REGION Rigshospitalet

FACULTY OF HEALTH SCIENCES
UNIVERSITY OF COPENHAGEN

CHIP COPENHAGEN HIV PROGRAMME

Virussygdomme anno 2009: En verden til forskel fra 1994

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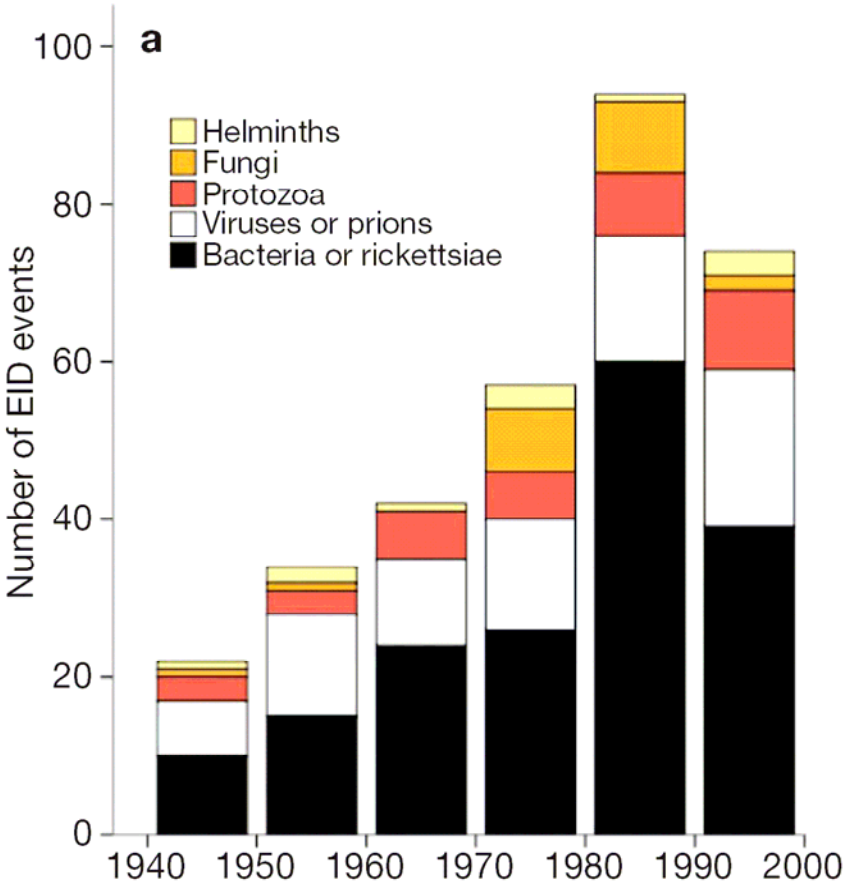
Virussygdomme vi ikke vidste

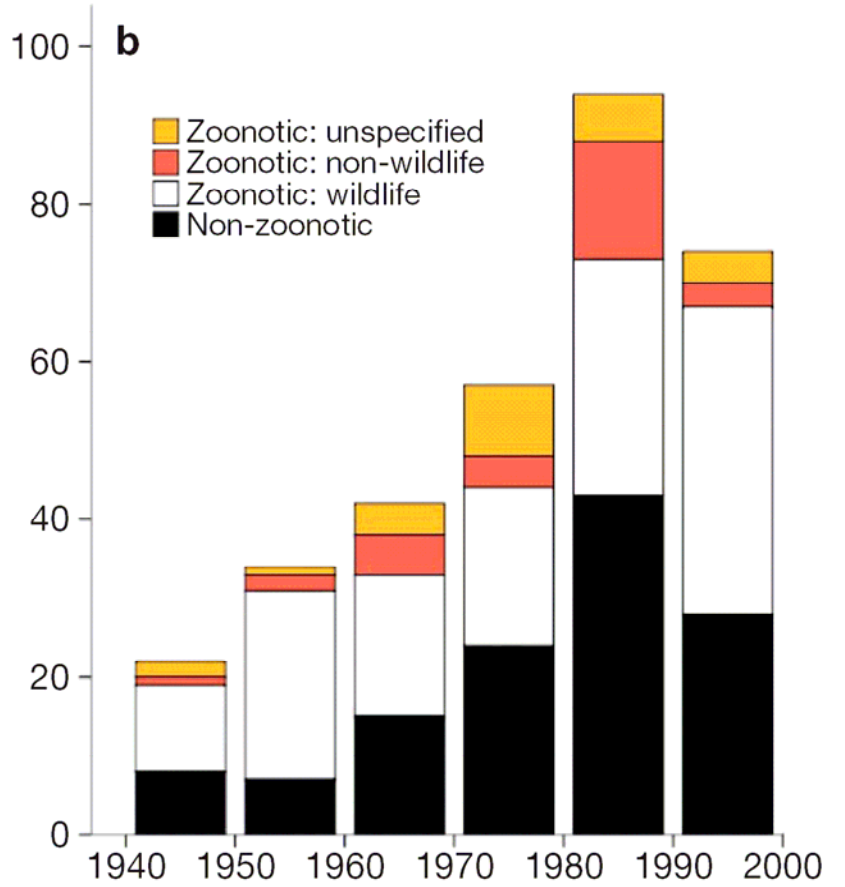
FANDTES

i 1994

Global trends in emerging infectious diseases (EID):

cluster of infectious diseases emerging for the first time in human population



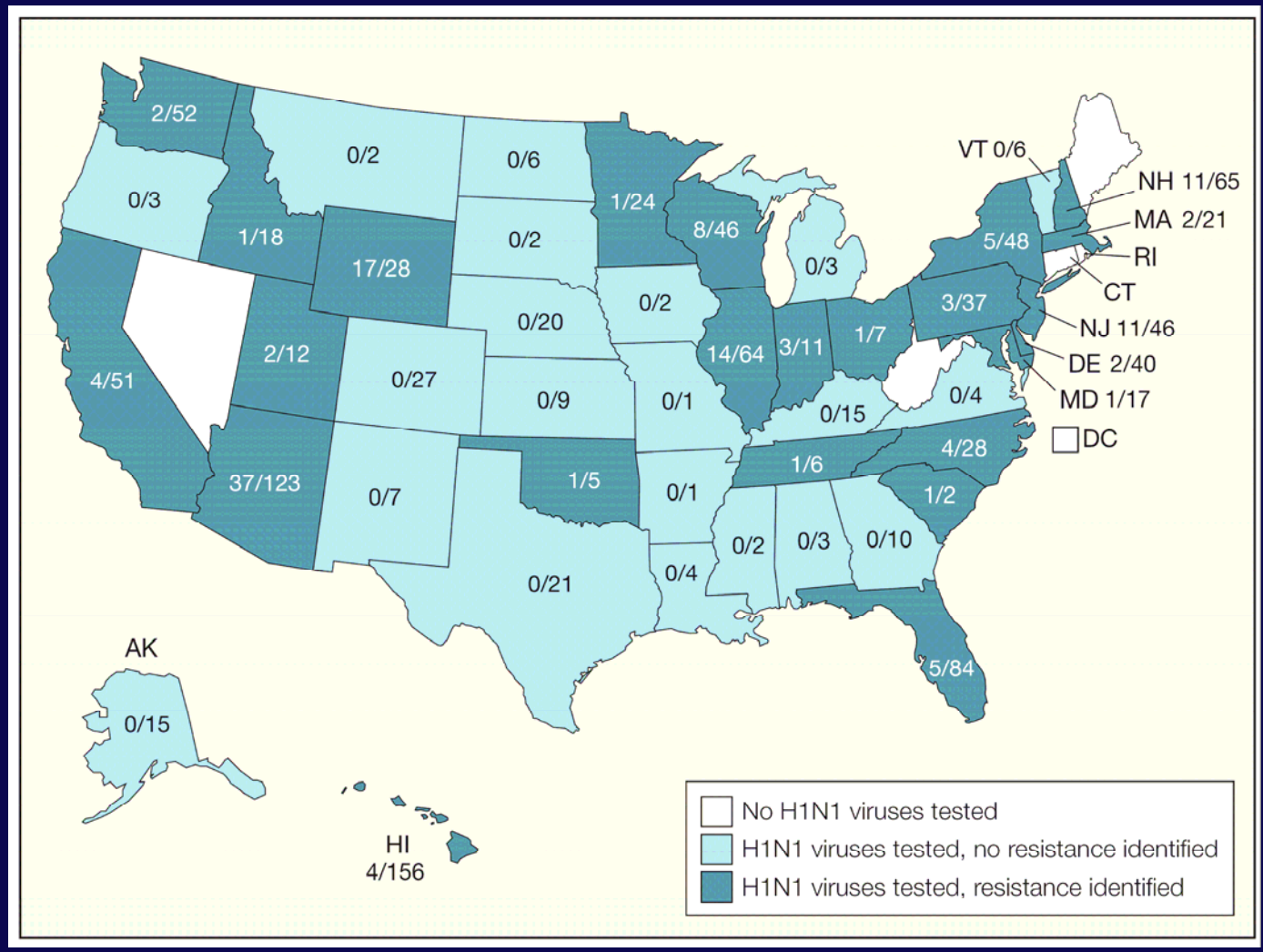


Jones *et al*, Nature 2008

Nogle eksempler

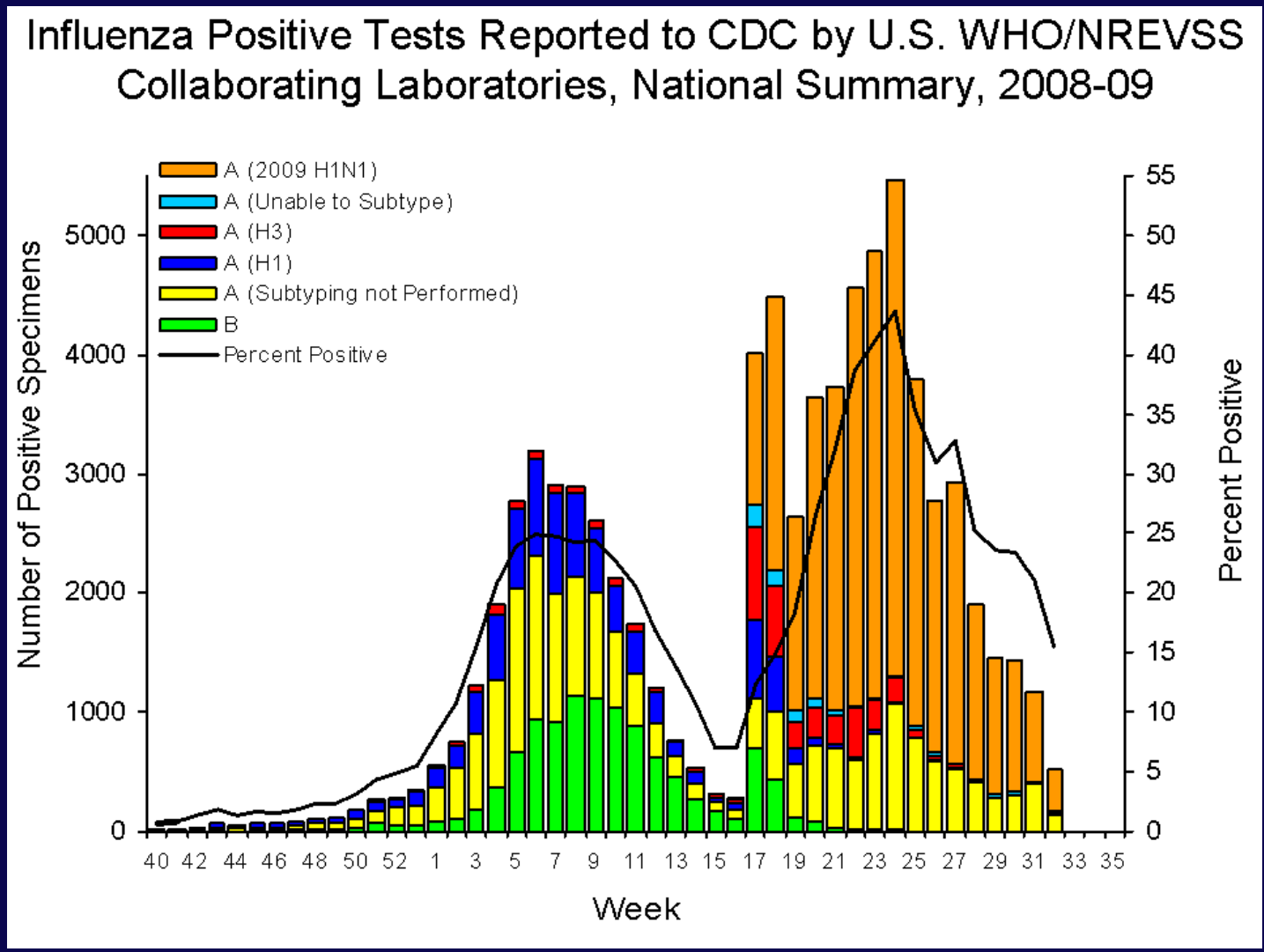
- Forklaring på sygdomme vi kendte til
  - Kaposi's sarcom
    - Human herpes virus 8 (1995)
  - Forkølelse
    - Parvo virussen "Boca virus" (identificeret i 2001)
  - Hæmorragisk feber
    - Lujo virus (identificeret i 2009)
- Nye virussygdomme
  - Severe acute respiratory syndrome (SARS)
    - SARS Corona virus (2003)
- Reintroduktioner i nye områder
  - West Nile virus i USA og Chikungunya virus i Italien

