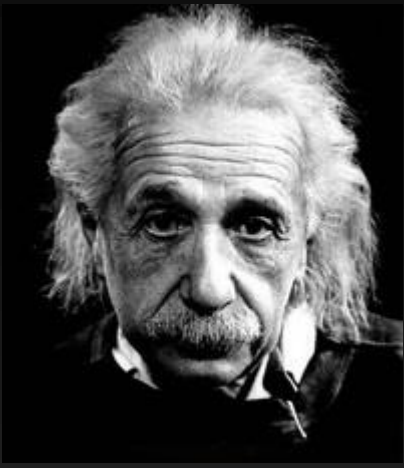


Astımda BİRİNCİL ve ikincil korunma

Dr. Ömer KALAYCI

ASTIMDA KORUNMA

- Astım bulgusu ve belirtisi baş göstermeden hastalığı önleme BİRİNCİL
- Astım riskini artıran (allerjik) hastalığı olanlarda astımı önleme İKİNCİL
- Astımı olanlarda çevresel önlemlerle tedavi ÜÇÜNCÜL



Bu seneki sorular geen
senekiyle aynı.

Evet,
ama bu sene yanıtlar farklı

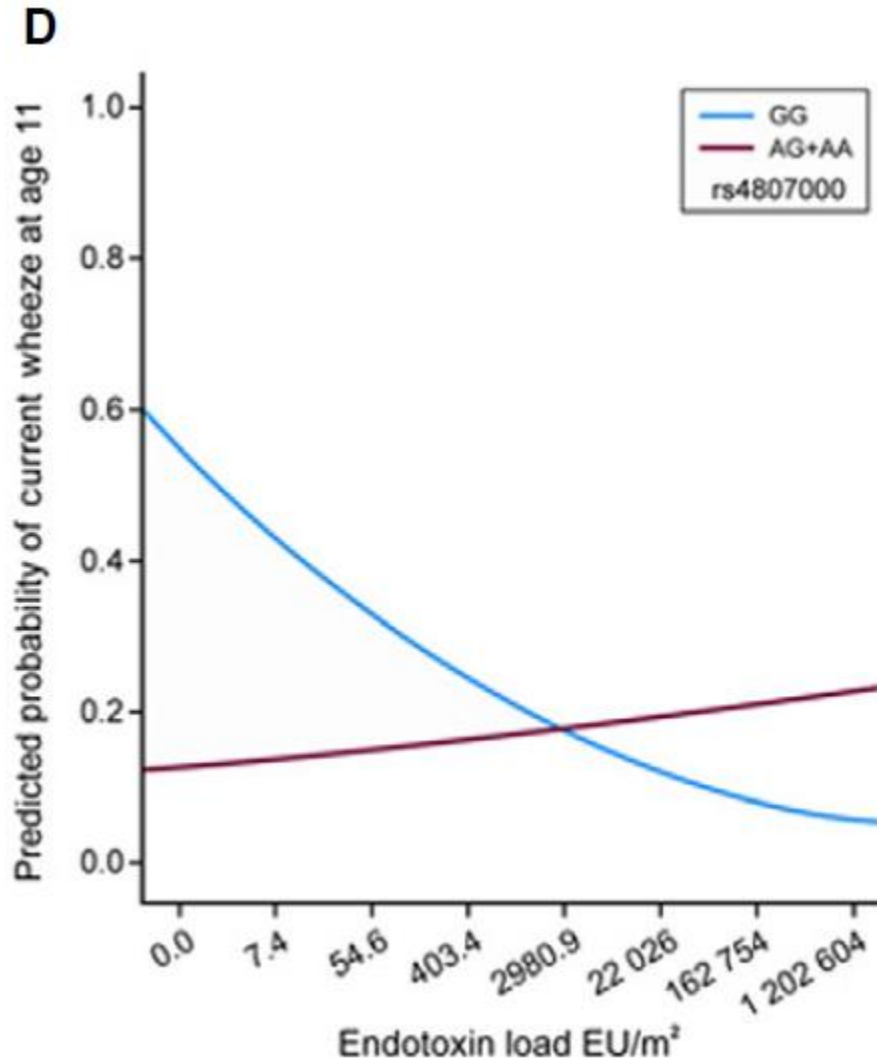
HAVA KİRLİLİĞİ

- Traffic-related air pollution (TRAP)
 - NO₂
 - PM 2.5
- Tütün dumanı

GINA 2017

Astımın ortaya çıkması ve devamı gen – çevre etkileşiminin bir sonucudur.

Astım heterojen bir hastalıktır



Sahiner U et al. Allergy 2014; 69: 1648–1658

Astında heterojenite

N=613	Mean(SD) % (N)
Age at follow-up (years)	9 (3.0)
Sex (male)	64% (392/613)
BMI	18.4 (3.6)
Age of asthma onset (years)	5 (3.4)
Family history of asthma (yes)	30% (184/613)
Exposure to tobacco smoke (yes)	39% (240/613)
Skin prick test positivity	59% (361/613)
FEV ₁ % predicted	87 (14.3)
FVC% predicted	96 (15.1)
FEV ₁ /FVC (%)	86 (7.0)
Bronchodilator Reversibility (%)	17.1 (12.9)
Total IgE(kU/L)	228 (458)
Blood eosinophil (%)	4.4 (3.5)
Asthma Severity	
Mild	78% (476/613)
Moderate	20% (126/613)
Severe	2% (11/613)

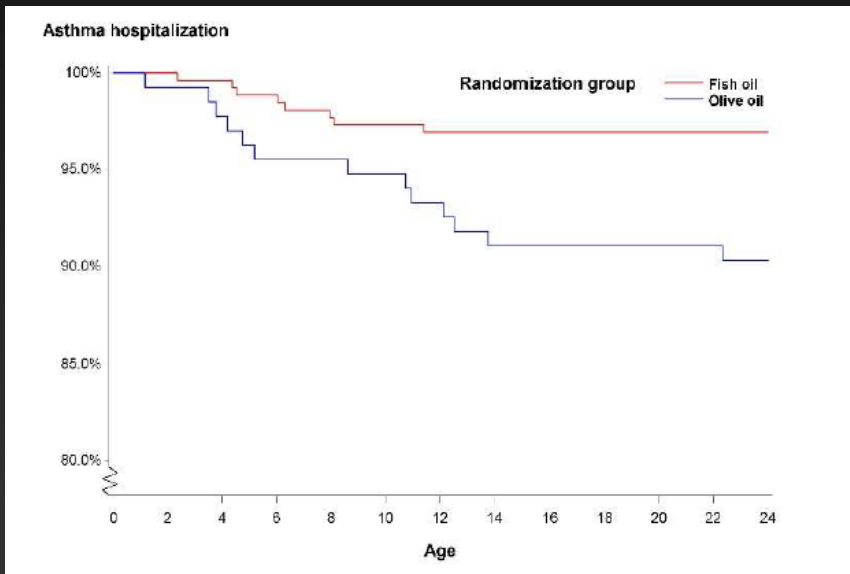
Türk çocuklarında astım fenotipleri

	Cluster 1 (n=132) <i>"Difficult asthma"</i>	Cluster 2 (n=210) <i>"Early-onset mild atopic asthma"</i>	Cluster 3 (n=153) <i>"Early-onset mild non-atopic asthma"</i>	Cluster 4 (n=105) <i>"Late-onset asthma"</i>	Cluster 5 (n=13) <i>"Exacerbation-prone asthma"</i>
Feature/domain					
Age of onset (years)	<u>4.9 (2.3-7)</u>	<u>4.4 (3-6)</u>	<u>3.8 (2-6)</u>	10.7 (9-12)	<u>4.1 (2-5)</u>
Asthma attacks Number, previous year	1.0 (0-1)	0.8 (0-1)	0.9 (0-1)	0.4 (0-1)	3.5 (0-7)
Allergic sensitization Sensitized	77/132 (58%)	183/210 (87%)	27/153 (18%)	67/105 (64%)	7/13 (54%)
Asthma severity					
Mild	46/132 (35%)	190/210 (90%)	141/153 (92%)	91/105 (87%)	8/13 (62%)
Moderate/severe	86/132(65%)	20/210 (10%)	12/153 (8%)	14/105 (13%)	5/13 (38%)
Cluster stability	1.00	0.99	0.99	1.00	1.00

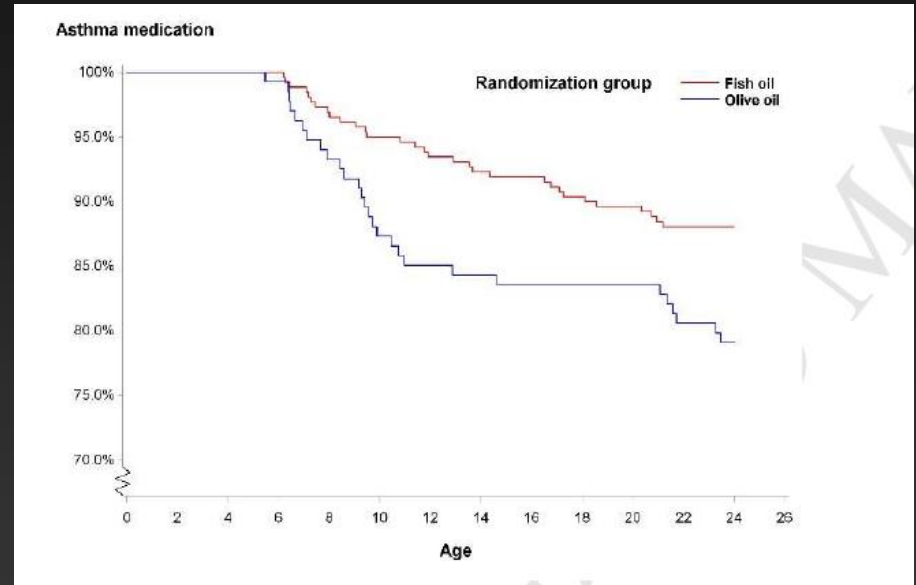
İNTRAUTERİN DÖNEM

Gebelikte balık yağı n-3 polyunsaturated fatty acids (PUFA)

	RANDOMİZASYON		
	Zeytinyağı N=136	Yağ yok N=131	Balık yağı N=266 (2.7g)
	İZLEM – 24 yıl		
Kayıt	134	126	262
Anket	104	90	188
Klinik	72	63	108



P= 0.01



P= 0.02

Fish Oil–Derived Fatty Acids in Pregnancy and Wheeze and Asthma in Offspring COPSAC

Table 1. Effects of n–3 LCPUFA on the Primary End Point.*

End Point	Children with Available Data (no. with primary end point/total no.)	n–3 LCPUFA (N=346) <i>percent</i>	Control (N=349)	Odds Ratio	Hazard Ratio	95% CI	P Value
Follow-up to 3–5 yr of age							
All	136/695	16.9	23.7		0.69	0.49–0.97	0.035
Stratified according to maternal pre-treatment blood levels of EPA + DHA as % of total fatty acids							
Lowest third (<4.3%)	49/203	17.5	34.1		0.46	0.25–0.83	0.011
Middle third (4.3–5.3%)	31/202	14.4	16.9		0.85	0.42–1.73	0.656
Highest third (>5.3%)	41/203	19.3	21.5		0.85	0.46–1.57	0.605

