



***Infettivologia: una disciplina in evoluzione***

***I successi a lungo termine della terapia  
antiretrovirale***

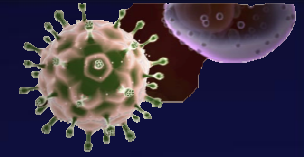
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***U.O. Malattie Infettive***

***Azienda Ospedaliero Universitaria - Ferrara***

***Ferrara, 18 marzo 2017***

# The HIV Virology Timeline



**HIV-1  
isolated**

**HIV-1  
genome  
sequenced**

**Virus replication  
causes  
immunological  
compromise**

**HAART**

**Viral load  
testing**

**Is HIV eradication  
possible?**

1982

1985

1991

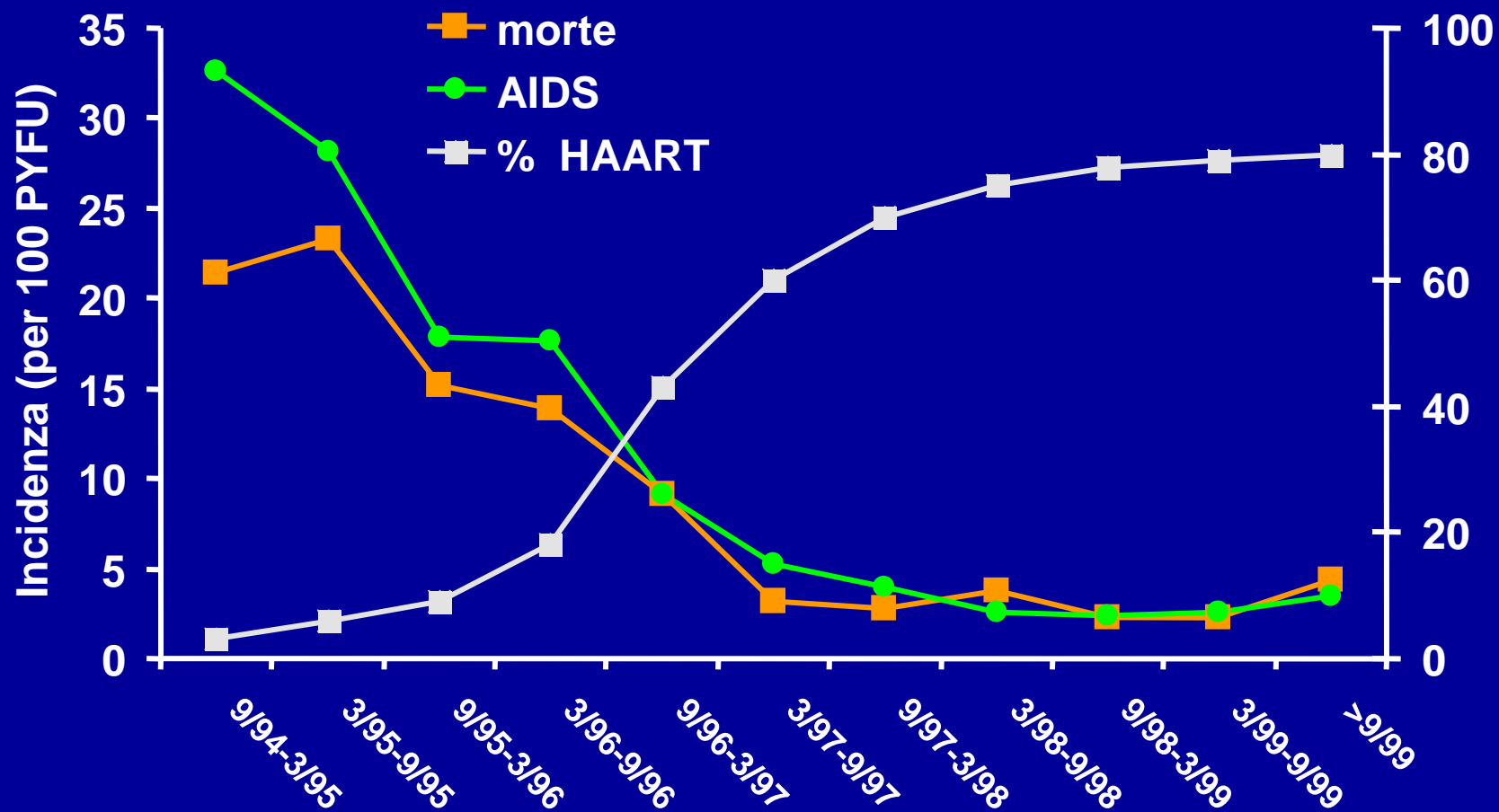
1995

1996

2009

2010 →

# Incidenza di AIDS e morte per AIDS in Europa: 1994-2000



Adattata da: EuroSIDA 2000

# La terapia antiretrovirale ( HAART) nella infezione da HIV

HIV

Sistema immunitario

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Replicazione virale,  
distruzione CD4