Sæson H1N1 bliver oseltamivir resistent i løbet af sæsonen 2007-2008



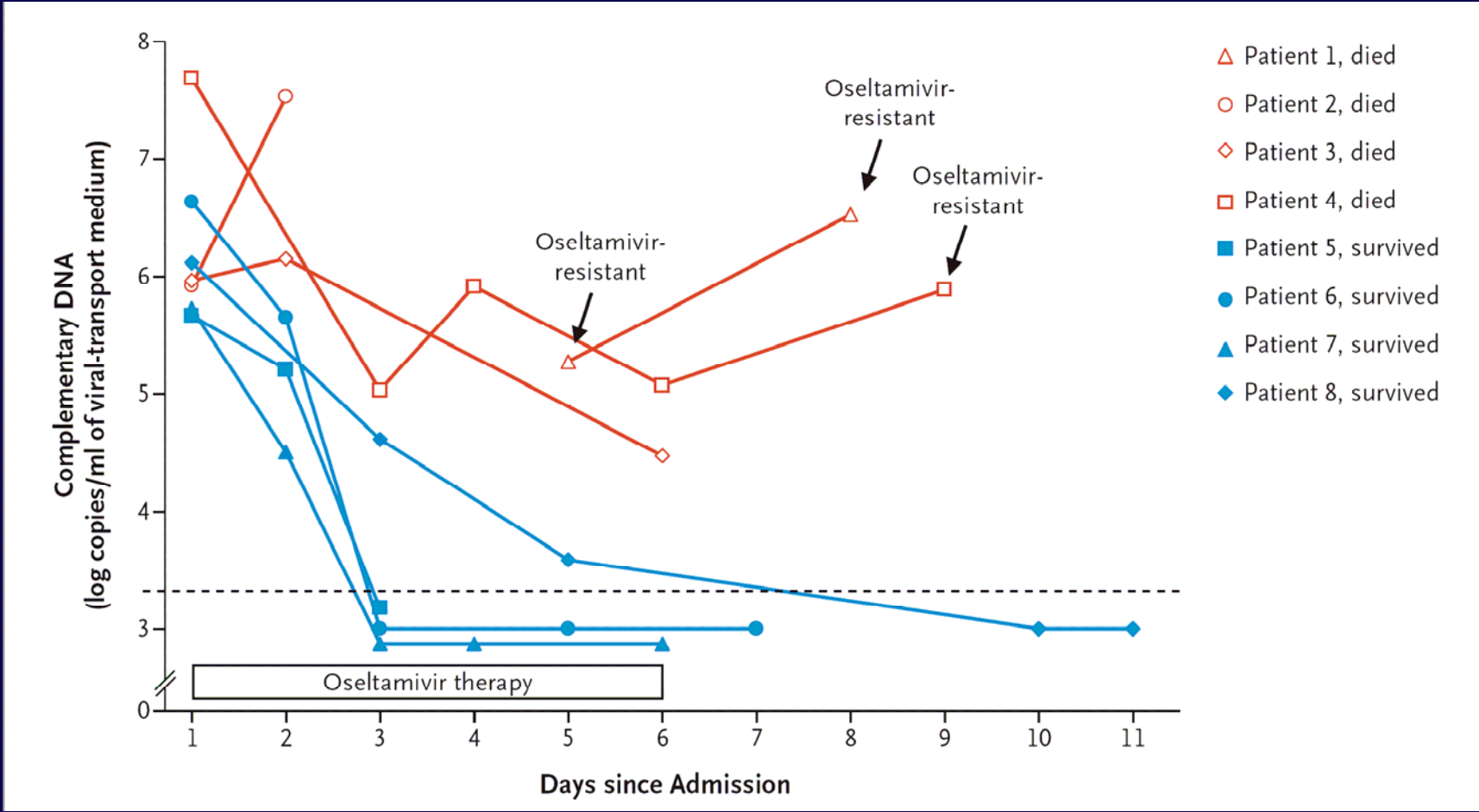
Dharan et al, JAMA 2009

Transition af sæson H1N1 og H1N1v i foråret 2009



http://www.cdc.gov/flu/weekly/index.htm#whomap

Oseltamivir resistent H5N1



de Jong *et al*, NEJM 2005

Virussygdomme vi ikke vidste

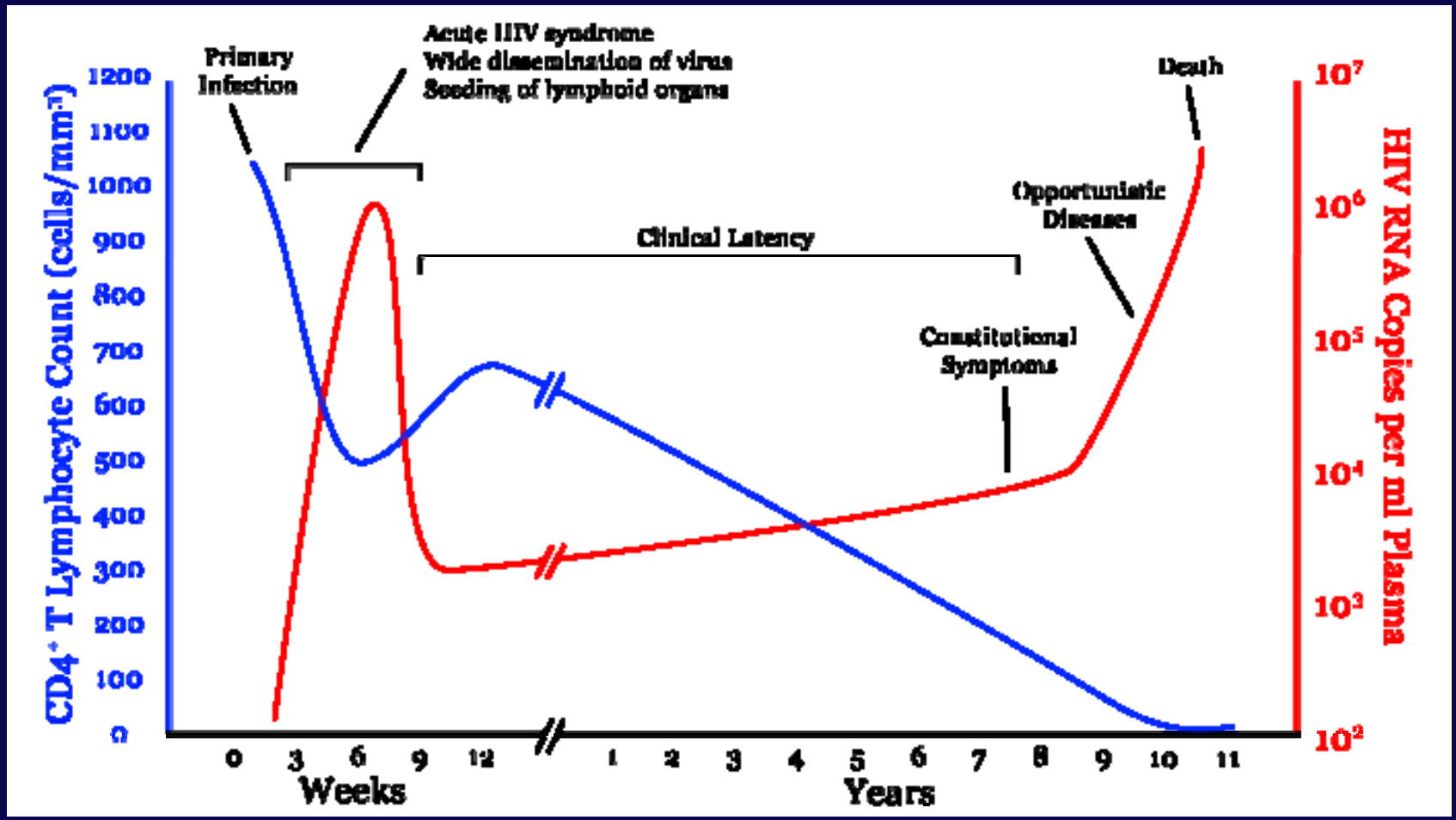
HVORLEDES UDVIKLEDE SIG

i 1994

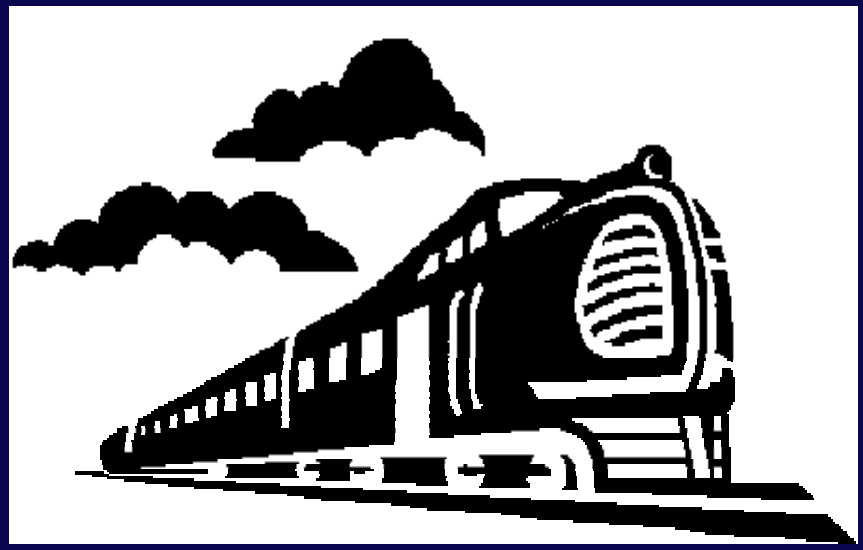
The temporary benefit on survival in AIDS patients of zidovudine monotherapy