İntrauterin 24 hafta - doğum sonrası 1 hafta

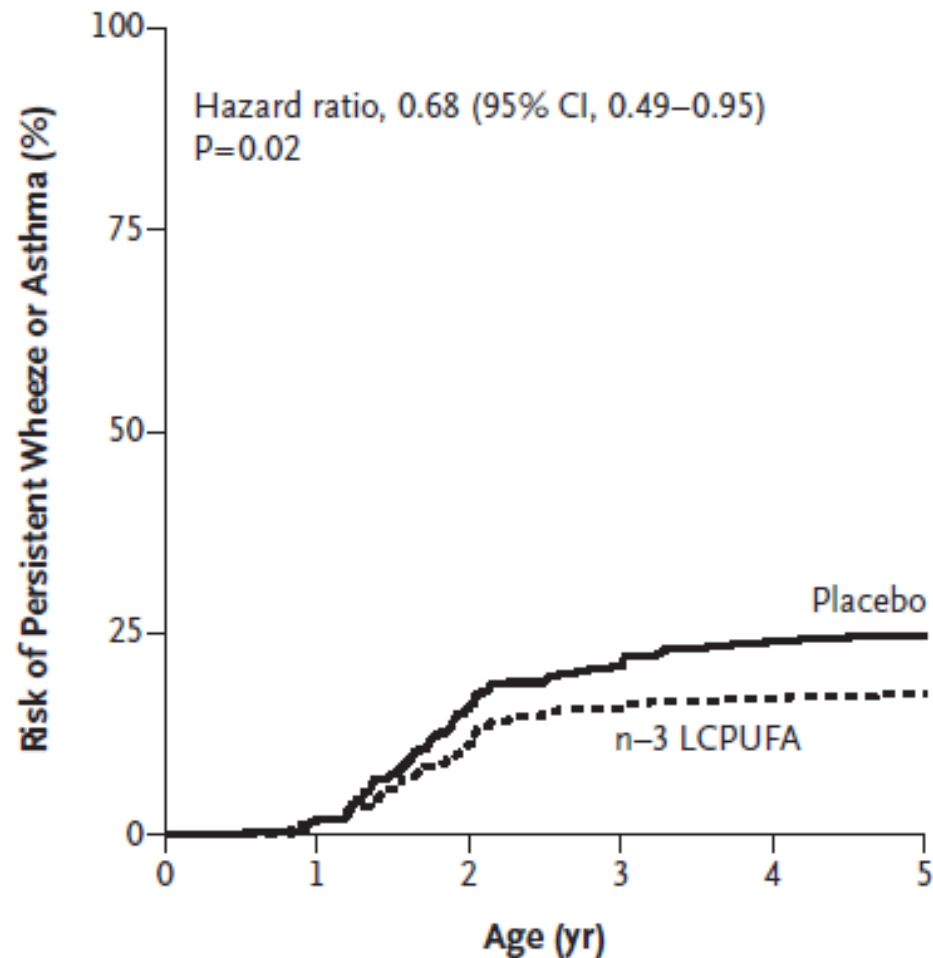
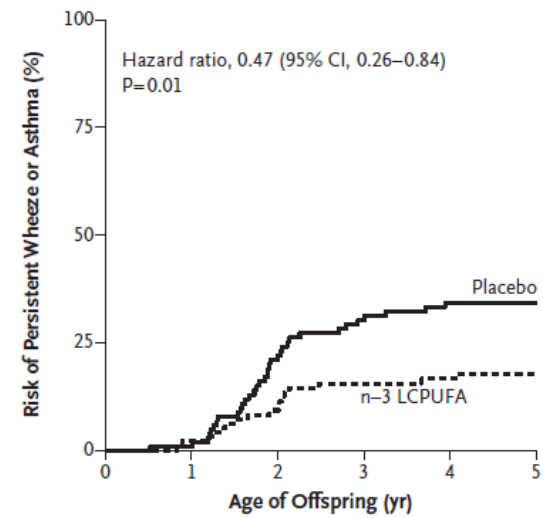


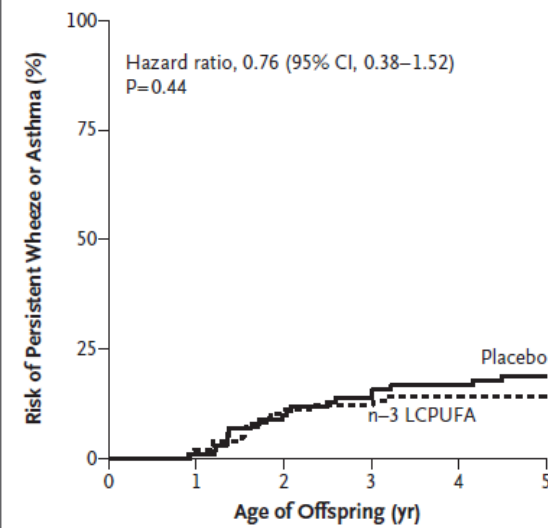
Figure 1. Risk of Persistent Wheeze or Asthma in Children According to n-3 LCPUFA Supplementation or Placebo during Pregnancy.

LCPUFA denotes long-chain polyunsaturated fatty acids.

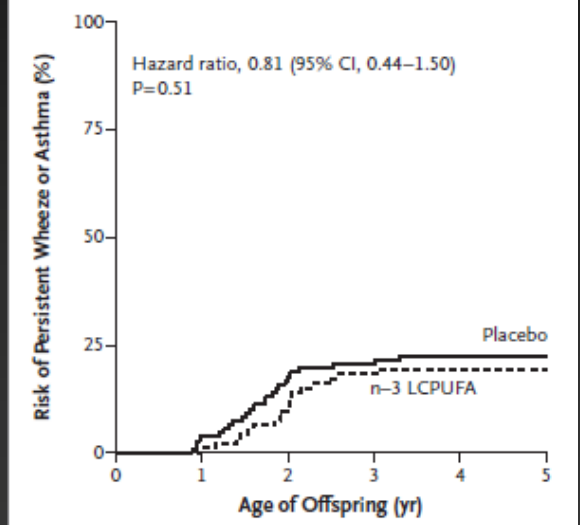
A Low EPA and DHA Blood Levels in Mother



B Moderate EPA and DHA Blood Levels in Mother



C High EPA and DHA Blood Levels in Mother



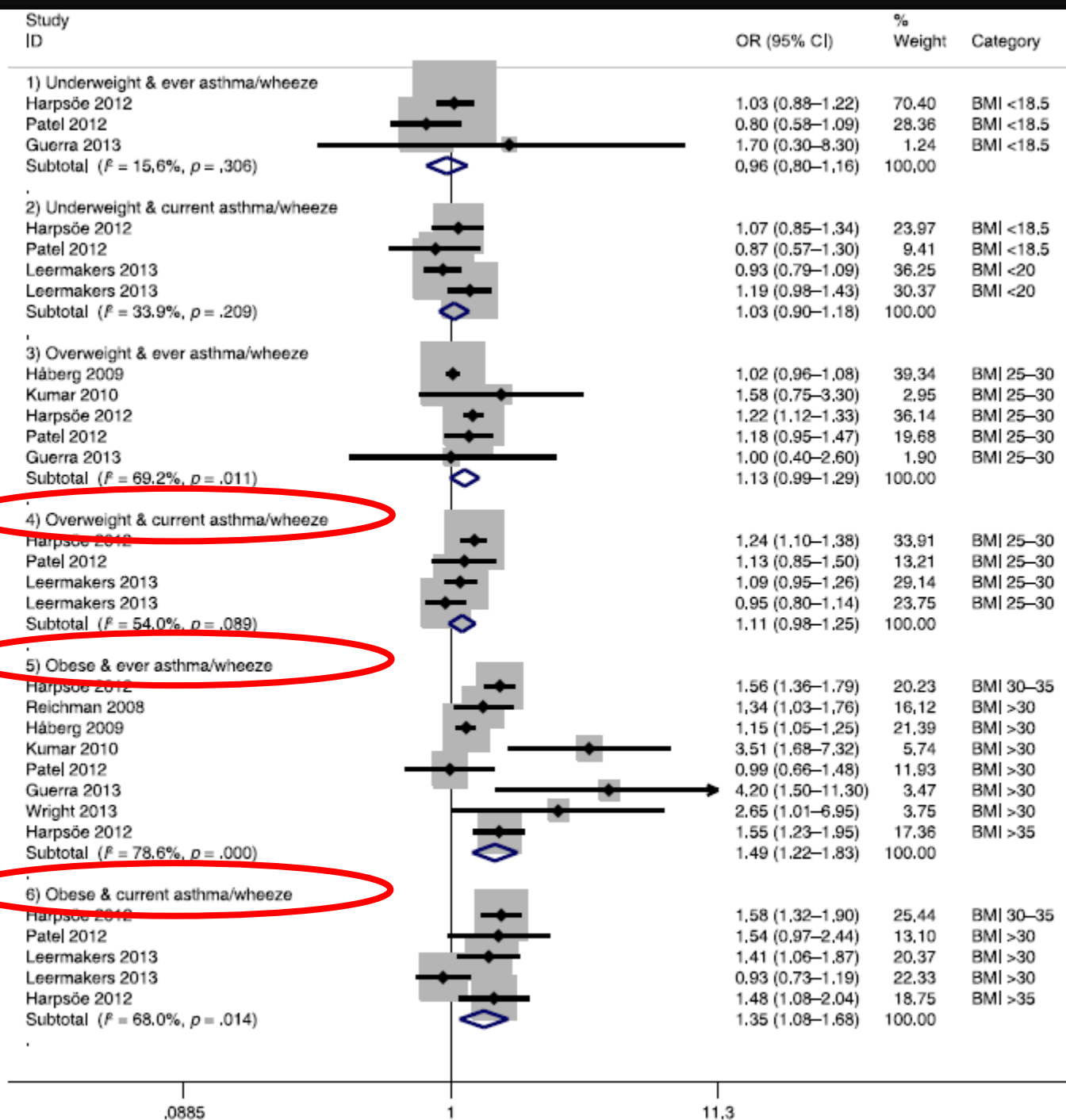
Öneriler

GINA

- Astımın önlenmesi için gebelikte diyet önerilmez
- Astımın önlenmesi için gebelikte diyet önermek için HENÜZ yeterli veri yoktur
- Ancak, bu umut vaat eden bir konudur

M

d



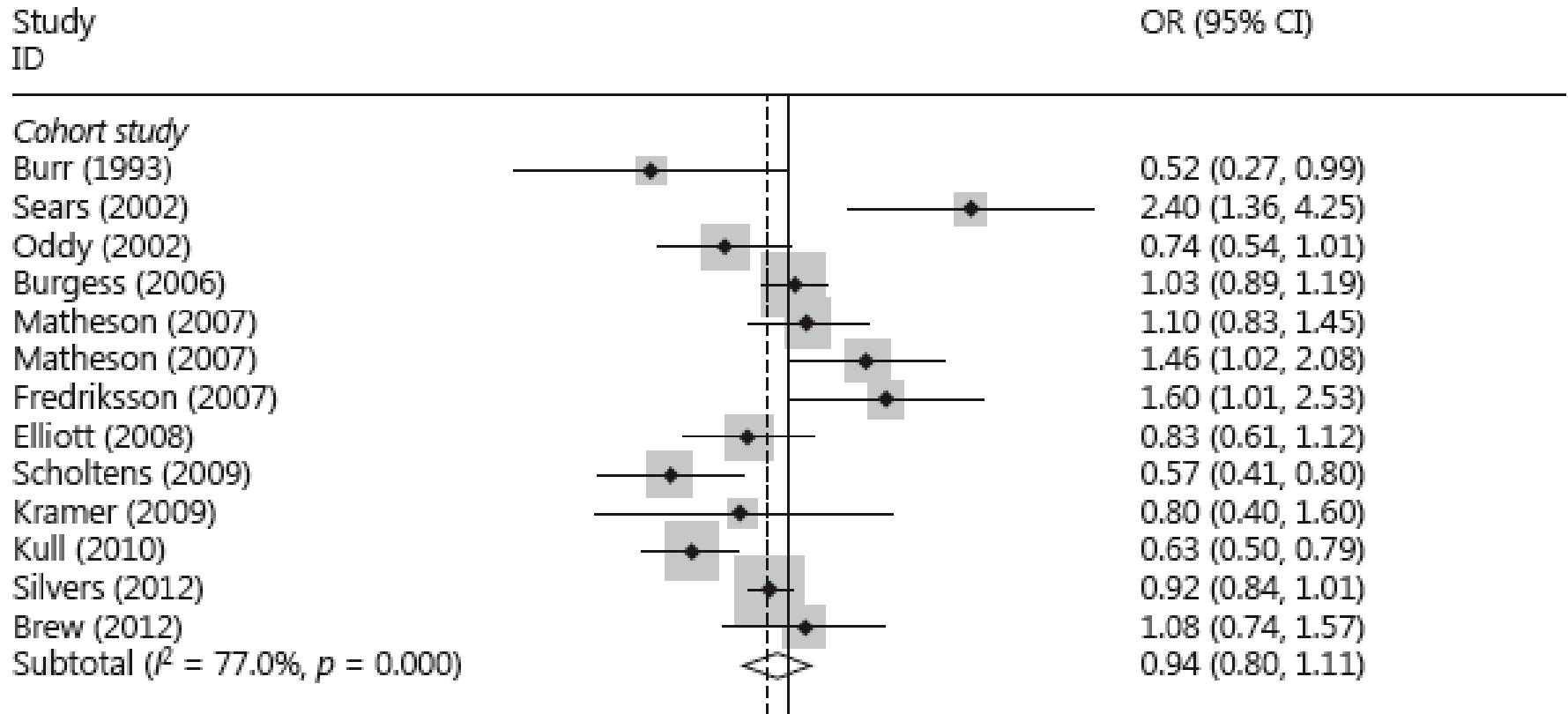
Gebelikte obesite ve hızlı kilo alımı çocuklarda astımla ilişkili olabilir

