



Tuberculosis in Greenland

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Historical perspective



Prevalence of *M. tuberculosis* infection

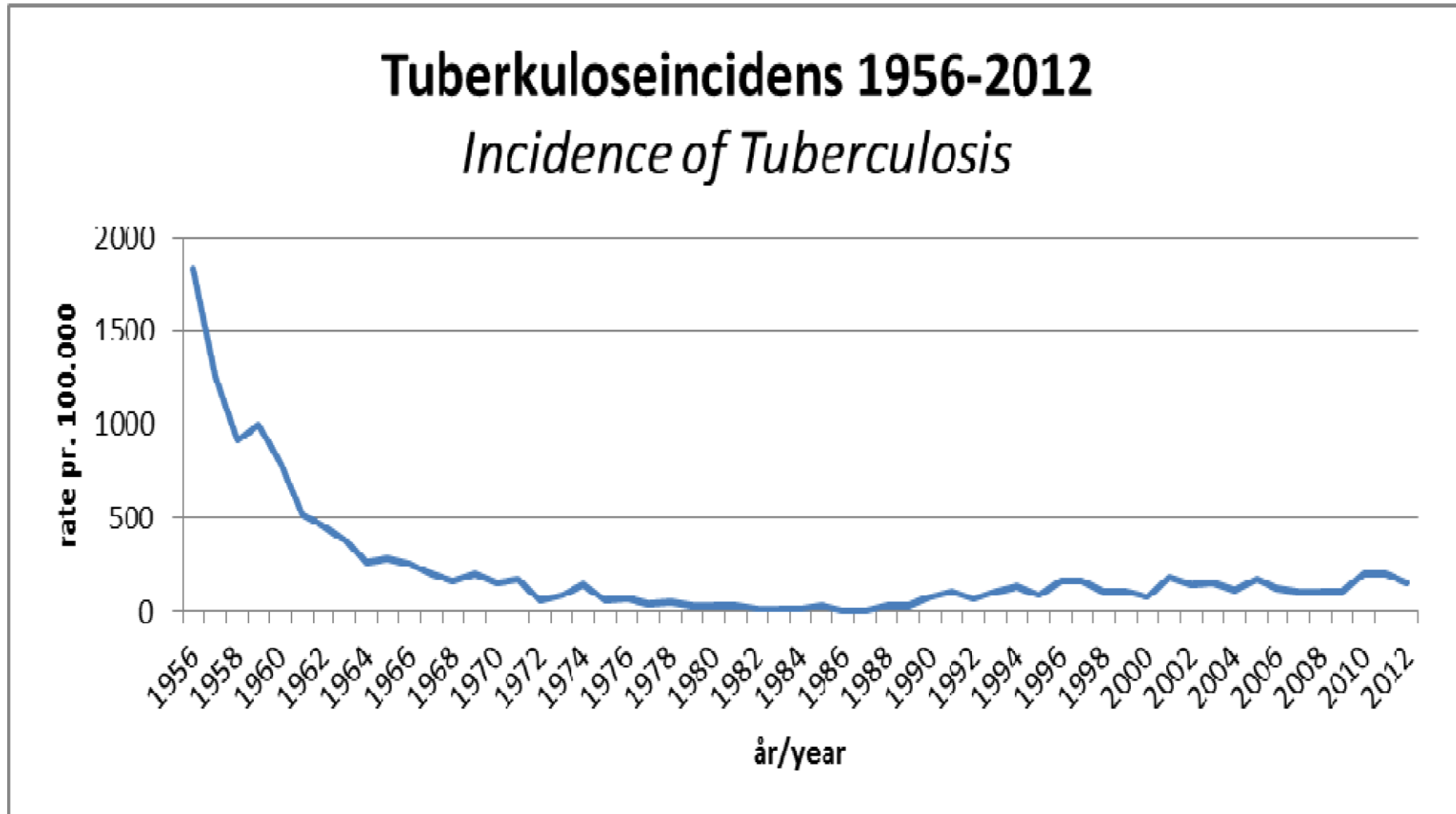
CROSS SECTIONAL TUBERCULIN SKIN TEST SURVEY CHILDREN, SOUTHERN GREENLAND, 1933

- 866 Participants, ½-20 years of age
(50% of relevant population)
- ½-6 years: 43% TST positive
- 7-13 years: 86% TST positive
- 14-19 years: 100% TST positive



Bertelsen, A. Grønlandsk medicinsk Statistik og Nosografi I-IV, Medd. om Grønland CXVII, 1943.