Lundgren *et al*, JAMA 1994

The interaction between HIV and the CD4+ lymphocytes

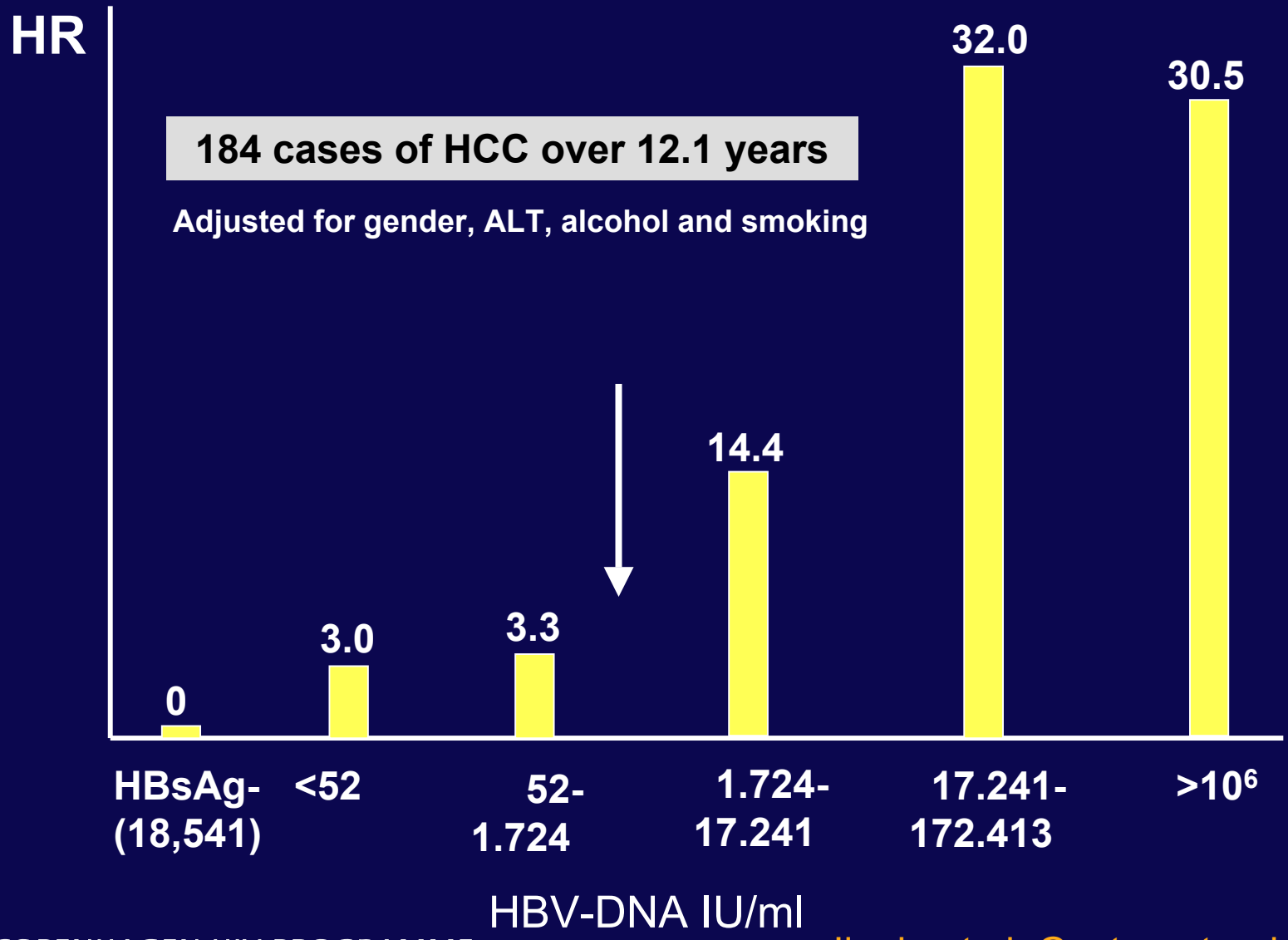


HIV pathogenesis: the train analogy



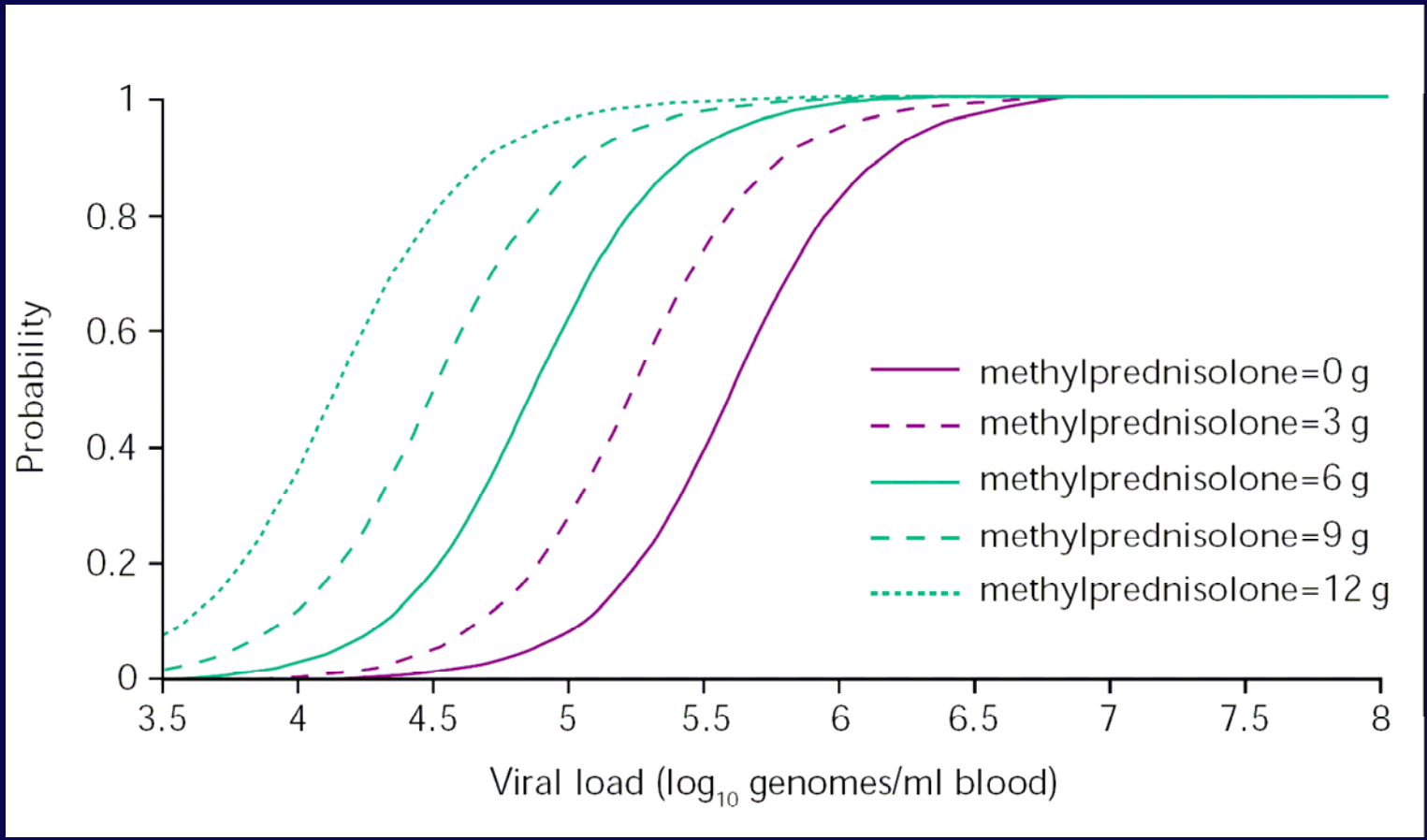
Distance: Number of CD_4 counts
Speed: Rate of HIV replication

Risk of HCC in 3584 HBsAg+ patients (REVEAL)



Iloeje et al. Gastroenterology 2007

Sandsynlighed for CMV sygdom blandt transplanterede patienter: betydning af virus-mængde og prednisolon



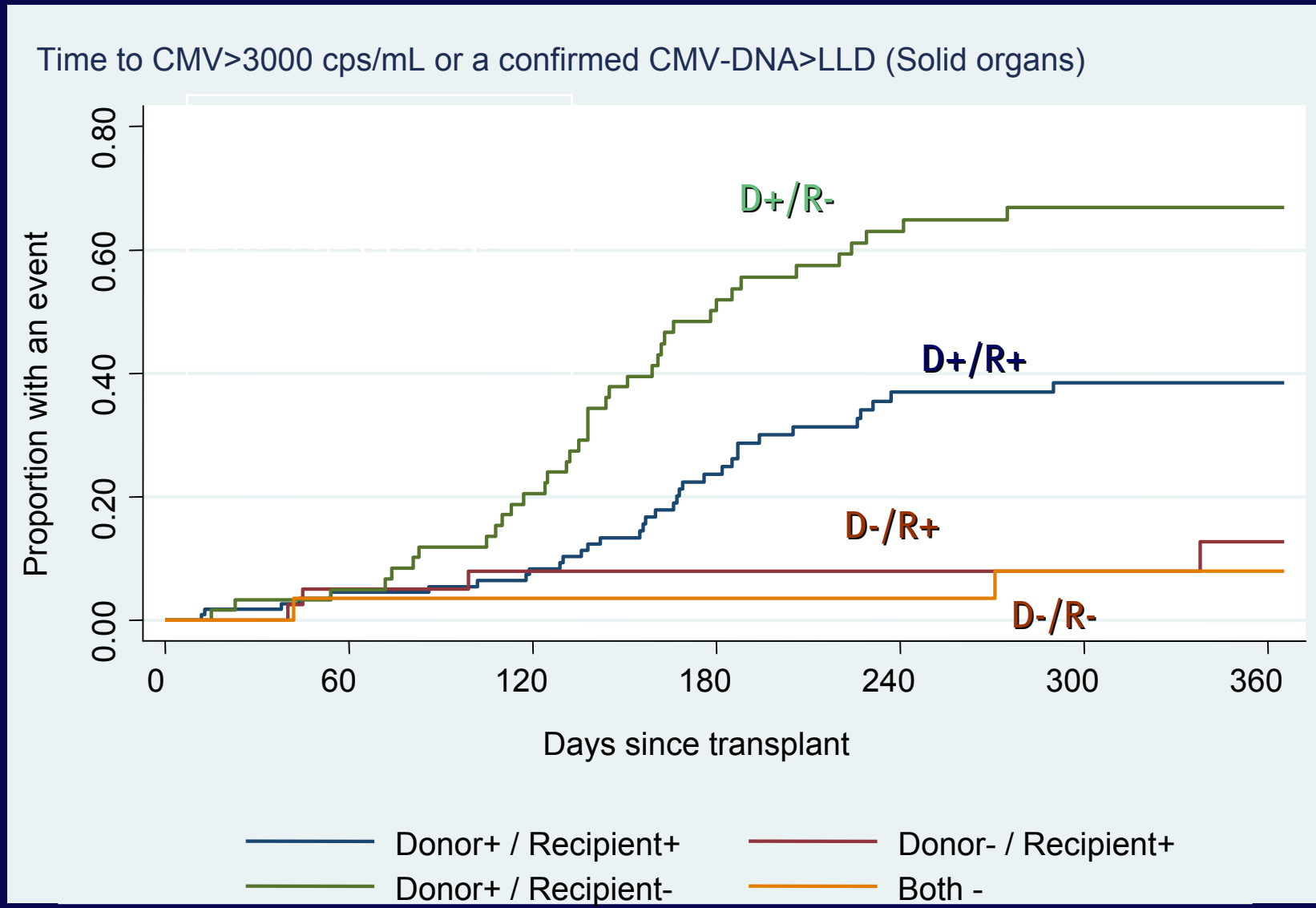
Cope *et al*. JID 1997;176:1484

Virussygdomme vi ikke vidste

HVORDAN VI SKULLE BEHANDLE

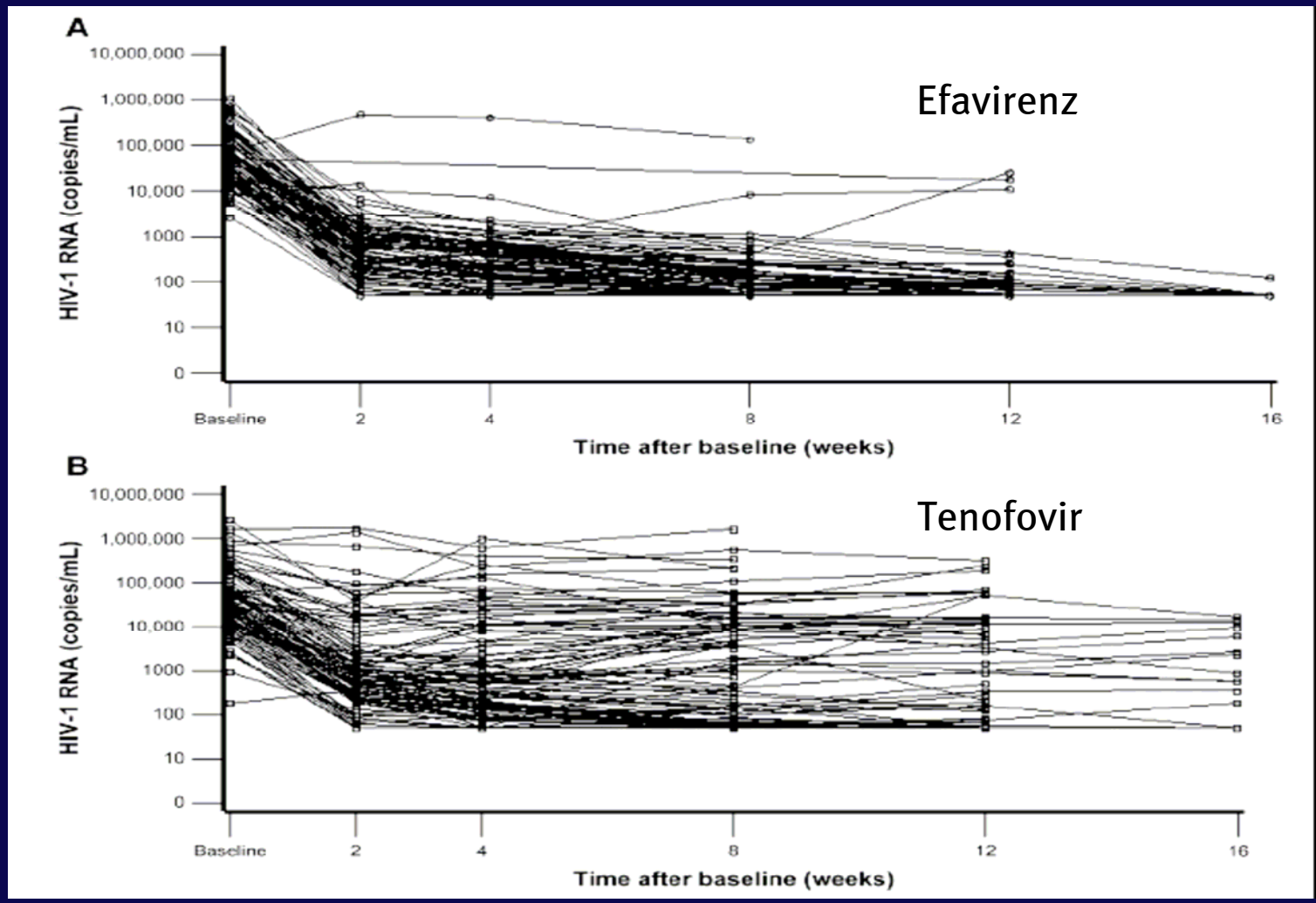
i 1994

Solid Organ Transplant: Risk of CMV infection according to serostatus at time of Tx



Cunha-Bang *et al*, IDSA 2009

Tenofovir vs efavirenz in combination with abacavir and lamivudine



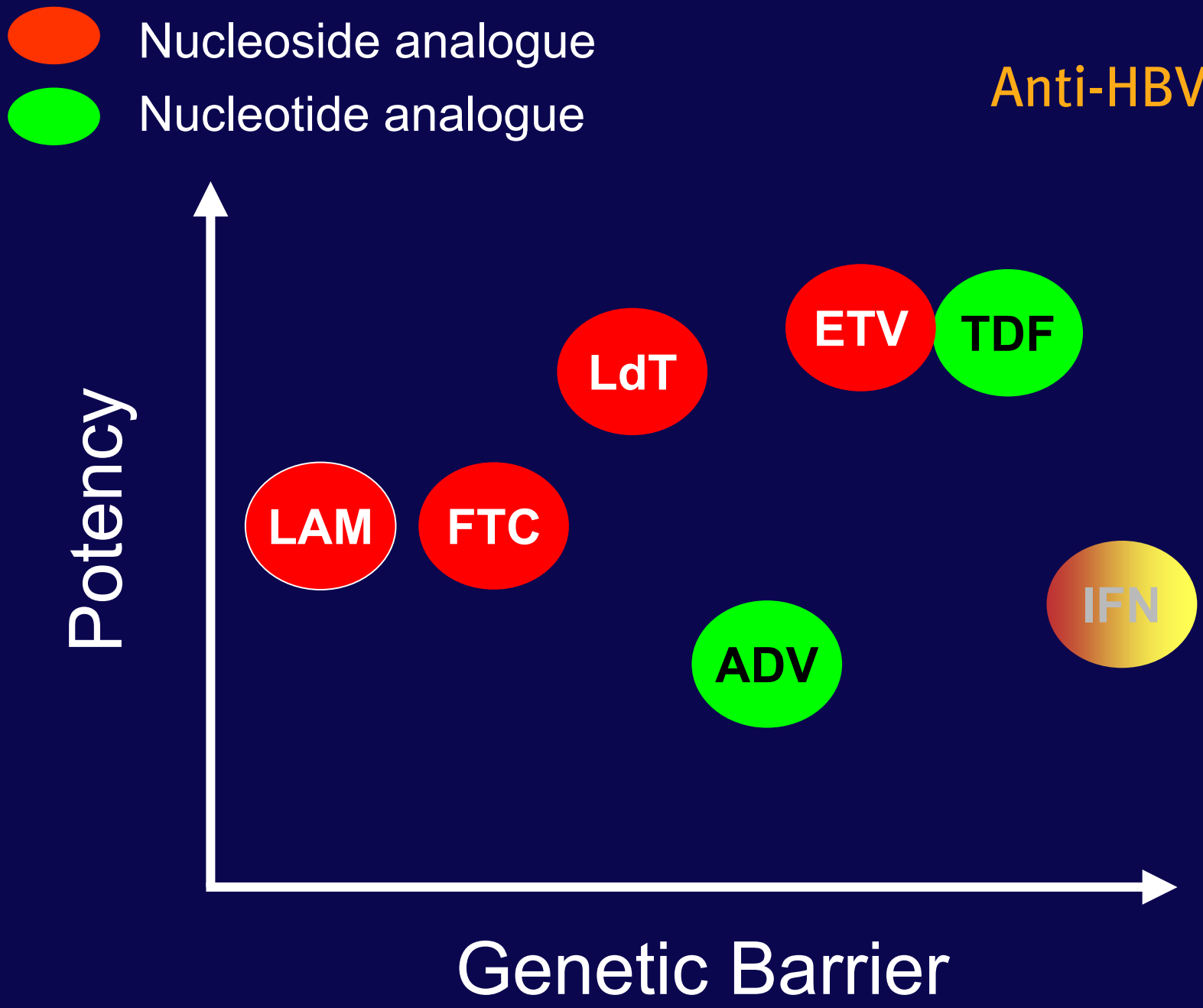
Mutations in RT:

