



***Patologia infettiva emergente e riemergente  
Ferrara, 5 maggio 2012***

# **Evoluzione della terapia antiretrovirale e nuove problematiche gestionali nel paziente HIV positivo**

**Laura Sighinolfi**

***U.O. Malattie Infettive  
U.S. Gestione Ambulatorio HIV/AIDS  
Azienda Ospedaliero-Universitaria Ferrara***





**1981-2011**  
**Infezione da HIV - Trent'anni dopo**

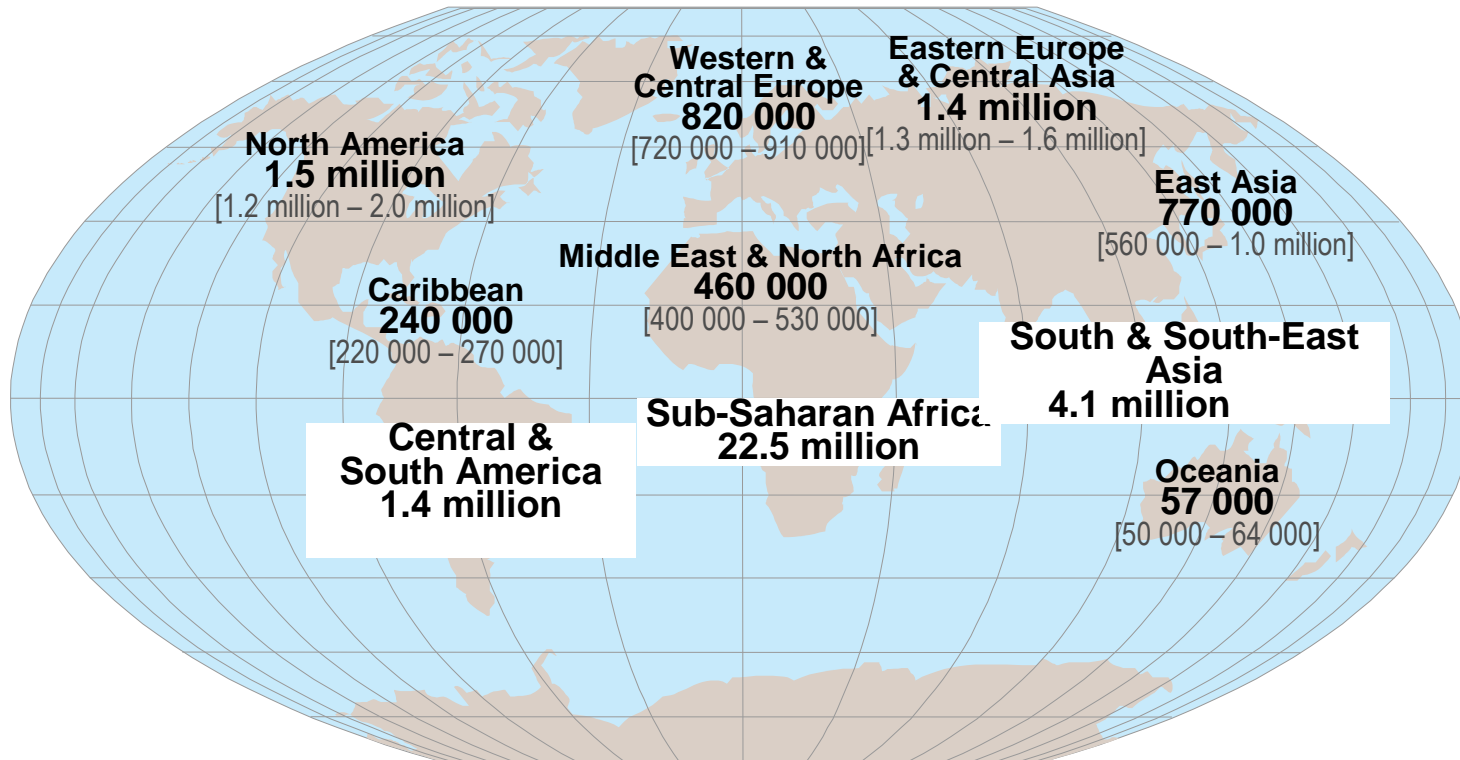
**COSA E' SUCCESSO?**

- **Epidemia mondiale**

**Nel 2010**

- **34 milioni di persone con infezione da HIV**
- **1.8 milioni sono morte per HIV/AIDS**
- **2.7 milioni di nuove infezioni**