Tuberculosis incidence 1956-2012



TB cases reported to the Chief medical officer of Greenland. 1956-2012
Courtesy of the Chief Medical Officer in Greenland, annual report 2013

21,75

Misigssut



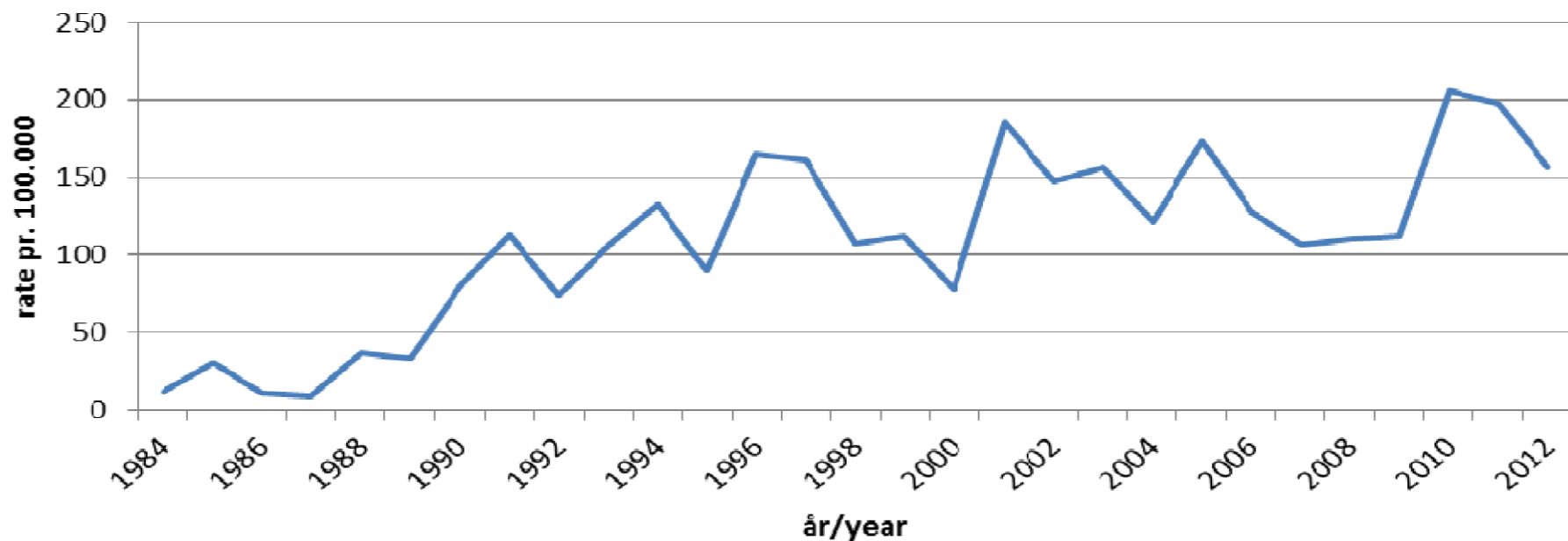
KALAALLIT NUNAAT GRØNLAND

2004

MARTIN MORCK f.c.