184L/V (97%)

65R (53%)

Gallant *et al*, JID, 2005

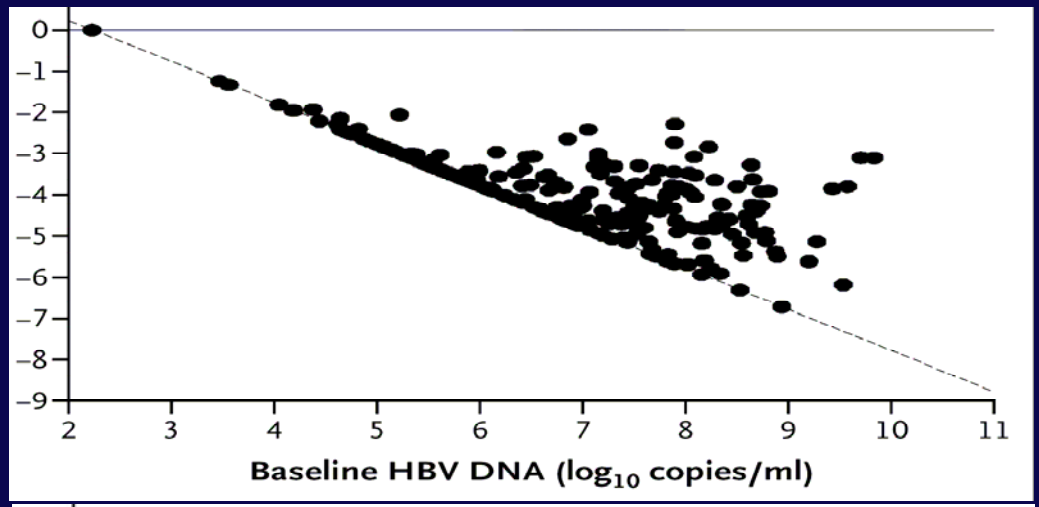
Anti-HBV Drugs



Garcia-Gasco *et al.* J HIV Ther 2007; 12: 1-5.

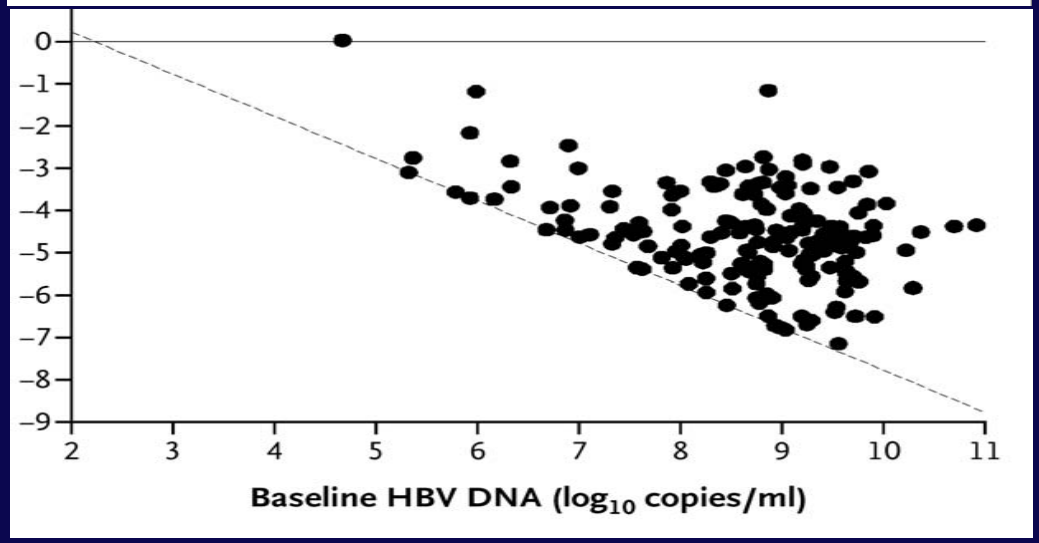
Week 12 full viral suppression response to tenofovir according to HBeAg status

Difference from baseline In HBV-DNA



HBeAg -

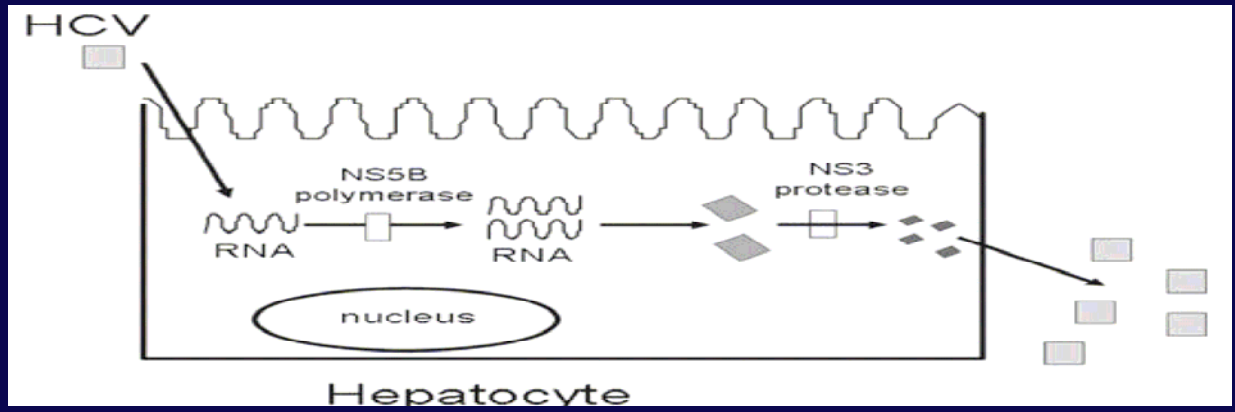
No evidence of resistance

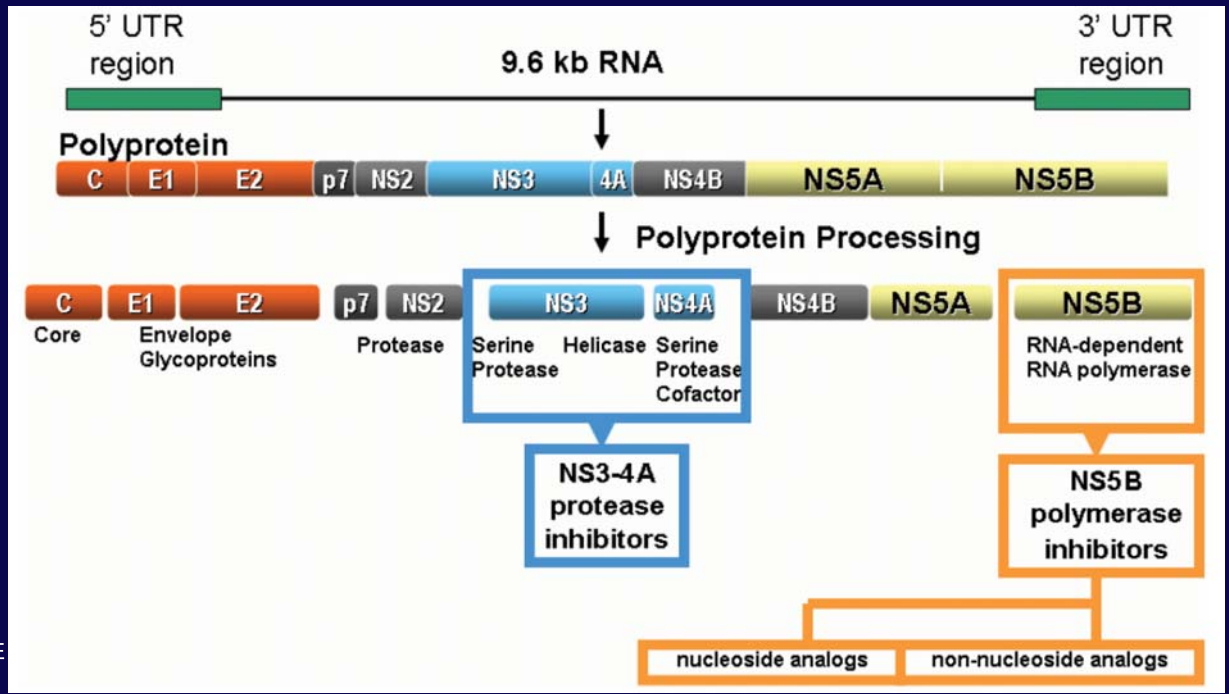


HBeAg +

Marcellin *et al*, NEJM 2008

Anti-HCV drug targets: HCV's life cycle & genome





Virussygdomme vi ikke vidste

HVORDAN VI BEDST UNDGÅR SMITTEOVERFØRSEL

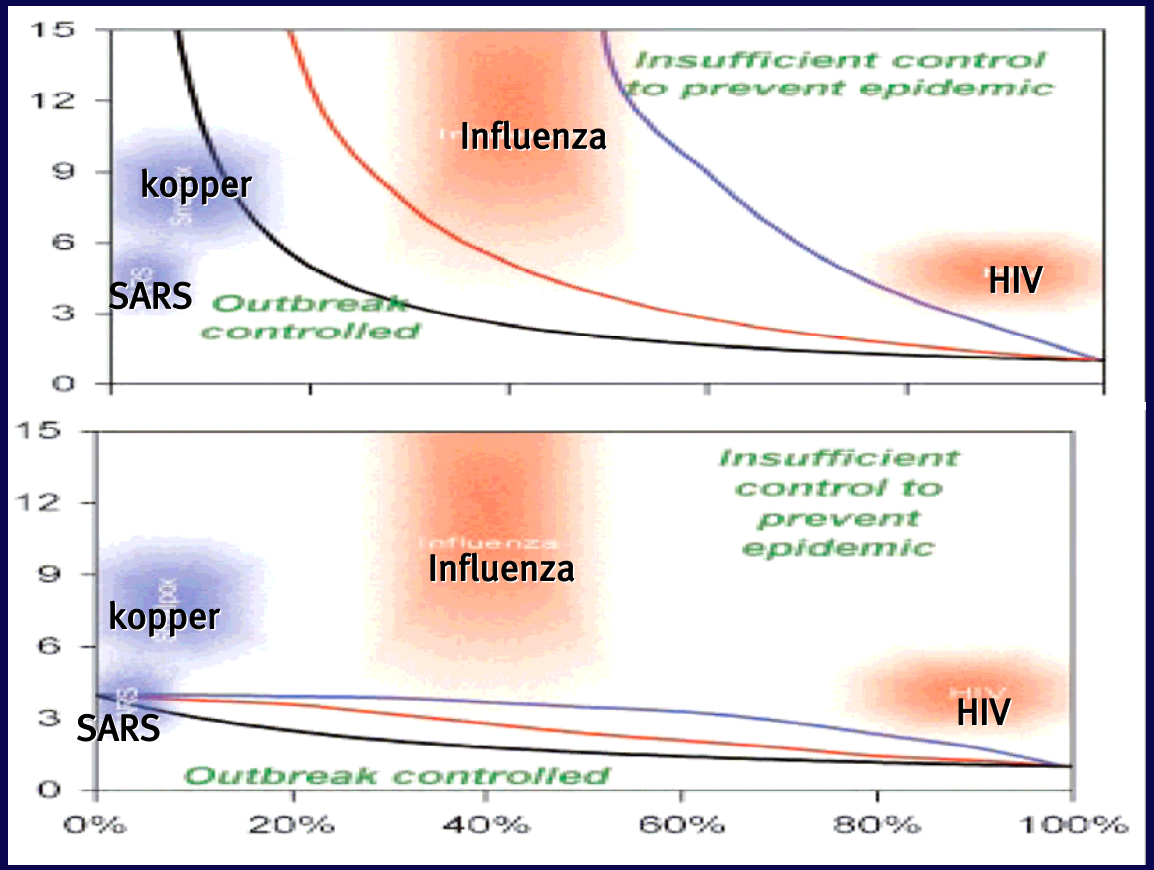
i 1994

3 scenarier (ud fra matematiske modeller) for mulighederne for at inddæmme 1 af 4 virus epidemier

(SARS, kopper, influenza og HIV)