# Adults and children estimated to be living with HIV | 2010



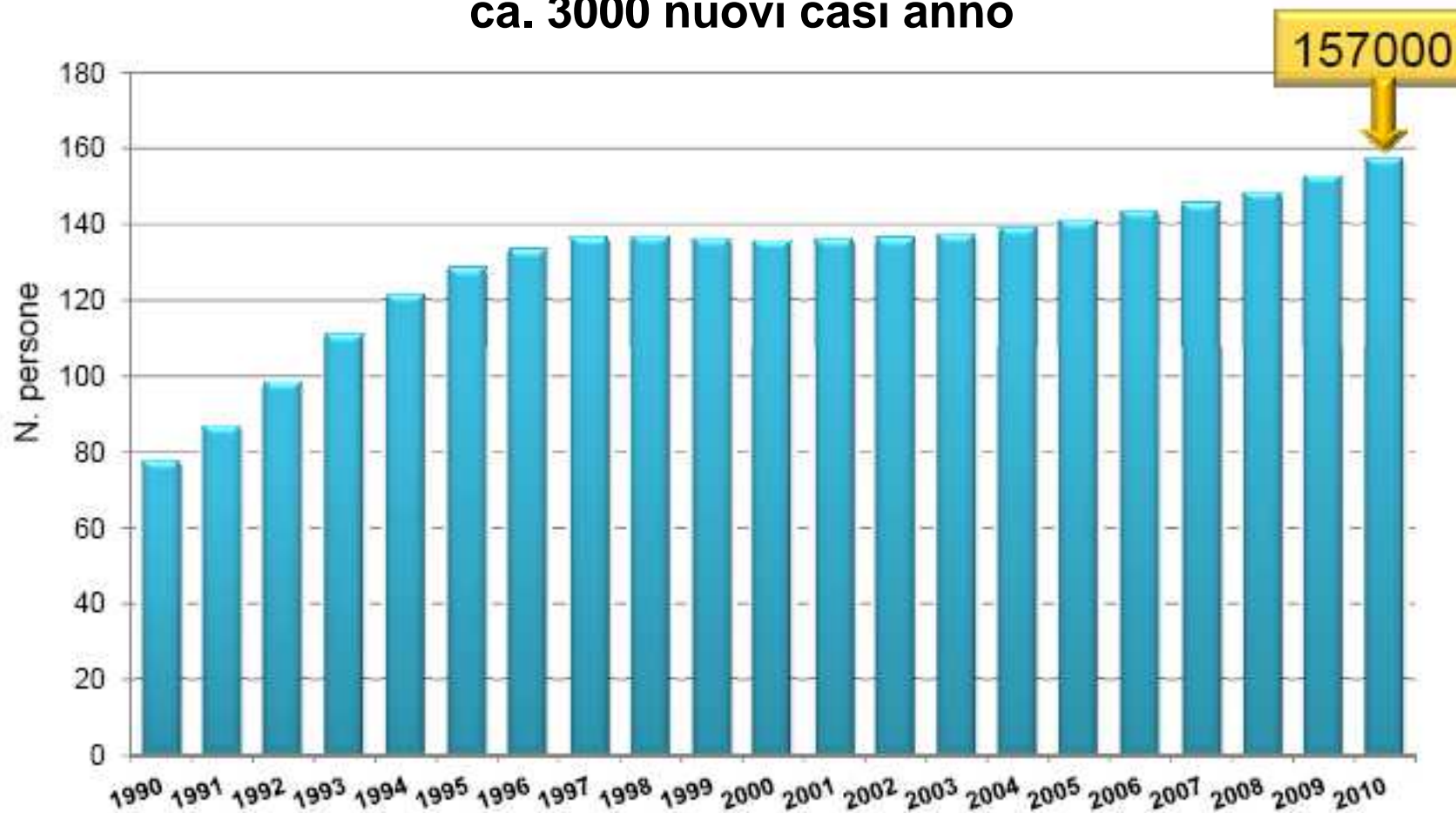
**Total: 34 million** [31.6 million – 35.2million]



# Stima del numero di persone viventi con HIV/AIDS in Italia, 1990-2010 (metodo UNAIDS)



**ca. 3000 nuovi casi anno**



# Farmaci antiretrovirali nel 2012

| NRTI               | NNRTI         | PI         | Entry                 |
|--------------------|---------------|------------|-----------------------|
| <b>Zidovudine</b>  | Nevirapine    | Saquinavir | ENF                   |
| Didanosine         | Delavirdine   | Ritonavir  |                       |
| Zalcitabine        | Efavirenz     | Indinavir  | <b>Inib.integrasi</b> |
| Stavudine          | Etravirina    | Nelfinavir | raltegravir           |
| Lamivudine         | Nevirapina RP | Amprenavir |                       |
| Abacavir           |               | Lopinavir  | <b>Inib.CCR5</b>      |
| Tenofovir          |               | Atazanavir | maraviroc             |
| Emtricitabine      |               | Fos-APV    |                       |
| <i>TDF/FTC</i>     |               | Tipranavir |                       |
| <i>ABC/3TC</i>     |               | Darunavir  |                       |
| <i>TDF/FTC/EFV</i> |               |            |                       |