HAART

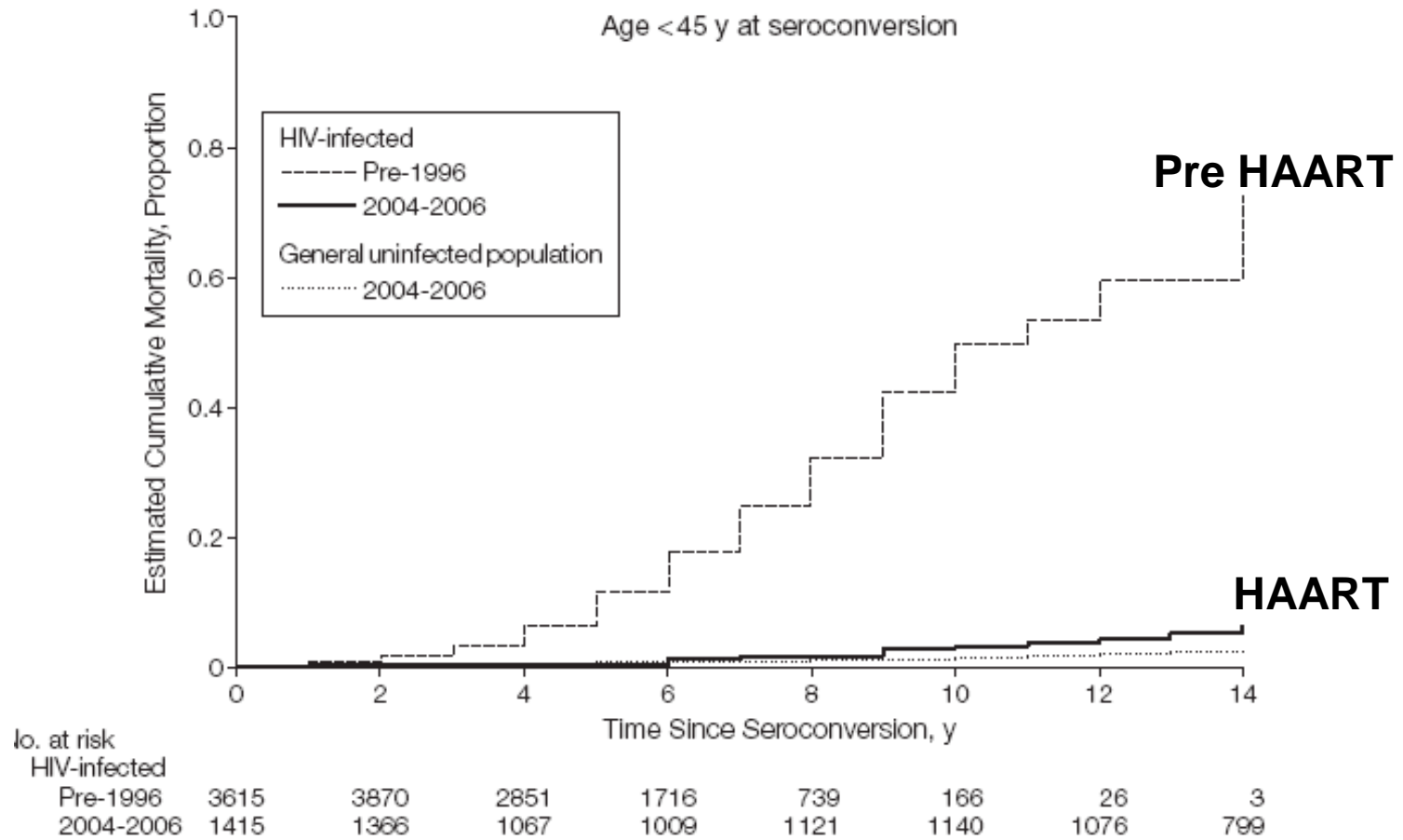
Attività antivirale,  
produzione CD4

Progressione malattia , infezioni opportunistiche

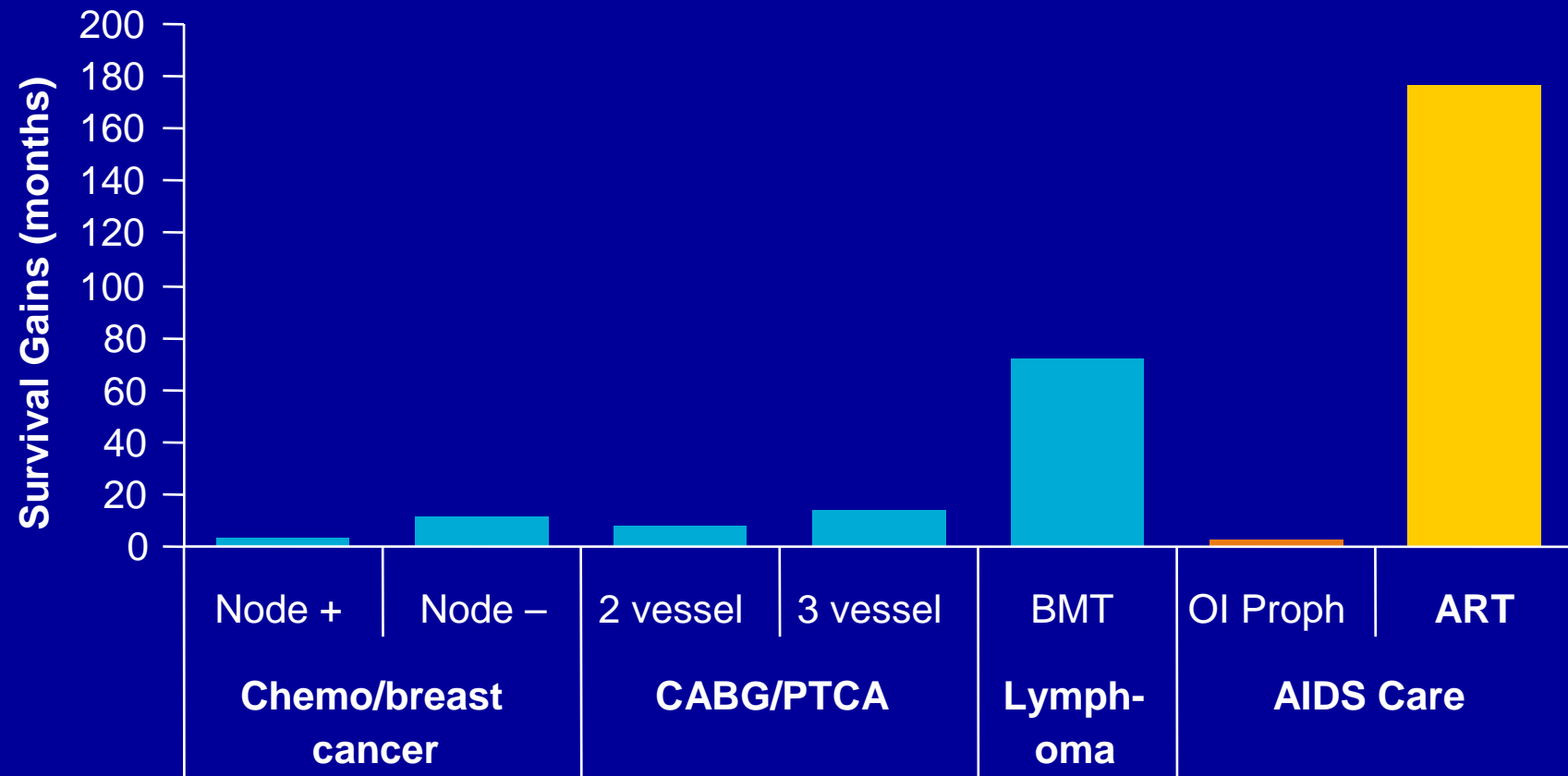
HIV → AIDS

RISK OF DEATH AFTER HIV SEROCONVERSION VS MORTALITY IN THE GENERAL POPULATION

**Cascade collaboration**



# Incremento della sopravvivenza dovuto alla ART vs. altri interventi sanitari

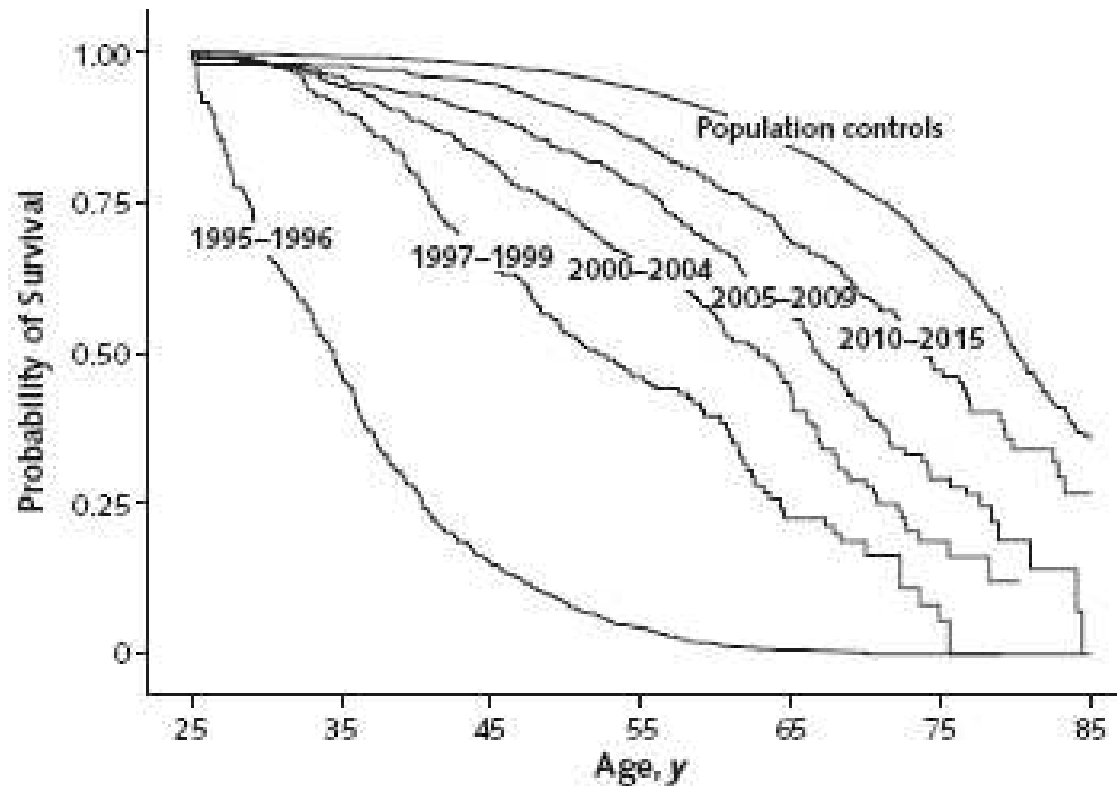




## Update of Survival for Persons With HIV Infection in Denmark

*Lohse et al .*

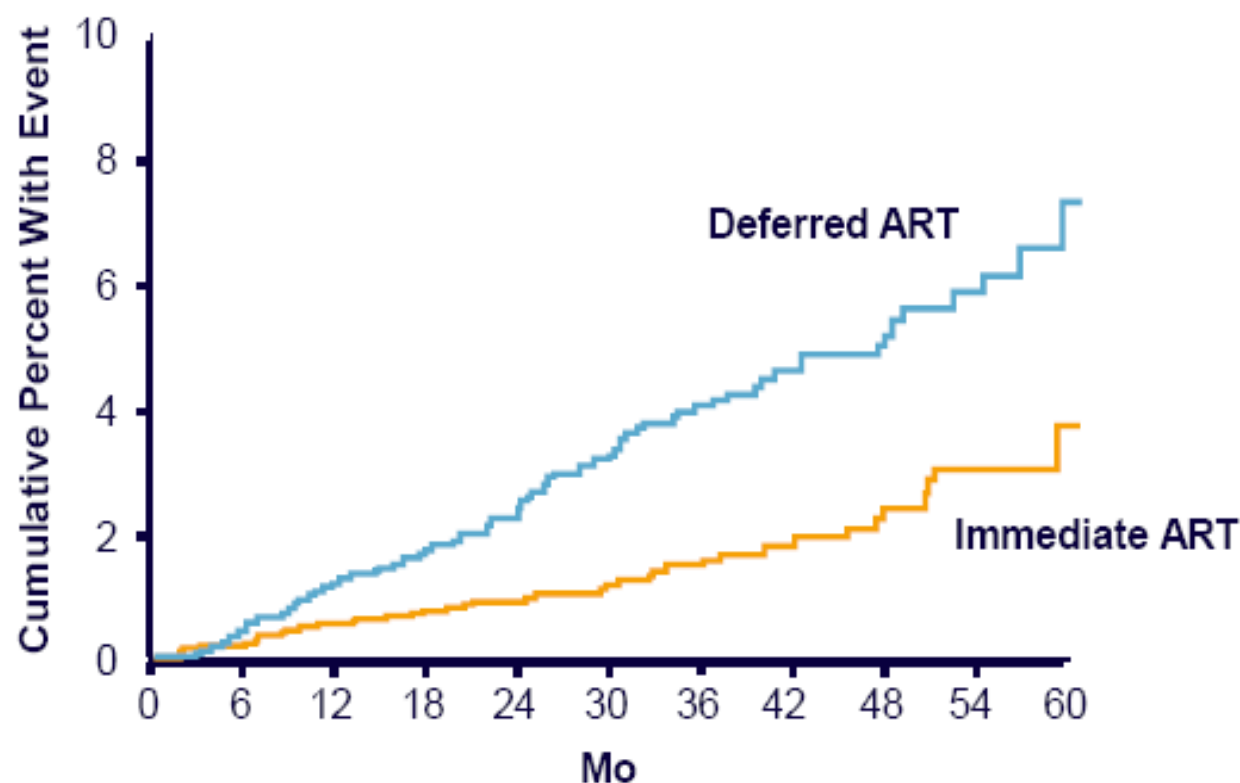
**Data 1995-2015**





## START: 57% Reduced Risk of Serious Events or Death with Immediate ART

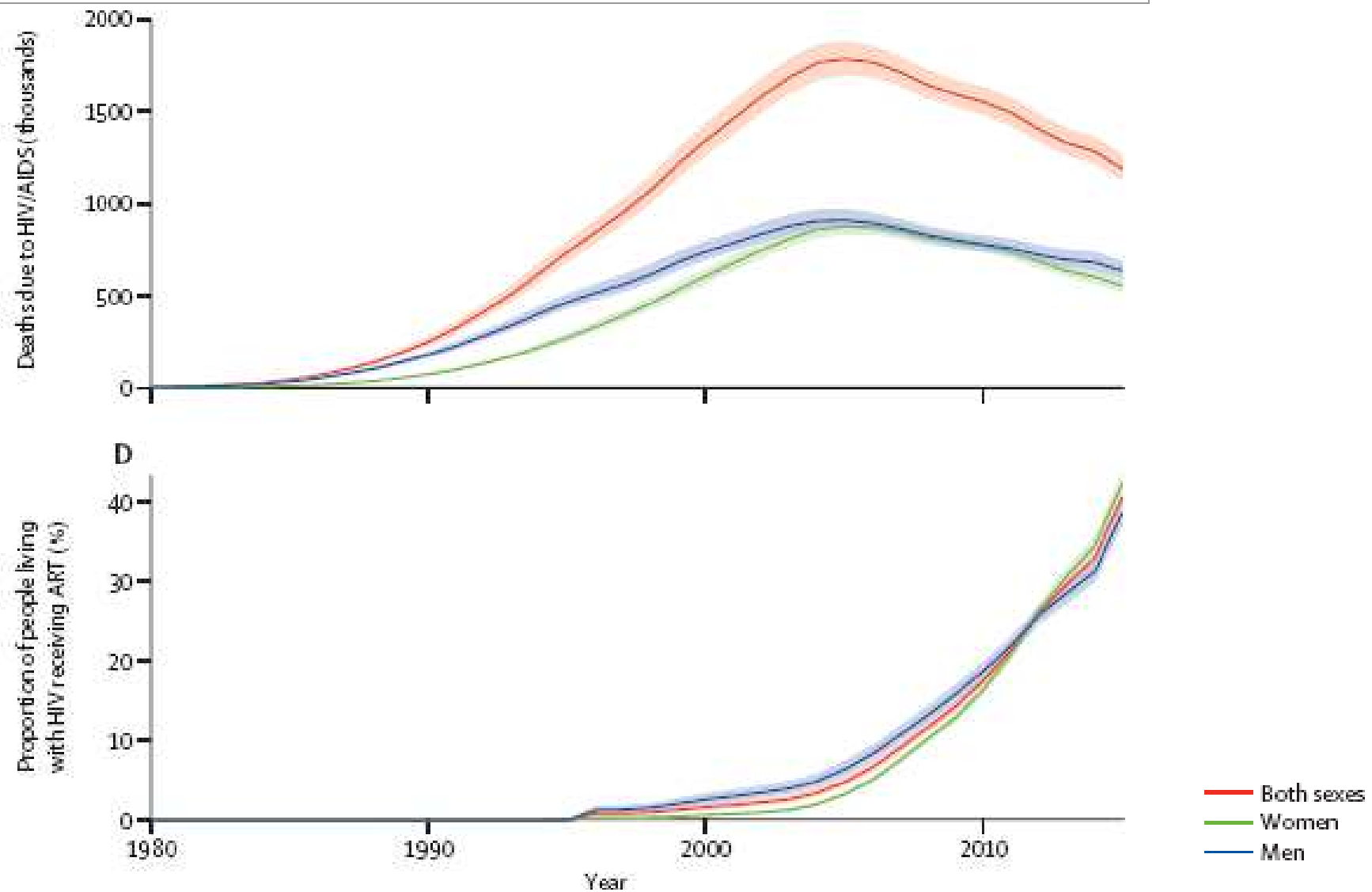
4.1% vs 1.8% in deferred vs immediate arms experienced serious AIDS or non-AIDS-related event or death (HR: 0.43; 95% CI: 0.30-0.62;  $P < .001$ )