R_0 værdi

% af sympto-matisk smittede der er kohorte isolerede



100%

75%

% af smitteoverførsler der sker før udvikling af symptomer

Fraser *et al*, PNAS 2004

Virussygdomme vi ikke vidste

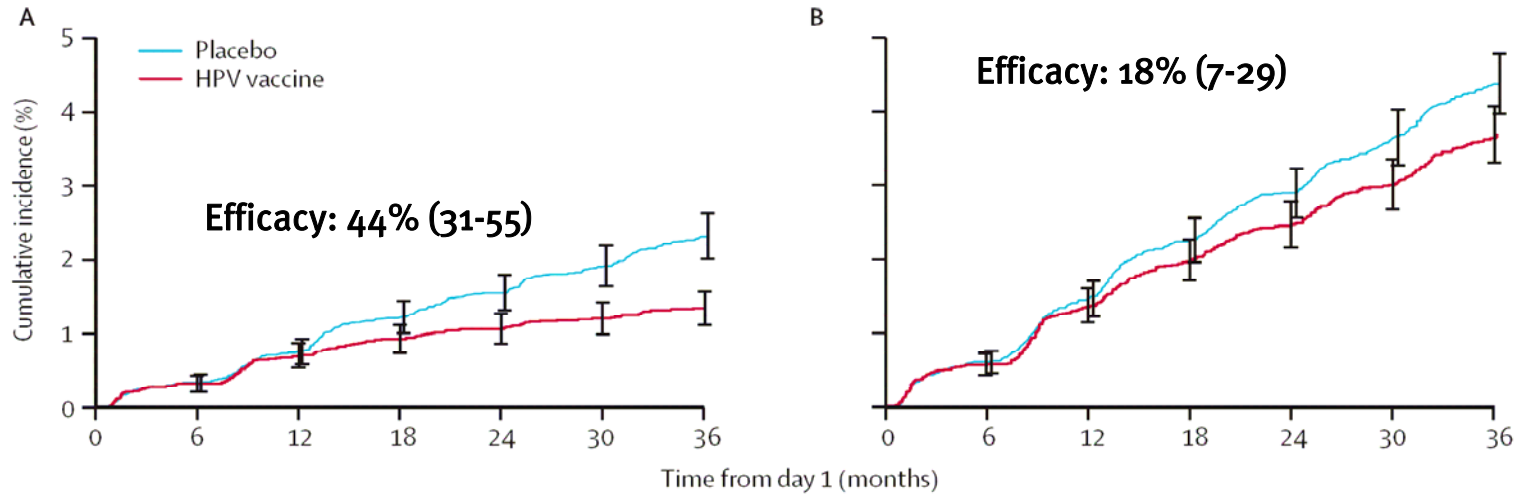
HVORDAN VI SKULLE VACCINERE IMOD

i 1994

Vaccine imod 6/11/16/18 HPV typer beskytter mod forstadier til cervical cancer

Risiko for HPV 16/18-relateret cervical intraepithelial neoplasi (CIN) grad 2/3 eller adenocarcinoma in situ (AIS)

Risiko for enhver form for HPV relateret CIN grad 2/3 eller AIS

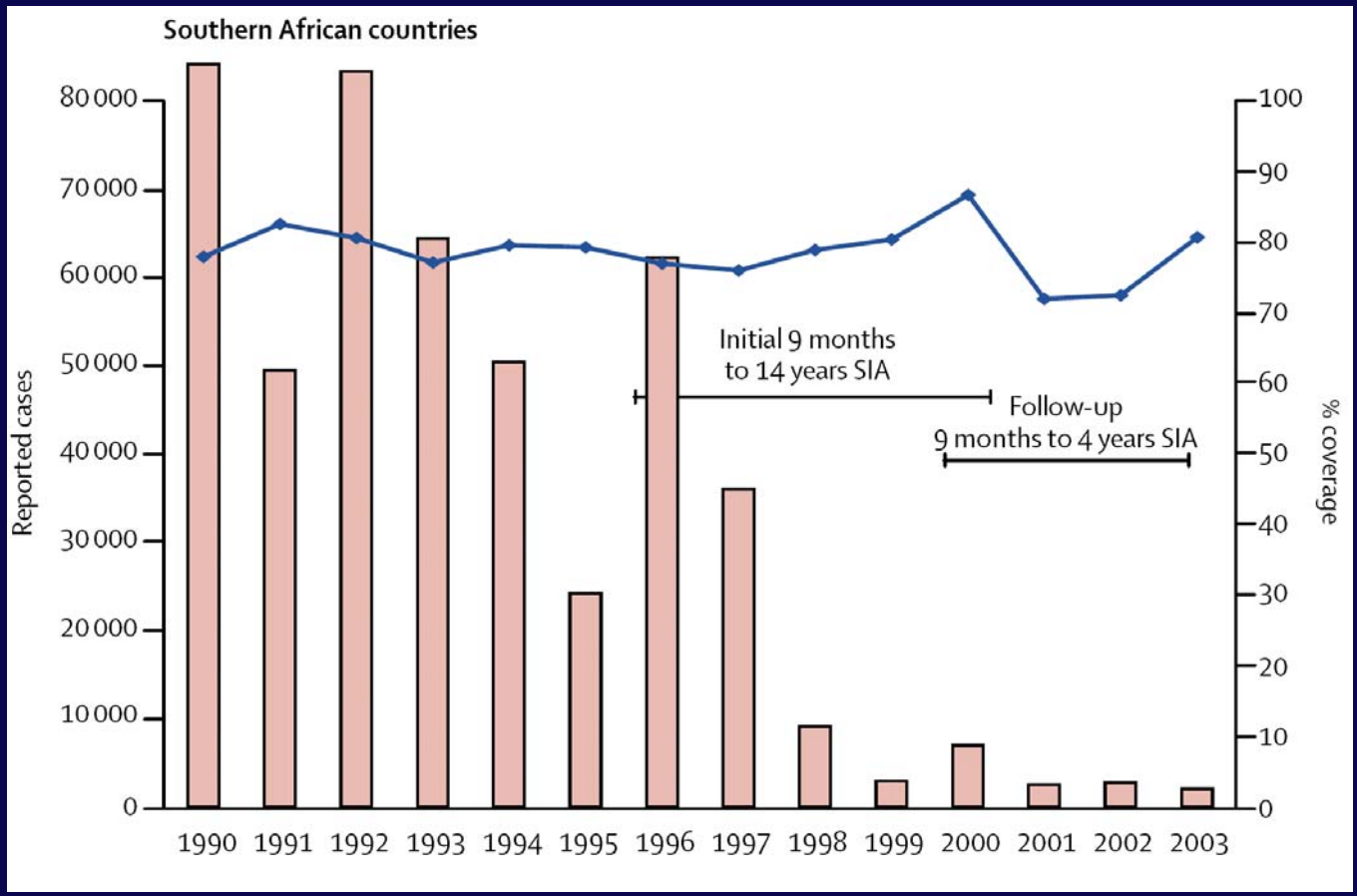


Number at risk													
HPV vaccine	10291*	9740	9554	9379	9146	8857	5141	10291*	9735	9531	9343	9110	8821	5111
Placebo	10292*	9815	9594	9390	9153	8849	5191	10292*	9802	9565	9359	9115	8803	5159
Cumulative number of cases													
HPV vaccine	0	31	69	90	103	116	128	0	55	132	191	236	285	343
Placebo	0	32	74	119	150	184	218	0	58	142	218	278	347	411

Efficacy improved if vaccinated prior to infection

The FutureII study group, Lancet 2007

Mæslinge-vaccination* og mæslinge-tilfælde i sydlige afrikanske lande



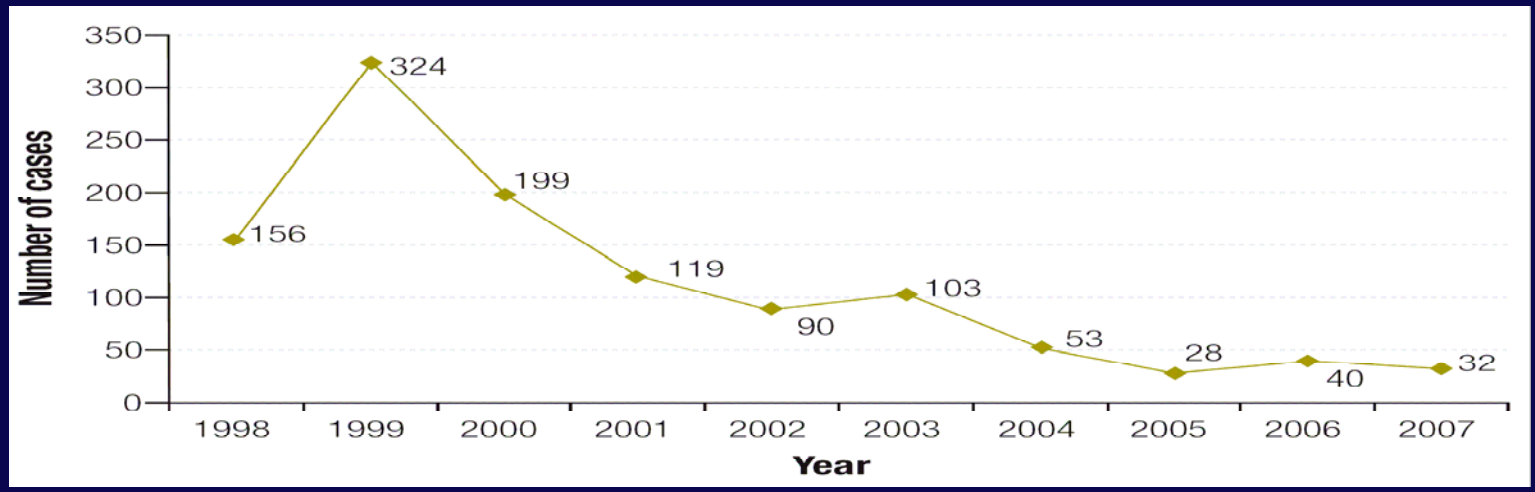
*SIA= supplemental immunization activities

Otten *et al*, Lancet 2005

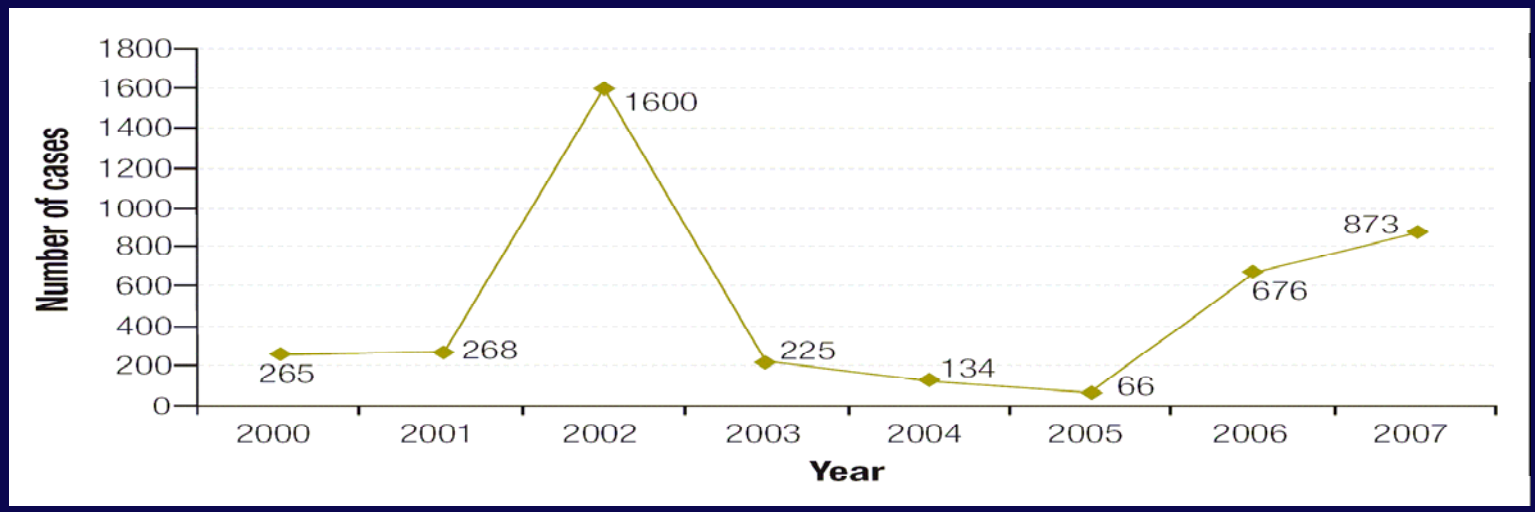
Udryddelse af Polio – startet i 1988:

stadig 4 lande med endemisk polio*

Pakistan



Indien



*: + Afganistan & Nigeria

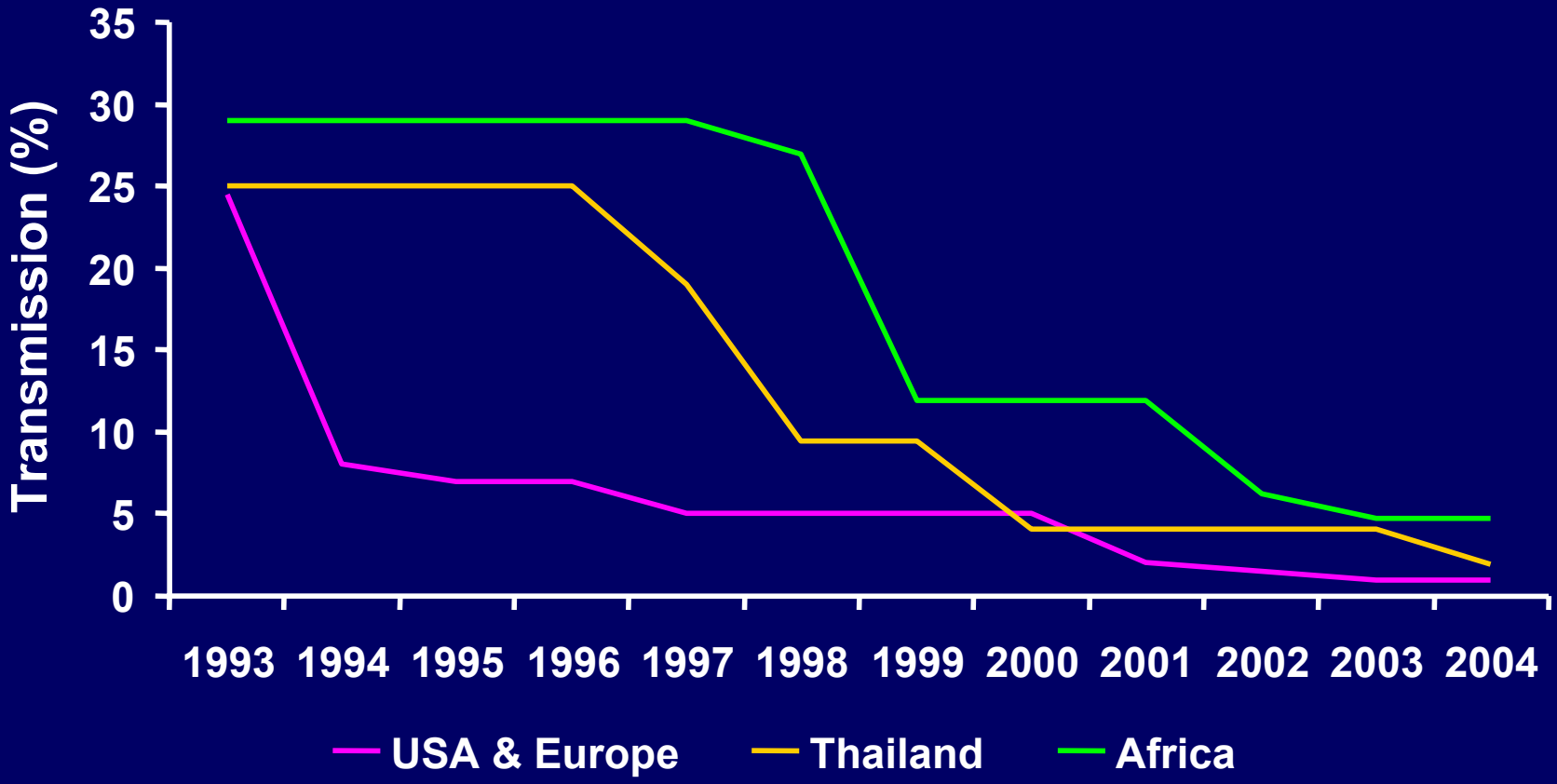
Obregon *et al.* Bull World Health Organ 2009