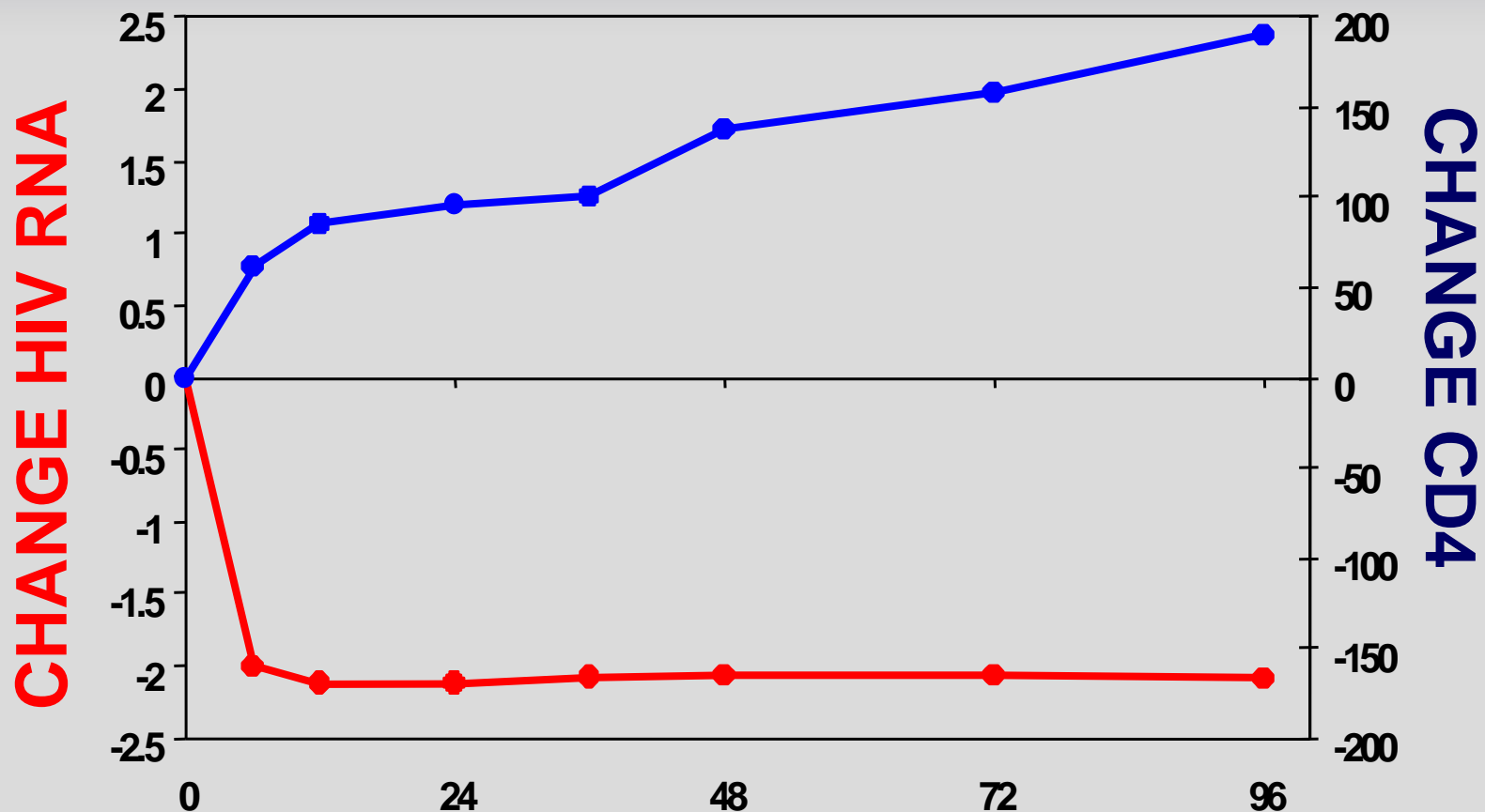
# Terapia antiretrovirale (HAART)

- **Costituita dalla associazione di 3 farmaci di almeno 2 classi diverse:**
- **2 NRTI + 1 NNRTI**
- **2 NRTI + 1 PI**

## Parametri di efficacia

- **Controllo replicazione virale :**  
**HIV RNA < 20 copie/ml**
- **Incremento linfociti CD4**