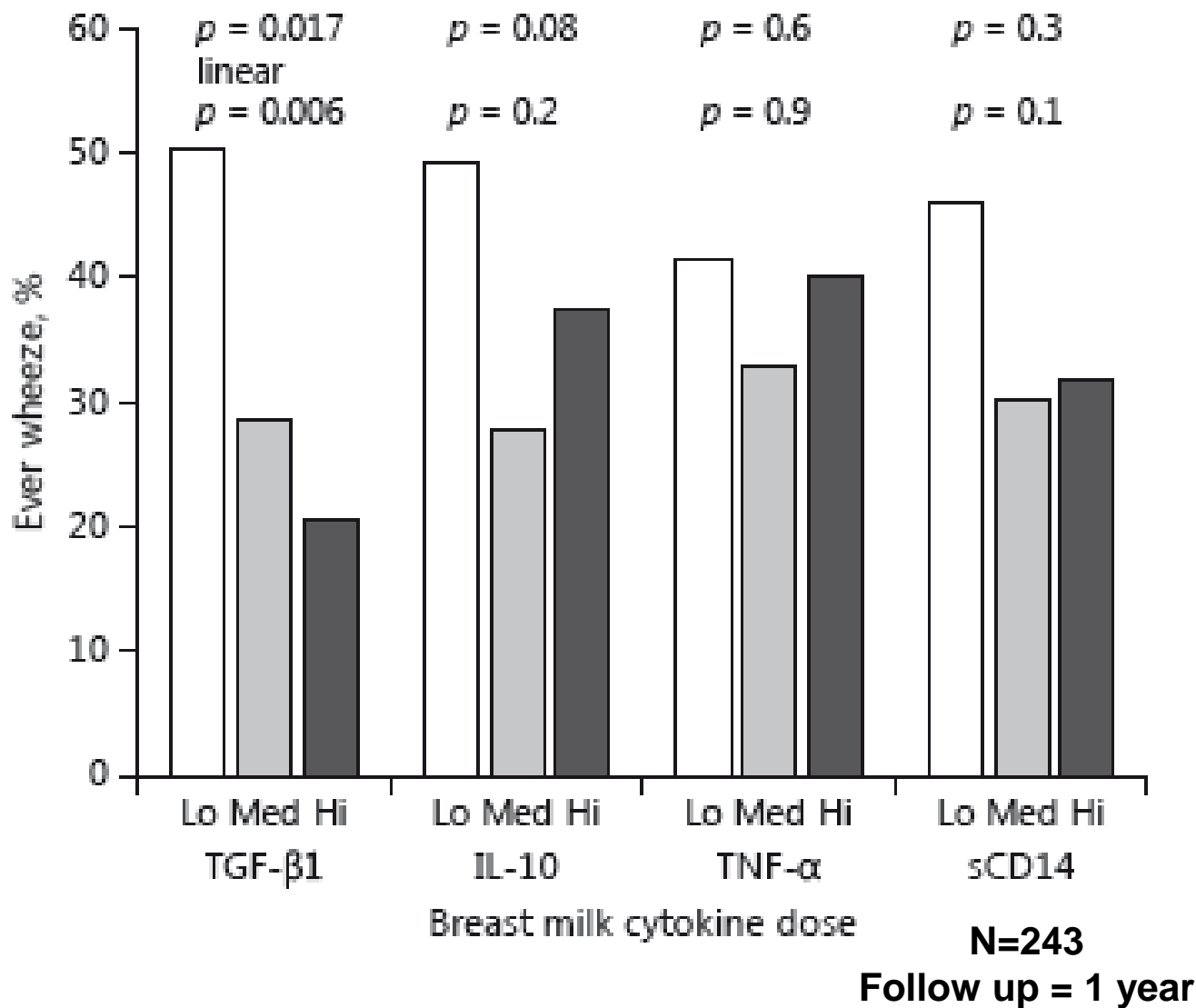
ANNE SÜTÜ

AAP

- En az üç ay YALNIZCA anne sütü erken döneminde hışıltıya karşı koruyucudur
- Daha büyük çocuklarda astıma karşı koruduğuna dair bir veri yoktur.
-

Meta-analysis: more versus less breastfeeding and risk of asthma in children aged 5–18 years.





Association of Breast Milk Fatty
Acids and Allergic Disease
Outcomes – a Systematic Review

n-3 PUFA anti-inflamatuvar

n-6 PUFA pro-inflamatuvar

Medline (74) + EMBASE (106) = 180

Duplicates removed

134 published papers

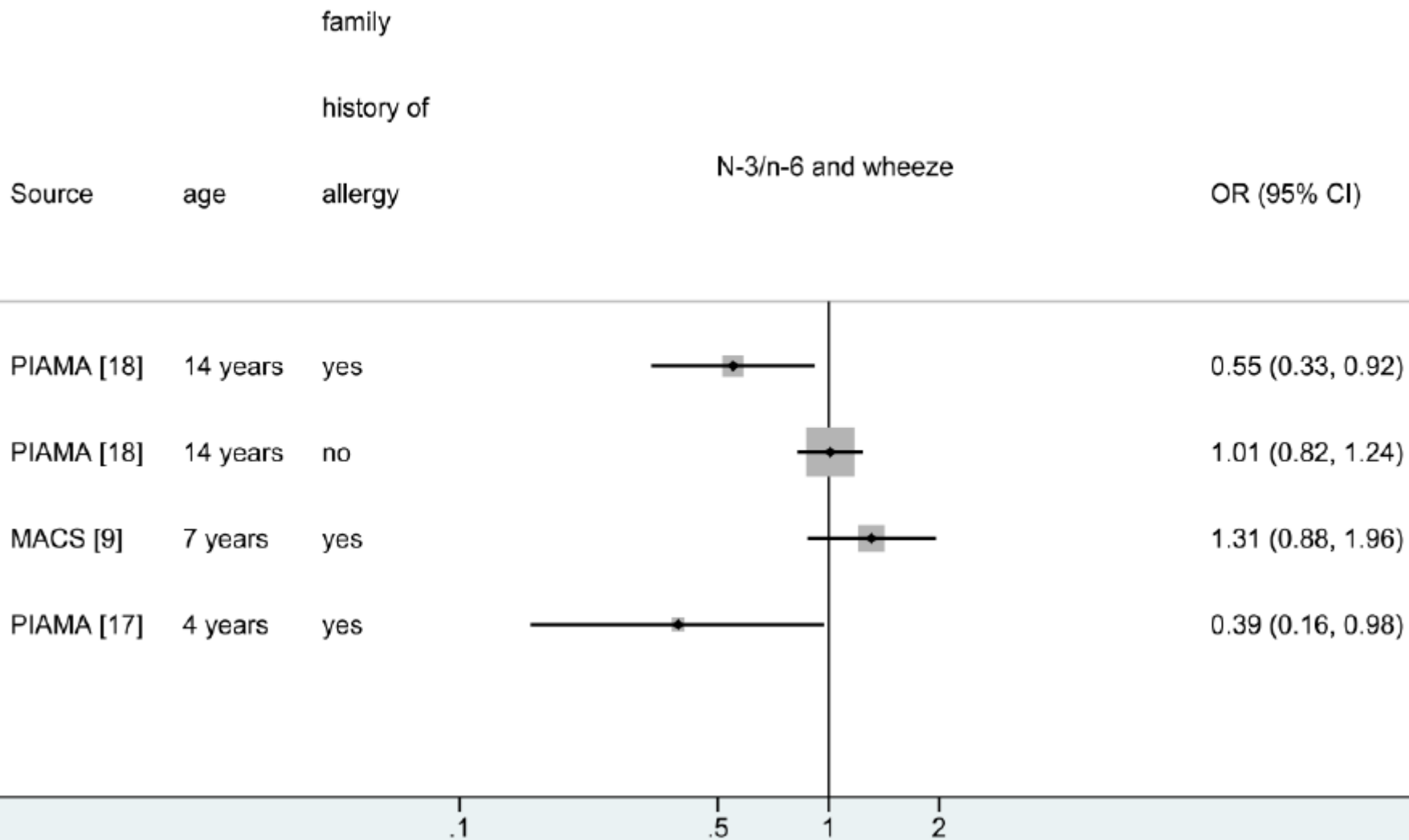
After title and abstract screening -39

Fatty acids not
quantified -7
Disease outcomes not
specified-2
Review- 5
Letters-1
Expert opinion-1
Editorial-4

11 birth cohort studies
(14 papers) +

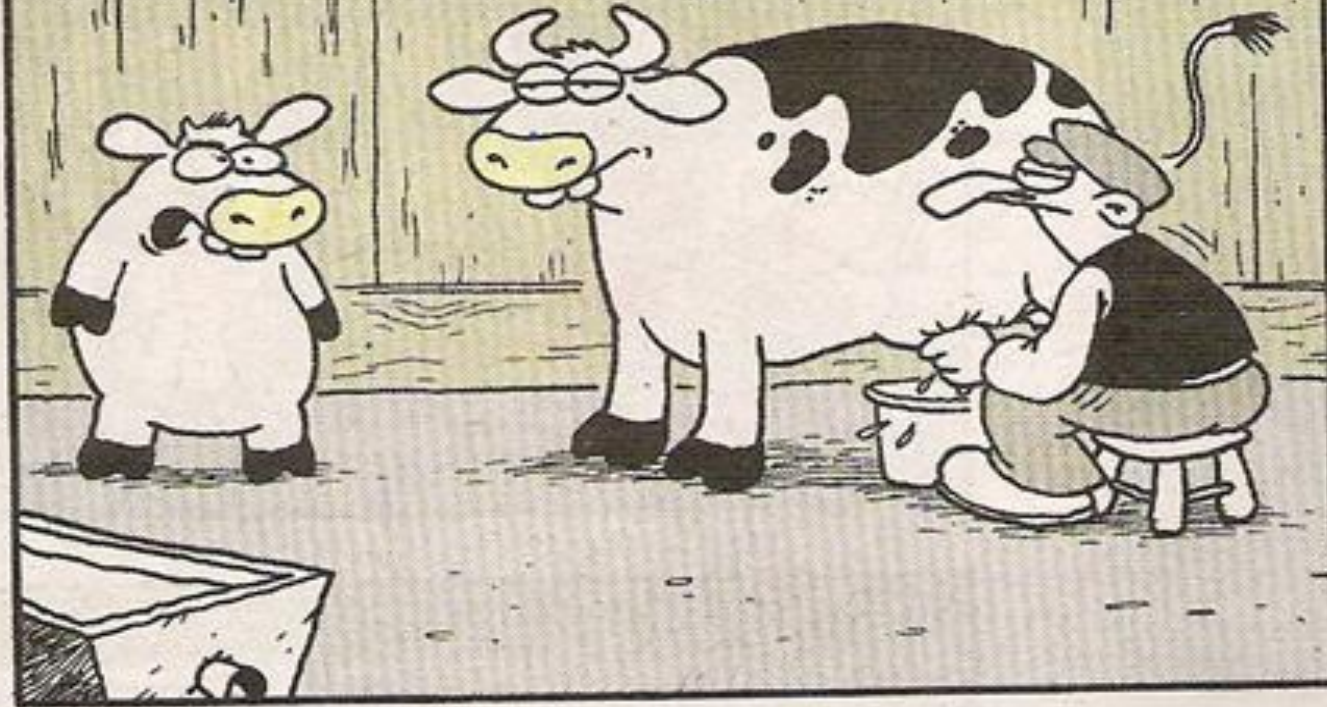
2 case control
studies (2 papers)

2 cross sectional
studies (2 papers)