Virussygdomme vi ikke vidste

HVORDAN SMITTE KUNNE FORHINDRES MEDICINSK

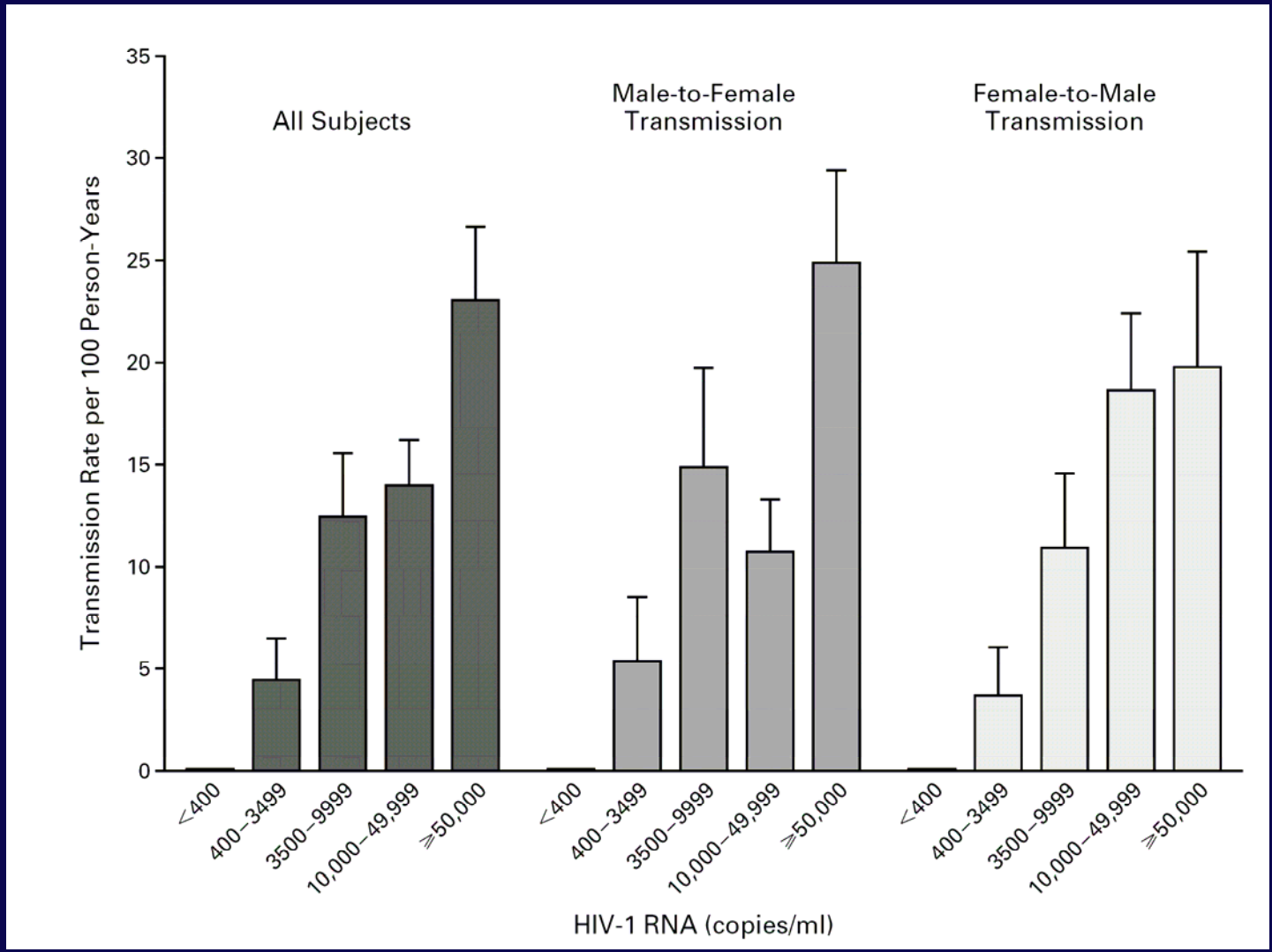
i 1994

Trends in reduction of Mother to Child Transmission of HIV: Trial* results over time



*Africa and Asia data obtained from trial results

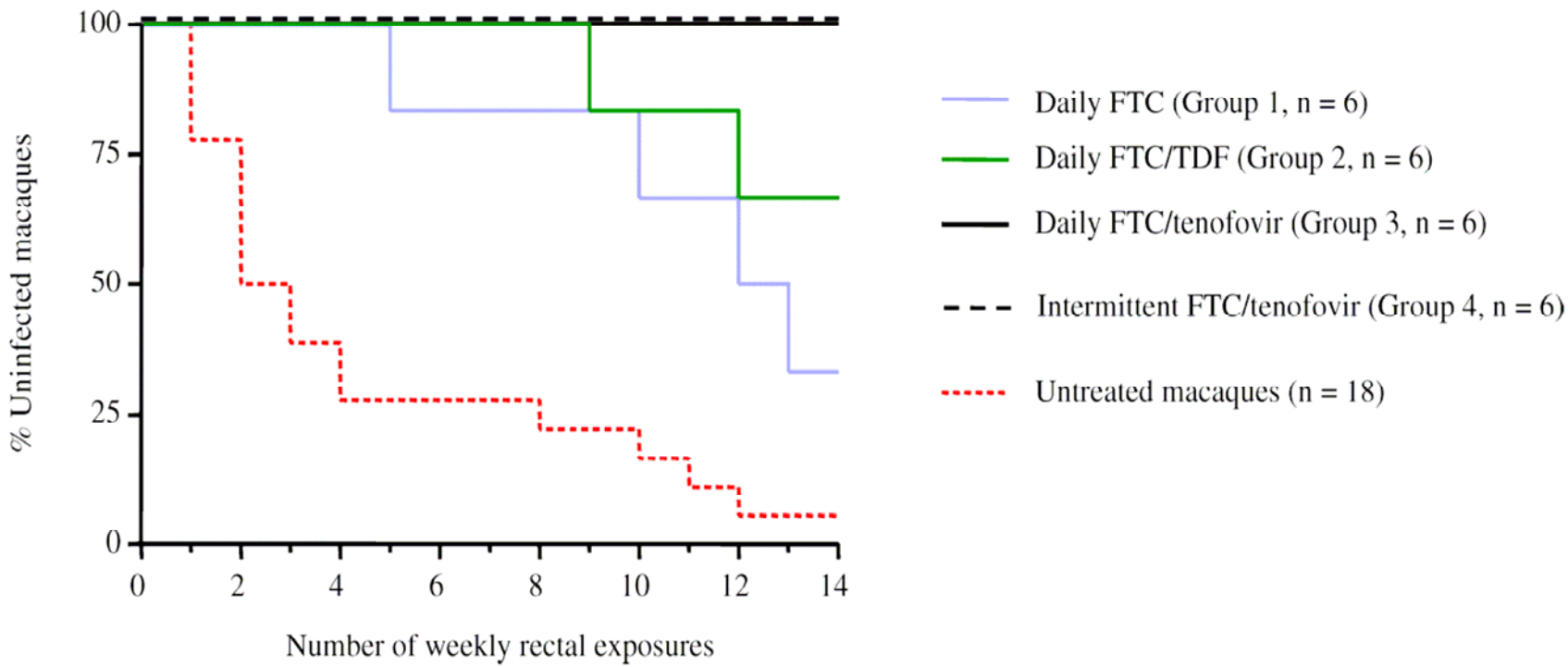
Heterosexual transmission risk



N=415 (50 for HIV-RNA ‹400)

Quinn *et al*, NEJM 2000

Pre-exposure (chemo)prophylaxis (PrEP) for infection with SHIV in macaque monkeys



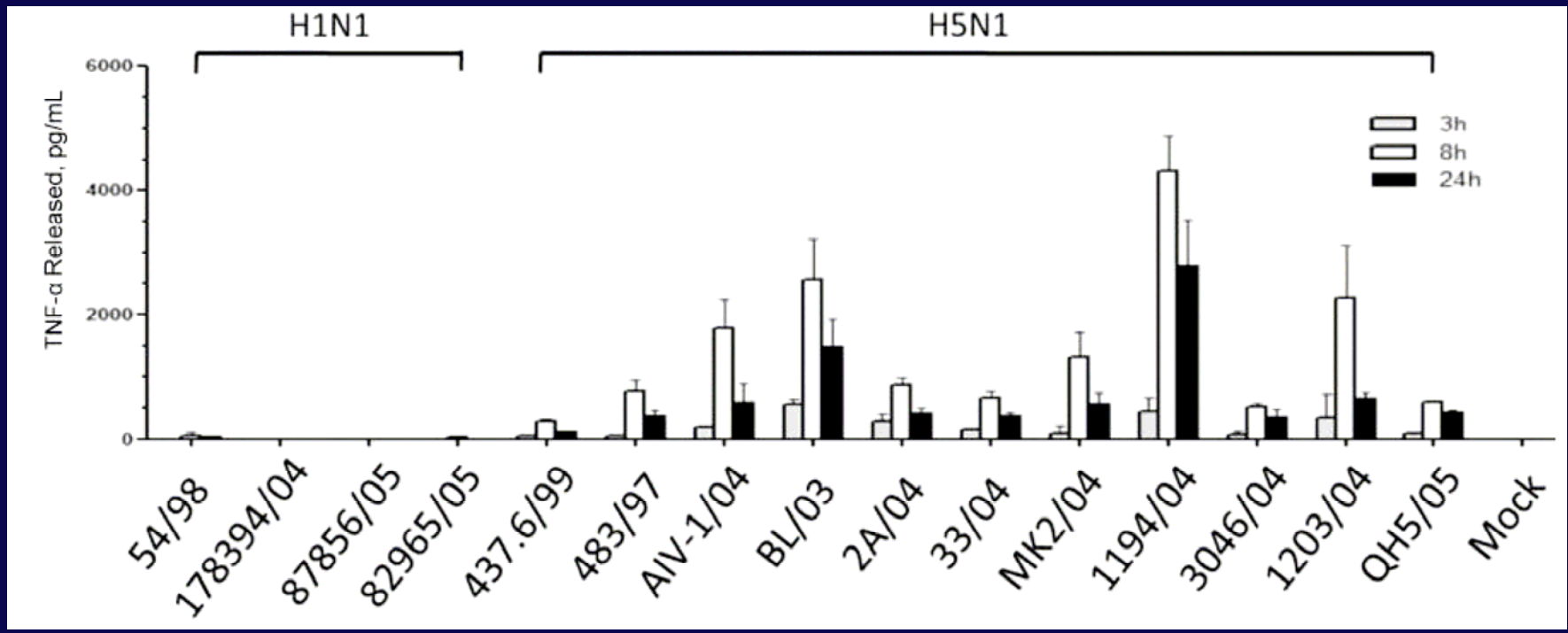
Garcia-Lerma et al, PLoS Med 2008

Virussygdomme vi ikke vidste

HVORFOR NOGLE VAR MERE VIRULENTE END ANDRE

i 1994

Human macrophage TNF-alfa production after infection with seasonal H1N1 and H5N1:
role of polymerase gene (PA in particular)



Pun Mok *et al*, JID 2009

Reverse genetics creating reassortants between 1918 and seasonal H1N1

Viral RNA polymerase complex promotes optimal growth of 1918 virus in the lower respiratory tract of ferrets

Tokiko Watanabe[a], Shinji Watanabe[a], Kyoko Shinya[b], Jin Hyun Kim[a], Masato Hatta[a], and Yoshihiro Kawaoka[a,b,c,d,1]

