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Hopkins Nutrition

Celebrating a Century of Nutritional Advances for Public Health

Vitamin A Interventions to Reduce Child Mortality, Blindness and Hearing Loss in Nepal

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Policy Questions on Vitamin A Deficiency

- Still a public health problem in Nepal?
  - Among children, mothers and infants?
  - Based on status or diet?
  - Where?
- Does VA reduce mortality?
  - In preschoolers?
  - In women/mothers?
  - In infants?
- Are there long-term benefits of early life VA intervention?
- Should Nepal maintain, expand, shift or integrate VAC?
- Does a “Dietary Safety Net” exist in Nepal?

Functions of Vitamin A

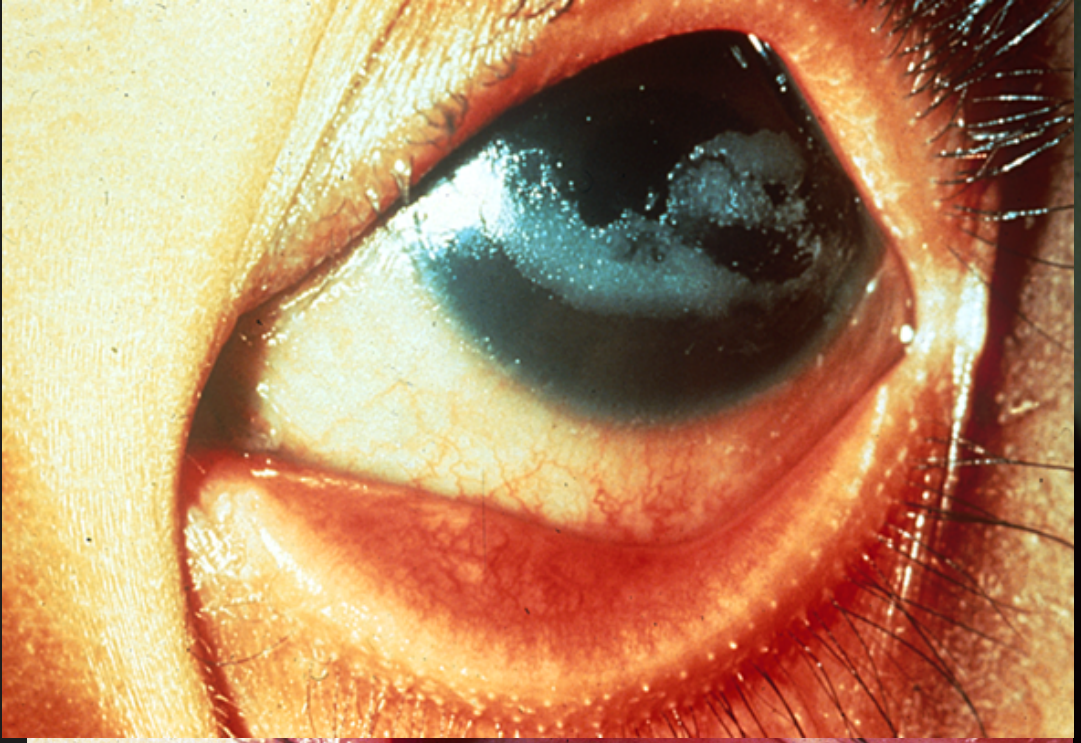
- Enables vision at night (thru the retinoid cycle)
- Regulates DNA transcription and cellular differentiation. Thus, required for -
  - Embryo-fetal development
  - Epithelial lining function (conjunctiva, all tracts)
  - Immunity: Innate and adaptive responses
  - Hematopoiesis (forming red blood cells)
  - Bone formation and growth (osteoblasts, - clasts)
- Likely need for healthy gut microbiome

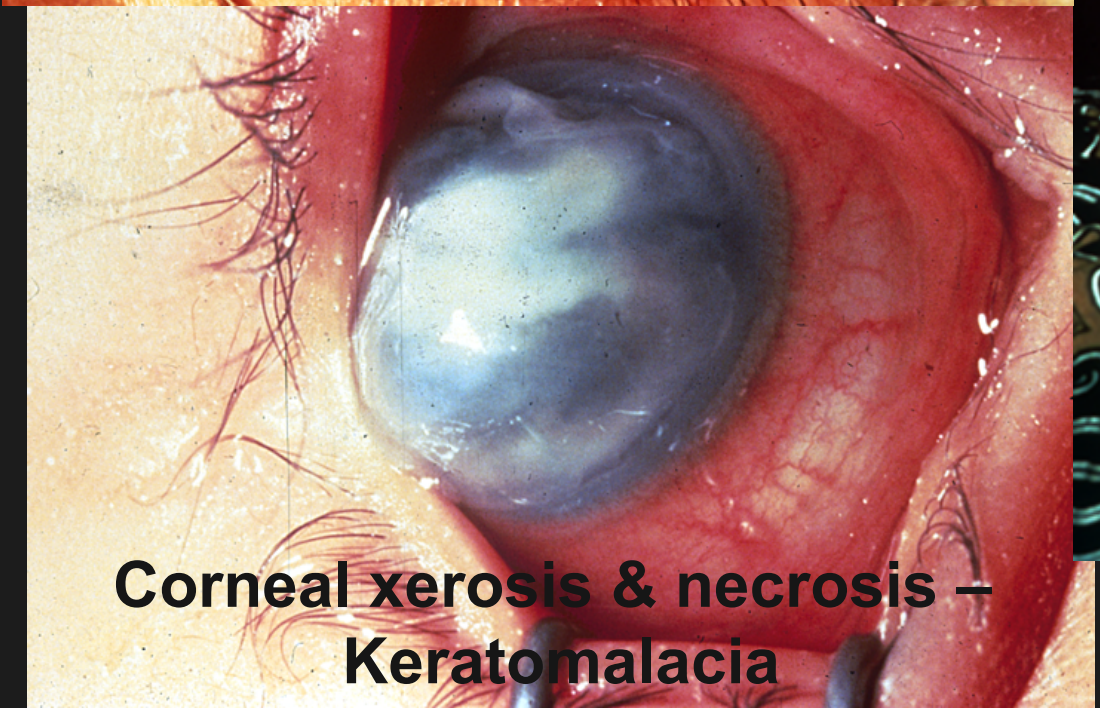
Thus, when Vitamin A is -

Adequate		Deficient
Bone growth	→	Growth retardation
Reproduction	→	Impaired fertility (M&F)
Embryogenesis	→	Teratogenesis
Night vision	→	Night blindness
Healthy linings	→	Epithelial metaplasia
Immune defenses	→	Impaired immunity & Inflammation
Energy balance	→	Excess adiposity?

Bitot's spot (X1B)

Photo: R Whitfield





Corneal xerosis & necrosis – Keratomalacia

Photos: Alfred Sommer

AMERICAN JOURNAL OF EPIDEMIOLOGY
Vol. 121, No. 1
Printed in U.S.A.

XEROPHTHALMIA AMONG NEPALESE CHILDREN[1]

Upadhyay MP et al Arch Ophthalmol 1985

Upadhyay, M. P. (Tribhuvan U. Institute of Medicine, Post Box
rajgunj, Kathmandu, Nepal), B. J. Gurung, K. K. Pillai and B. P.
mia among Nepalese children. *Am J Epidemiol* 1985;121:
A nationwide sample survey was conducted be
to determine the prevalence of xerophthalm
lation proportionate random samples
visions of the country by emplo
population was defined a
of 0 and 14 years. T
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Bitot's s
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1980-1: 1.65% or ~75,000 children with X1B, ~1000 with corneal disease

subdi-
he survey
etween the ages
mia in Nepal was 1.65
corneal scar. While cases of
s of Nepal, followed by the moun-
ror corneal lesions. Vitamin A deficiency
one-third of acquired bilateral blindness in
al cases in the study were accompanied by diarrhea
ating xerophthalmia to be symptomatic of the whole spec-
uon.