# Estimates of global, regional, and national incidence, prevalence, and mortality of HIV, 1980–2015: the Global Burden of Disease Study 2015

Lancet HIV 2016; 3: e361–87

GBD 2015 HIV Collaborators\*



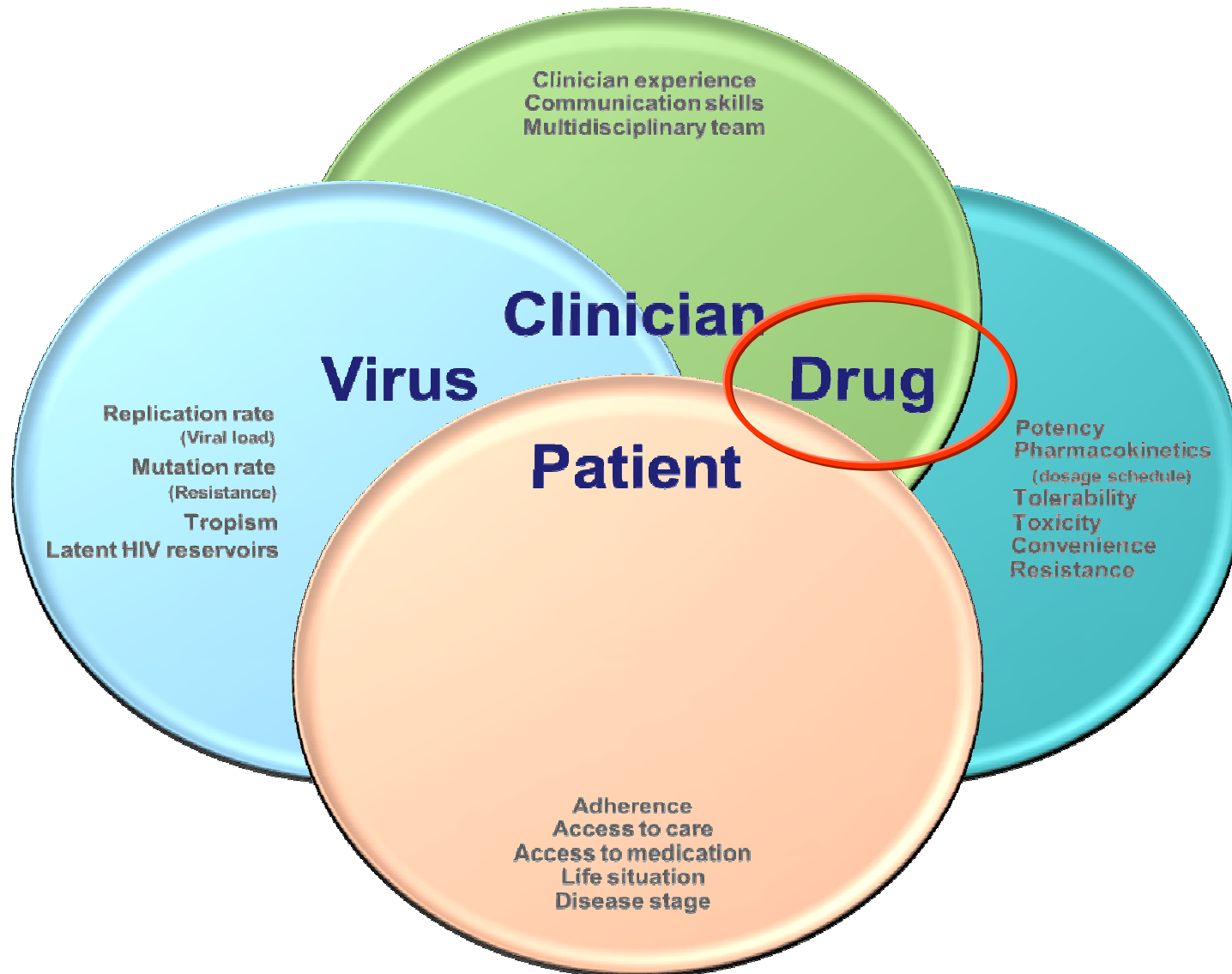
# Gli effetti della HAART



- **Efficace e duratura soppressione della replicazione virale**
- **Conservazione della funzione immunitaria**
- **Riduzione della mortalità e morbilità HIV-correlata**
- **Miglioramento della qualità della vita**



## Fattori che influenzano il successo della terapia



# Farmaci antiretrovirali nel 2017

## NRTIs

- Abacavir
- Didanosine
- Emtricitabine
- Lamivudine
- Stavudine
- Tenofovir
- Zidovudine

## NNRTIs

- Efavirenz
- Nevirapine
- Etravirine
- Rilpivirine

## Protease Inhibitors

- Atazanavir
- Darunavir
- Fos-Amprenavir
- Indinavir
- Lopinavir
- Nelfinavir
- Ritonavir
- Saquinavir
- Tipranavir