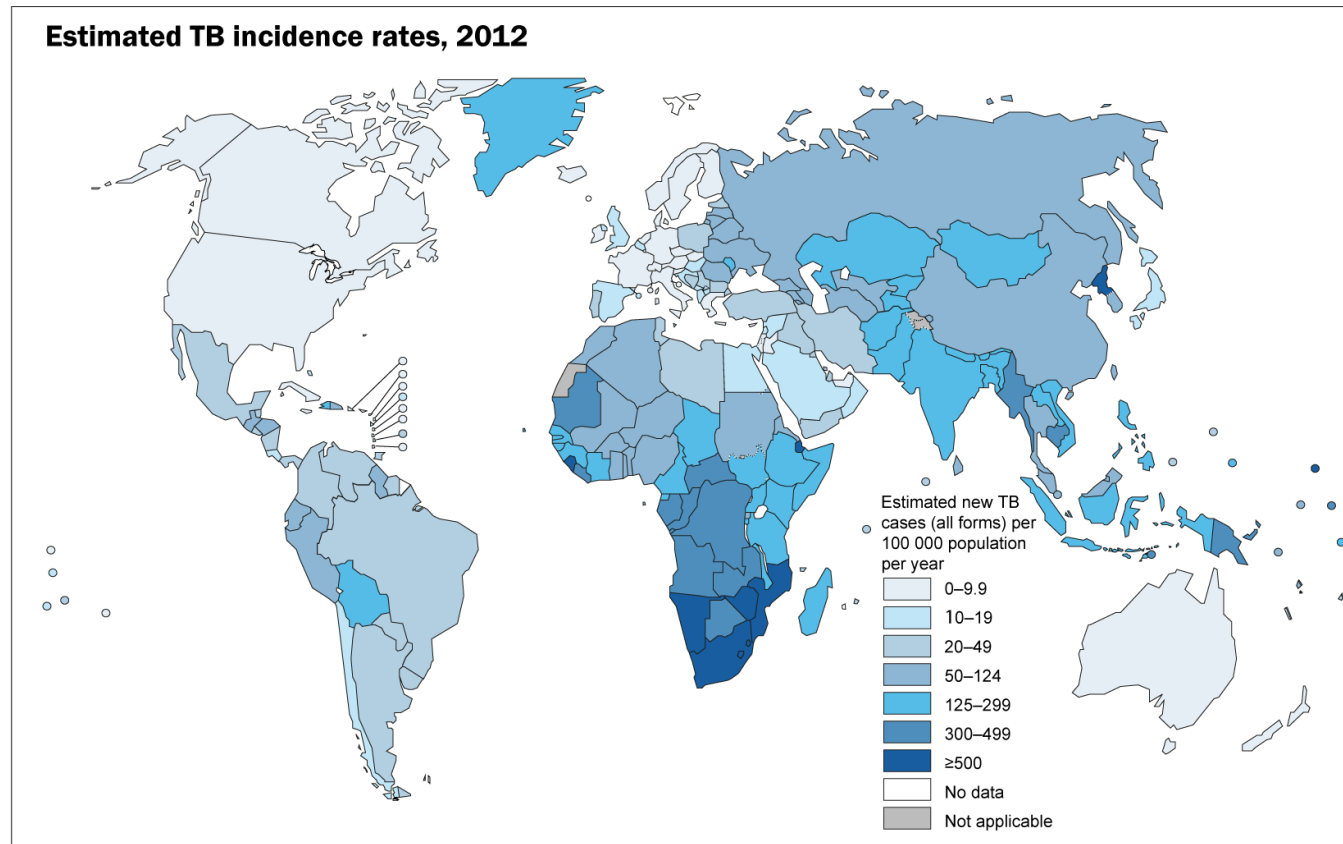
Tuberkuloseincidens 1984-2012

Incidence of Tuberculosis



TB cases reported to the Chief medical officer of Greenland 1984-2012
Courtesy of the Chief Medical Officer in Greenland, annual report 2013

Tuberculosis notification, WHO 2012



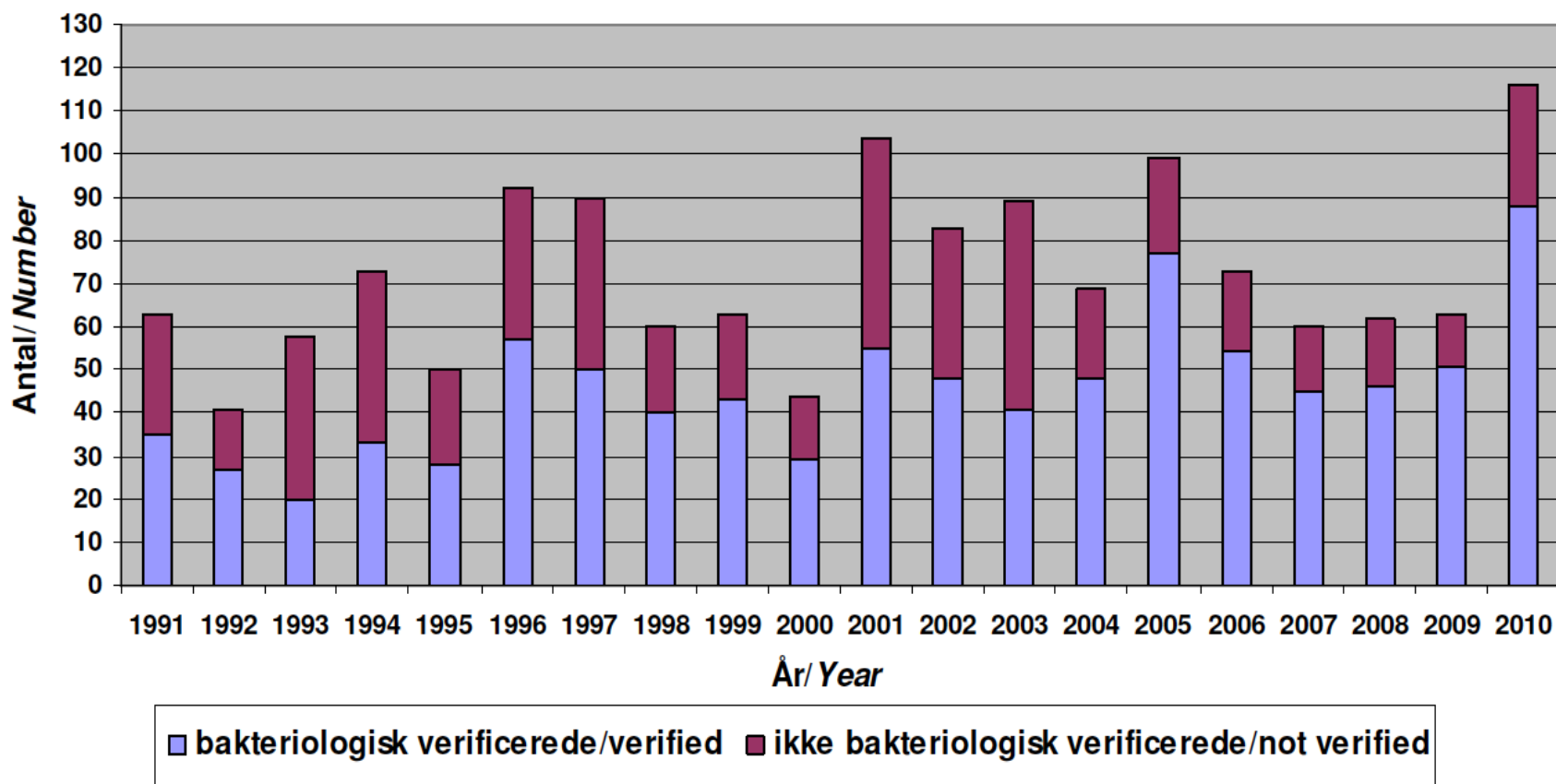
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: *Global Tuberculosis Report 2013*. WHO, 2013.