Food Items	Spearman's rank correlation	P-value
Preformed vitamin A sources		
Meat (with liver)	0.38	< 0.002
Fish	0.39	< 0.002
Animal milk	0.66	< 0.001
Other breast milk	0.50	< 0.001
Eggs	0.53	< 0.001
Carotenoid sources		
Mango	0.54	< 0.001
DGLV	0.33	< 0.010
Papaya	0.14	0.270
Low vitamin A foods		
Sweet potato (white)	0.44	< 0.001
Rice and dal	0.42	< 0.001
Other vegetables	0.25	< 0.050
Watery rice and dal mix	0.45	< 0.001
Unleavened wheat bread	0.20	0.100
Honey	0.24	< 0.050
Banana	0.22	< 0.080

Gittelsohn J et al Eur J Clin Nutr 1997

Epidemiology of Xerophthalmia in Nepal

A Pattern of Household Poverty, Childhood Illness, and Mortality

Khatry S et al Arch Ophthalmol 1995

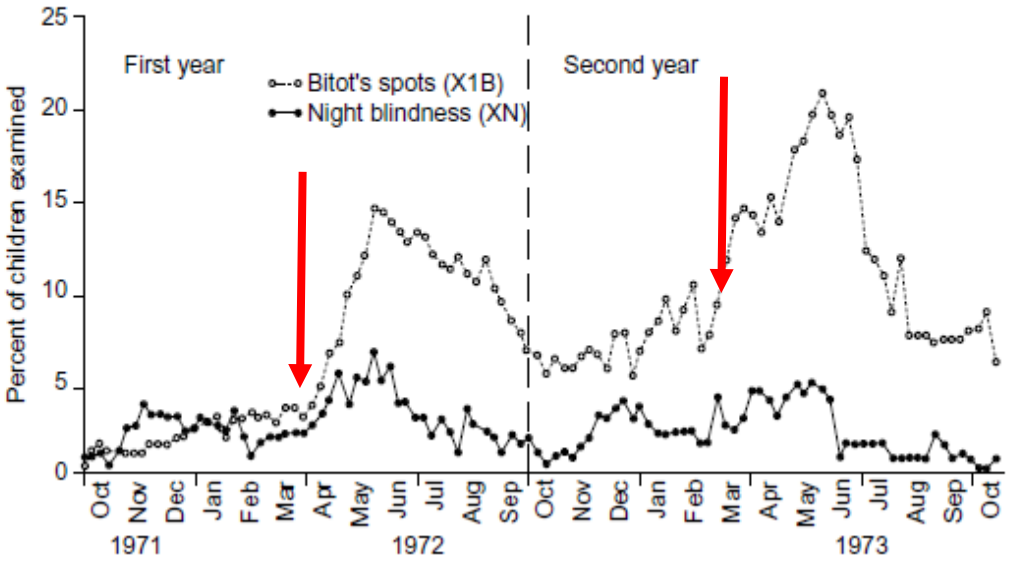
A case-control study of xerophthalmia (120 cases, two with corneal disease; 3377 children without xerophthalmia, 12 to 60 months of age) was conducted in th
of Nepal. Relative household wealth (ownership of anim
and social standing (parental education
inversely related to risk of xerophthalm
die than mothers of co
holds wi

Risk factors for xerophthalmia: Inadequate breastfeeding, wasting, stunting, dysentery, previous sib with xerophthalmia or sib death, low SES; poor diet (Shankar et al AJCN 1996)

se manner
justing for age and other
ted duration of dysentery in the previous
ions of 1 to 6 days and ≥7 days, respectively, vs none).
ective of a lower, local standard of living within which child health, nu-
survival are compromised.

(Arch Ophthalmol. 1995;113:425-429)

The Epidemiology of Eye Disease



Sinha DP & Bang FB Am J Clin Nutr 1976


Alfred Sommer

The "Aceh Study": 1982-84

IMPACT OF VITAMIN A SUPPLEMENTATION ON CHILDHOOD MORTALITY
A Randomised Controlled Community Trial

ALFRED SOMMER
EDI DJUNAEDI
A. A. LOEDEN
IGNATIUS TARWOTJO
KEITH P. WEST, JR
ROBERT TILDEN
LISA MELE
AND THE ACEH STUDY GROUP

The Lancet · Saturday 24 May 1986

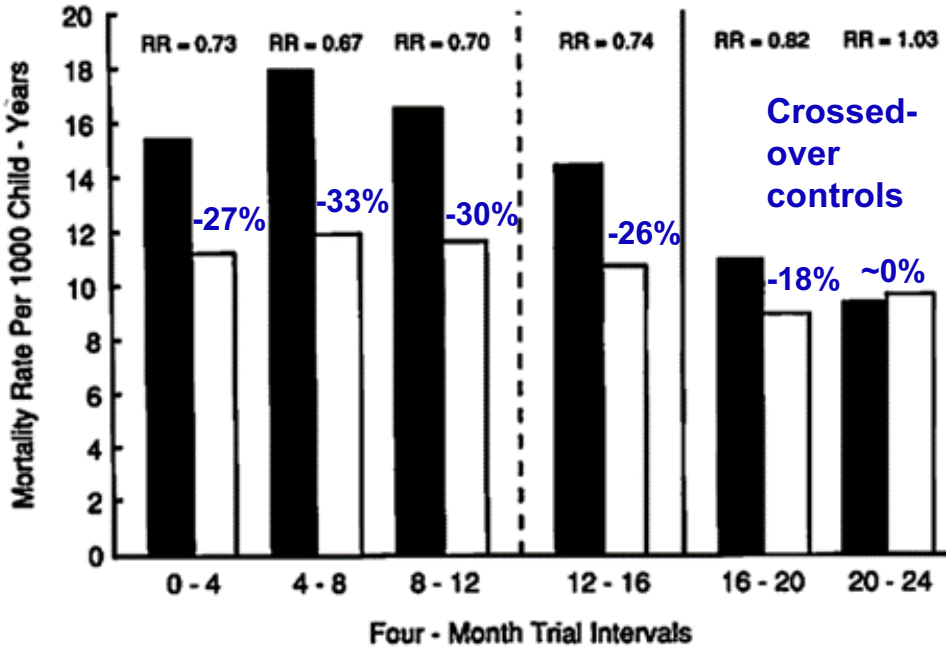
- 450 N Sumatran villages randomized to semi-annual, 200,000 IU vitamin A, or not.
- ~26,000 preschool children enrolled, dosed, followed
- **vitamin A reduced 1-6 yr mortality by 34%**

THE LANCET
July 15, 1994
Vol 338 No 875

ORIGINAL ARTICLES

Efficacy of vitamin A in reducing preschool child mortality in Nepal

KEITH P. WEST, JR R. P. POKHREL JOANNE KATZ
STEVEN C. LECLERQ SUBARNA K. KHATRY
SHARADA R. SHRESTHA ELIZABETH K. PRADHAN
JAMES M. TIELSCH M. R. PANDEY ALFRED SOMMER



Pokhrel RP et al Lancet 1994

Childhood mortality after a high dose of vitamin A in a high risk population

Nils M P Daulaire, Eric S Starbuck, Robin M Houston, Mary S Church, Therese A Stukel, Mrigendra R Pandey

British Med J 1992

Abstract

Objectives—To determine whether a single high dose of vitamin A given to all children in communities with high mortality and malnutrition could affect mortality and to assess whether periodic community wide supplementation could be readily incorporated into an ongoing primary health programme.

Design—Opportunistic controlled trial.

Setting—Jumla district, Nepal.

Subjects—All children aged under 5 years; 3786 in eight subdistricts given single dose of vitamin A and 3411 in remaining eight subdistricts given no supplementation.

Main outcome measures—Mortality and cause of death in the five months after supplementation.