## New Classes

### Fusion Inhibitors

- Enfuvirtide

### R5 Inhibitors

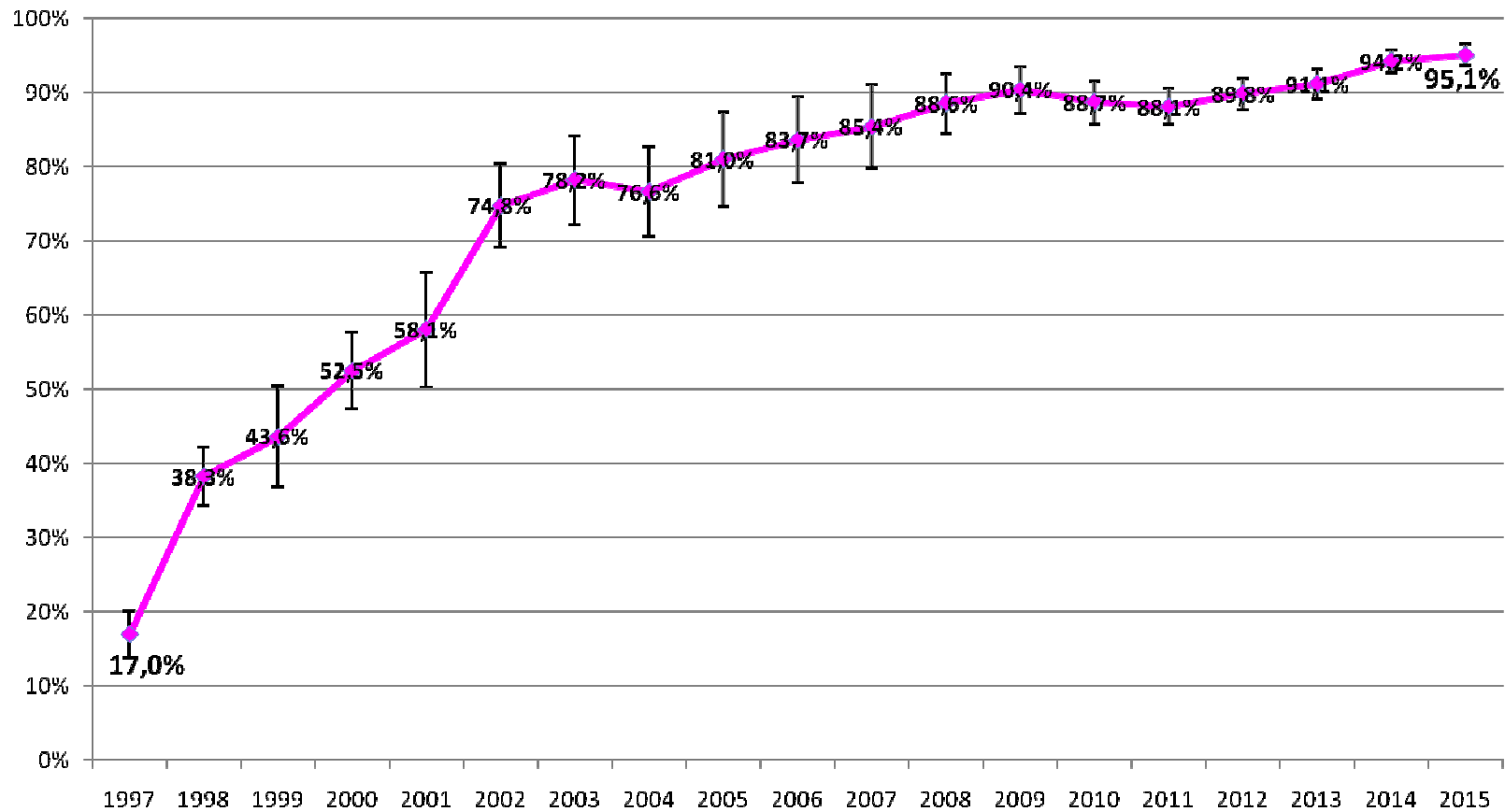
- Maraviroc

### Integrase Inhibitors

- Raltegravir
- Elvitegravir
- Dolutegravir

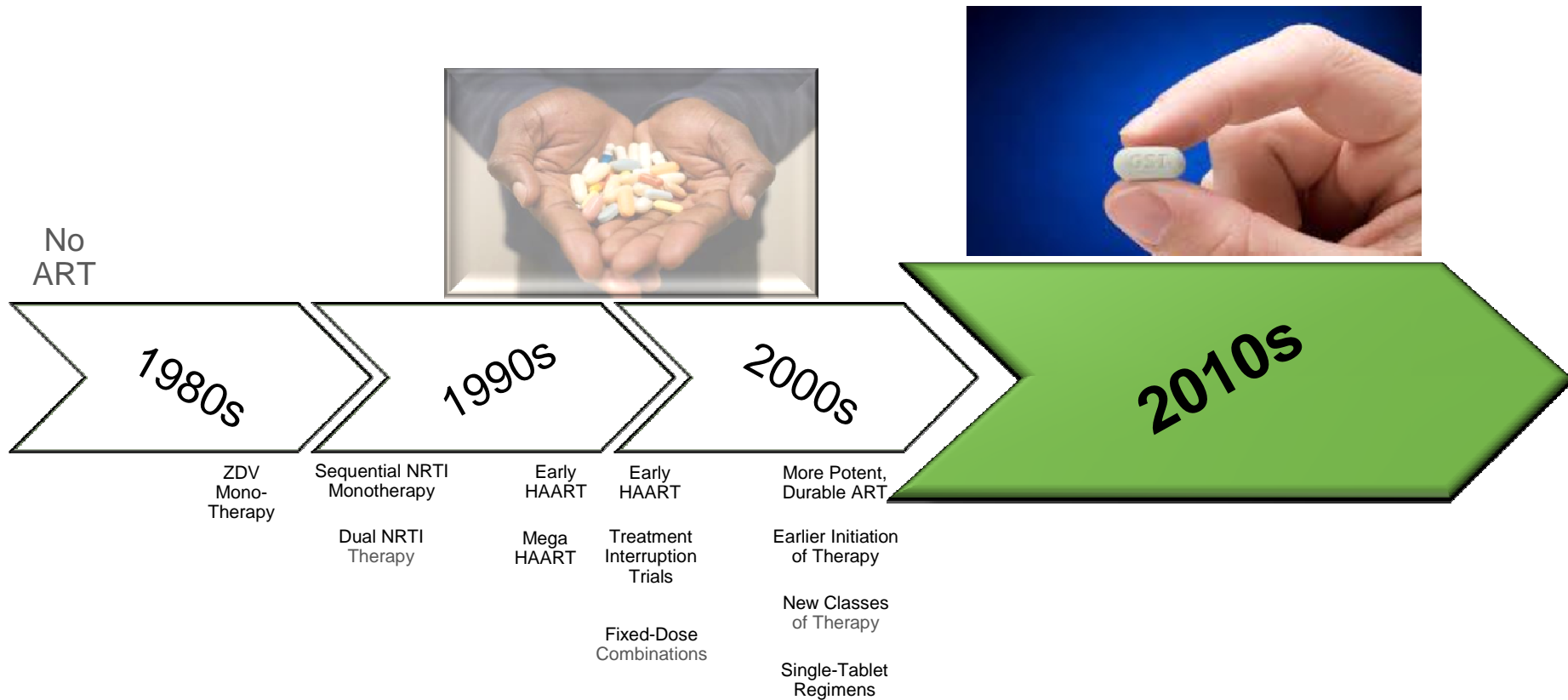


**Proportion of patients with a VL $\leq$ 80 copies/mL at 12 months from starting their first ART regimen by calendar year of initiation**

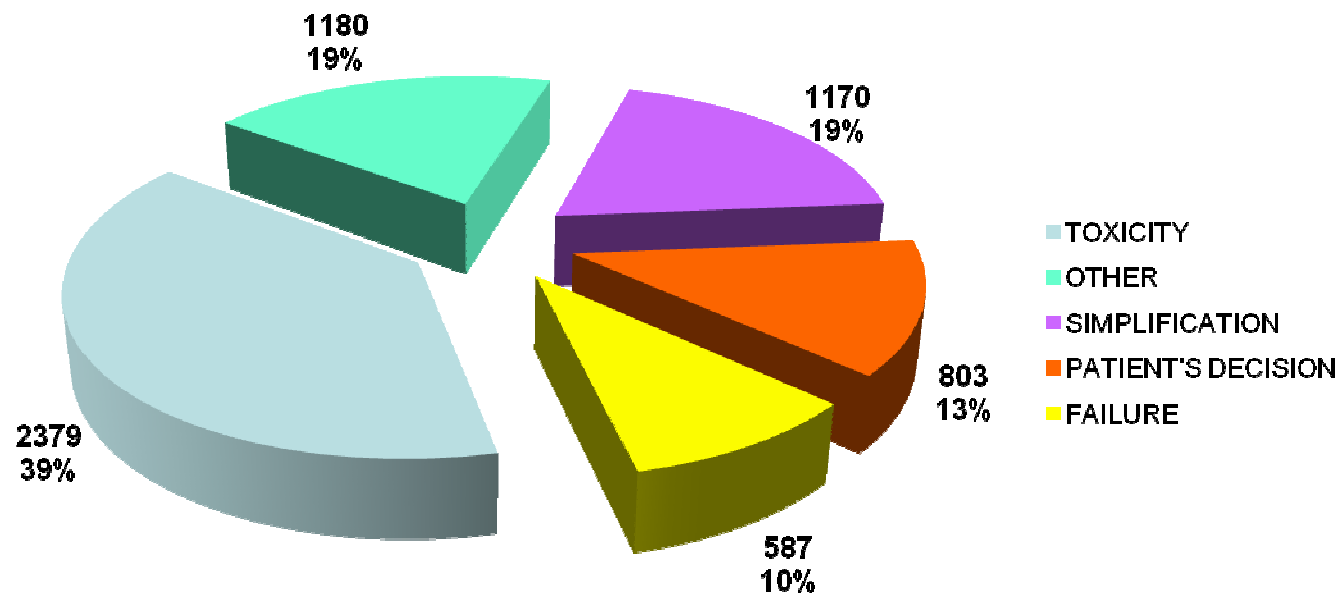


# Today's ART

## Once-Daily, Single-Tablet Regimens

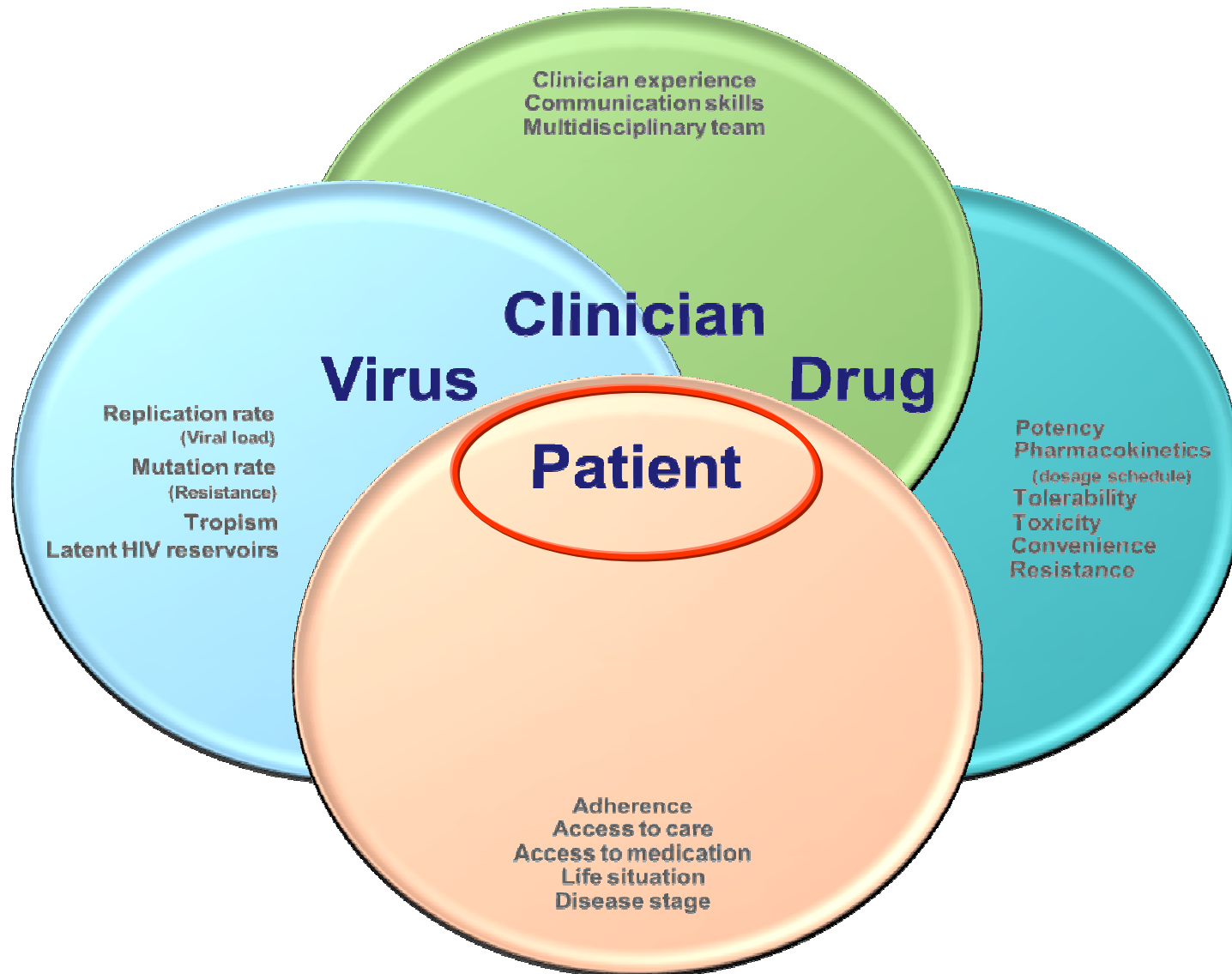


## Distribution of reasons for stopping at least one drug included in the first regimen N=6119



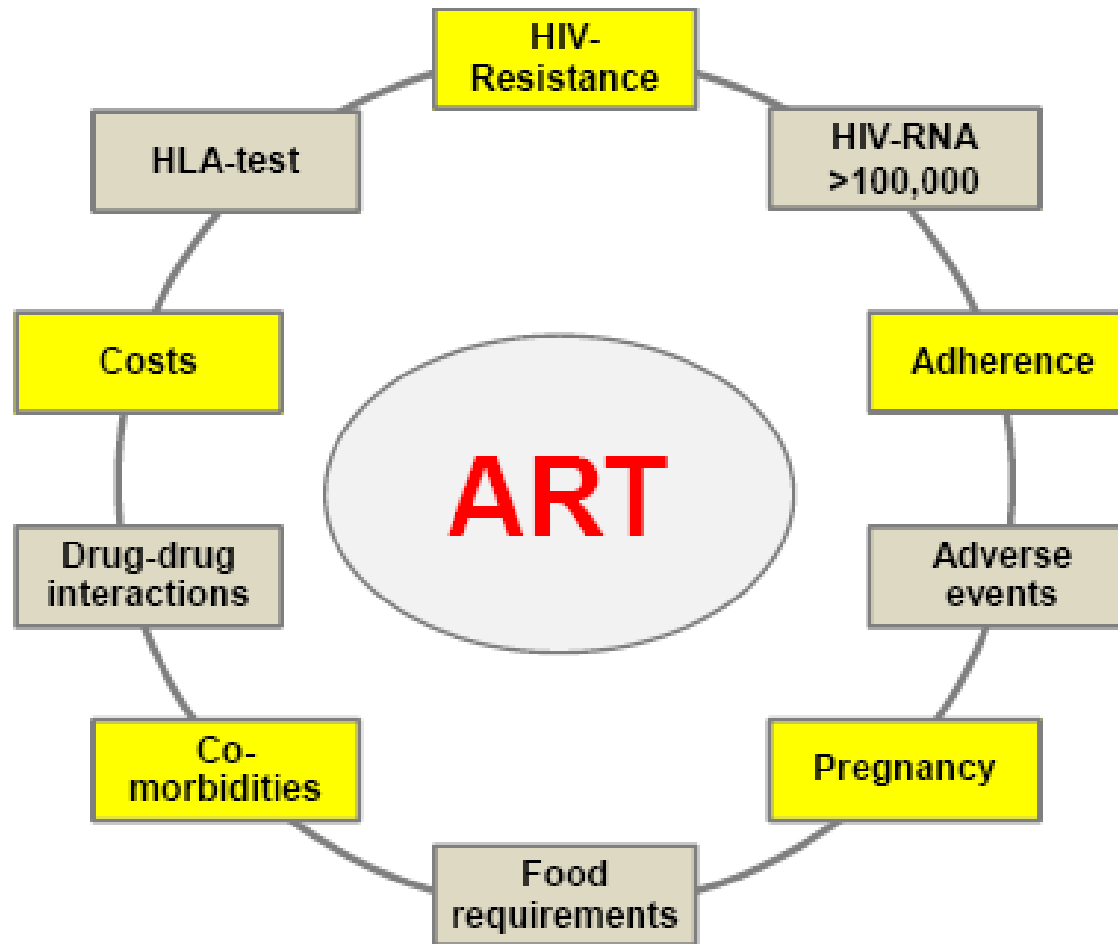


## Fattori che influenzano il successo della terapia





## Fattori che condizionano la scelta della ART



# Gli effetti della HAART



- **Efficace e duratura soppressione della replicazione virale**
- Conservazione della funzione immunitaria
- Riduzione della mortalità e morbilità HIV-correlata
- Miglioramento della qualità della vita
  