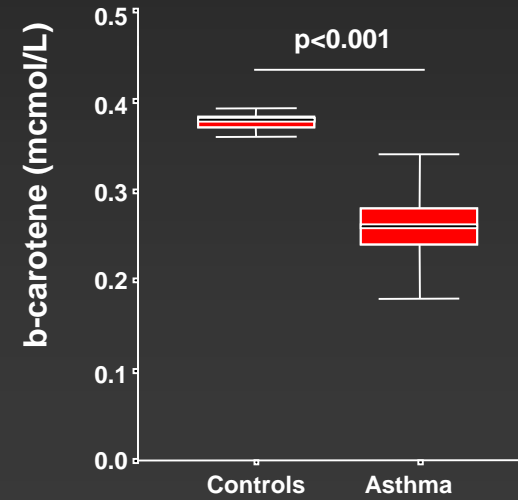
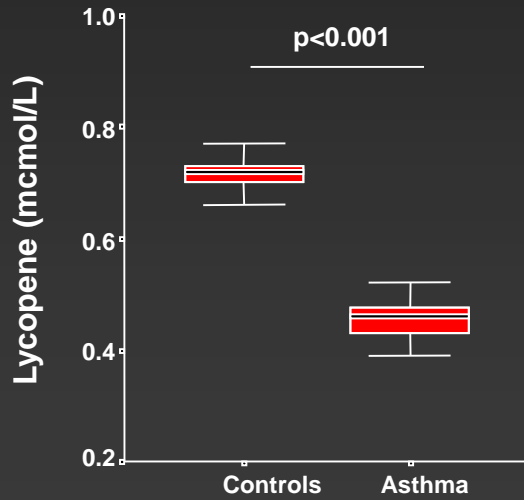
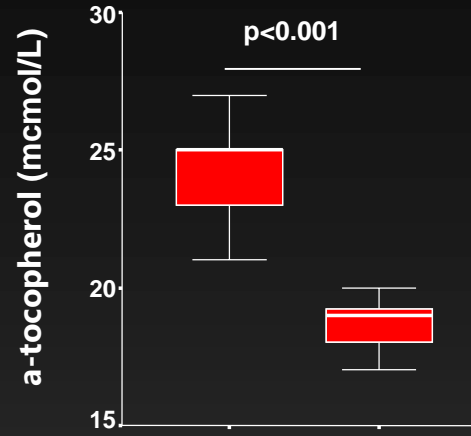
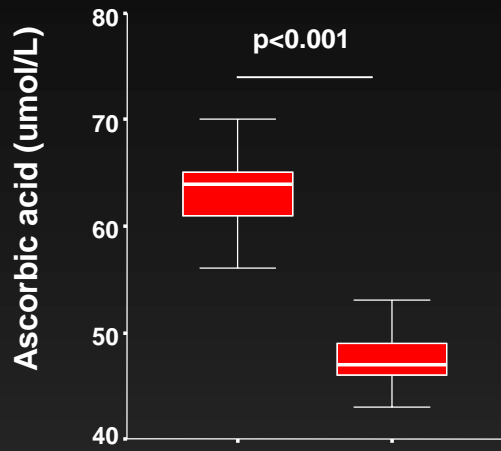


ANNEEAA !!
BEN DE SÜT
İSTİYÖÖM ...!

Aynı anda hem
çocuk yapmak hem
de kariyer
yapmak ne kadar
zor ya...



Antioksidanlar Vit C, E Vit D



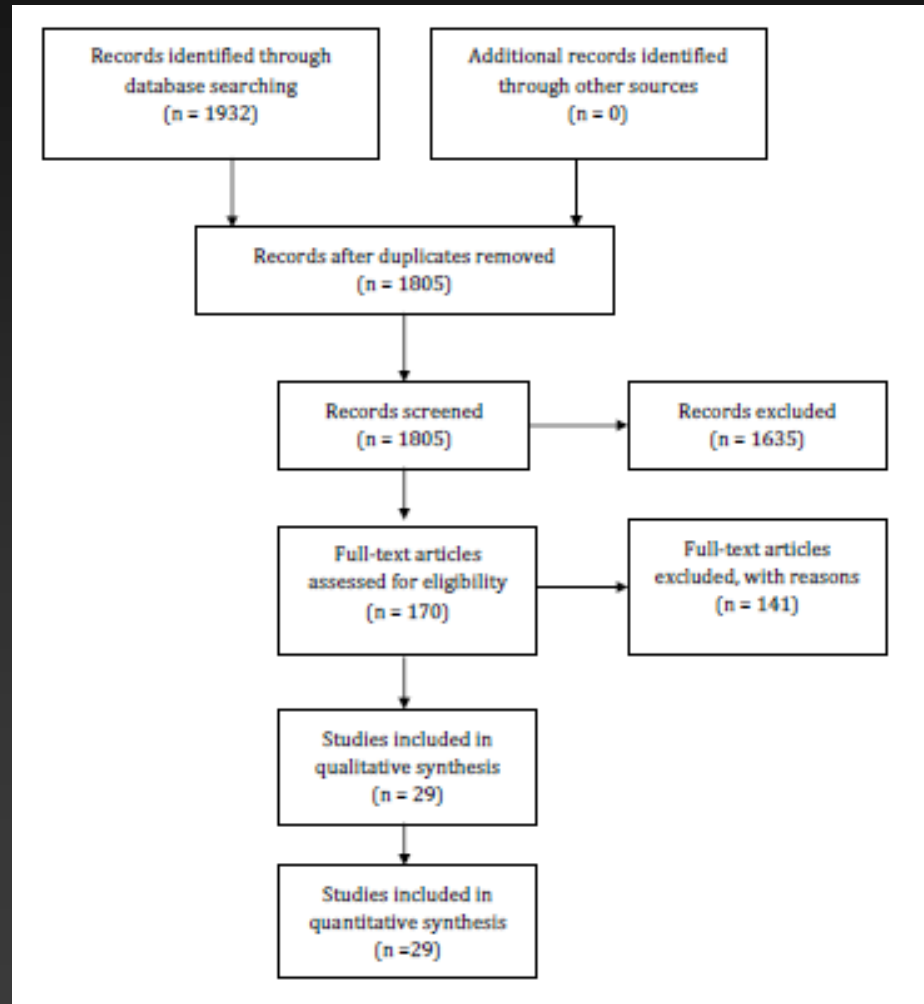
Respiratory outcomes in early childhood following antenatal vitamin C and E supplementation

Anne Greenough,¹ Seif O Shaheen,² Andrew Shennan,³ Paul T Seed,⁴ Lucilla Poston⁵

Table 4 Infant outcomes by maternal randomisation status

	Vitamins (n=386)	Placebo (n=366)	Comparison (99% CI)	p Value
Chest symptoms in first 12 months				
Asthma	6.0%	6.3%	0.94 (0.42 to 2.11)	0.855
Eczema	25.4%	23.5%	1.10 (0.70 to 1.74)	0.586
Cough				
At all	70.5%	74.9%	0.81 (0.50 to 1.29)	0.245
More than once/week	10.6%	11.5%	0.90 (0.47 to 1.74)	0.679
Wheeze				
At all	23.3%	28.1%	0.78 (0.50 to 1.21)	0.144
More than once/week	3.9%	4.6%	0.81 (0.32 to 2.06)	0.568
Chest symptoms in second 12 months				
At all	86.8%	85.8%	1.08 (0.59 to 1.97)	0.752
More than once/week	13.2%	10.1%	1.33 (0.71 to 2.51)	0.246
Wheeze				
At all	25.9%	26.5%	0.97 (0.62 to 1.52)	0.852
More than once/week	2.6%	3.0%	0.83 (0.26 to 2.59)	0.669

Vitamin D supplementation in primary allergy prevention



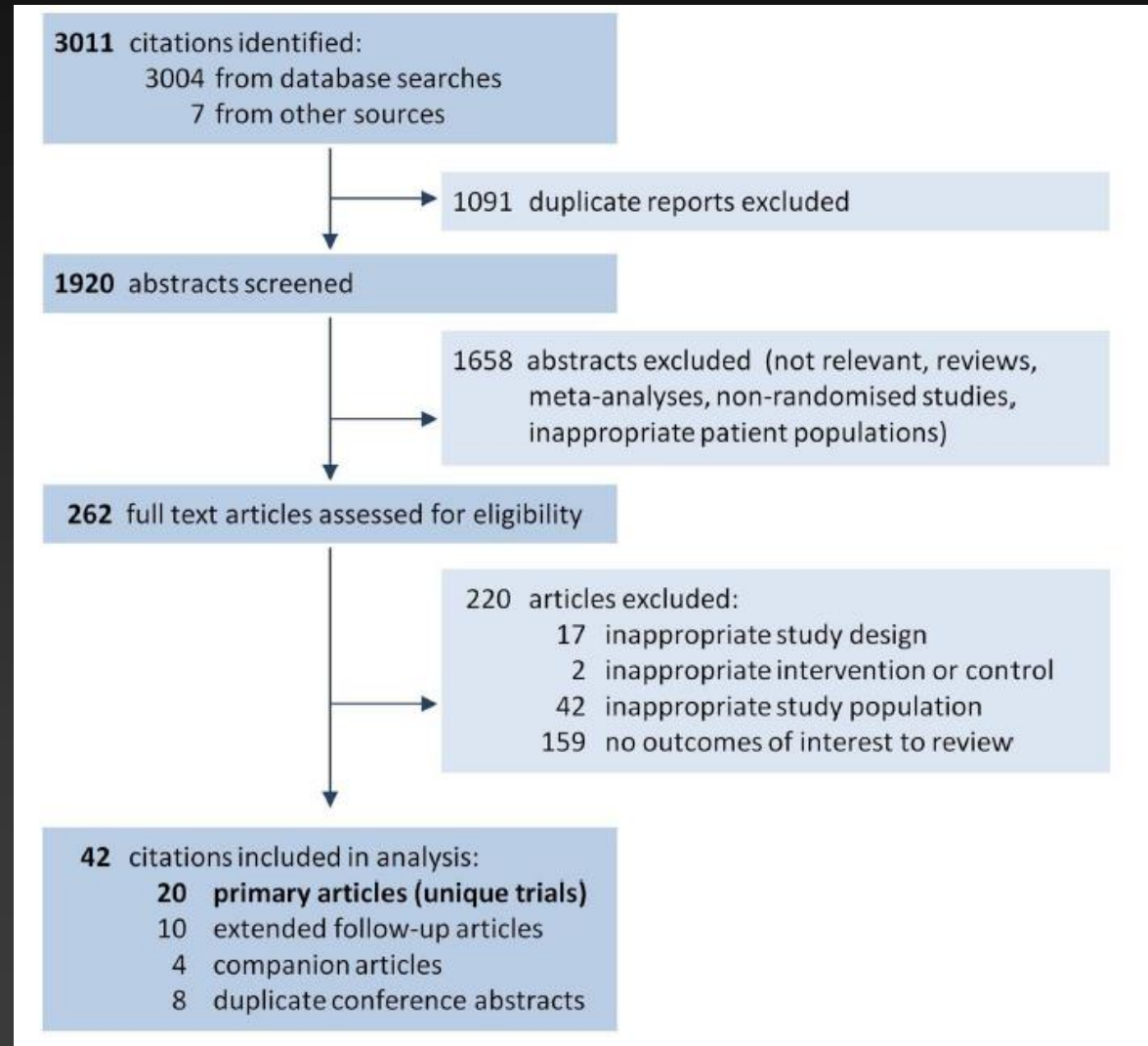
Dönem	Sonuç	Olgu sayısı (çalışma sayısı)	Öneri kuvveti (GRADE)	RR (CI)
Gebelik	Astım Wheezing 3 yıl izlem	151 1	Çok düşük	1.12 0.50-2.54
Emzirme	Astım 16 yl izlem	483 olgu 483 kontrol	Çok düşük	1.09 (0.84-1.40)
Süt çocukluğu	Astım 31 yıl	6768 (1) Gözlemsel	Çok düşük	3.07 (0.19-51.0)
Çocukluk	-	-	-	-