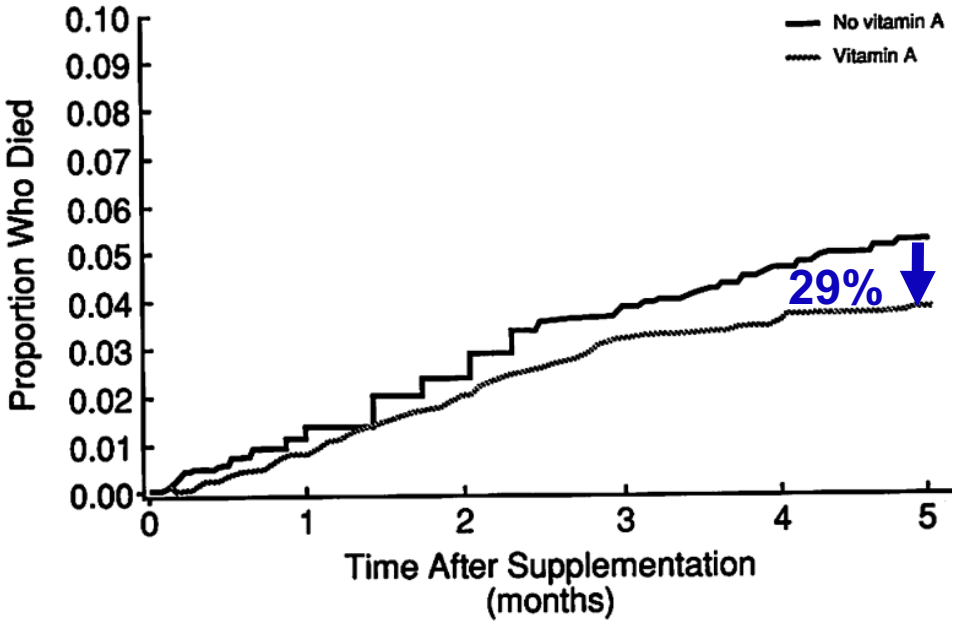
Results—Risk of death for children aged 1-59 months in supplemented communities was 26% lower (relative risk 0·74, 95% confidence interval 0·55 to 0·99) than in unsupplemented communities.

major problem in mountainous areas,[8] this observation suggested that serious deficiency might exist.

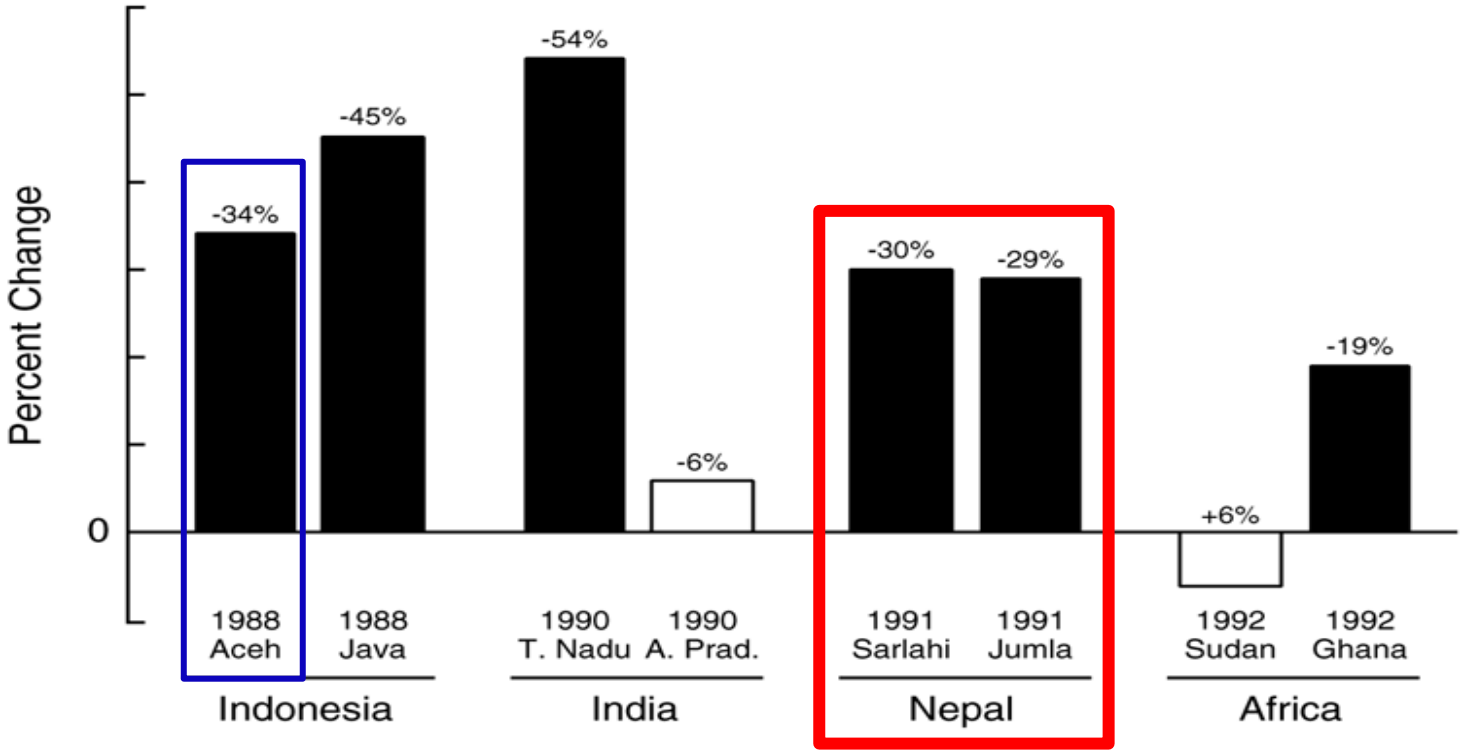
At the end of the pneumonia trial we initiated routine periodic vitamin A supplementation for all children under 5 years. Because new field implementation systems were required and immediate full coverage was impracticable the programme was phased in over six months, resulting in an initial period in which only half the children were given supplementation. We assessed the difference in mortality between supplemented and unsupplemented populations and analysed the cost and impact on the health programme.

Subjects and methods

Jumla district lies in a remote mountainous region of northwestern Nepal. The district's population is about 80 000, with 12 000 children under 5 years. It is one of