- **Riduce la trasmissione di HIV**



# HIV e gravidanza

Terapia antiretrovirale in  
gravidanza

Parto cesareo

Allattamento artificiale

**Tasso di trasmissione < 1%**

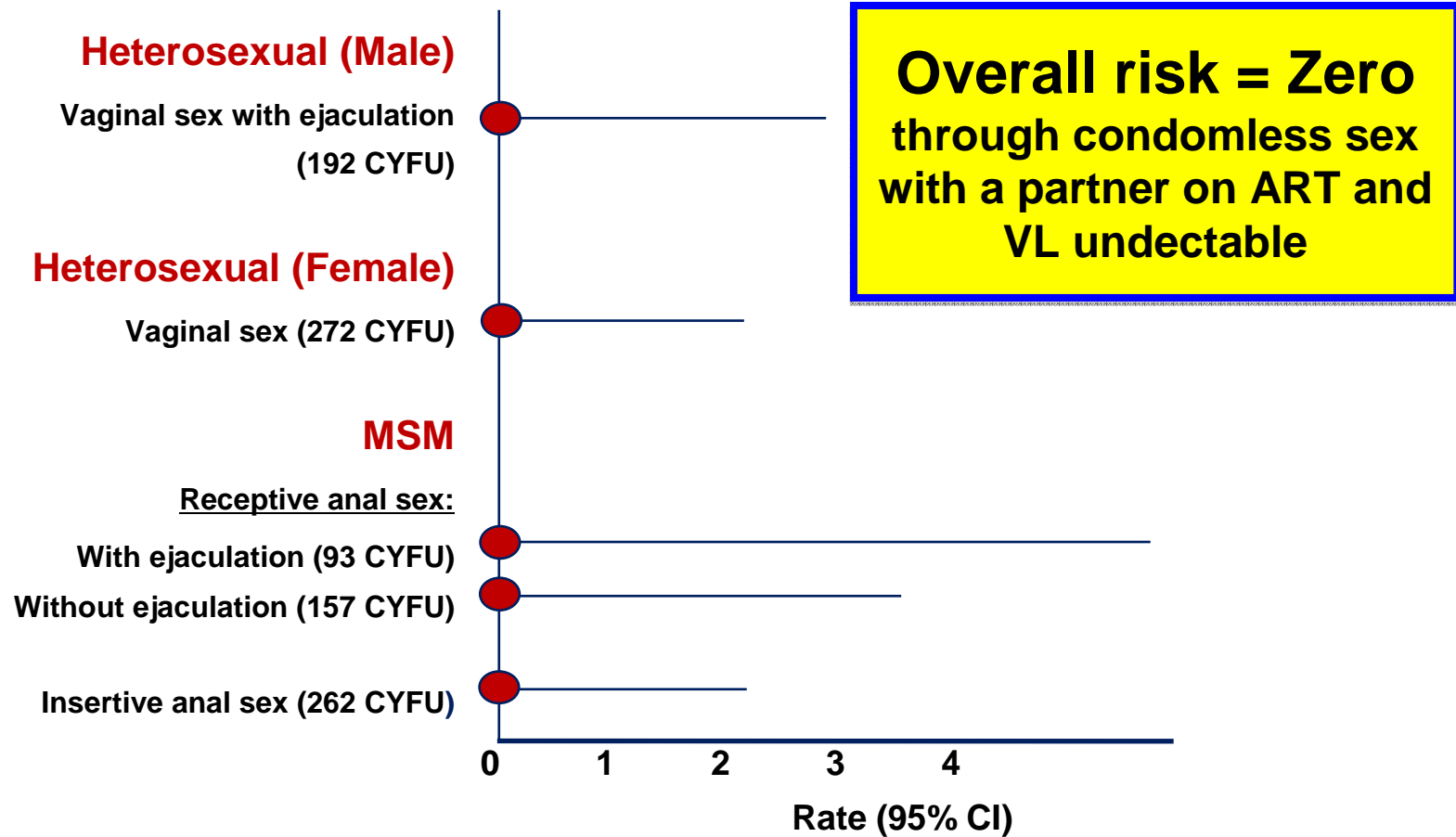


- **Diffuso uso della terapia**
- **Screening delle gestanti**



# HIV Transmission According to Sexual Behavior Reported by HIV-Negative Partner

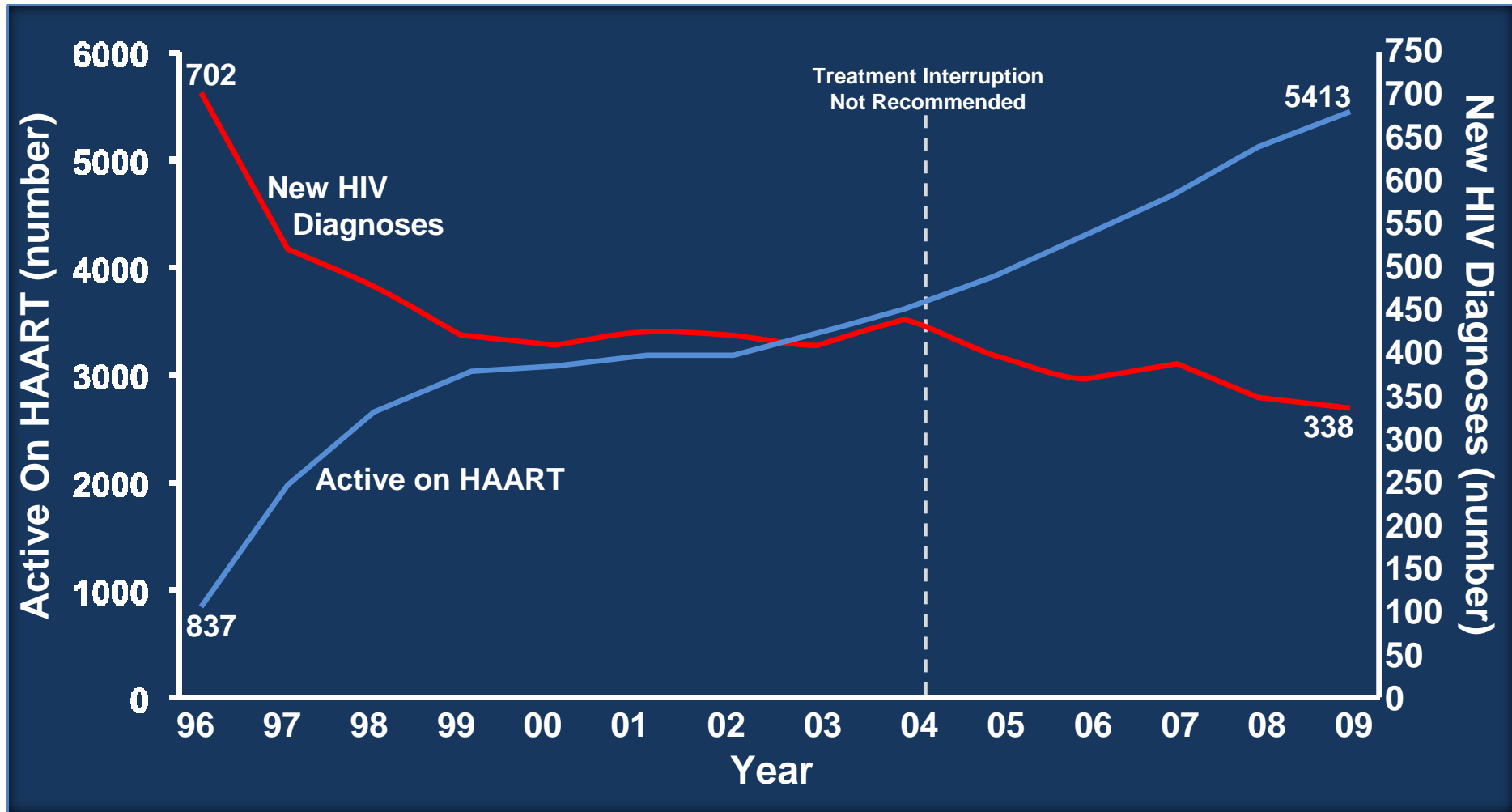
Rate of Couple Transmission  
(per 100 Couple-Years Follow-Up)



Source: Rodger A, et al. 21<sup>st</sup> CROI. Boston, 2014. Abstract 153LB

# HAART Coverage and New HIV Diagnoses

## British Columbia, Canada

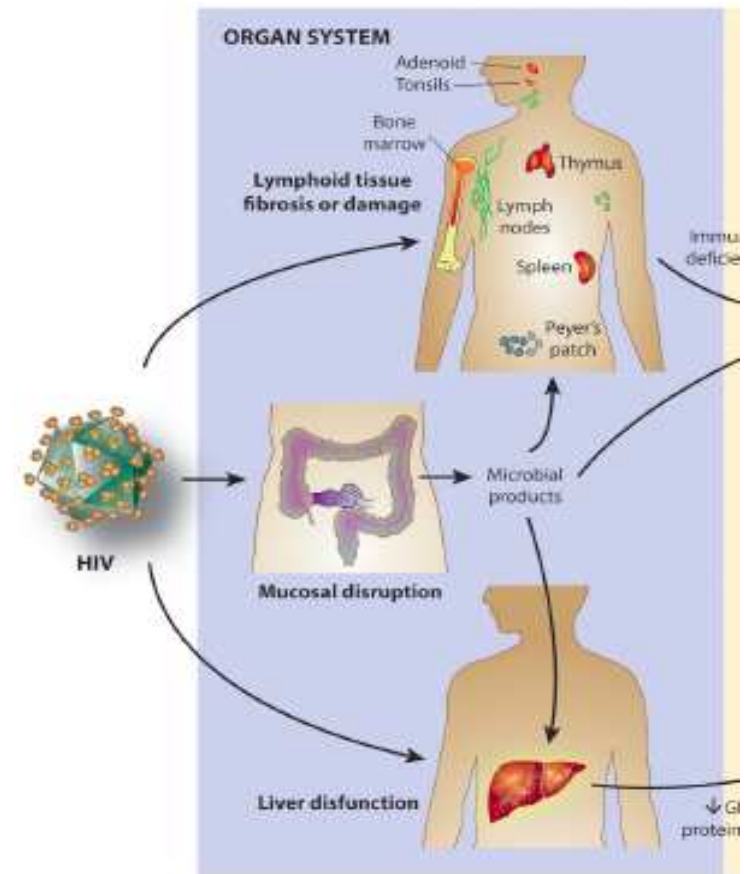


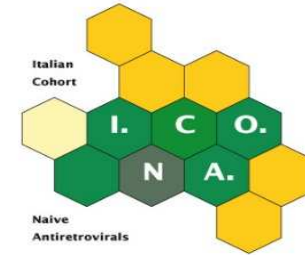
Montaner JS, et al. *Lancet*. 2010;376:532-539.