Antioksidan vitaminler ve Vit D

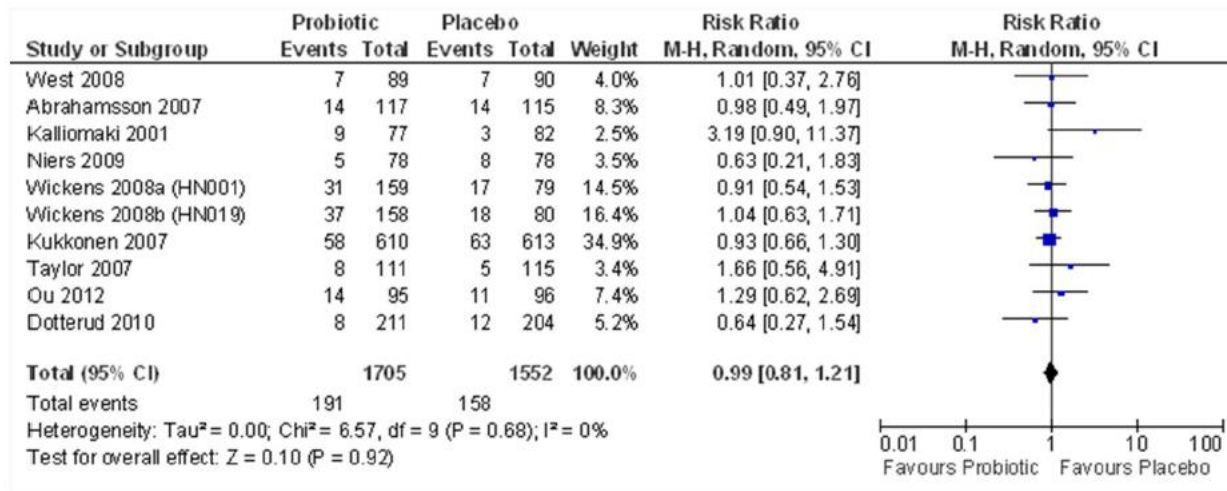
Astımdan birincil korunmada
saptanmış yararları yoktur

MİKROBİYATA ENFEKSİYONLAR

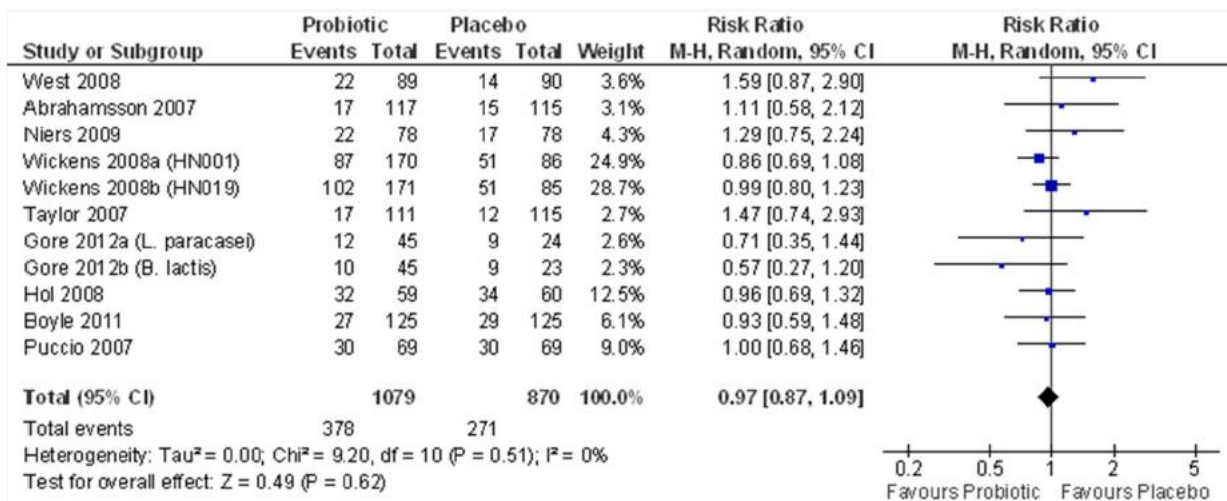
Probiotic supplementation during pregnancy or infancy for the prevention of asthma and wheeze: systematic review and meta-analysis



ASTIM TANISI



HIŞILTI

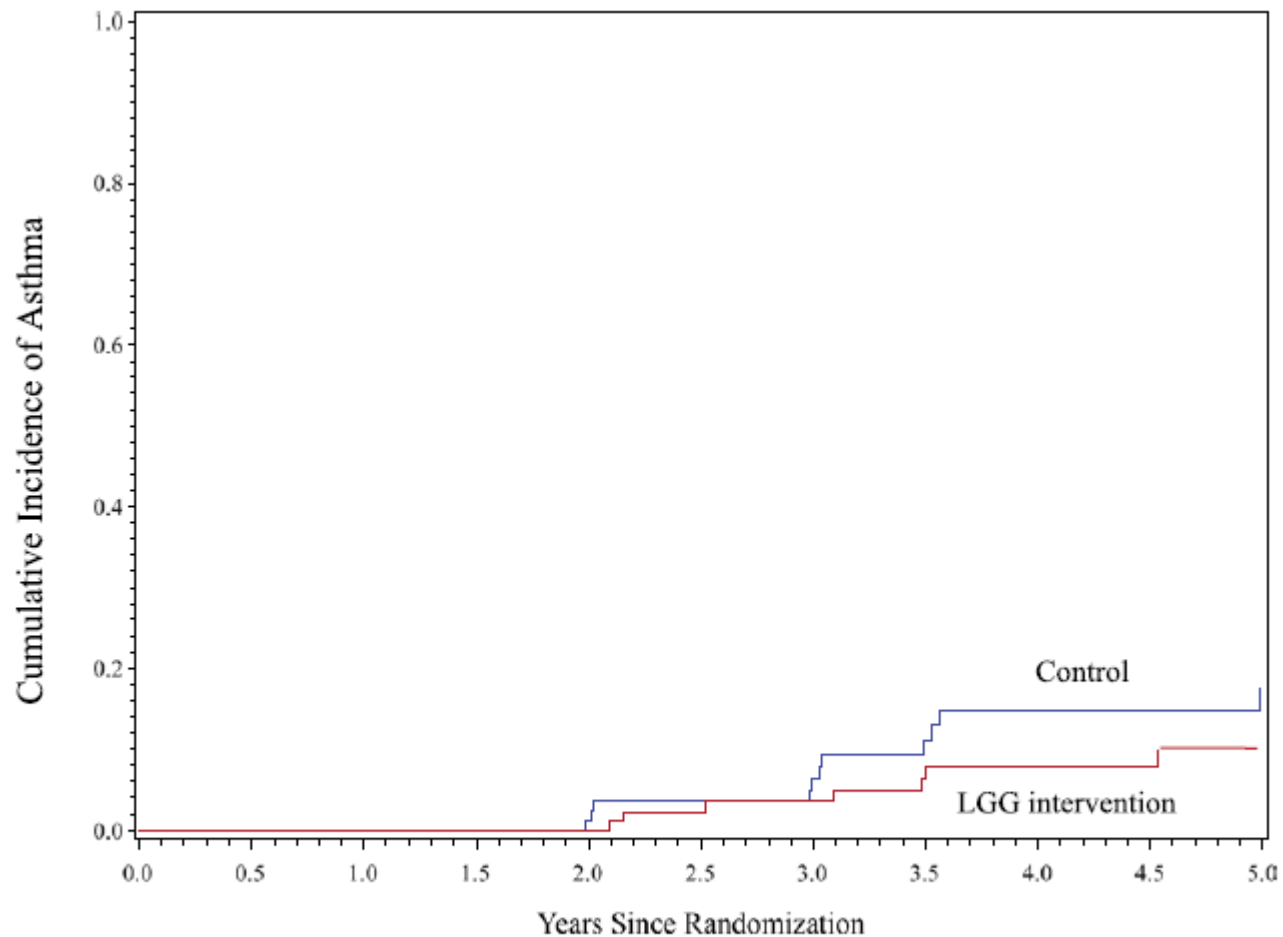


Early Probiotic Supplementation for Eczema and Asthma Prevention: A Randomized Controlled Trial

Michael D. Cabana, MD, MPH,^{a,b,c} Michelle McKean, RD, MPH,^a Aaron B. Caughey, MD, PhD,^d Lawrence Fong, MD,^e Susan Lynch, PhD,^e Angela Wong, MD,^f Russell Leong, MD,^g Homer A. Boushey, MD,^e Joan F. Hilton, ScD, MPH^b

Pediatrics, Haziran 2017

- Anne ve / veya babada astım
- 10 milyar cfu *Lactobacillus rhamnosus* /placebo
- Tedavi süresi 6 ay
- Sonuç parametresi: 5 yıl içinde astım



Number at risk											
Control	92	91	89	88	85	80	64	51	41	39	32
LGG	92	91	89	89	89	85	77	64	52	48	43

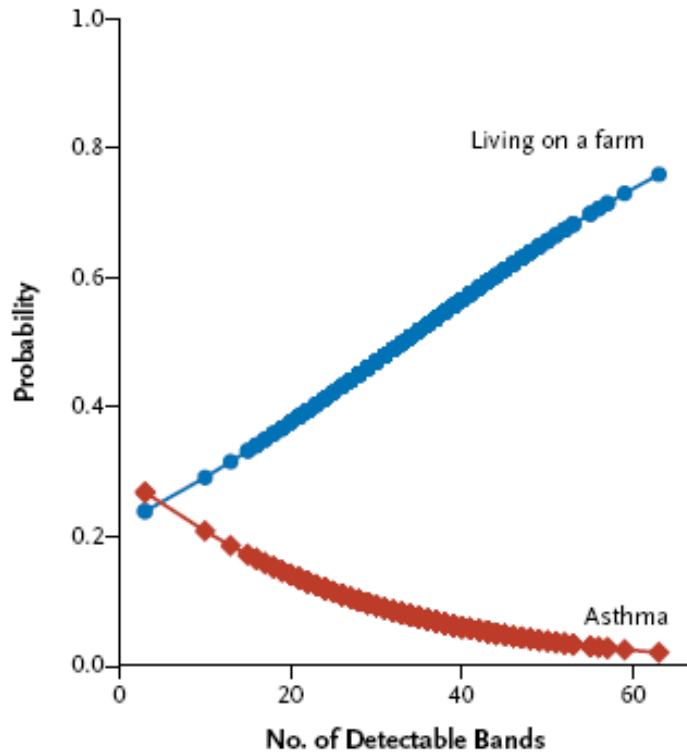
5 yaşında Cumulative incidence of asthma
17.4% (95% CI, 7.6%–27.1%) Kontrol
9.7% (95% CI, 2.7%– 16.6%) LGG
RR 0.88 (95% CI, 0.41–1.87)

Prebiyotik, Probiyotik, Synbiotik

- Astımdan korunmada yararlı olduklarına dair delil yoktur.

Mikrobik çeşitlilik - astım

A Bacteria (PARSIFAL)



B Fungi (GABRIELA)

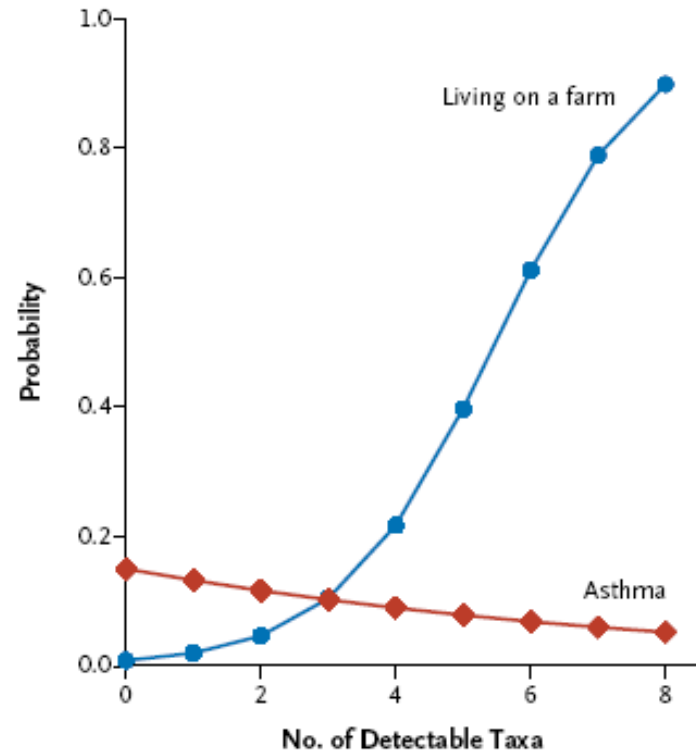


Figure 3. Relationship between Microbial Exposure and the Probability of Asthma.