588–592 | PNAS | January 13, 2009 | vol. 106 | no. 2

Virussygdomme vi ikke vidste

HVOR MEGET SUNDHEDSSKADE DE FORÅRSAGEDE

i 1994

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 30, 2006 VOL. 355 NO. 22

CD4+ Count–Guided Interruption of Antiretroviral Treatment

The Strategies for Management of Antiretroviral Therapy (SMART) Study Group*

CD4+ cell count >350 cells/mm^3

n = 2752

Continous Strategy: Virologic Suppression (VS)

n = 2720

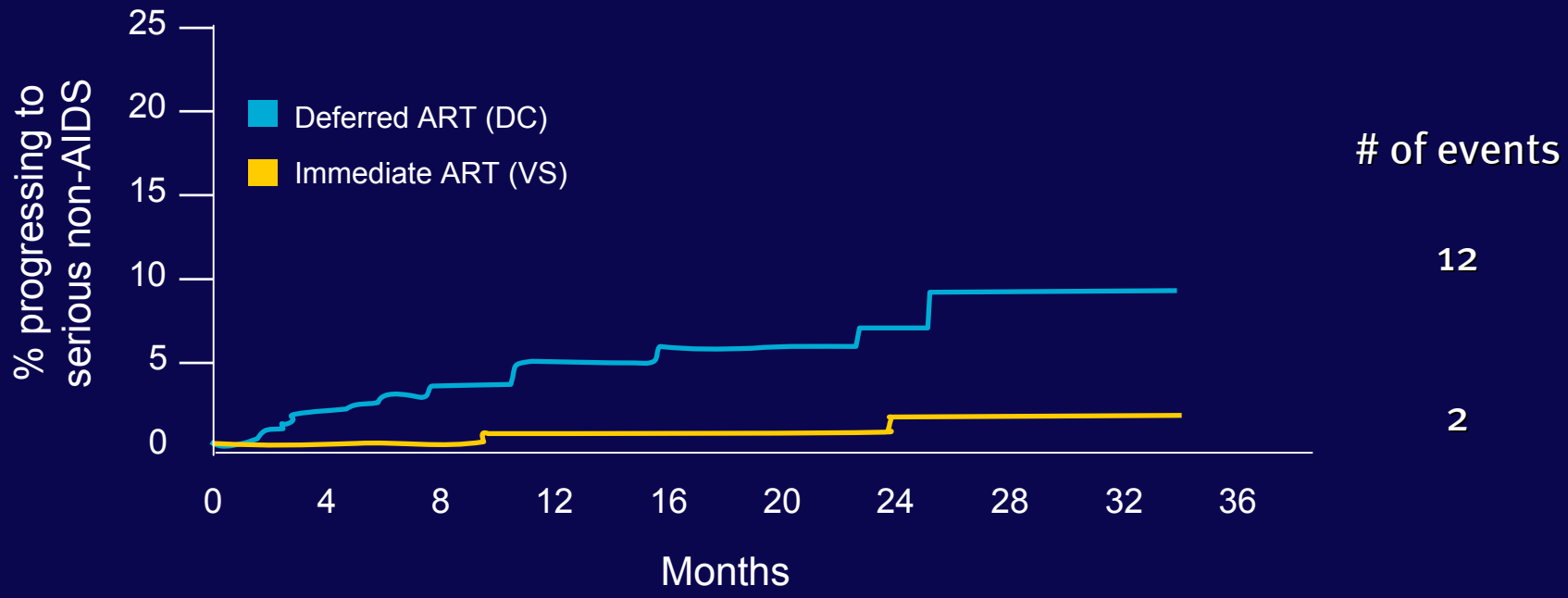
Intermittent Strategy: Drug Conservation (DC)

Plan: 910 primary endpoints; 8 years average follow-up.

Intervention interrupted on 11 January 2006

Subgroup in SMART either naïve or not currently on ART: early versus deferred

Serious Non-AIDS*



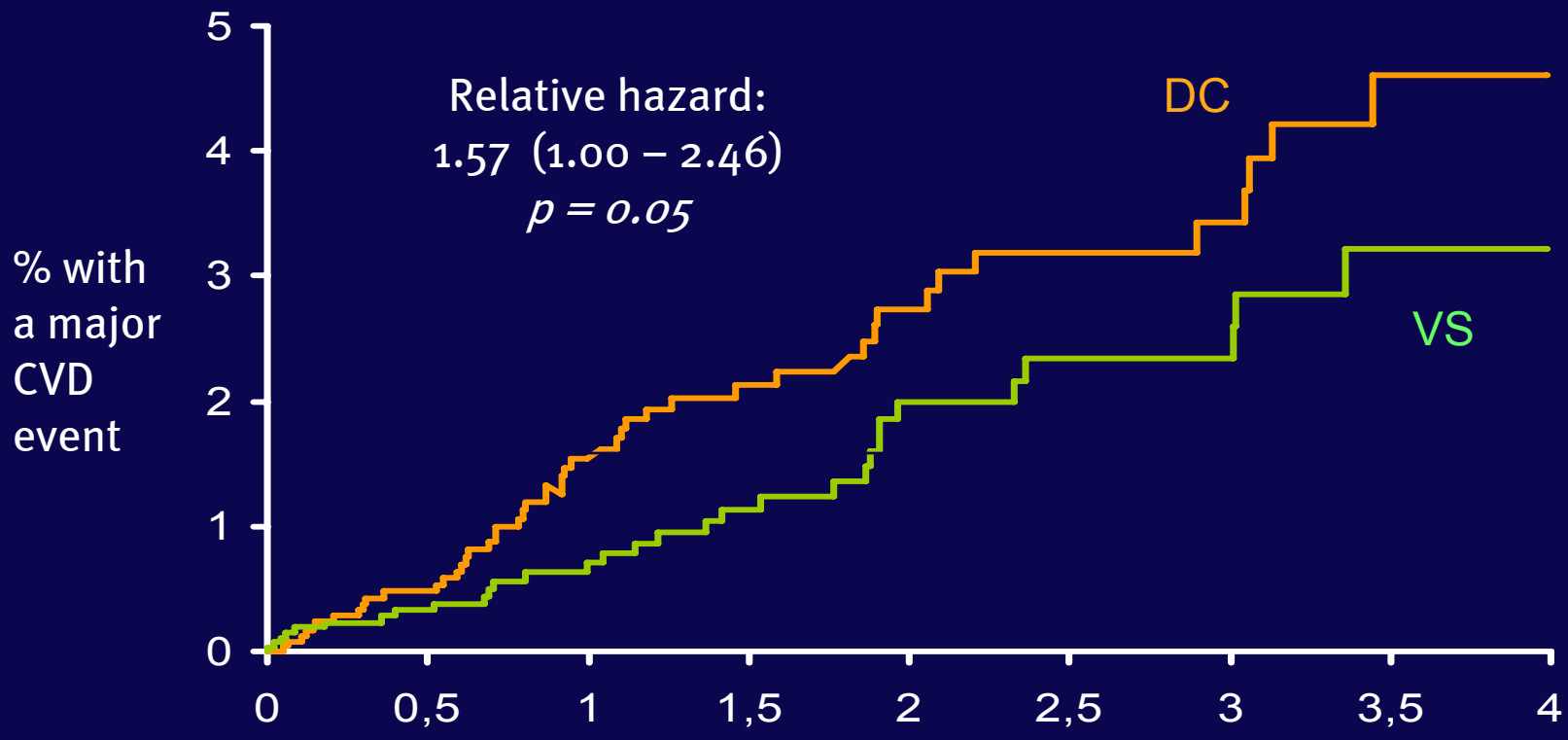
No. at risk

Def. ART	228	189	159	128	96	73	59	36	27	24
Imm. ART	249	210	180	145	125	106	80	58	44	36

*: Cardiovascular, liver & renal disease + non-AIDS cancers (non-fatal and fatal)

SMART Study Group. Emery *et al* J Inf Dis 2008

Risk of major CVD events* by treatment arm

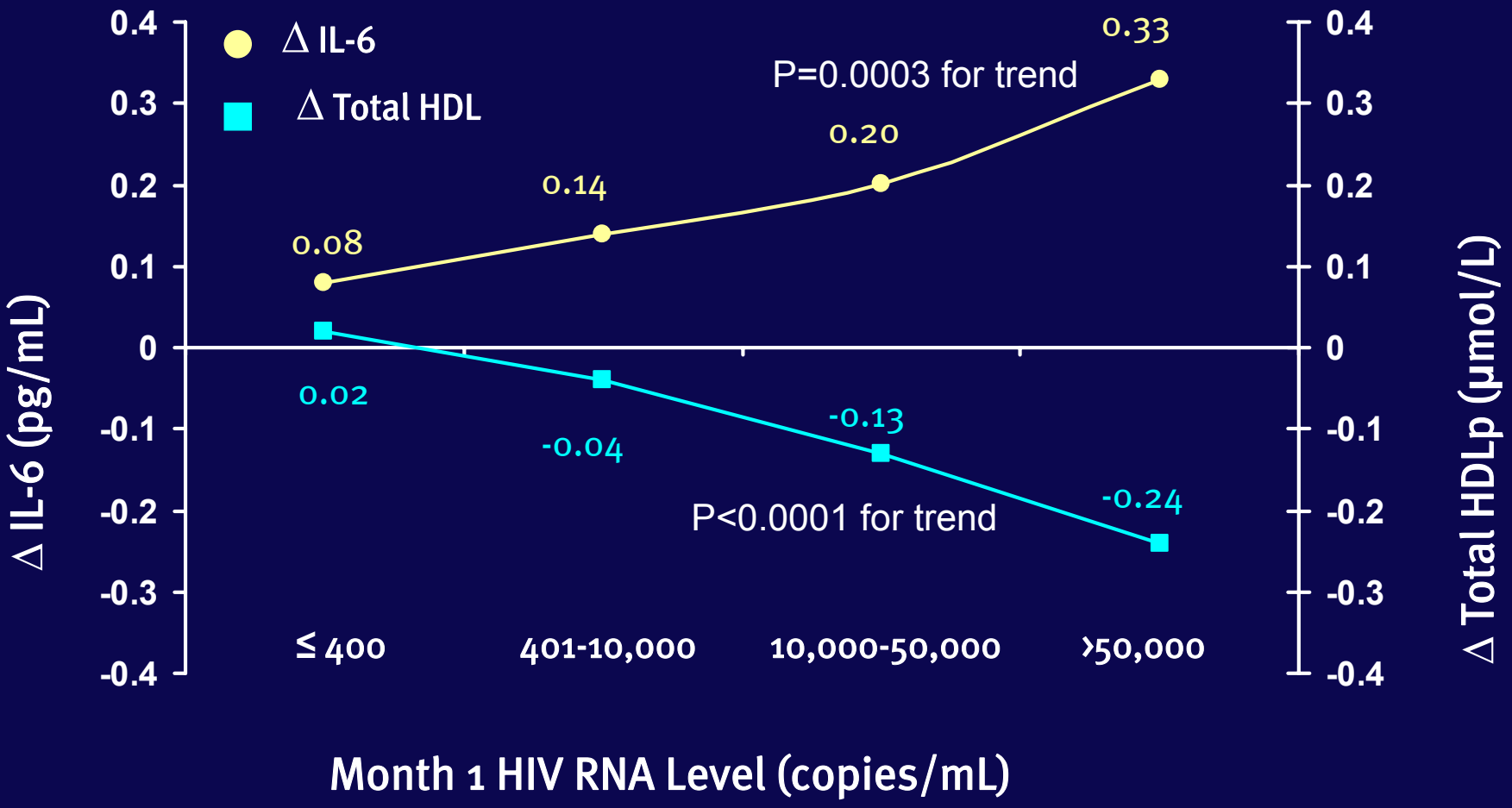


No. at risk					
DC	2752	1306	713	379	10
VS	2720	1292	696	377	10

* death from CVD, silent or clinical MI, stroke CAD requiring invasive procedure

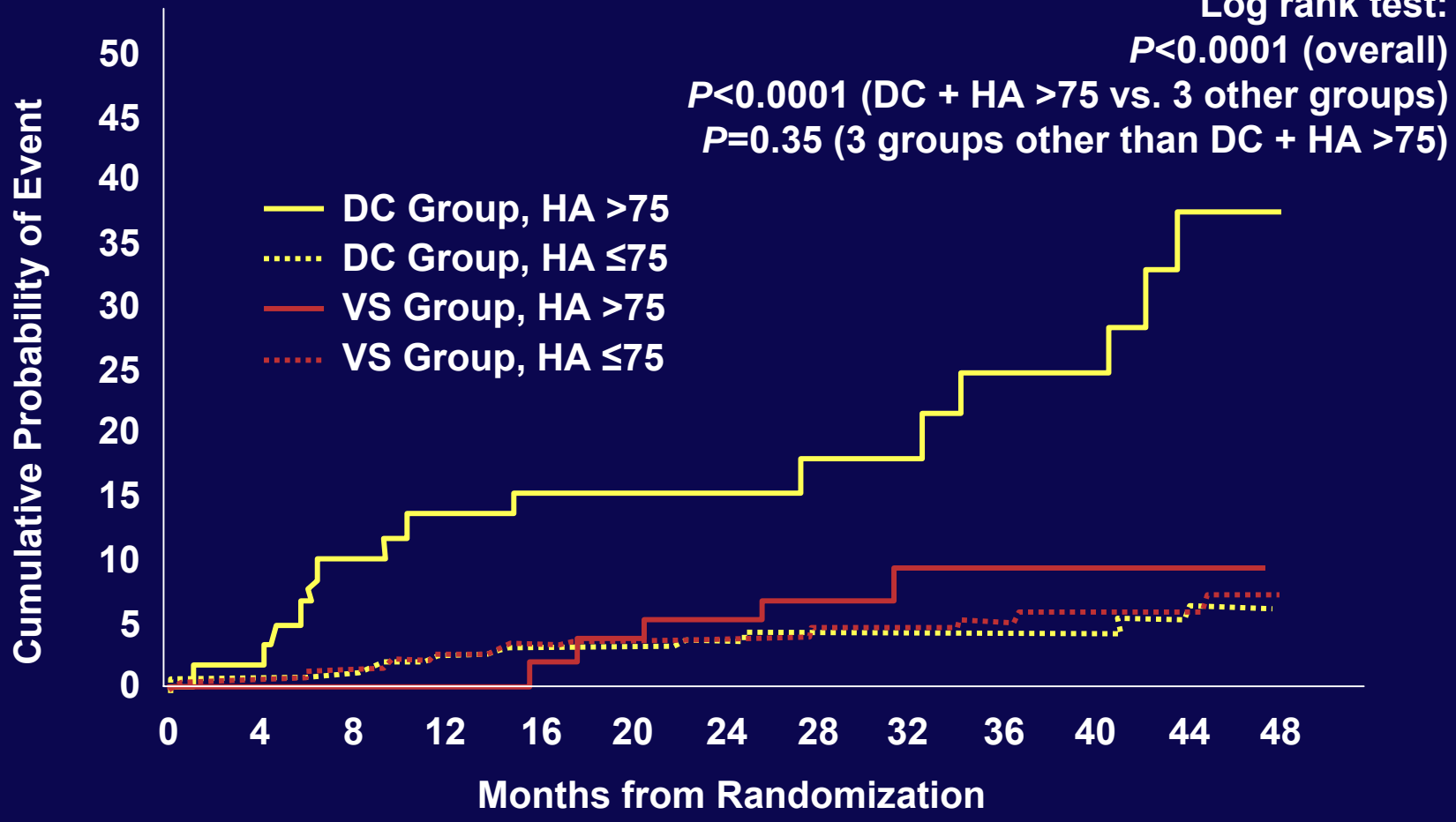
SMART/CVD: Phillips *et al*, AVT 2008

Change in Log IL-6 (pg/mL) and Total HDLp concentration (µmol/L) from Baseline to 1 Month*