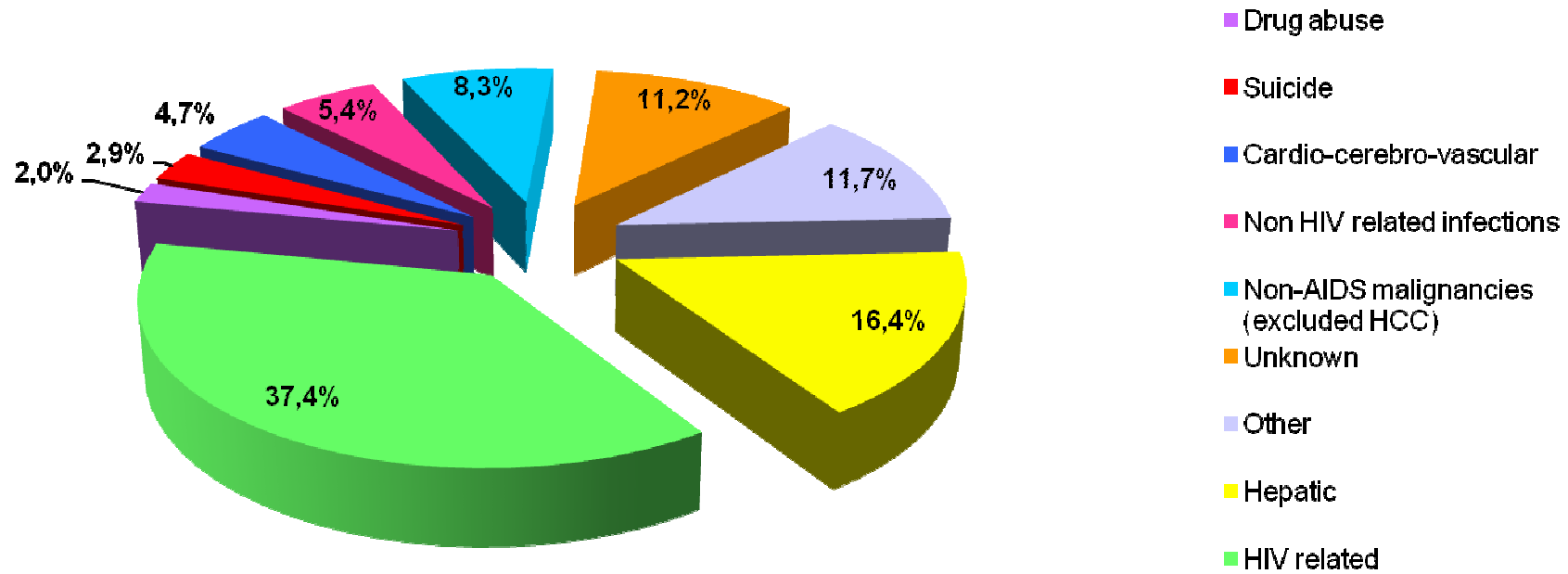
## Limiti della HAART

- La HAART efficace controlla la replicazione di HIV e favorisce il recupero di linfociti CD4
- **L'infezione da HIV è una patologia sistemica in cui oltre al danno immunologico vi è un danno d'organo**