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Bakteriologisk verificerede Tuberkulose tilfælde 1991 - 2010 *Bacteriological verified cases of tuberculosis*



Figur 12

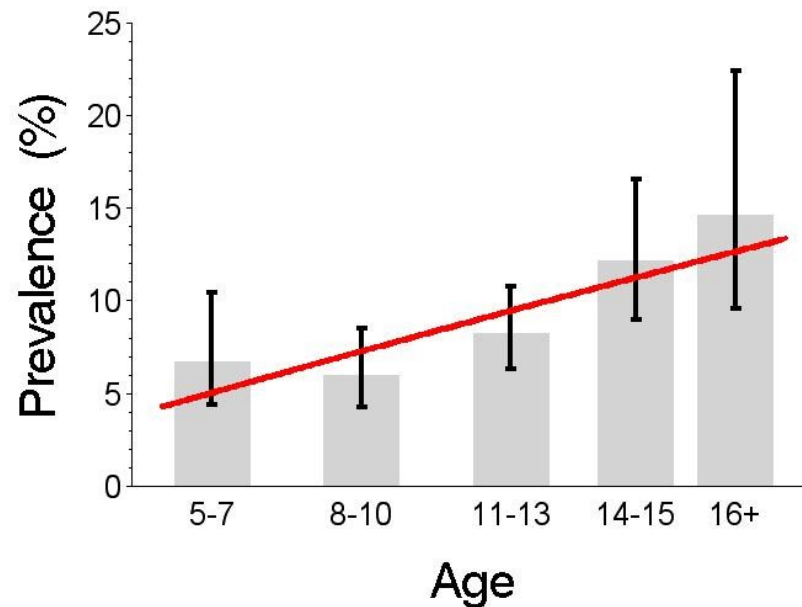
Number of TB cases in periods with high and low incidence

	TB-tilfælde	
Total	1597	
1975-1989	207	13%
1990-2010	1390	87%

TB cases per age group

Age groups in years	TB incidence* 1975-1989	TB incidence* 1990-2010	Trend for the period 1990-2010 (p-value)
0-4	6	59	0.3
5-14	8	67	0.7
15-24	27	173	<0.0001
25-34	29	135	0.0003
35-44	33	113	0.02
45-54	66	137	0.35
55-64	88	159	0.08
65+	49	163	0.04

Prevalence of *M. tuberculosis* infection by age



Effect of national interventions



Ten years of tuberculosis intervention in Greenland - Has it prevented cases of childhood tuberculosis?