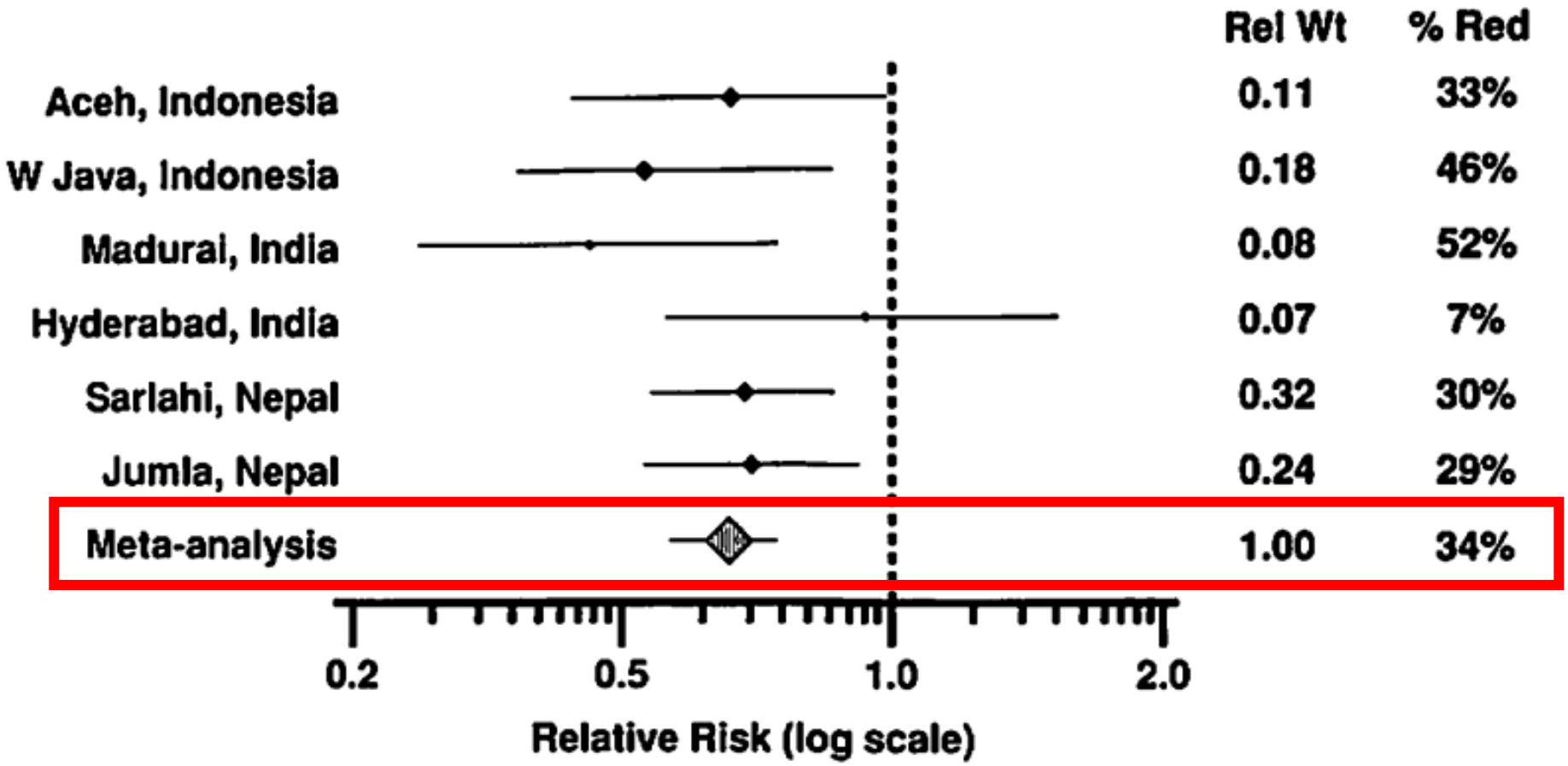


Eight Major Vitamin A Intervention Trials
25-35% Reduction in Preschool Child Mortality



Sommer A & West KP. Vitamin A Deficiency: Health Survival and Vision. Oxford Press, 1996

Meta-analysis of Vitamin A-Child Mortality Trial Findings in Southern Asia



Beaton G, McCabe G et al CIDA Report 1992

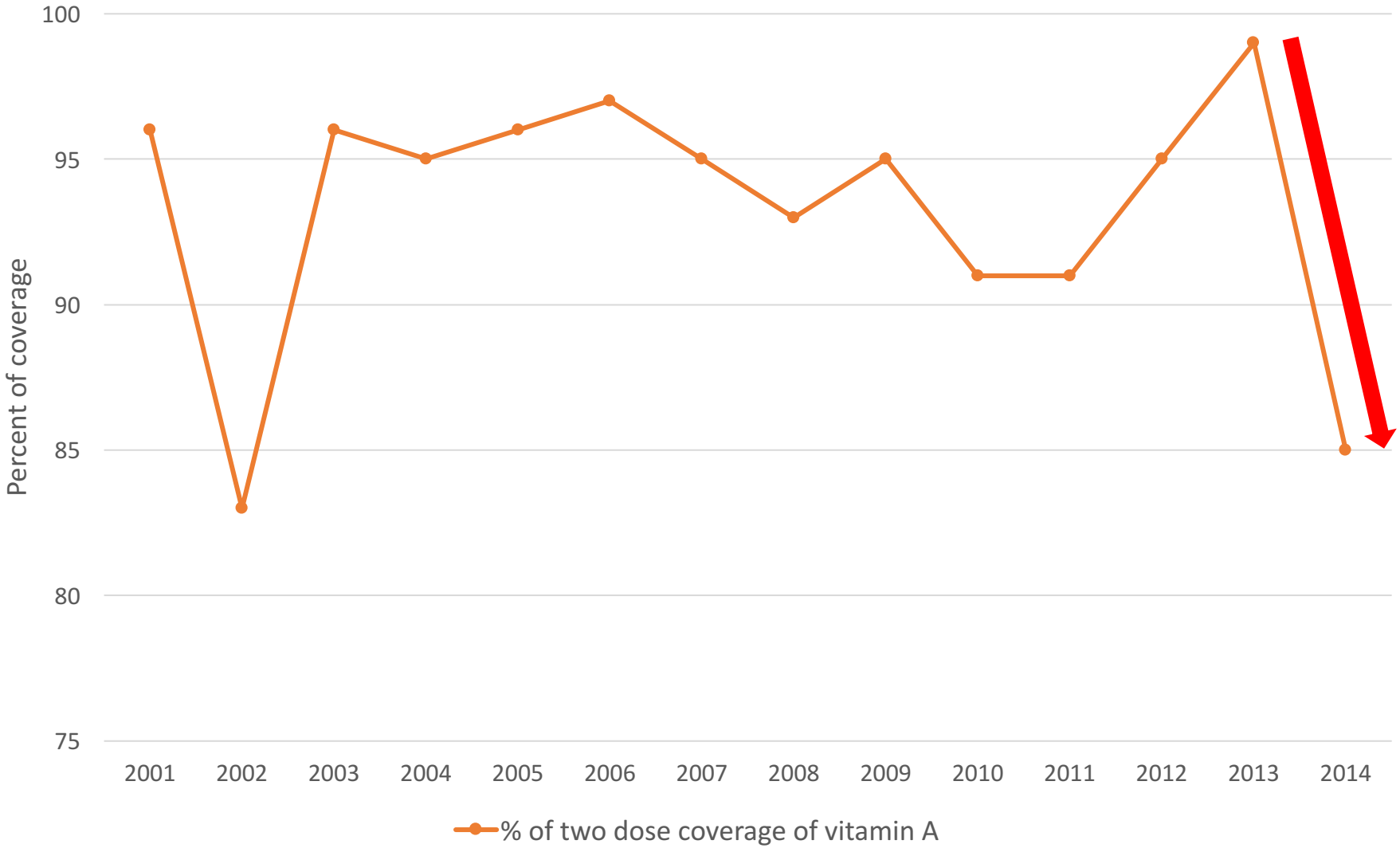
Hearing Loss from Childhood Ear Infections: Reduced 42% by Preschool Vitamin A Supplementation

Supplement	Total No.	No. Cases (%)	Odds ratio (95% CI)	% risk difference (95% CI)
Overall	2370	140 (5.9†)	—	—
Placebo	1116	72 (6.5)	1.00	—
Vitamin A	1254	68 (5.4)	0.83 (0.62 to 1.12)	–1.0 (–2.7 to 0.7)
No ear discharge				
Placebo	902	30 (3.3)	1.00	—
Vitamin A	1012	36 (3.6)	1.07 (0.64 to 1.80)	0.2 (–1.5 to 1.9)
Ear discharge				
Placebo	214	42 (19.6)	1.00	—
Vitamin A	242	32 (13.2)	**0.58 (0.37 to 0.92) [= 42% reduction]**	**–7.2 (–13.0 to –1.4)**