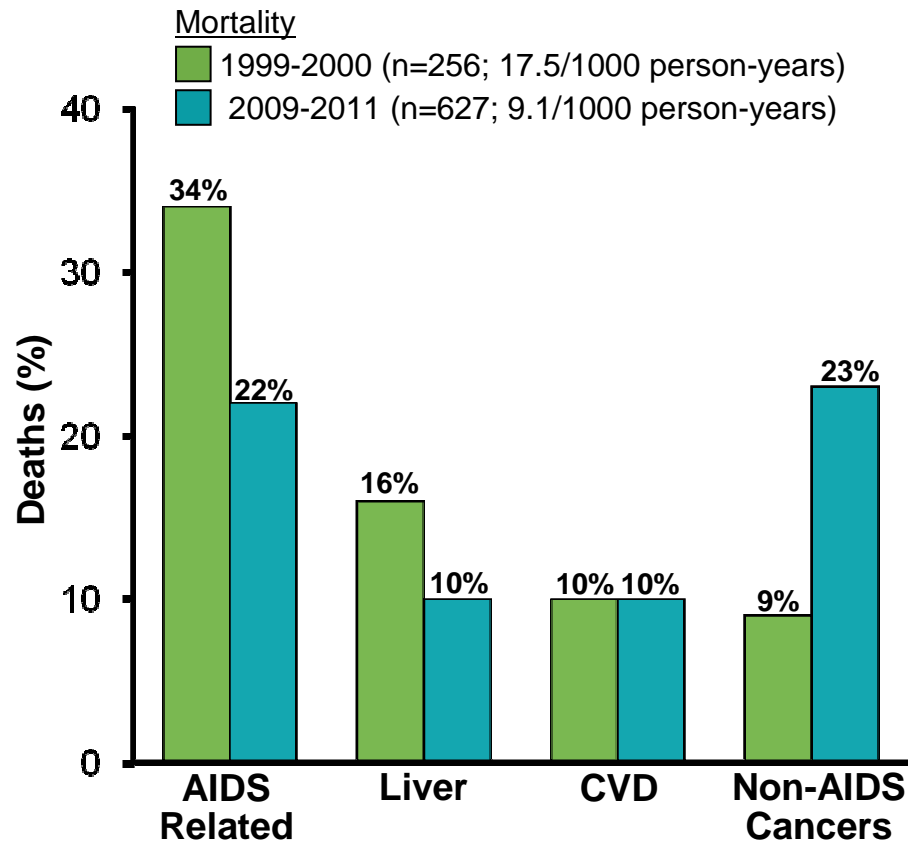


## Cause of death, n=48

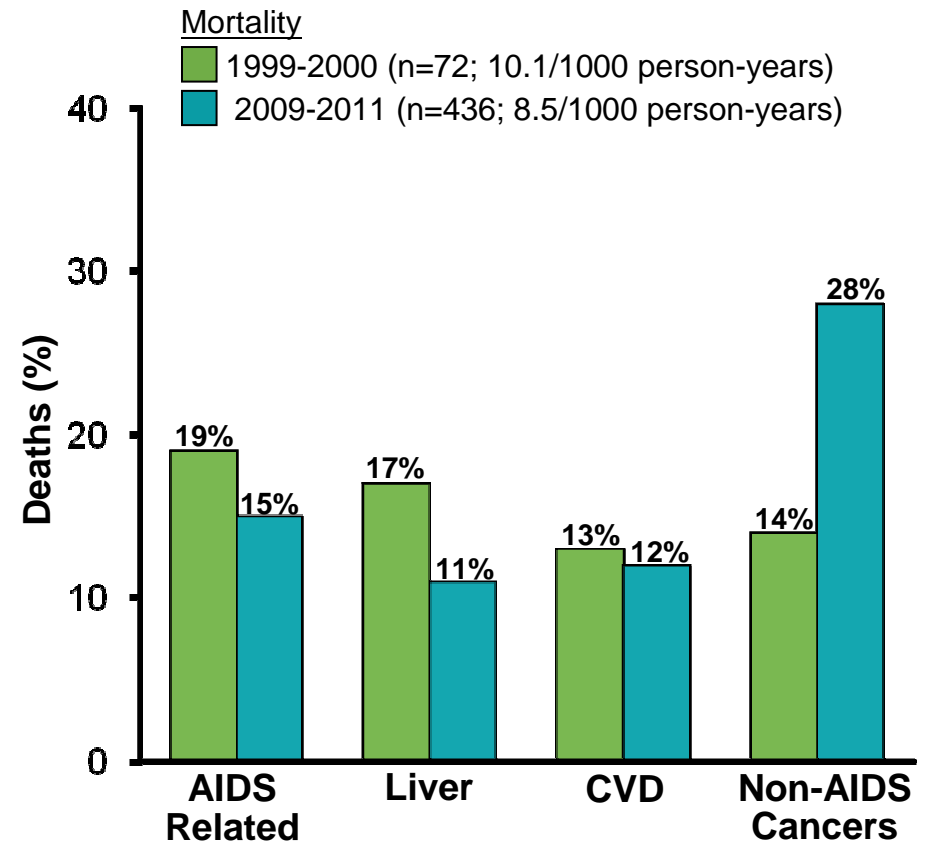


# D:A:D Study: Trends in the Underlying Causes of Death in HIV Patients

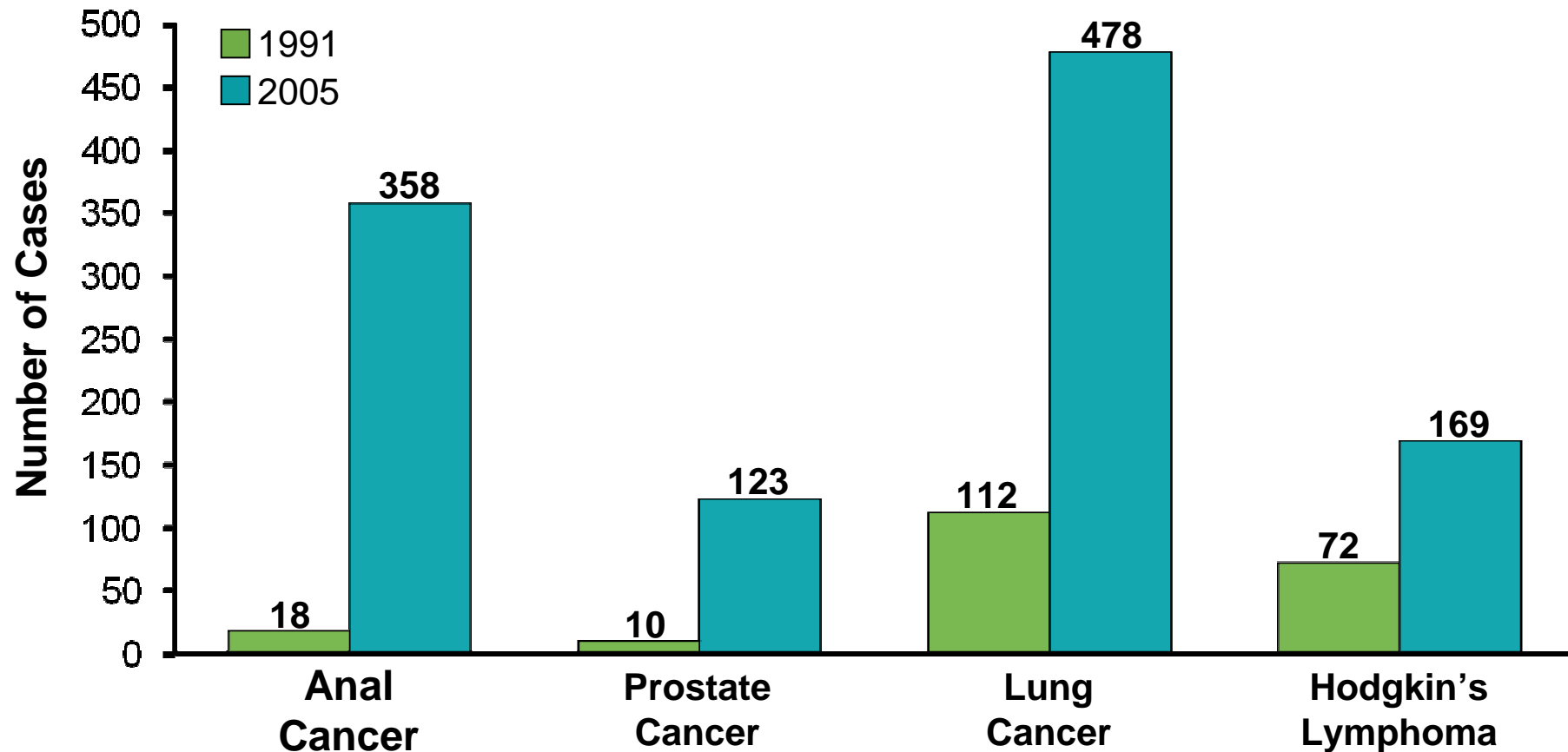
## Overall D:A:D Cohort



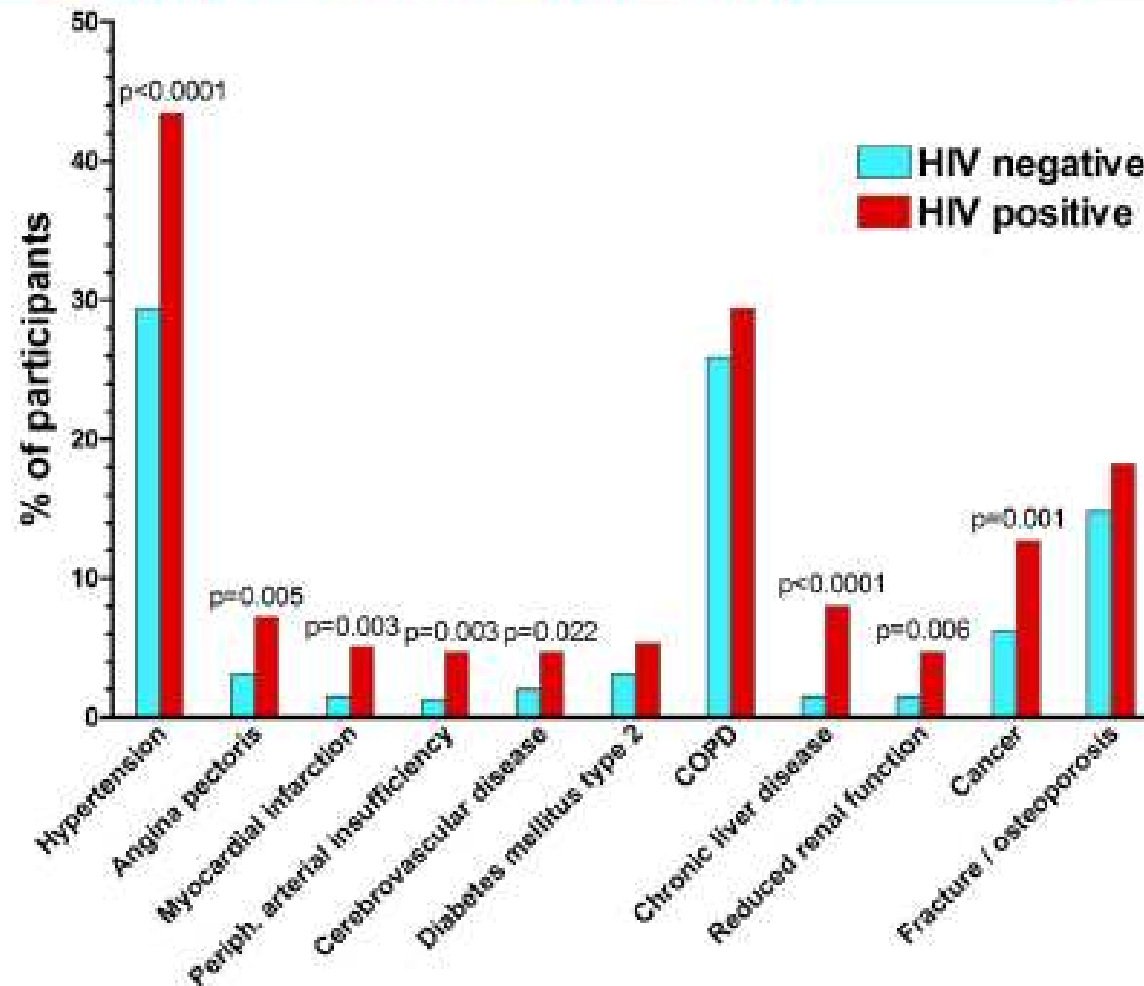
## Current HIV RNA <50 Copies/mL



# CDC: Changes in Non-AIDS-Defining Cancer Among HIV-Infected Patients



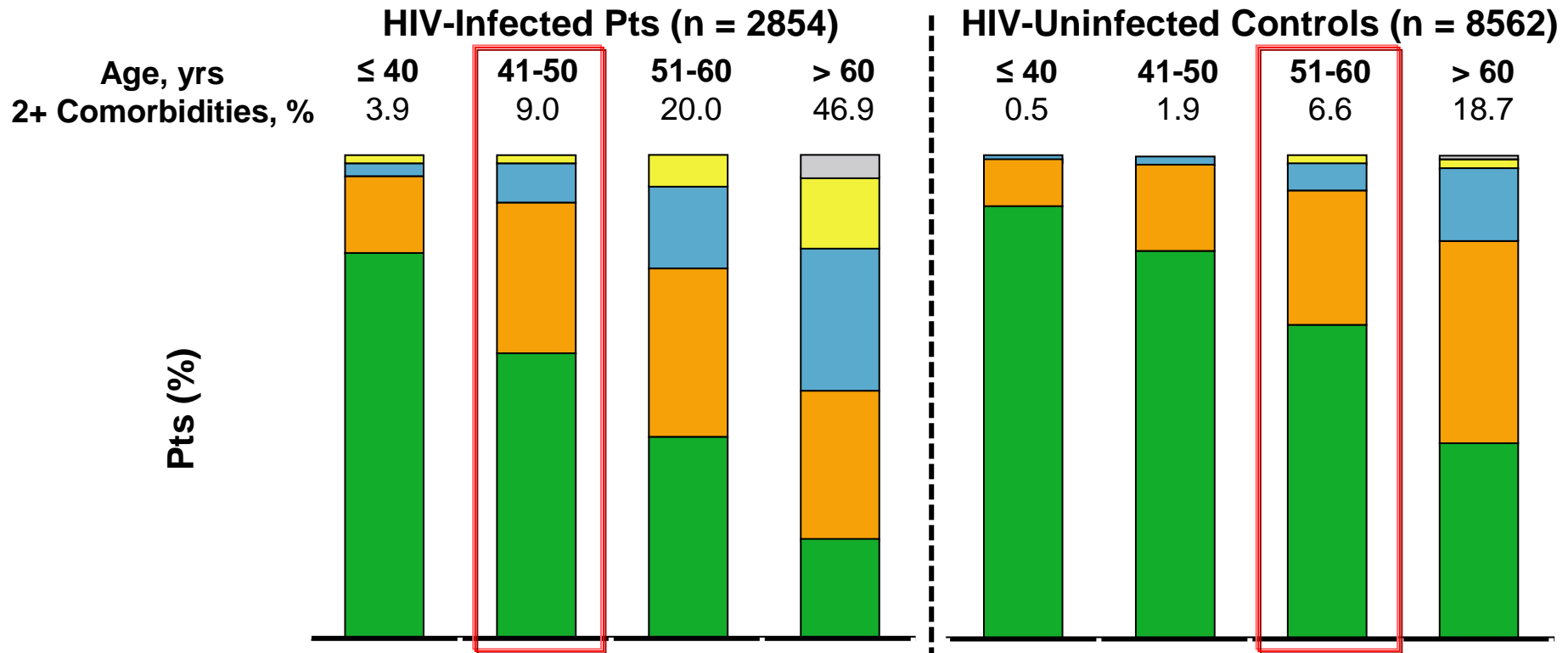
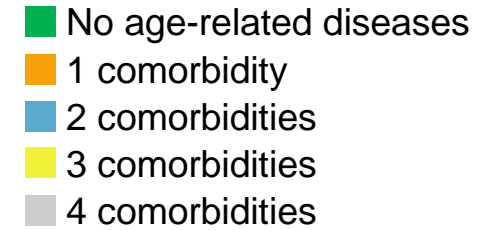
# Comorbidity distribution