Period	TB cases	IRR	95% CI	p
1990-1994	23	0.47	(0.28-0.75)	0.002
1995-1999	64	1 (Ref.)	-	-
2000-2006	93	1.05	(0.76-1.45)	0.78
2007-2010	29	0.62	(0.39-0.95)	0.03
Total	209			0.0004

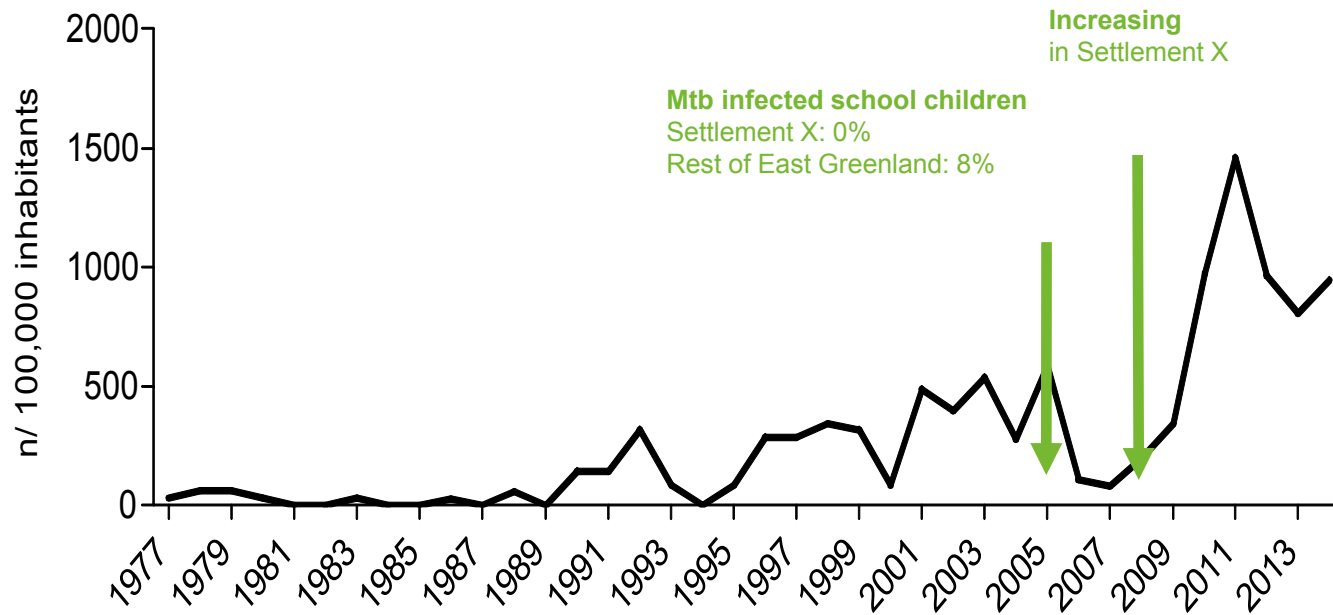


Outbreak 1994



Outbreak 2010-2012

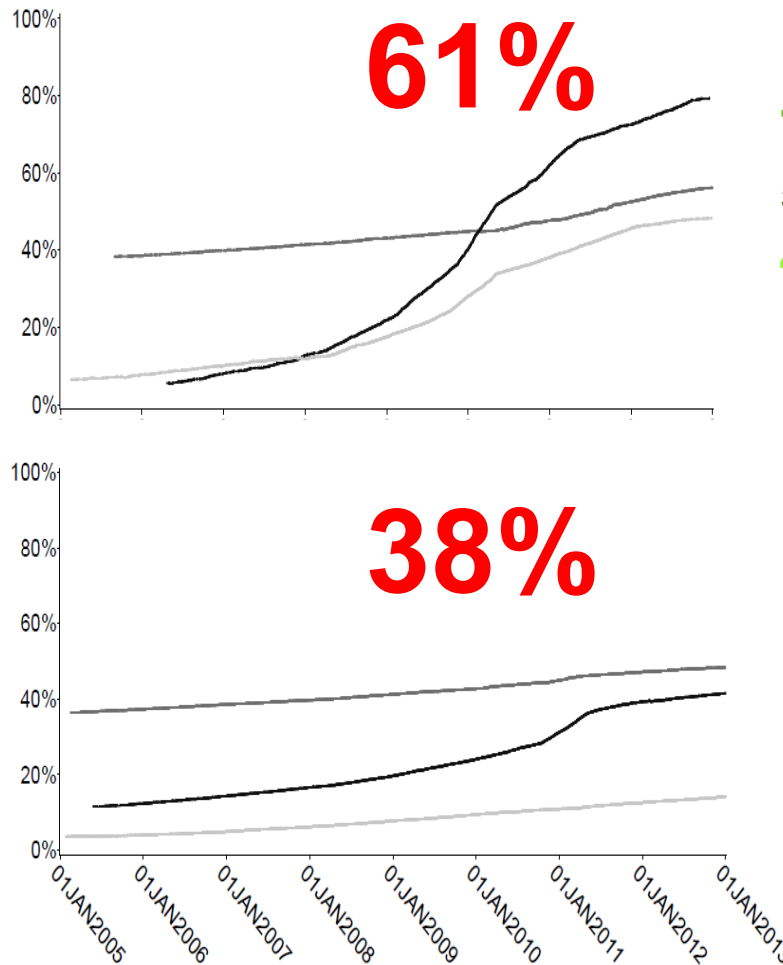
TB notification rate East Greenland 1977-2014