# SCOPE cohort (SF): incremento dei CD4 durante soppressione virale



*JID 2000; 181:946-53*

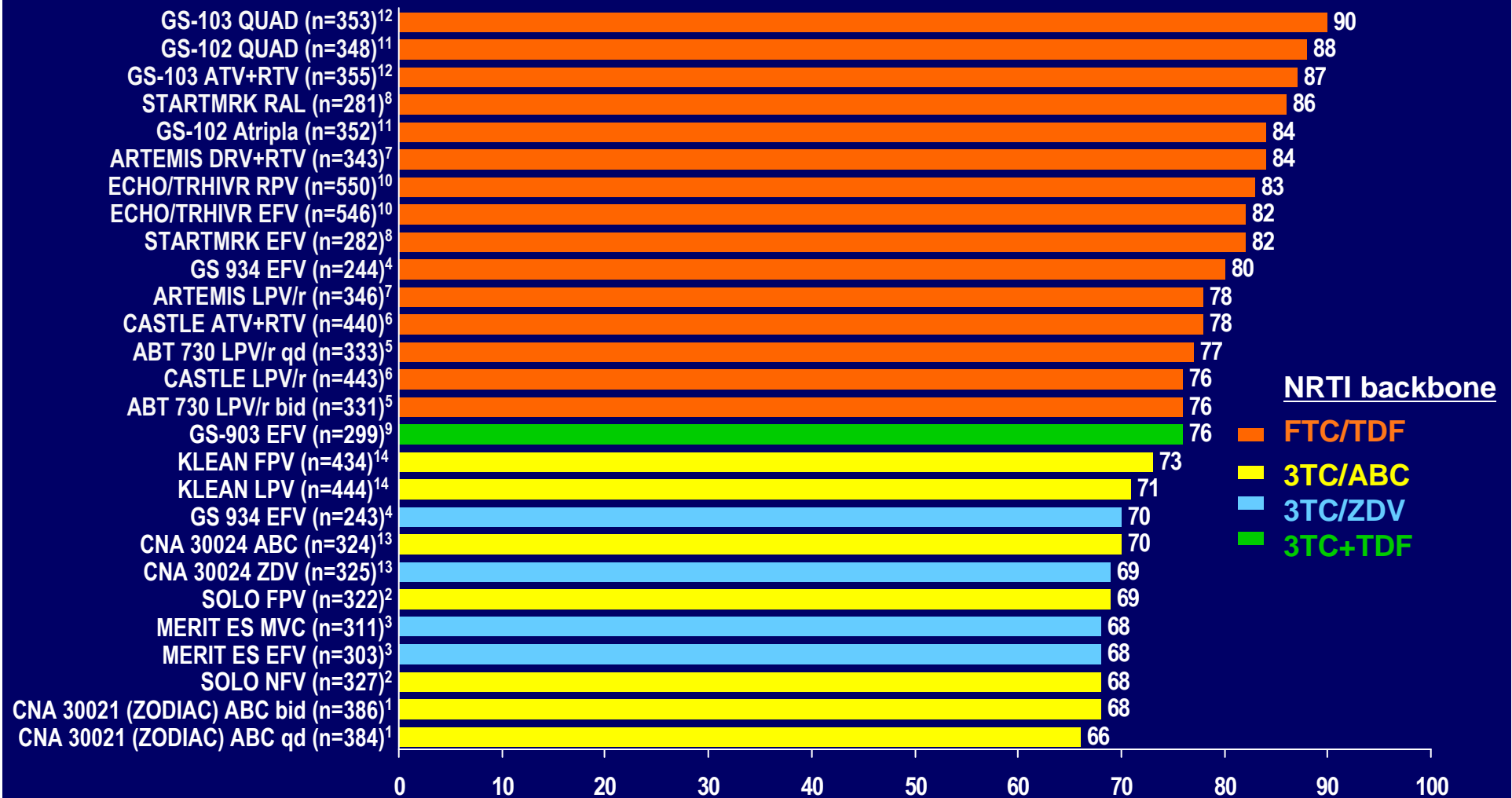
*AIDS 2003; 17(13):1907-1915*

# Background:



## Cross-Study Comparison of Registrational Treatment-Naive Clinical Trials

### HIV RNA <50 c/mL at Week 48



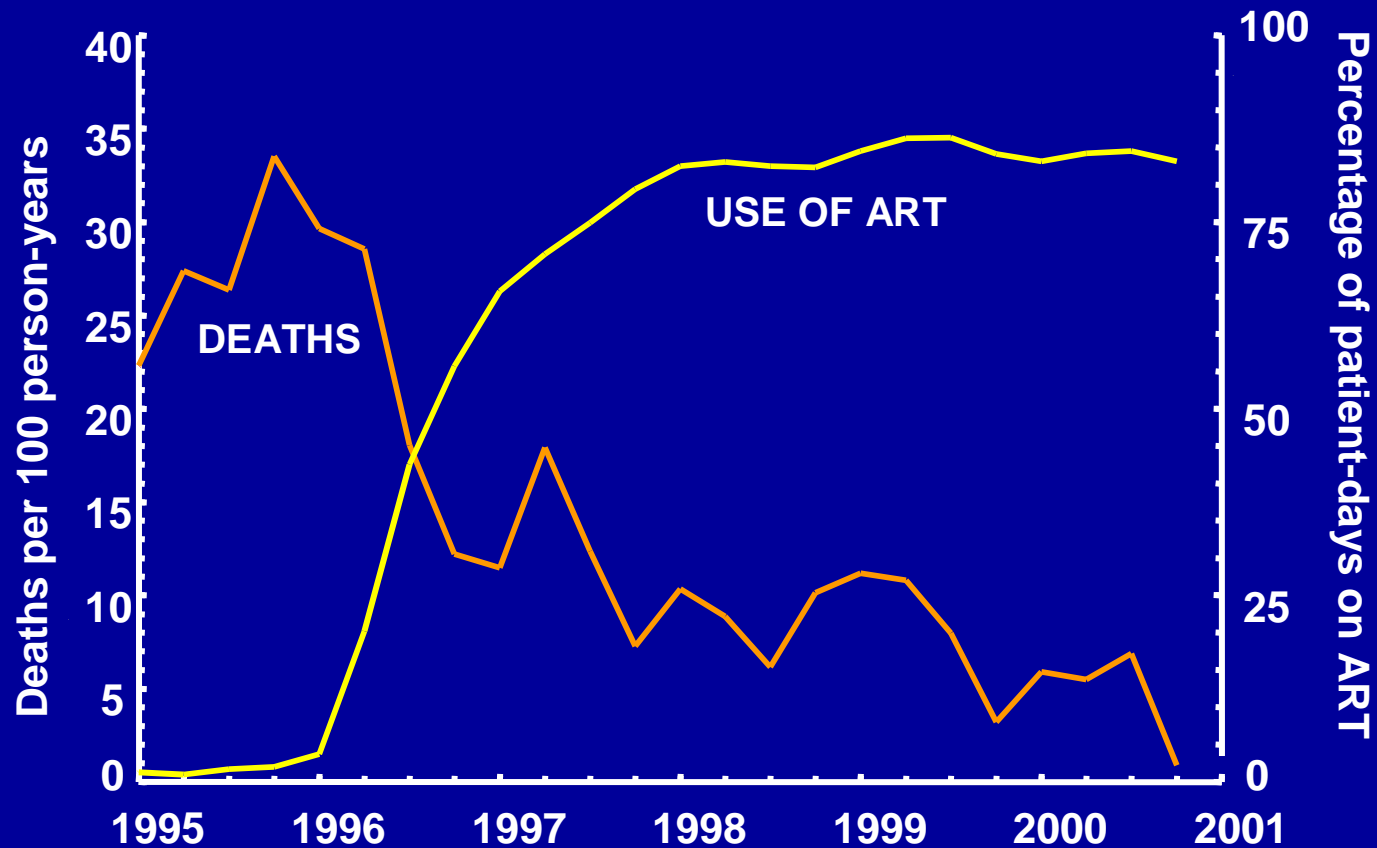
% of Patients with HIV-1 RNA <50 copies/mL at Week 48