* DC patients on ART at baseline with HIV RNA ≤ 400 copies/mL

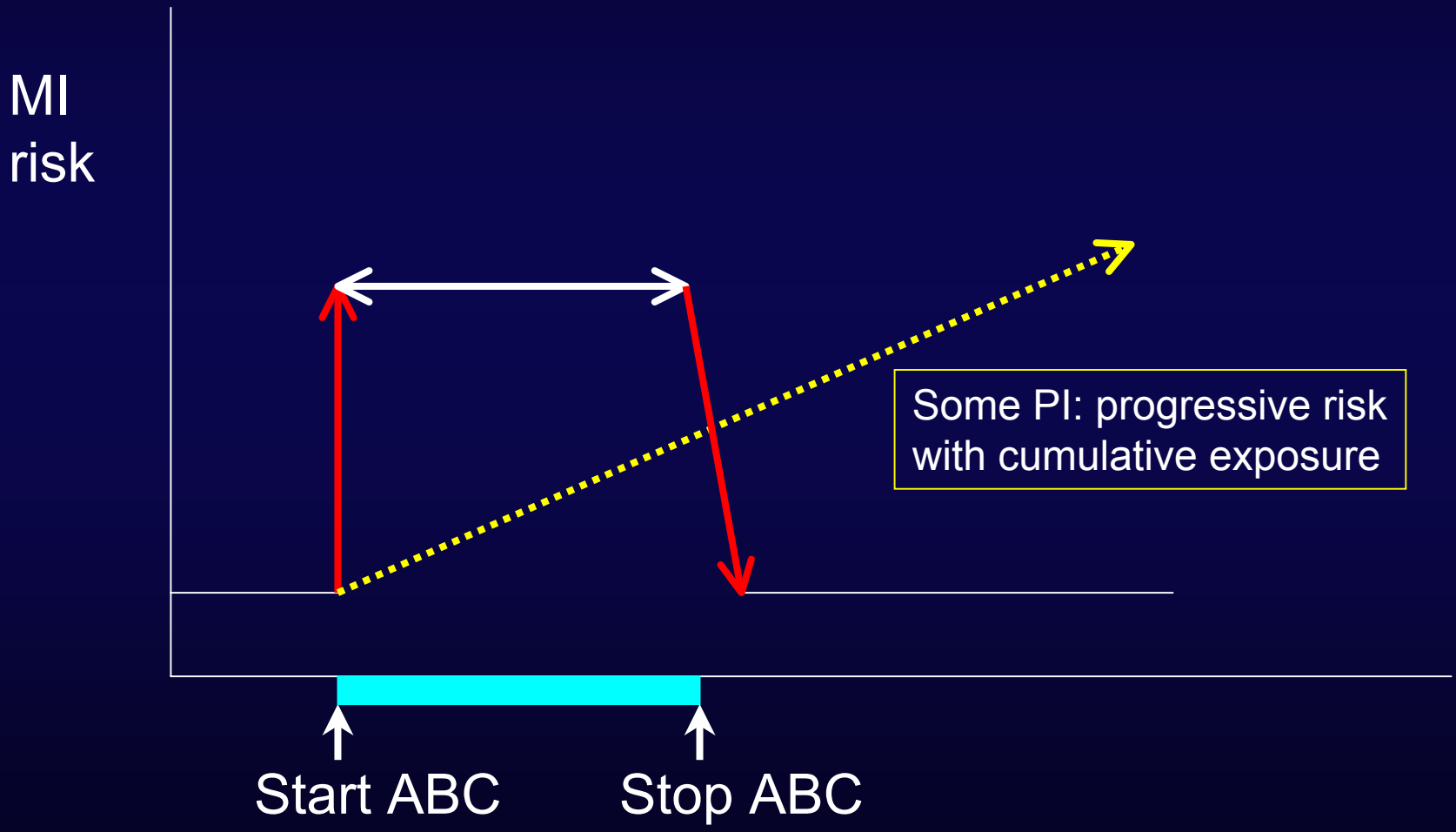
Risk of non-AIDS death in viral hepatitis co-infected according to level of surrogate of liver impairment (hyaluronic acid (>75 – abnormal)) and treatment arm in SMART



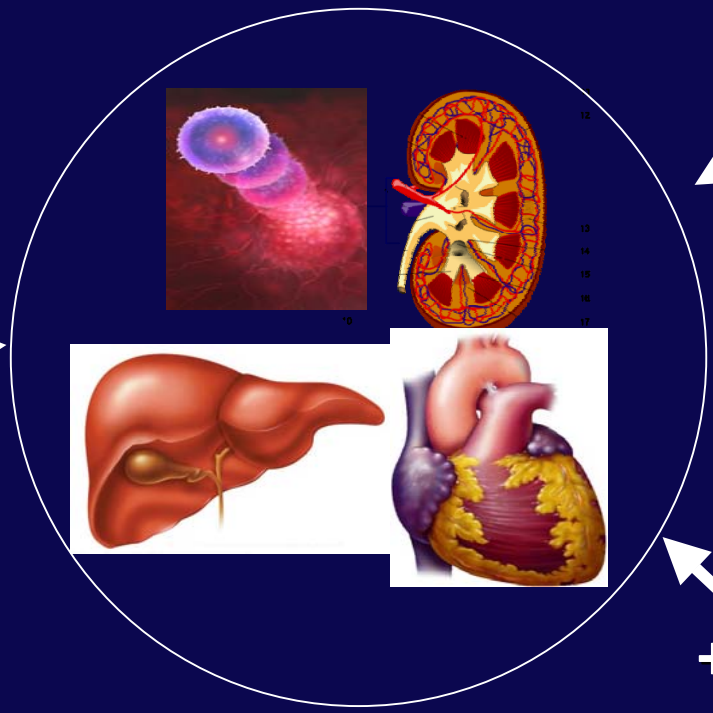
DC =Drug Conservation (ART interruption); VS=Virologic Suppression

Peters et al. CROI 2009

Time-course for association between ARV drug exposure and risk of MI



Principal factors affecting risk of serious non-AIDS events* in HIV



Traditional risk factors

+

+

+

ART

*: Cardiovascular disease, Liver disease, Kidney disease Non-AIDS related cancers

Virus vi ikke vidste

KUNNE SKABE SÅ VOLDSOMME SAMFUNDSMÆSSIGE & POLITISKE REAKTIONER

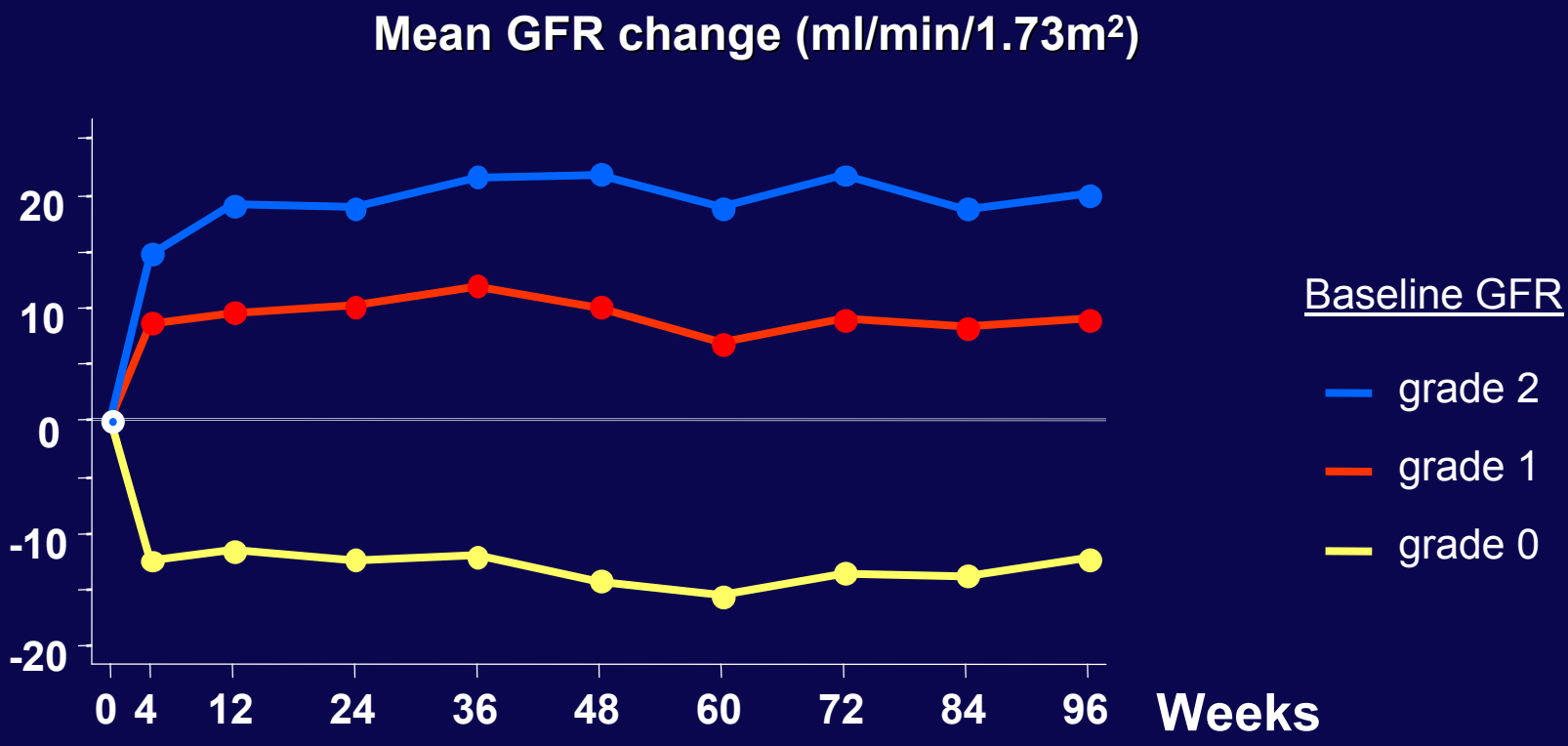
i 1994

Videnudvikling vedr. virussygdomme fra 1994 til 2009 – og fremover

- Fremskridt i høj grad betinget af
  - udvikling af molekylær-biologiske teknologi
  - specifik drug design teknologi
- Virussygdomme har
  - multiple årsager,
  - Diagnose kræver specifikt rettet klinisk mistanke og målrettede metoder
  - Skal behandles med som regel specifikt udviklede anvirale midler (få ”bred-spektrede” antivirale stoffer)
- I takt med at behandlingsmulighederne udvikler sig, vil den kliniske håndtering af virussygdomme kræve en tiltagende målrettet og specialiseret viden af dem, der varetager denne funktion

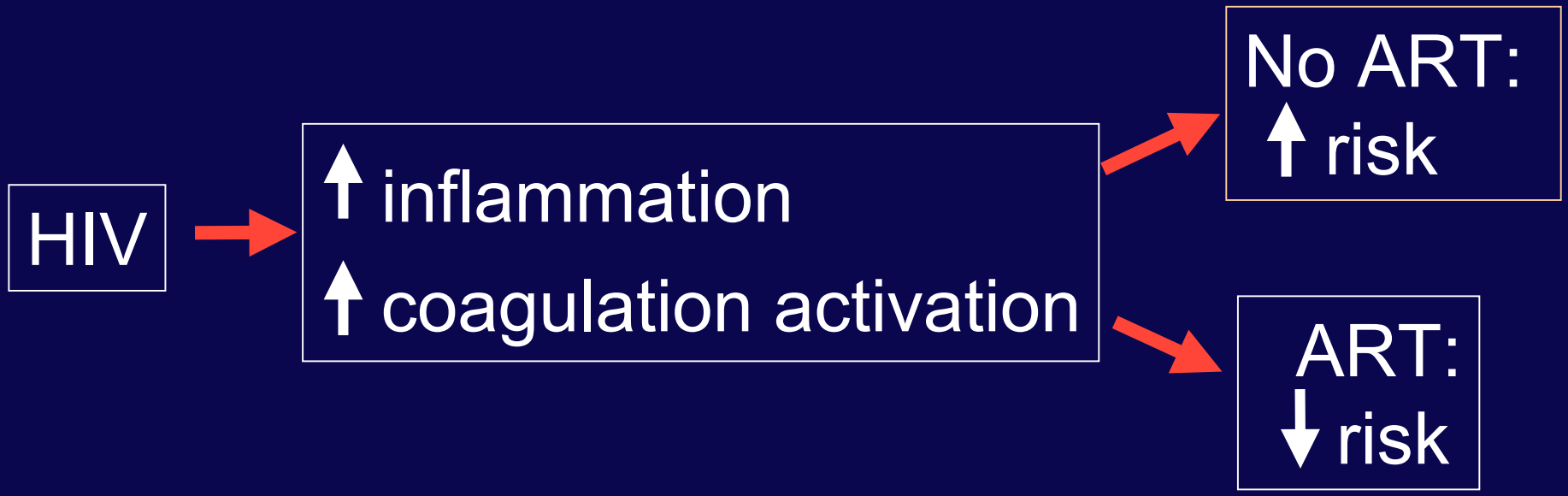
Glomerular filtration rate (GFR) over time by baseline GFR:

Impaired baseline GFR improved



DART: Reid *et al.* XVI IAC (2006). Abst. THAB0105

Hypothesis: HIV and non-AIDS disease risk



Magnitude of absolute risk ↑ depends on other factors

INSIGHT study group, 2007