TB incidence rates (IR) and incidence rate ratios (IRR) East Greenland 2008-2012

	Settlement X			Rest of East Greenland			IRR
	Cases	Person-years	IR /100,000	Cases	Person-years	IR /100,000	
Total	28	1,668	1,730	99	15,360	704	2.48
0-12 yrs	-	380	-	3	3,631	90	-
13-19 yrs	18	251	7,389	39	2,056	2,210	4.08
20+ yrs	10	1,036	1,000	57	9,671	633	1.49

Mtb infection prevalence Jan 1, 2013, East Greenland (IGRAs, n= 4,060)



Settlement X

79% teenagers
56% adults
48% children

Rest of East Greenland

48% adults
42% teenagers
14% children

Effect of BCG vaccination



Host Immunity to

Tuberculosis in Greenland

Sascha Wilk Michelsen, MD, PhD student



Supervisors: Melbye M, Soborg B, Koch A, Agger EM, Hoff ST

How effective is the BCG vaccine in preventing tuberculosis infection and disease?

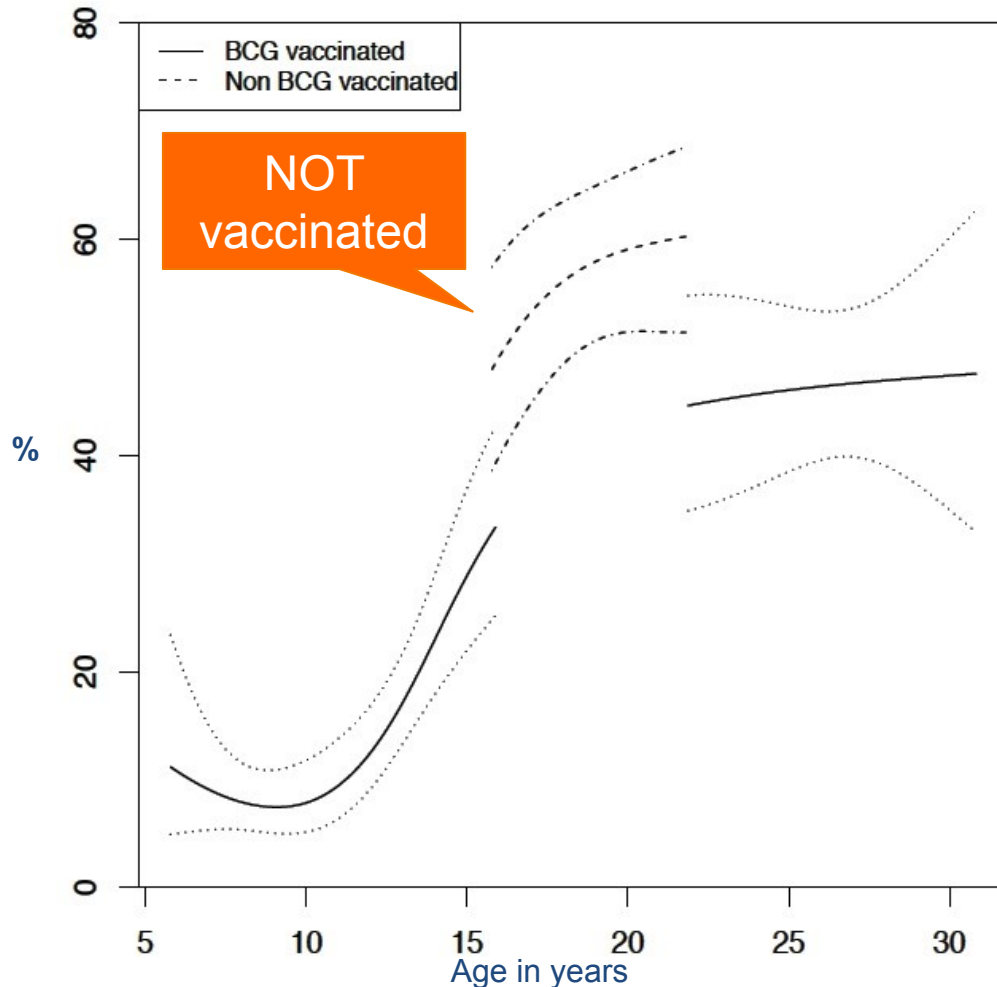
Is immunity to latency antigens associated with prevention of progression to TB?

Is immunity to *Mtb* antigens specific for infection stages and is immunity sustained over time?