This slide depicts data from multiple studies published from 2004-2012. Not all regimens have been compared head-to-head in a clinical trial

Internal Use Only

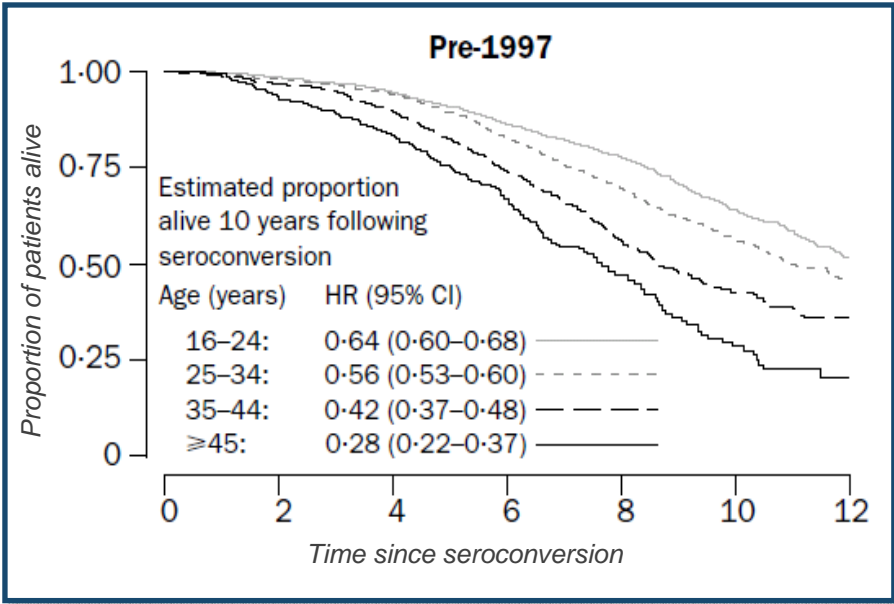
# AIDS Mortality Rates: 1996-2001

## Mortality vs. ART utilization

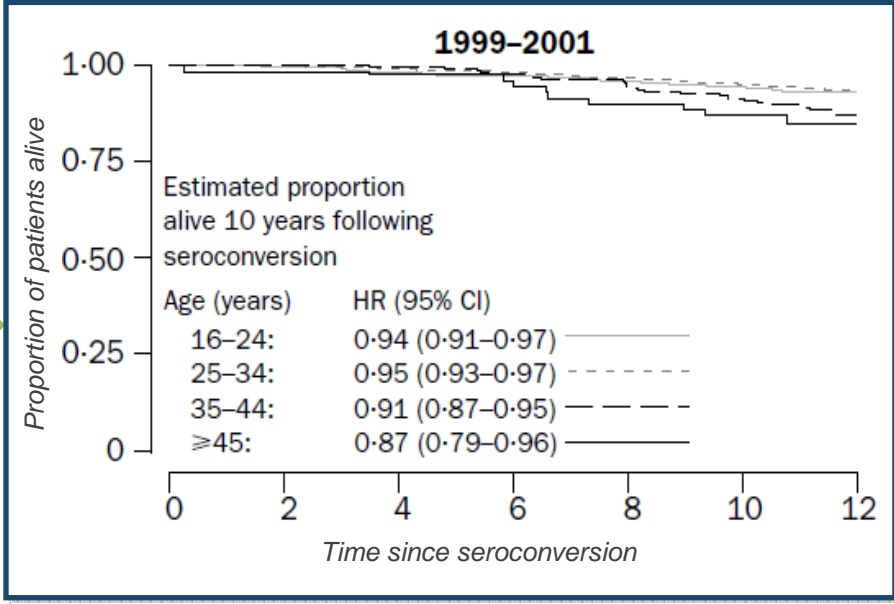


# La introduzione della HAART ha reso l' infezione da HIV una patologia