# Comorbidities Increase With Age and With HIV Infection

- Single-center, case-control study



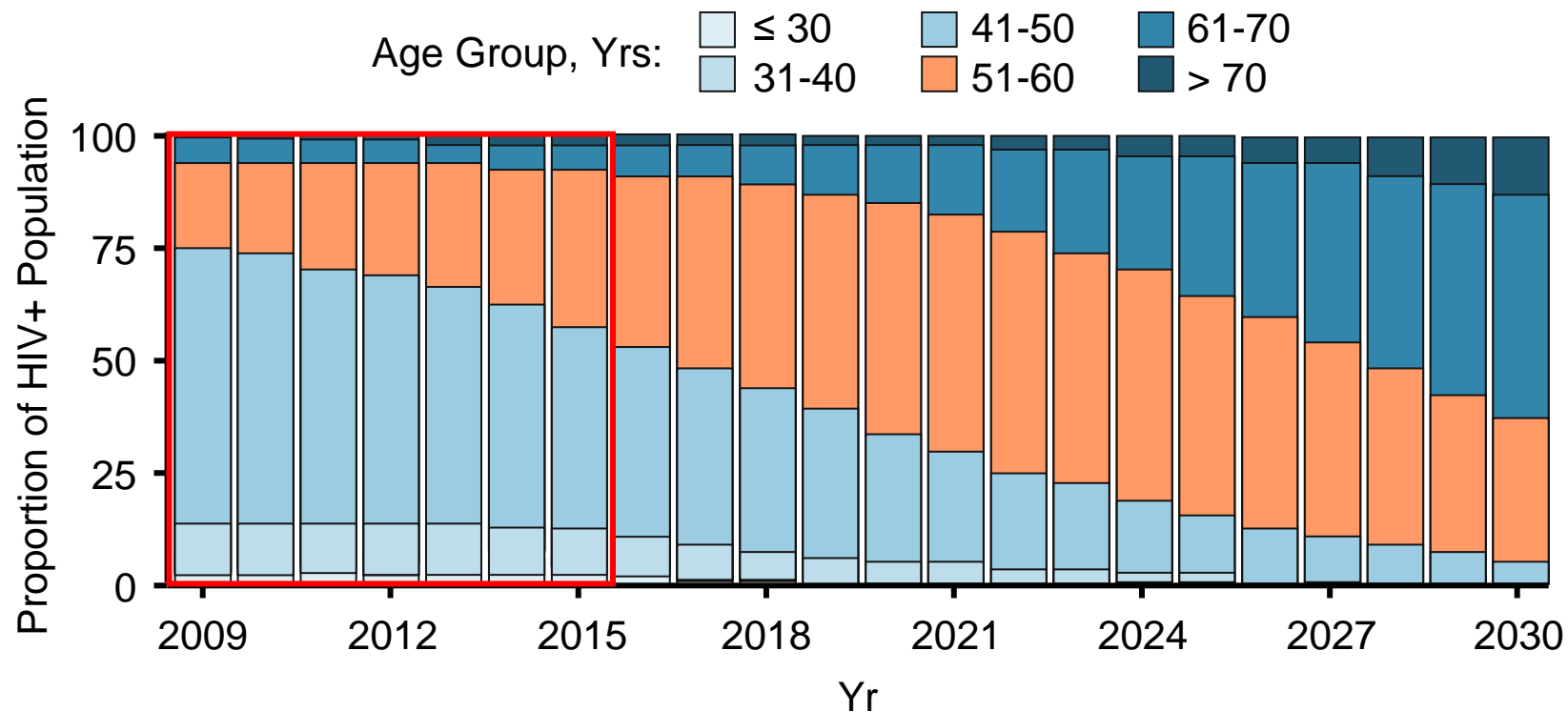
\*Comorbidities: bone fractures, CVD, diabetes, HTN, hypothyroidism.

Guaraldi G, et al. Clin Infect Dis. 2011;53:1120-1126.

# Model Simulation Predicts Growth of Aging HIV+ Population

- By 2030, ~ 60% of HIV+ pts predicted to be older than 60 yrs of age, with ~ 10% older than 70 yrs of age

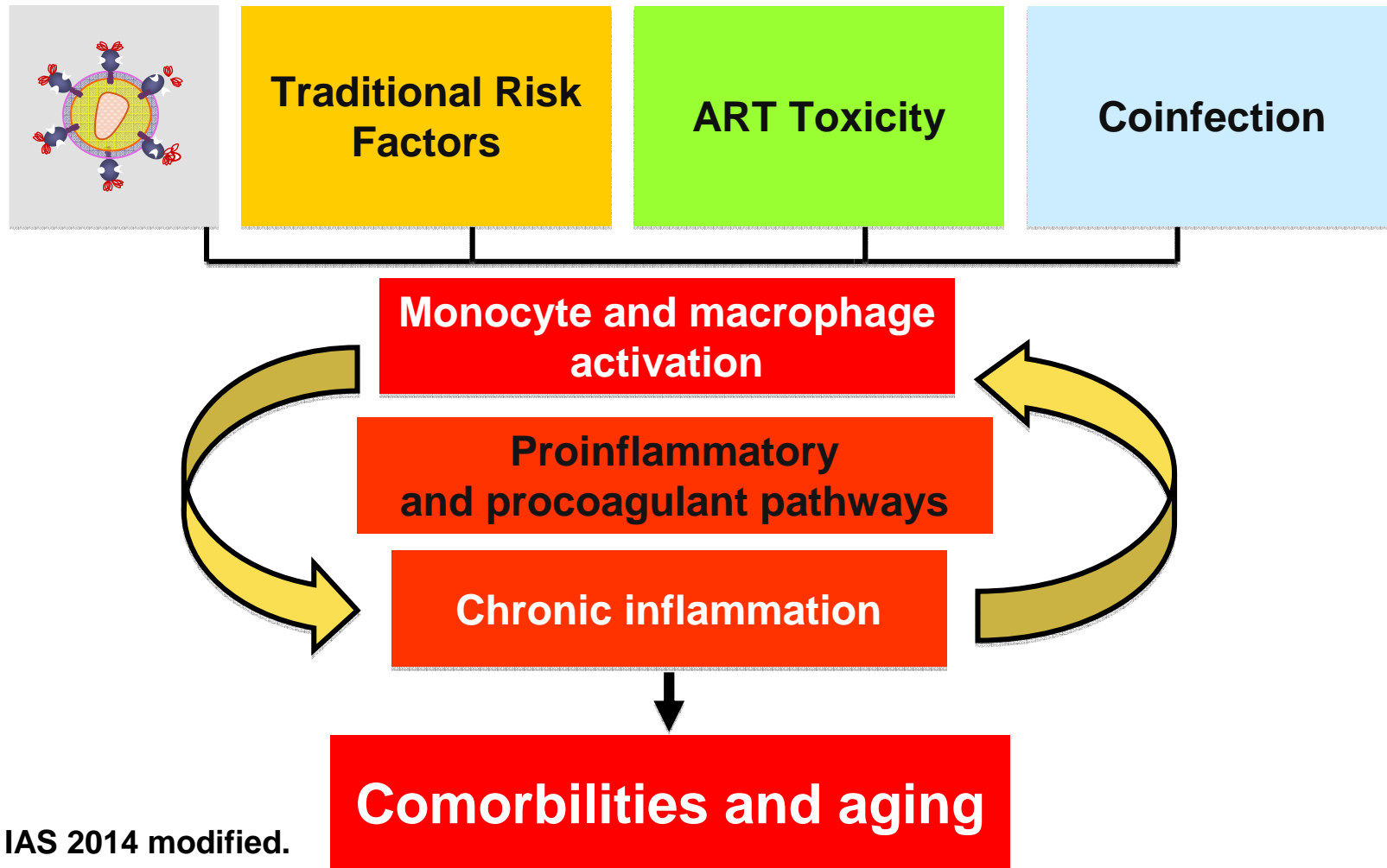
Observed (Red Box) and Projected Age Distribution of HIV+ Pts 2009-2030



Guaraldi G, et al. International Comorbidities WS 2016. Abstract P06.  
Reproduced with permission.

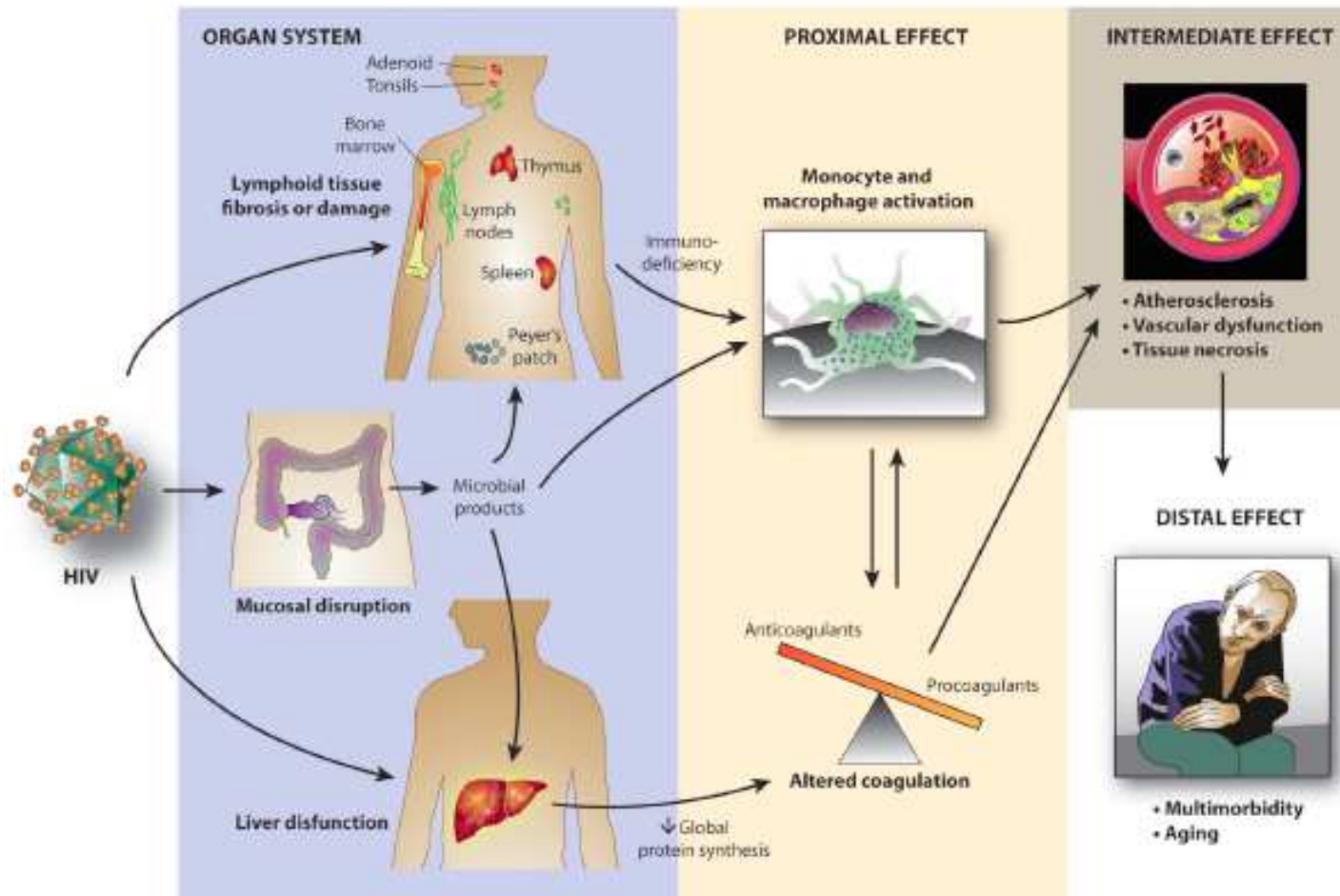


# Factors Contributing to “inflammaging” in HIV-Positive Pts



Crowe S. IAS 2014 modified.

# Systemic Effects of Inflammation on Health During Chronic HIV Infection



*....And miles to go before ....*

**(R.Frost)**