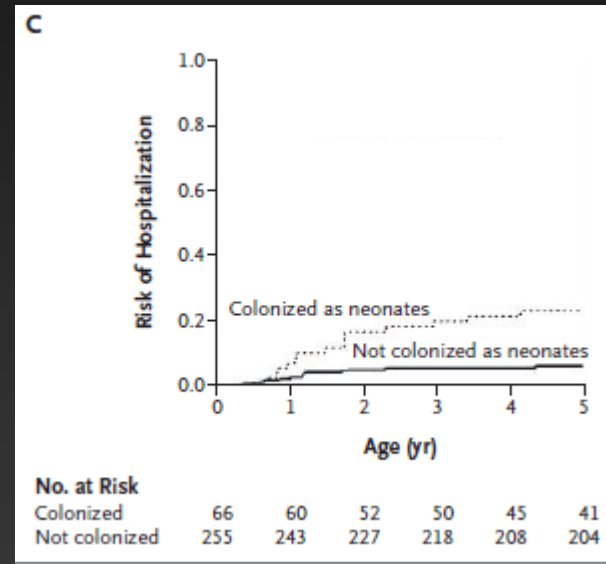
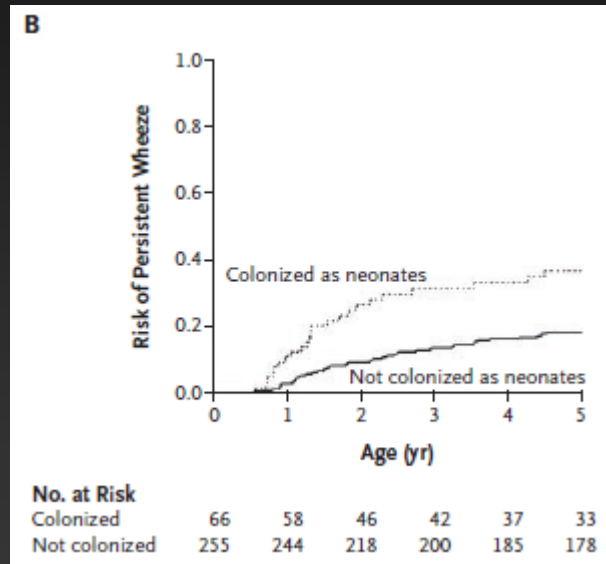
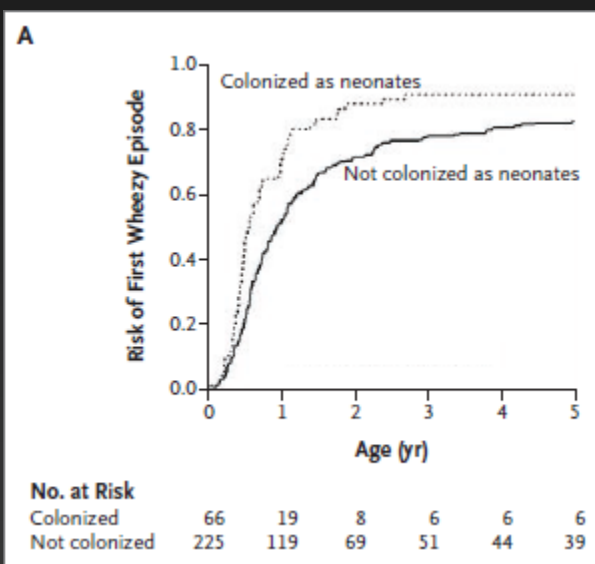
In both the PARSIFAL study and GABRIELA, the range of microbial exposure was inversely associated with the probability of asthma.

Mikrobiyal kolonizasyonu etkileyen faktörler

- Vajinal / sezeryan doğum
- Erken antibiyotik kullanımı
- Evcil hayvan
- Makro çevre : Çiftlik / ahır / şehir
- Beslenme

Childhood Asthma After Bacterial Colonization of the Airways in Neonates

S aureus, S pneumoniae, M catarrhalis, H Influenza



Bisgaard H N Engl J Med 2007;357:1487-95.

RSV - RV

- Süt çocukluğu döneminde geçirilen (ağır) RSV ve RV enfeksiyonları astım için risk faktörleridir
- Alt solunum yolu enfeksiyonları astımın ilk belirtisi midir?
- Astım ve RSV/RV sekeli için ortak bir genetik yatkınlık mı vardır?
- RSV /RV ile astım arasında sebep sonuç ilişkisi var mıdır?

Respiratory Syncytial Virus and Recurrent Wheeze in Healthy Preterm Infants

Maarten O. Blanken, M.D., Maroeska M. Rovers, Ph.D., Jorine M. Molenaar, M.D., Pauline L. Winkler-Seinstra, M.Sc., Adam Meijer, Ph.D., Jan L.L. Kimpen, M.D., Ph.D., and Louis Bont, M.D., Ph.D., for the Dutch RSV Neonatal Network

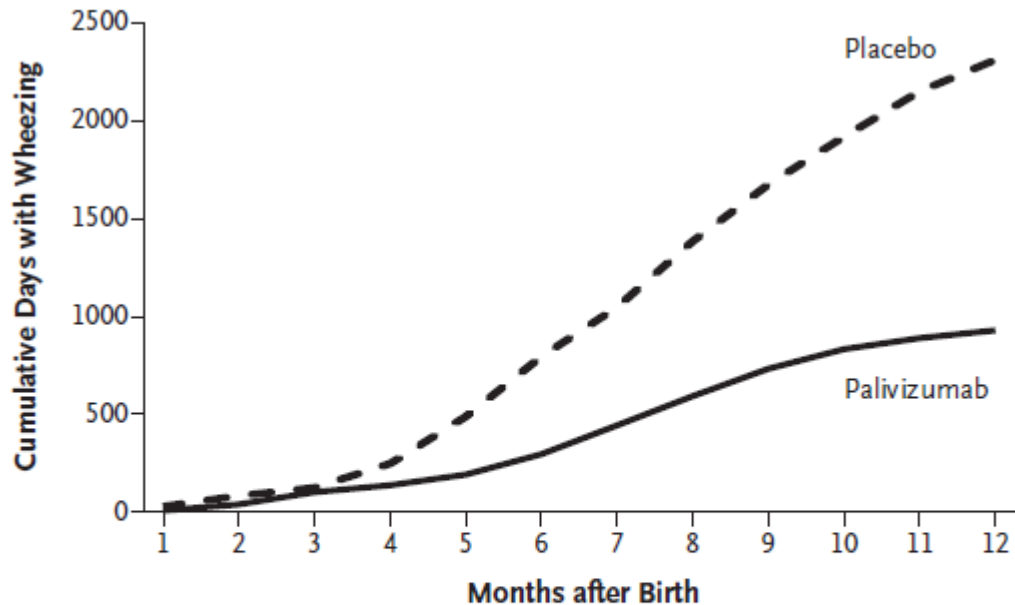


Figure 2. Cumulative Wheezing Days for 429 Preterm Infants during the First Year of Life.

$P < 0.001$ for the comparison between palivizumab and placebo with the use of Poisson regression.

Respiratory syncytial virus immunoprophylaxis in high-risk infants and development of childhood asthma



Kecia N. Carroll, MD, MPH,^{a,e} Tebeb Gebretsadik, MPH,^{b,e} Gabriel J. Escobar, MD,^{f,g,h} Pingsheng Wu, PhD,^{b,c,e} Sherian Xu Li, MS,^g Eileen M. Walsh, RN,^g Ed Mitchel, MS,^{d,e} Chantel D. Sloan, PhD,^{e,i} William D. Dupont, PhD,^{b,e} and Tina V. Hartert, MD, MPH^{c,e} *Nashville, Tenn, Oakland and Walnut Creek, Calif, and Provo, Utah*

**RSV İMMUNOPROFLAKSİSİNE UYUM -ASTİM
PRIMA, 1996-2003
4.5- 6 yaş**

Tüm grup	N=6566	Adjusted OR
Kullanmamış		Reference
< % 70		0.93 (0.78 – 1.10)
≥ % 70		1.17 (0.98-1.39)

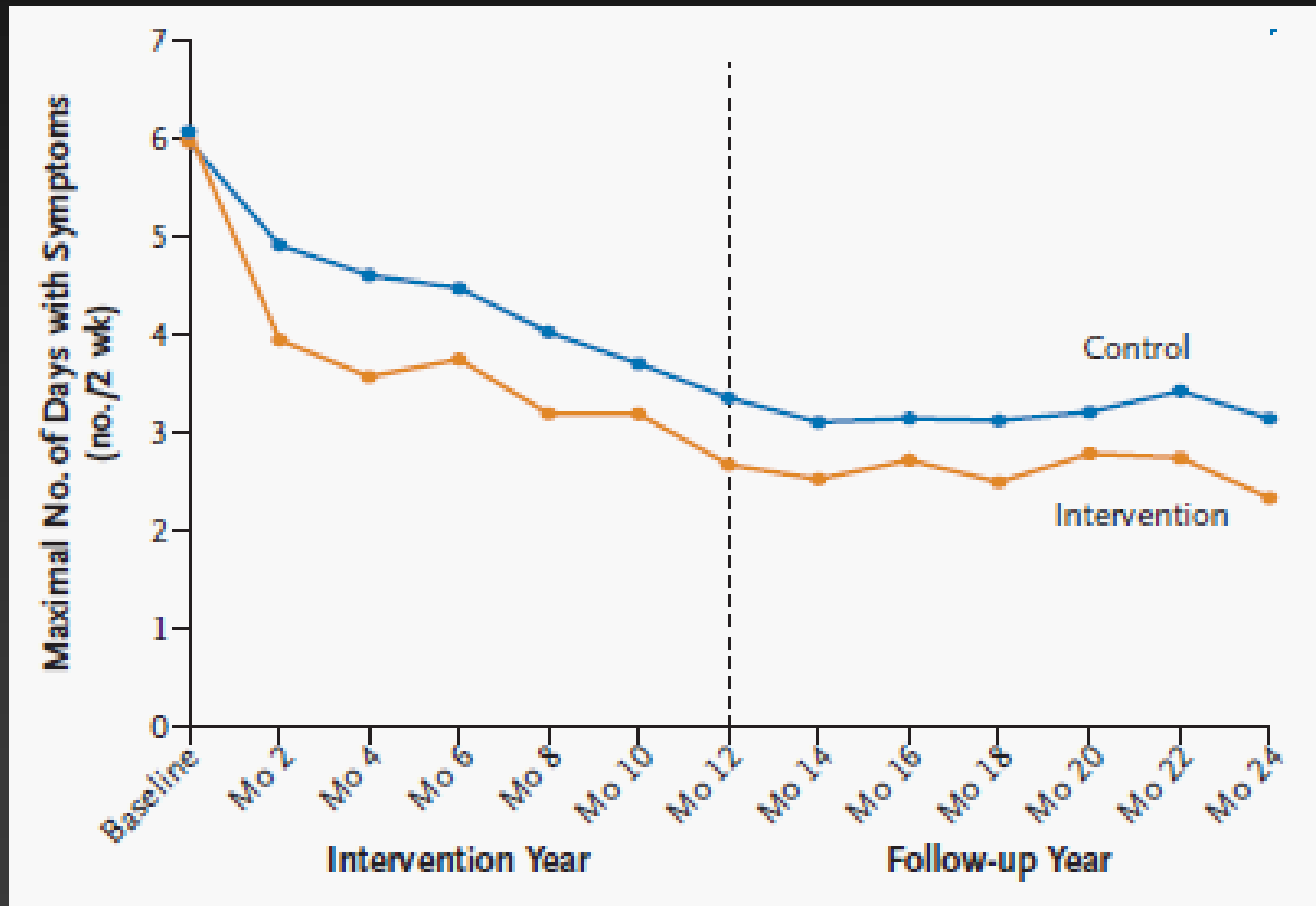
Cinsiyet, EGA, doğum ağırlığı, ırk, anne yaşı, eğitim , doğum sayısı, sigara , kardeş sayısı