cronica (Cascade collaboration)

## Pre-HAART



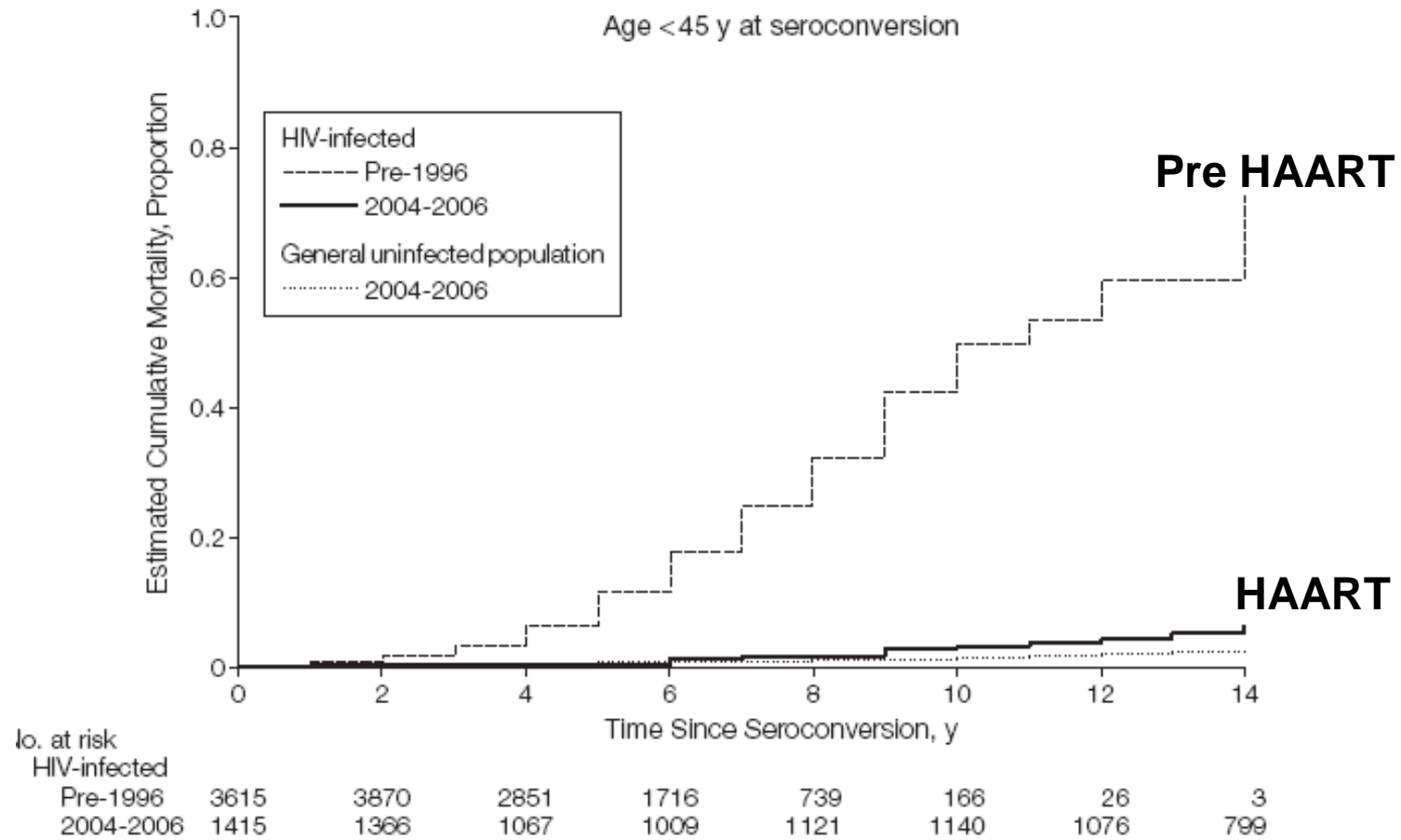
## HAART



Porter K, *Lancet* 2003; 362:1267-74

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

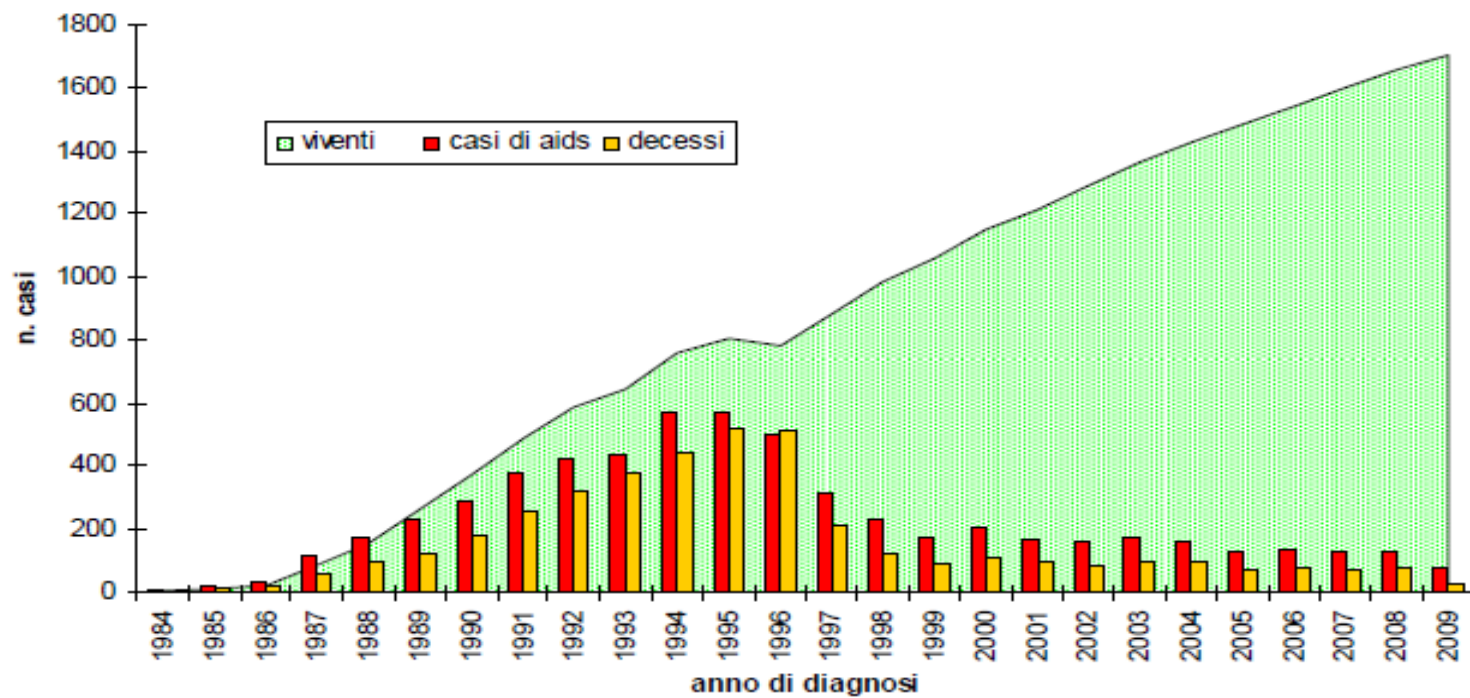
## Cascade collaboration





## Mortalità per AIDS

Figura 36 – Andamento epidemico di AIDS in Emilia-Romagna, 1984-2009. (valori assoluti)