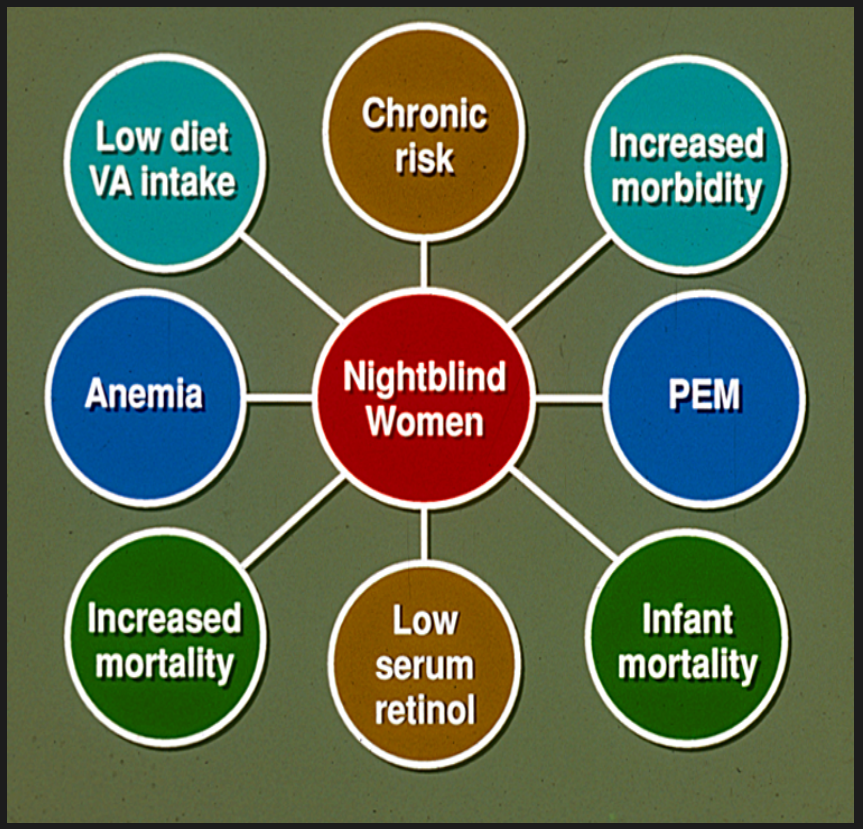
Based on following the NNIPS-1 vitamin A trial cohort 16 years later.

Schmitz J et al BMJ 2012

Coverage of Two-Dose Vitamin A Supplementation in Nepal, 2001-2014



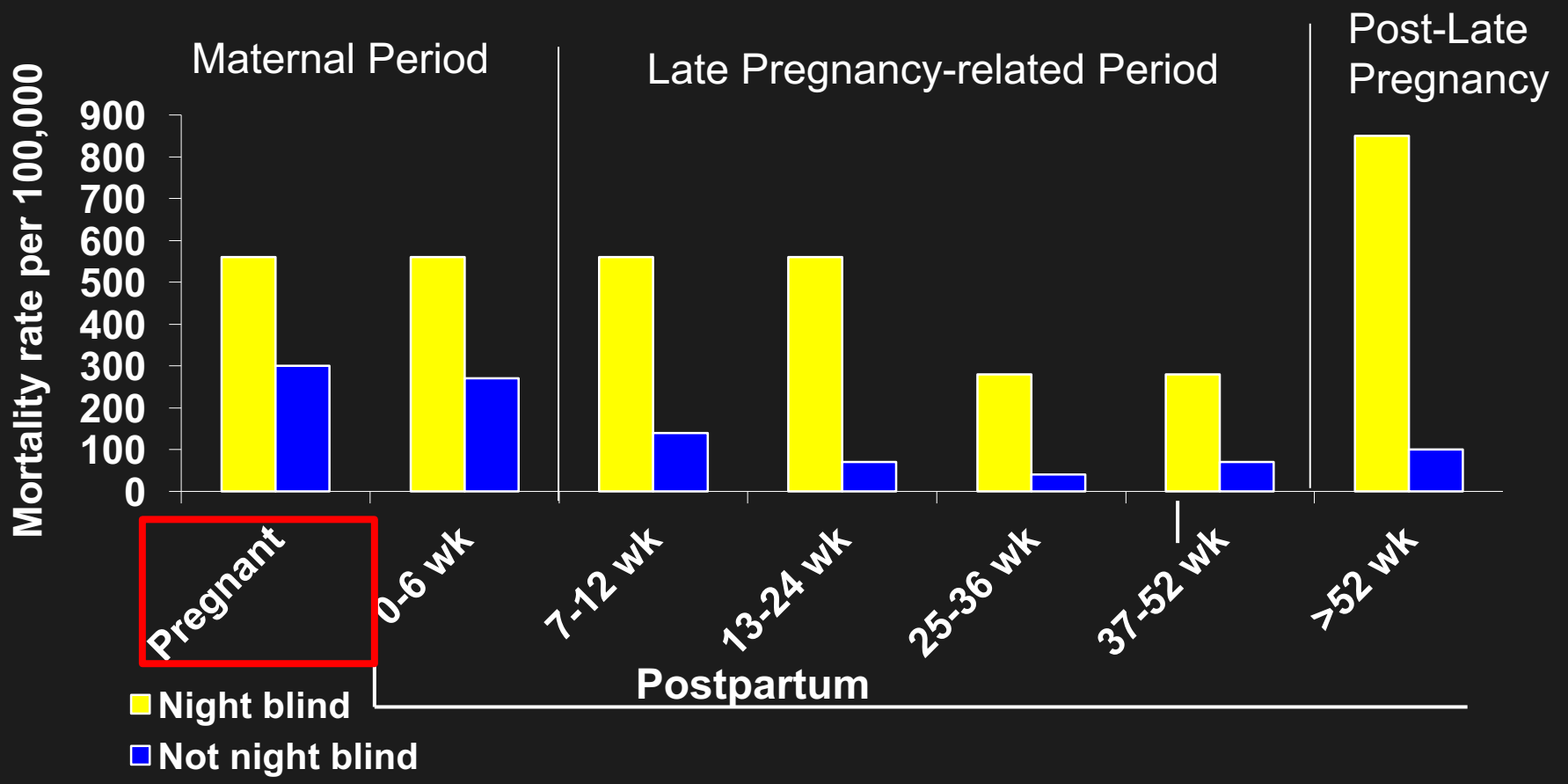
UNICEF. 2017. Vitamin A deficiency: Current Status + Progress. Vitamin A Supplementation. UNICEF Data: Monitoring the Situation of Children and Women.
Available: //data.unicef.org/topic/nutrition/vitamin-a-deficiency/.



Maternal Night Blindness: ~10%
during latter half of pregnancy in undernourished South Asian populations