Diğer faktörler

- Psikososyal
- İlaçlar
 - Parasetamol

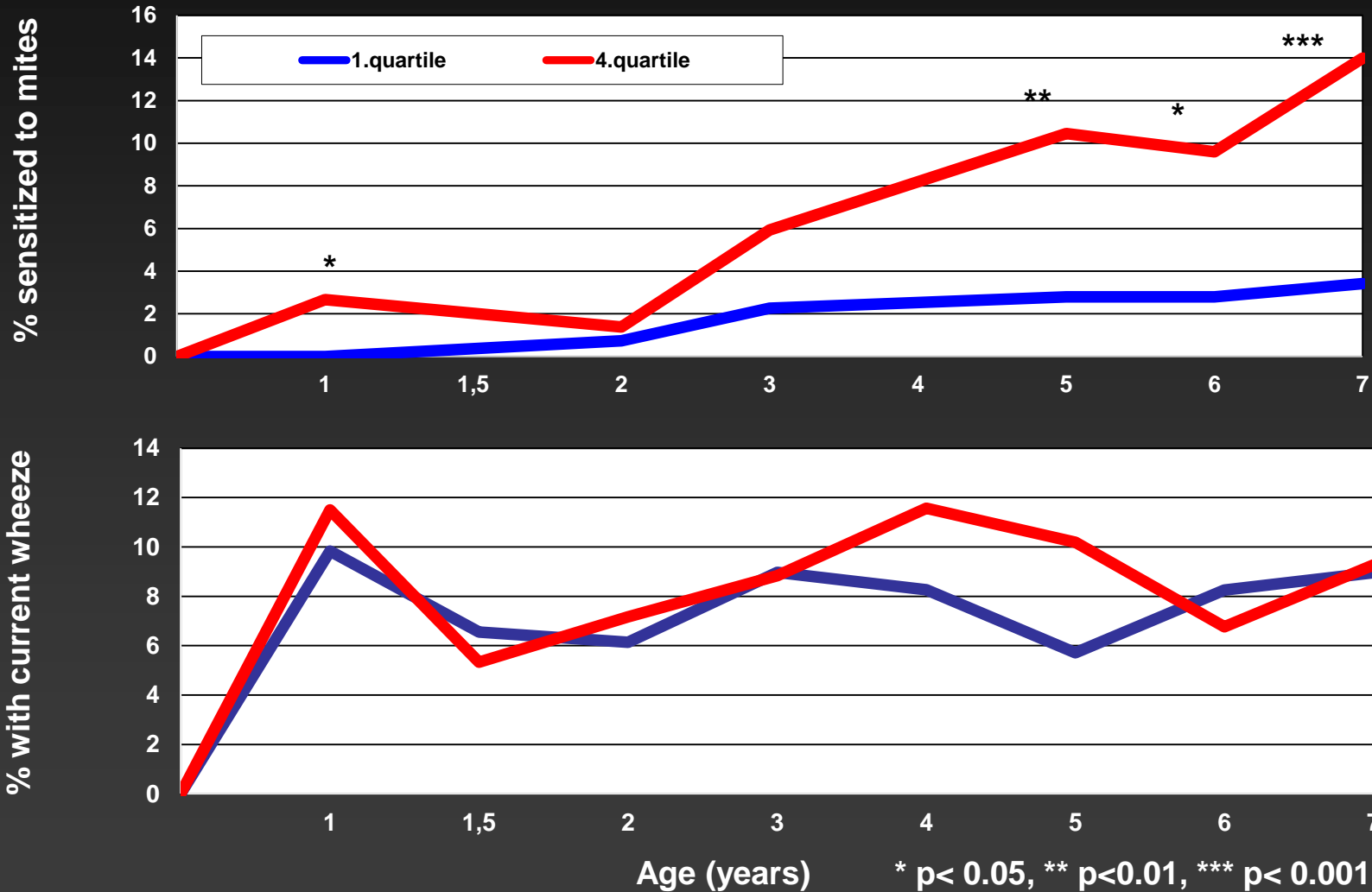
SOLUNAN ALLERJENLER

Results of a Home-Based Environmental Intervention among Urban Children with Asthma



Inner-City Asthma Study Group* N Engl J Med 2004;351:1068-80.

EV AKARI DUYARLILIĞI – KARŞILAŞMA WHEEZING



(Lau et al, Lancet 2000, 1392-1397)

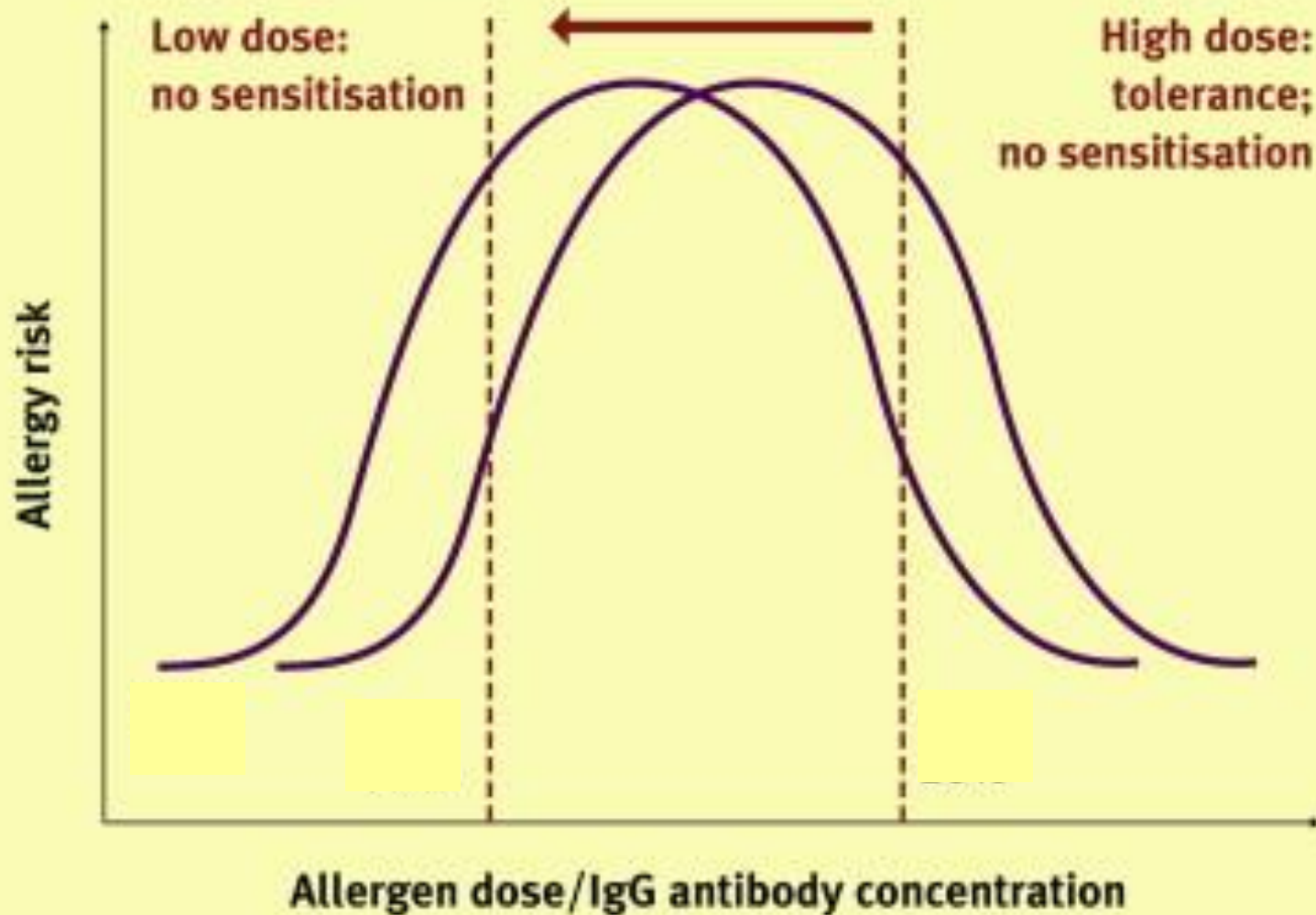
Early-life home environment and risk of asthma among inner-city children

George T. O'Connor, MD, MS,^a Susan V. Lynch, PhD,^b Gordon R. Bloomberg, MD,^c Meyer Kattan, MD,^d Robert A. Wood, MD,^e Peter J. Gergen, MD, MPH,^f Katy F. Jaffee, MS,^g Agustin Calatroni, MS,^g Leonard B. Bacharier, MD,^c Avraham Beigelman, MD,^c Megan T. Sandel, MD, MPH,^h Christine C. Johnson, PhD,ⁱ Ali Faruqi, MS,^b Clark Santee, BS,^b Kei E. Fujimura, PhD,^b Douglas Fadrosh, MS,^b Homer Boushey, MD,^b Cynthia M. Visness, PhD,^g and James E. Gern, MD^j *Boston, Mass, San Francisco, Calif, St Louis, Mo, New York, NY, Baltimore and Rockville, Md, Chapel Hill, NC, Detroit, Mich, and Madison, Wis*

TABLE II. Association between home dust allergen concentration in the first 3 years of life and asthma at 7 years of age

	Allergen concentration*		Adjusted OR (95% CI)†	P value
	No asthma (n = 312)	Asthma (n = 130)		
Cockroach (Bla g 1 [U/g])				
Age 3 mo	1.20 (0.20-7.15)	0.20 (0.20-3.70)	0.69 (0.45-1.06)	.09
Cumulative‡	7.00 (0.59-36.7)	2.19 (0.59-15.2)	0.55 (0.36-0.86)	<.01
Mouse (Mus m 1 [µg/g])				
Age 3 mo	0.57 (0.13-2.80)	0.22 (0.07-2.52)	0.75 (0.55-1.01)	.06
Cumulative‡	4.29 (0.71-19.0)	3.66 (0.28-11.5)	0.68 (0.49-0.94)	.02
Dust mite (Der f 1 [µg/g])				
Age 3 mo	0.28 (0.26-0.33)	0.27 (0.26-0.30)	0.98 (0.91-1.04)	.46
Cumulative‡	0.85 (0.80-1.15)	0.83 (0.79-1.16)	0.94 (0.82-1.09)	.42
Dog (Can f 1 [µg/g])				
Age 3 mo	0.005 (0.005-0.050)	0.005 (0.005-0.005)	0.62 (0.37-1.03)	.06
Cumulative‡	0.046 (0.015-0.684)	0.015 (0.015-0.265)	0.78 (0.56-1.09)	.15
Cat (Fel d 1 [µg/g])				
Age 3 mo	0.36 (0.20-1.33)	0.28 (0.19-0.59)	0.78 (0.62-0.98)	.03
Cumulative‡	1.17 (0.64-9.79)	0.94 (0.64-2.86)	0.71 (0.51-1.00)	.05
Sum of exposures index§				
Age 3 mo	3.99 ± 2.29	3.16 ± 2.28	0.59 (0.44-0.80)	<.001
Cumulative‡	11.33 ± 5.63	8.95 ± 5.05	0.52 (0.36-0.74)	<.001

Hayvan allerjenleri



Primer koruma alıřmaları

alıřma	Giriřim	Astım
Isle of Wight 2003	Akar - besin	8 yař azalma
Kanada (CaPPS) 2005	Akar - besin	7 yař azalma
Avrupa (SPACE) 2006	Akar - besin	2 yař -
Avustralya (CAPS) 2006	Akar besin	5 yař -

Primer koruma alıřmaları

alıřma	Giriřim	Astım
PREVACS (NL) 2005	Akar – hayvan- besin – sigara	2 yař -
PIAMA (NL) 2012	Akar	8 yař –
MAAS (UK) 2004	Akar	3 yař - Duyarlanmada artıř

SOLUNAN ALLERJENLER – PRİMER KORUNMA

- Bireye özgü çok deęişkenli yaklaşımlar yapılmalıdır
- Uzun soluklu çalışmalar yapılmalıdır