Fonte: Sistema di Sorveglianza delle nuove diagnosi di infezioni da HIV - Regione Emilia-Romagna



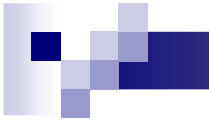
# Problemi attuali

- **Gestione clinica**
- **Gestione economica**
- **Controllo diffusione infezione**



# **Gestione clinica**

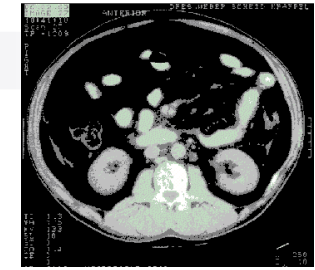
- **Patologia cronica**
- **Comorbidità non infettive**
- **Invecchiamento precoce**



Glucose metabolism impairment



Dyslipidaemia



Abnormalities of body composition



# Comorbidità HIV correlate non infettive

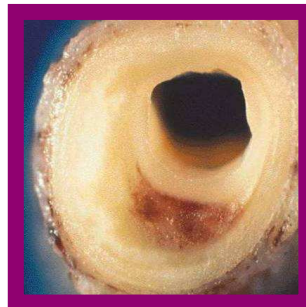
- Ruolo della HAART
- Ruolo di HIV



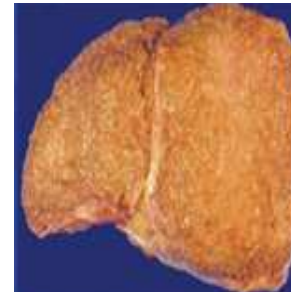
Body image alterations



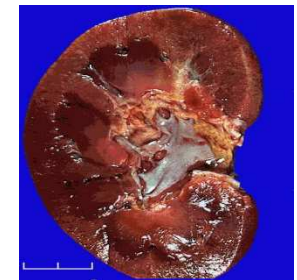
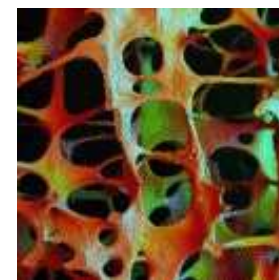
HAND



CVD



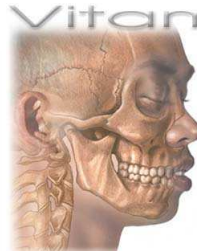
Hepatic steatosis Bone & Kidney disease



Depression



HT



Vit D

**Vitamin D**  
Vitamin D promotes the body's absorption of calcium, essential to development of healthy bones and teeth  
DRI: 5 µg  
Fat-soluble  
©ADAM.