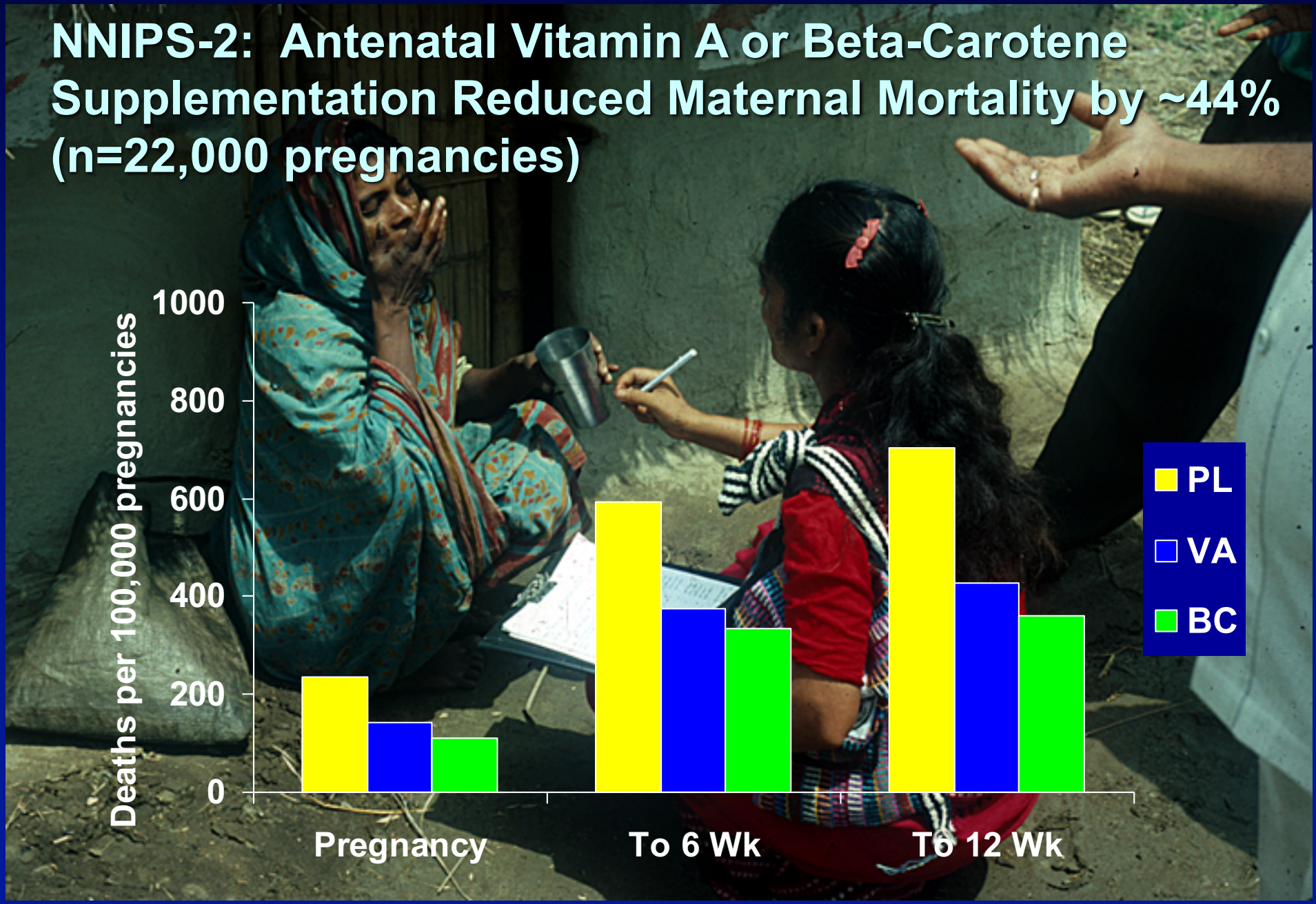
India:
Dixit, 1967; Mandal, 1973;
Nepal:
Katz et al, 1995;
Christian et al: Int J Epidemiol 1998;
Christian et al: Eur J Clin Nutr 1998;
Christian et al: Am J Clin Nutr 1998;
Christian et al: Soc Sci Med 1998;
Christian et al: Am J Epidemiol 2000;
Christian et al: J Nutr 2002

Mortality of Women by Night Blindness in Pregnancy, Sarlahi, Nepal



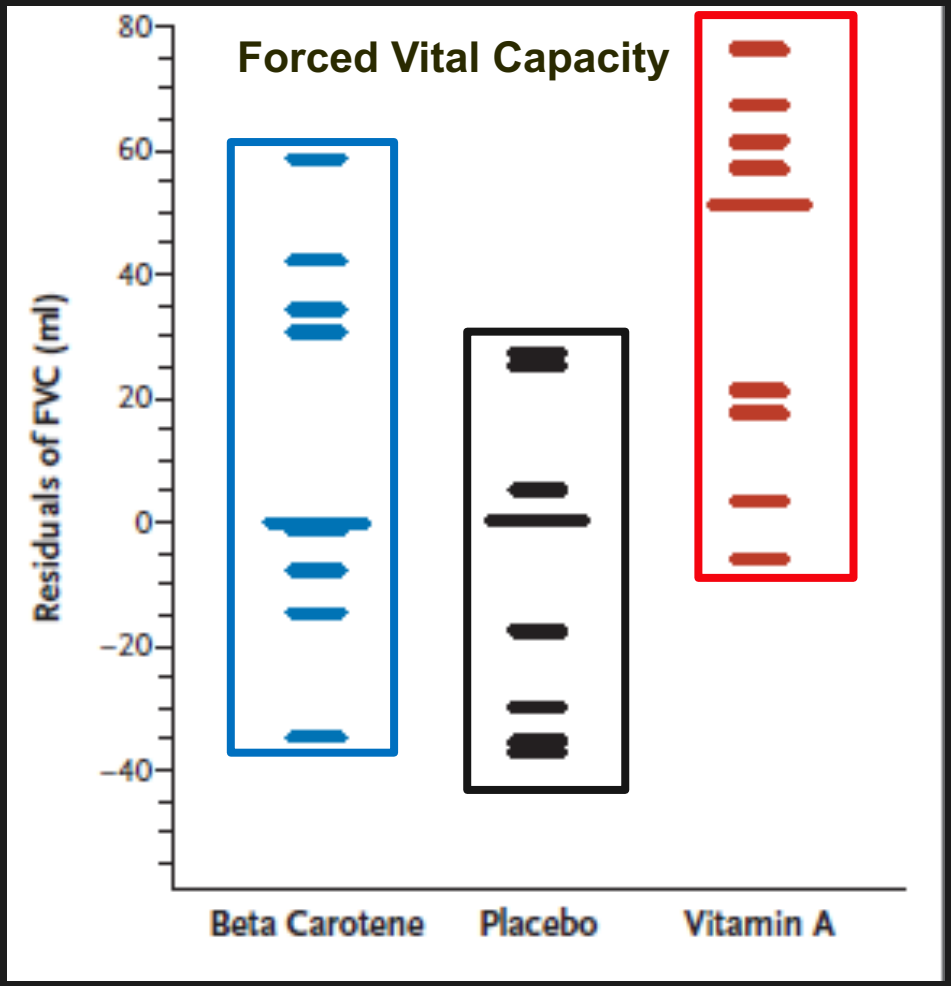
Christian et al, Am J Epidemiol 2000

NNIPS-2: Antenatal Vitamin A or Beta-Carotene Supplementation Reduced Maternal Mortality by ~44% (n=22,000 pregnancies)



West KP, Katz J, Khatry SK et al, BMJ 1999

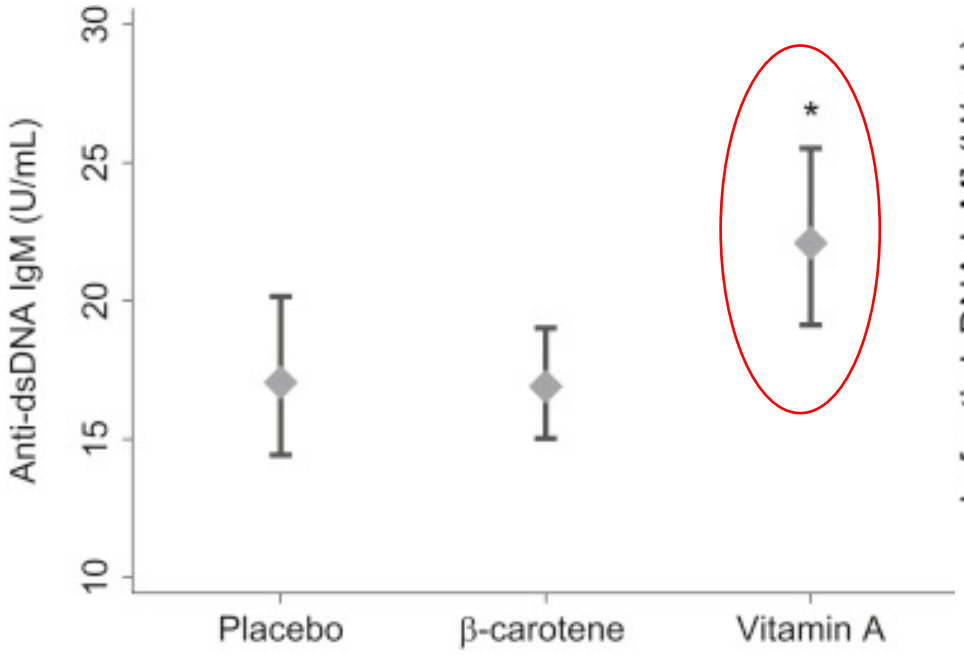
In Nepal: Antenatal Vitamin A Increased Lung Volume of Offspring by 9-13 Years of Age