BCG REDUCED THE ODDS OF TB INFECTION

N = 953, BORN IN GREENLAND, AGE 5-30 YEARS, PARTICIPATION RATE 80%

Predicted TB infection prevalence by age (%)



TB infection overall 29%

- Among vaccinated 23%
- Among non-vaccinated 56%

Odds ratio for TB infection in BCG vaccinated

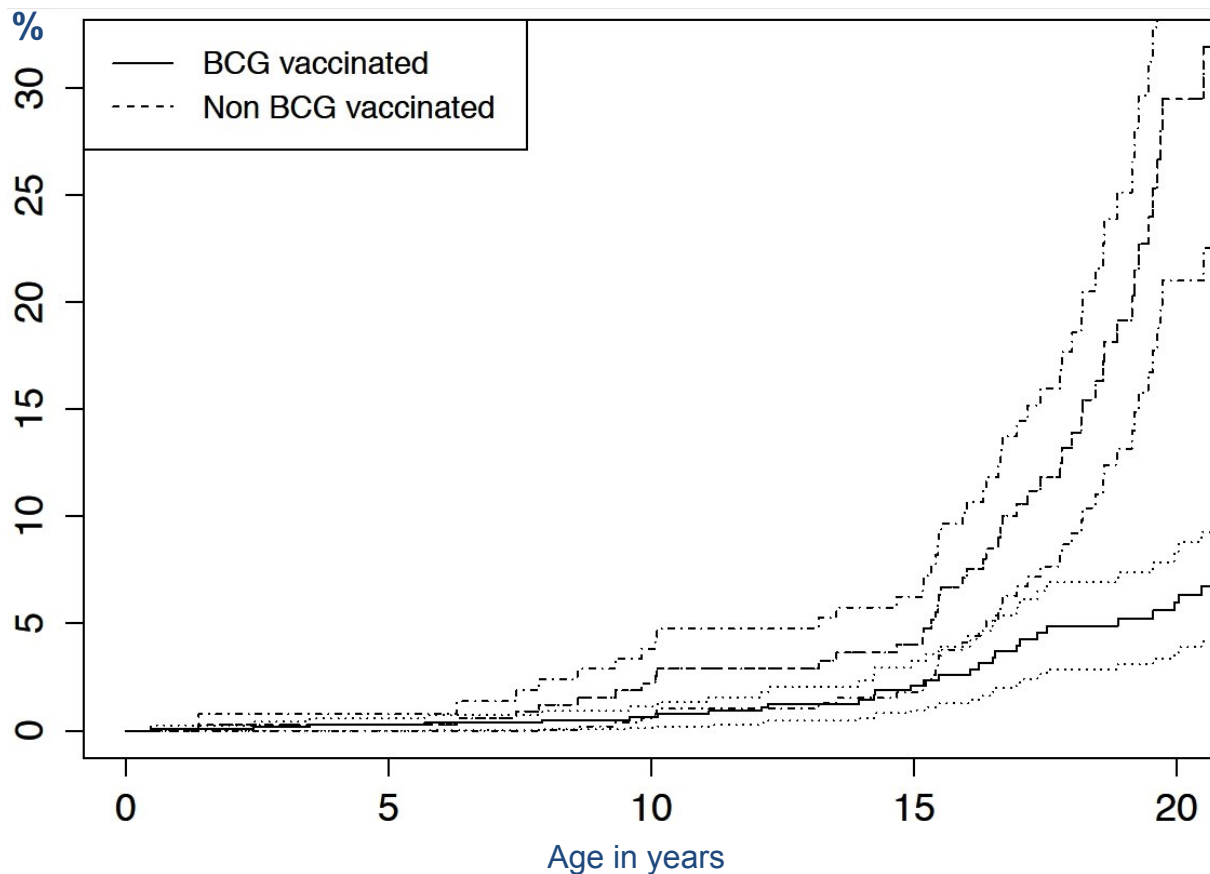
- Adjusted OR 0.52
(95% CI 0.32-0.85) $p = 0.01$

BCG reduced the risk of TB infection by 20%

BCG REDUCED THE RISK OF TB DISEASE

COHORT N = 1,597, AGE 5-30 YEARS, FOLLOW UP: 21,148 PERSON YEARS

Cumulative risk of TB disease by age (%)