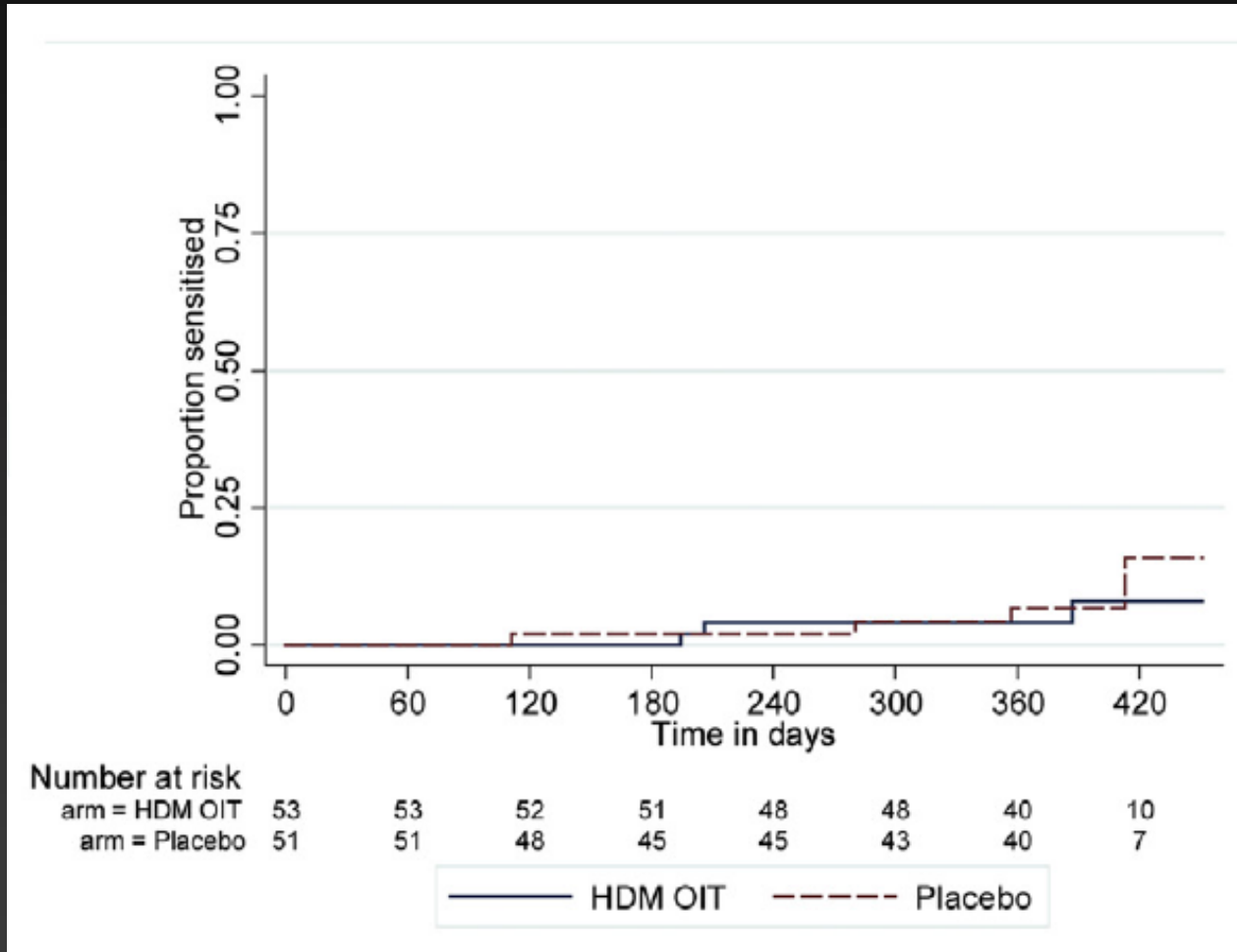
İMMÜNÖTERAPİ

Randomized controlled trial of primary prevention of atopy using house dust mite allergen oral immunotherapy in early childhood

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- Katılım: 5-9 ay
 - ≥ 2 birinci derece akrabada
Astım, rinokonjonktivit, ekzema veya besin allerjisi
 - SPT Negatif
 - HDM OIT (53); placebo (51)
 - İzlem 450 gün
- J Allergy Clin Immunol. 2015;136(6):1541-1547

Akar duyarlanma



Results from the 5-year SQ grass sublingual immunotherapy tablet asthma prevention (GAP) trial in children with grass pollen allergy

Erkka Valovirta, MD,^{a,b} Thomas H. Petersen, MD,^c Teresa Piotrowska, MD,^d Mette K. Laursen, MSc,^e Jens S. Andersen, MSc, PhD,^g Helle F. Sørensen, MSc, PhD,^g and Rabih Klink, MD,^f on behalf of the GAP investigators*
Turku, Finland, Kolding and Hørsholm, Denmark, Białystok, Poland, and Laon, France

- Yaş: 5-12 yıl
- n
 - SLIT 300
 - Placebo 308
- İzlem
 - 3 yıl tedavi
 - 2 yıl tedavi sonrası

Birincil sonlanım noktası

- Astım (rev obs) başlamasına kadar geçen zaman
- FARK YOK

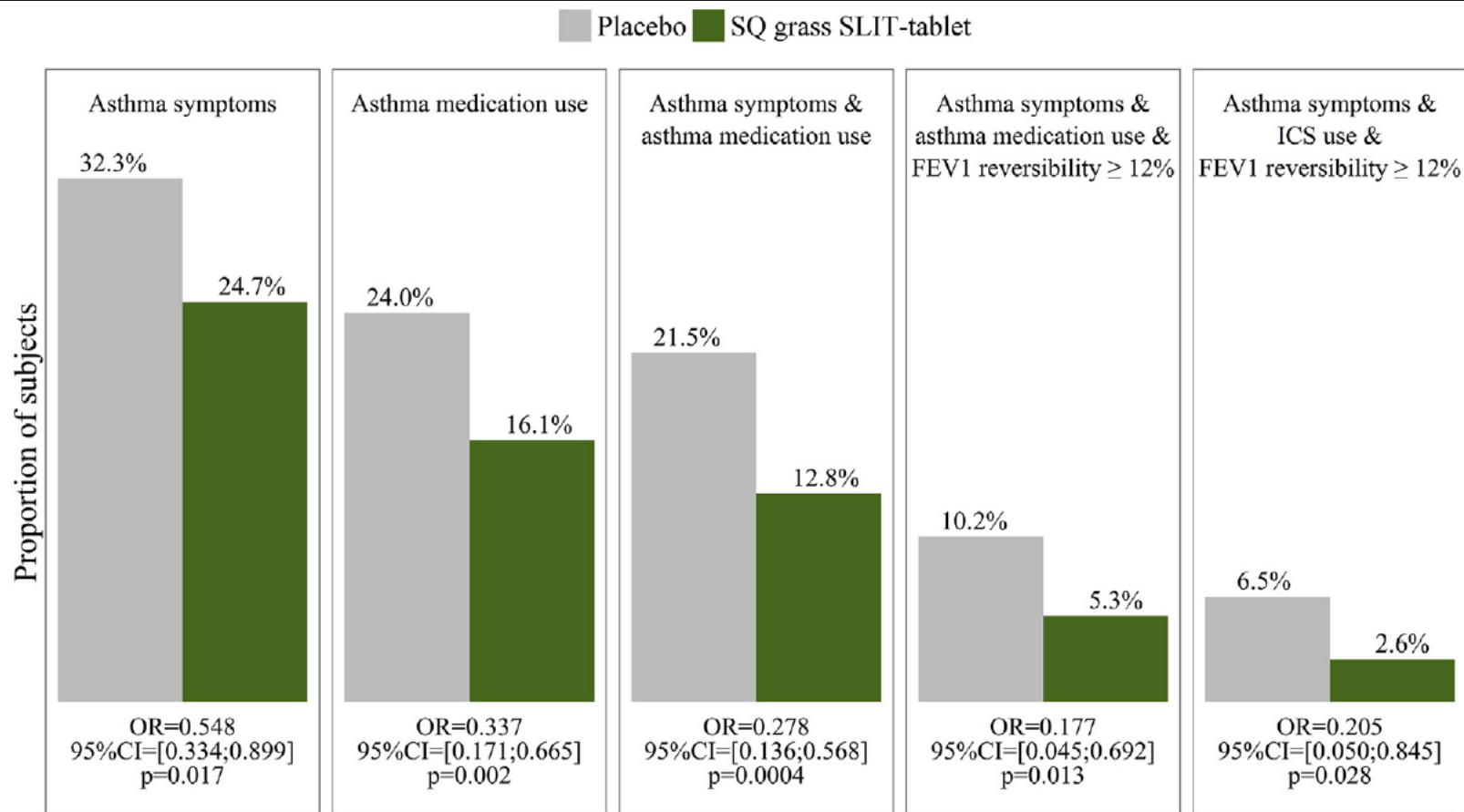
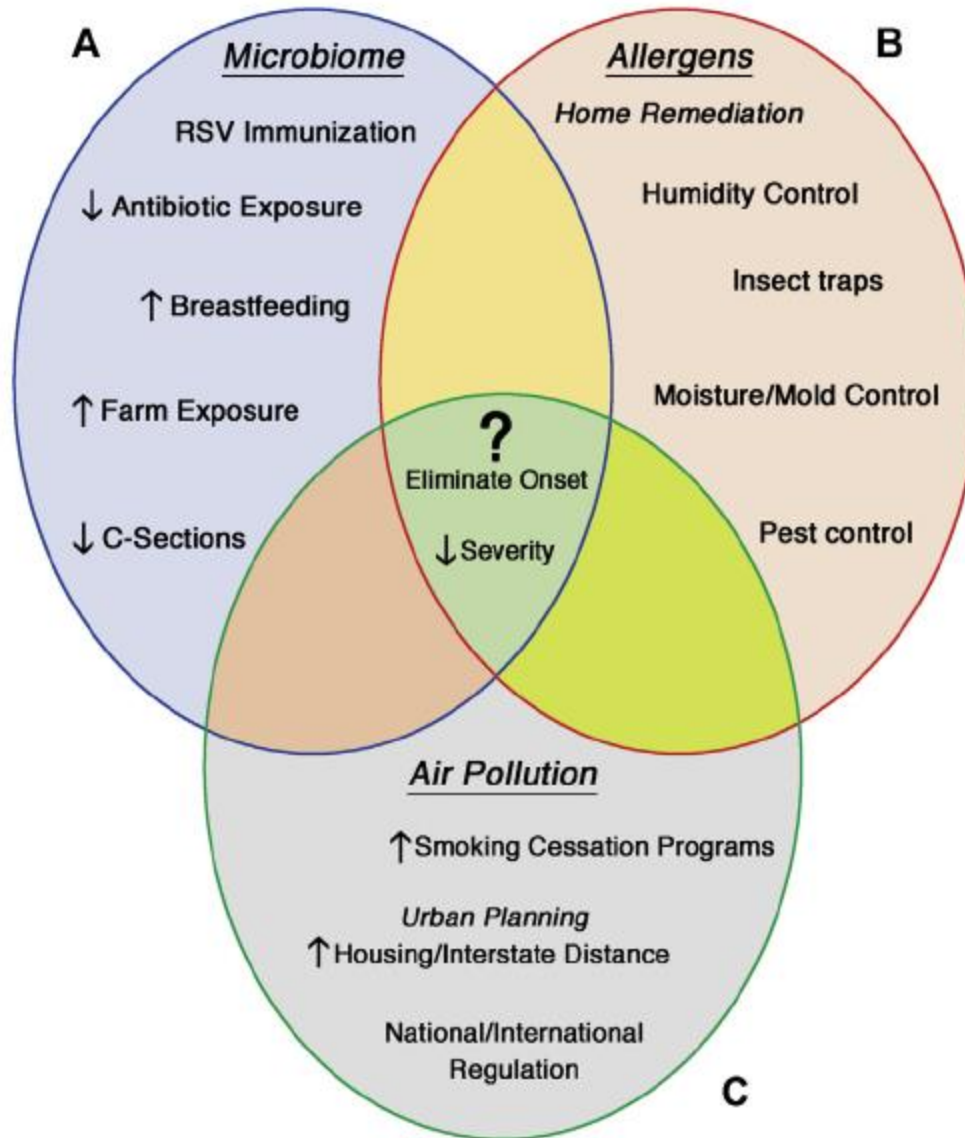


FIG 4. Proportion of subjects experiencing asthma symptoms, asthma medication use, asthma symptoms and asthma medication use, asthma symptoms and asthma medication use, and having a documented FEV₁ reversibility ≥12%, asthma symptoms and inhaled corticosteroids use, and documented FEV₁ reversibility ≥12% during the 2-year follow-up period.

SONUÇ

Potential Interventions to Reduce Risk of Allergic Disease



Öneriler

- Tütün dumanından sakınma
- Hava kirliliğinden sakınma
- Vajinal doğum
- Gereksiz ilaç özellikle antibiyotik kullanımından kaçınma



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