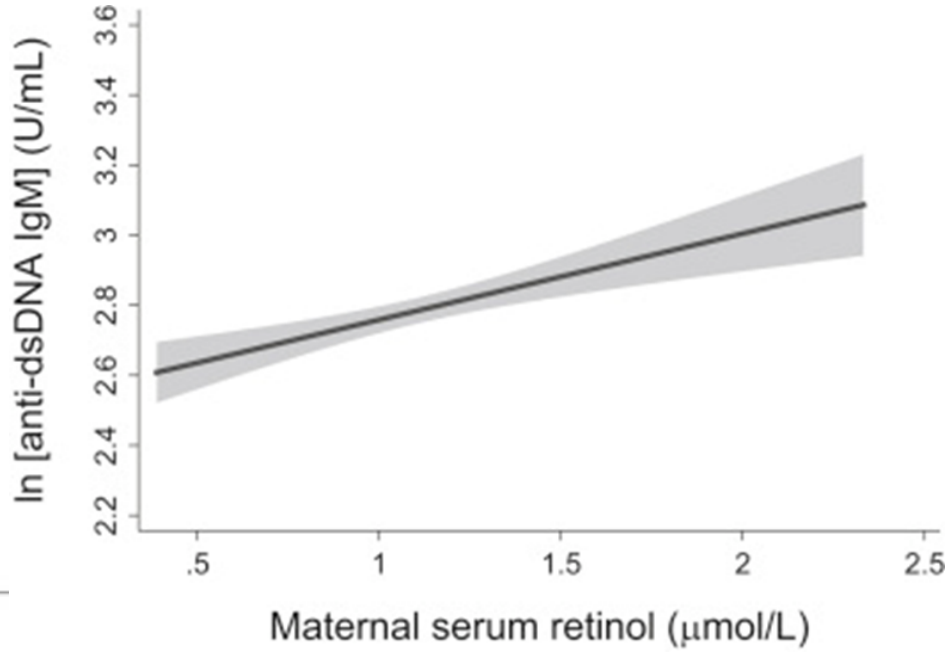


Checkley W, West KP, Wise RA et al New Eng J Med 2010

Weekly Antenatal Vitamin A and Maternal Serum Retinol in Pregnancy Increased Natural Antibody of Offspring 9 to 13 years of age in rural Nepal (n=250)

Values are geometric means (±95% confidence intervals).

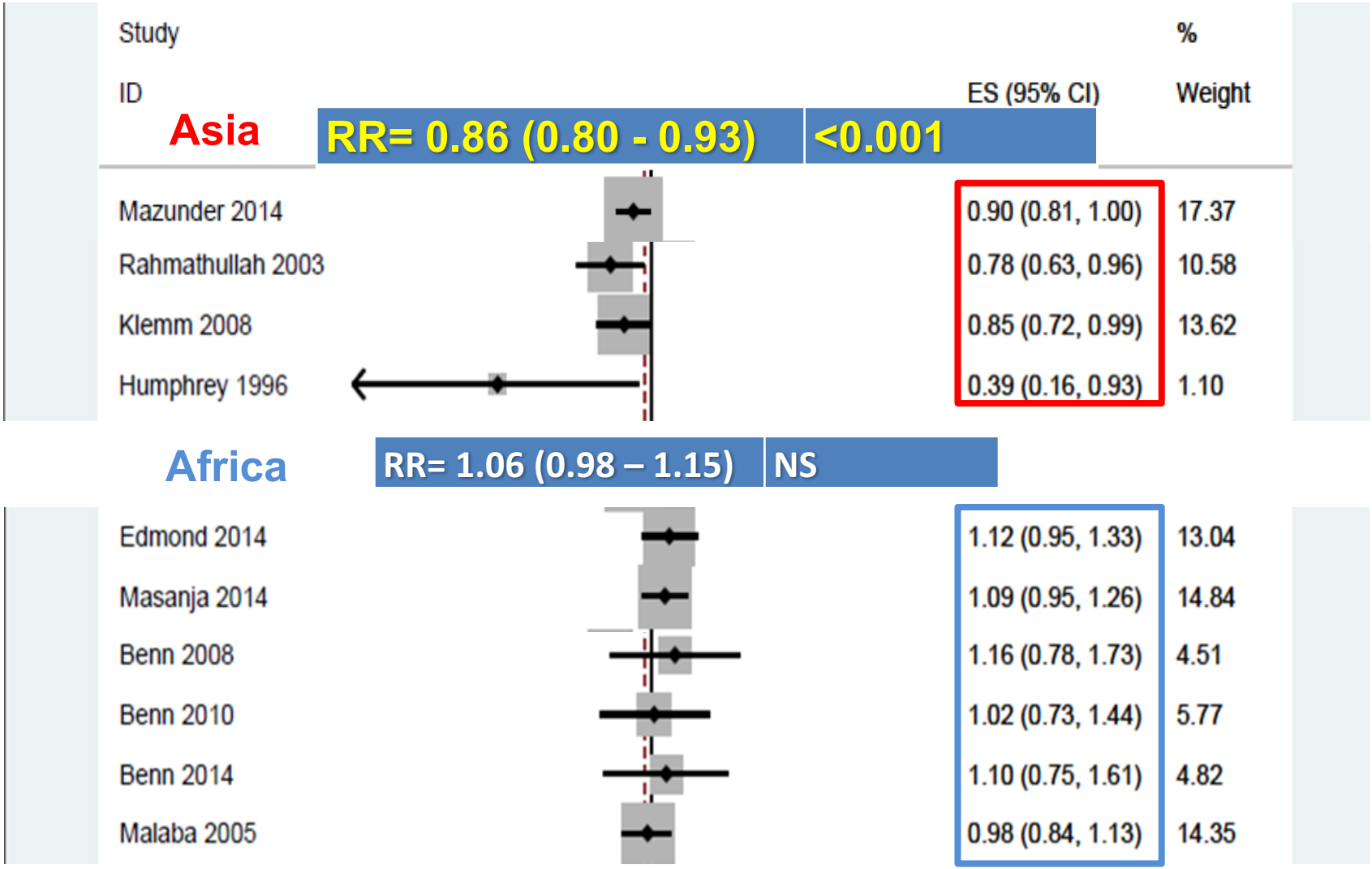




Palmer AC, Schulze KJ, Khatry SK, De Luca L, West KP Jr. Nutrition 2015;31:813-19