TB disease overall 6%

- Among vaccinated 4%
- Among non-vaccinated 11%
- TB incidence 440/100,000

Hazard ratio for TB disease in BCG vaccinated

- Adjusted HR 0.50
(95% CI 0.26-0.95) p = 0.03

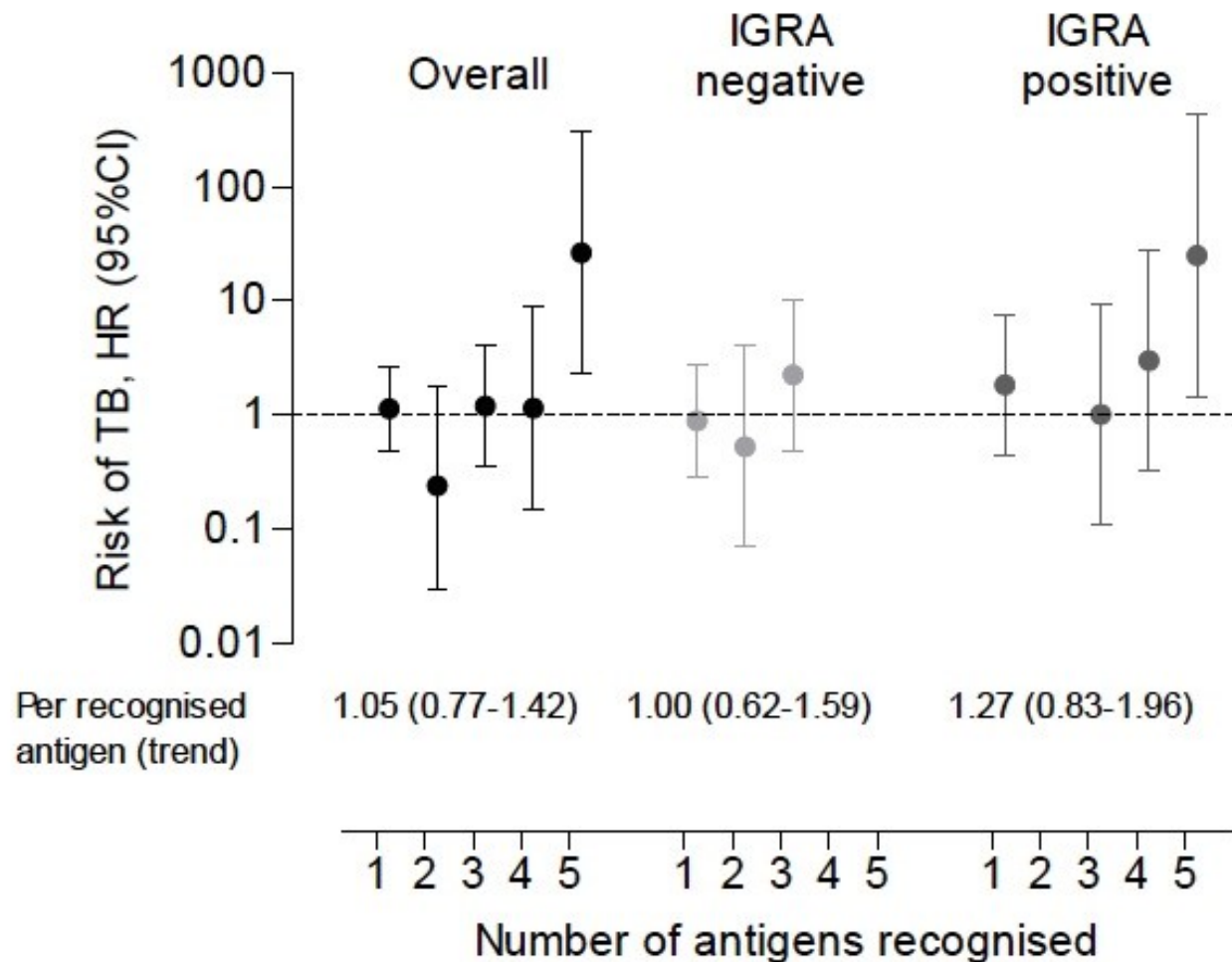
BCG reduced the risk of TB disease by 50%





IMMUNITY TO LATENCY ANTIGENS DID NOT REDUCE RISK OF SUBSEQUENT TB

COHORT N=911, AGE 5-31 YEARS, FOLLOW UP 1,985 PERSON YEARS



Unpublished data

Michelsen SW, Soborg B, Agger EM, Diaz LJ, Hoff ST, Koch A, Sorensen HC F, Andersen P, Wohlfahrt J, Melbye M

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CHANGES IN IMMUNITY TO *MTB* ANTIGENS AND RISK OF TB

TB FOLLOW UP 2 YEARS

- Neither increasing nor decreasing immunity to non-IGRA antigens was found to be associated with risk of subsequent TB.
- A substantial increase in immunity to IGRA antigen CFP10 was associated with 10-fold increased risk of subsequent TB
HR 10.06 (95% CI 1.05-96.25)

Thank you for listening