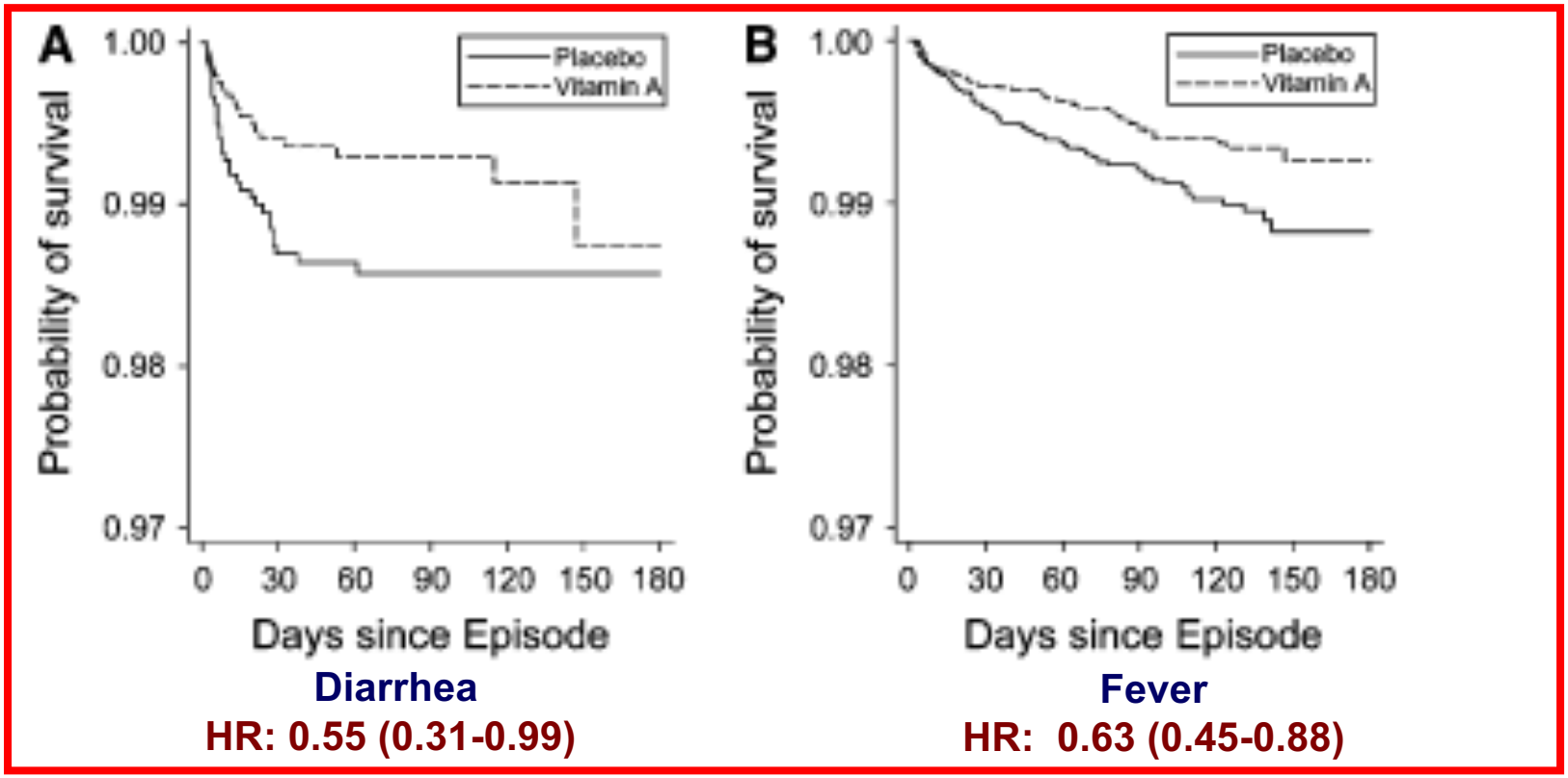
Newborn Vitamin A:
Life Saving Intervention in South Asia (not Africa)

Effects of Neonatal Vitamin A Supplementation on Six-Month Mortality In Asia and Africa



WHO Neonatal Vitamin A Supplementation Evidence Group (draft ms, 2017)

Causes of Death Affected by Neonatal Vitamin A? Diarrhea and Fever, also NEC, but not ALRI



Tielsch JM et al J Nutr 2007

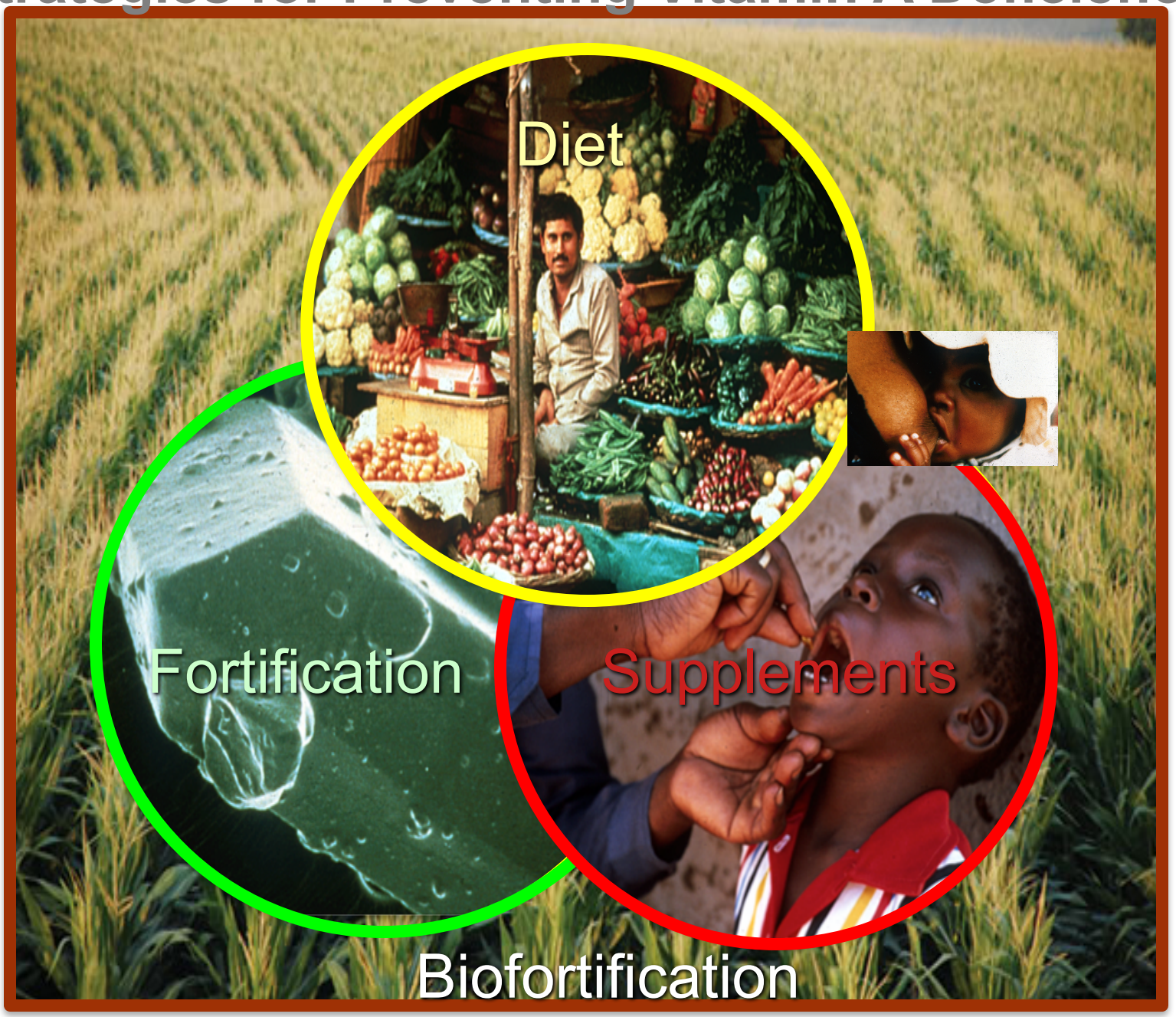
Estimate of Infant Deaths Avertable in South Asia: ~180,000 per Year

Country	Live Births (000)	IMR per 1000	No. Deaths < 6 mo (@85%)	Dx avertable (@14%)
Afghanistan	1081	66	60,645	8,941
Bangladesh	3134	31	82,581	11,561
Bhutan	13	27	299	42
India	25794	38	833,146	116,641
Nepal	577	29	14,223	1,991
Pakistan	5451	66	305,801	42,812
Sri Lanka	323	8	2,196	308
Total				**181,846**

UNICEF SOWC 2016. South Asia only, assumes only deaths < 6 mo averted;
129,890 deaths averted if assume 10% reduction.

Strategies for Preventing Vitamin A Deficiency

Deficient Population



Policy Recommendations for Discussion

- Maintain VAC program in preschool children at high coverage until -
  - Prevalence of VA deficiency is reliably <5%*
  - Dietary safety net is assured
  - Intensify exclusive breast feeding (<6 mo)
- Assure dietary adequacy, especially for women and children (Dr. Ramesh Adhikari)
- Consider newborn VA supplementation as part of safe birthing kit and essential neonatal care

Palmer AC et al Publ Health Nutr 2012

Thank you!

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Bill and Melinda Gates Foundation

Canadian Government

Sight and Life Foundation/DSM