T2D



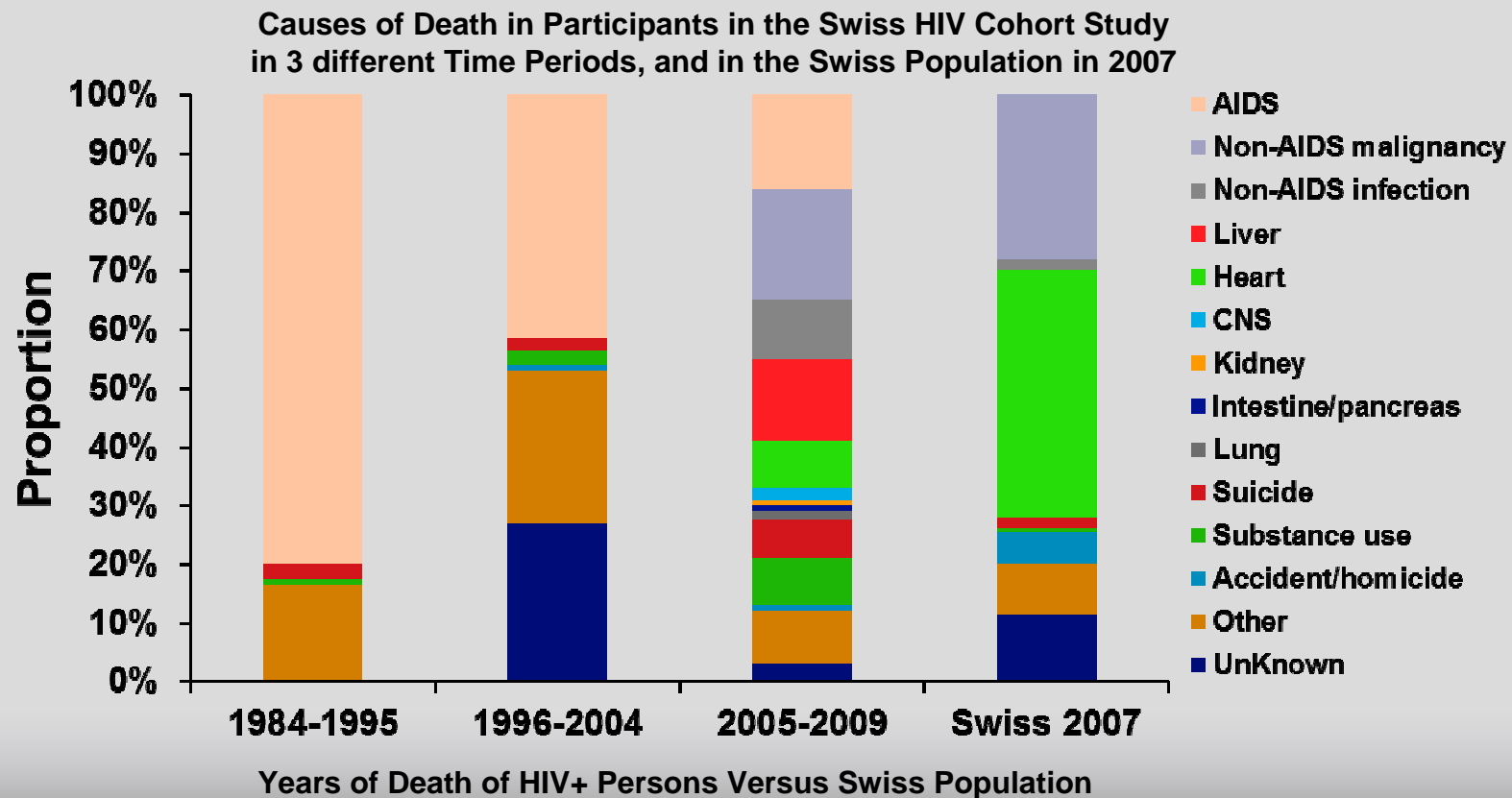
Cancer



Sexual Dysfunction

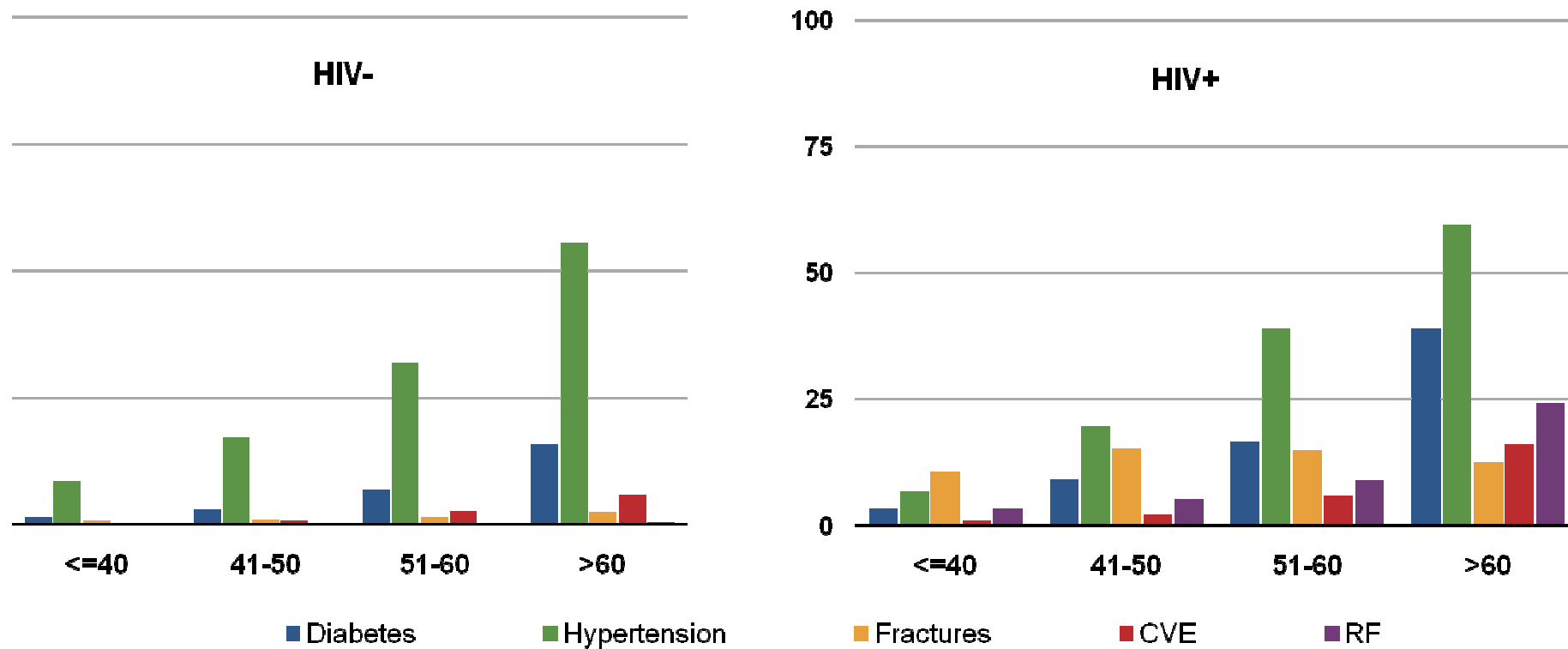
# Changing Patterns of the Causes of Death in a Swiss Cohort (SHCS)

- SHCS is a prospective observational cohort
- Characteristics of participants that died from 2005-2009
- 459 deaths/9,053 participants (5.1%)



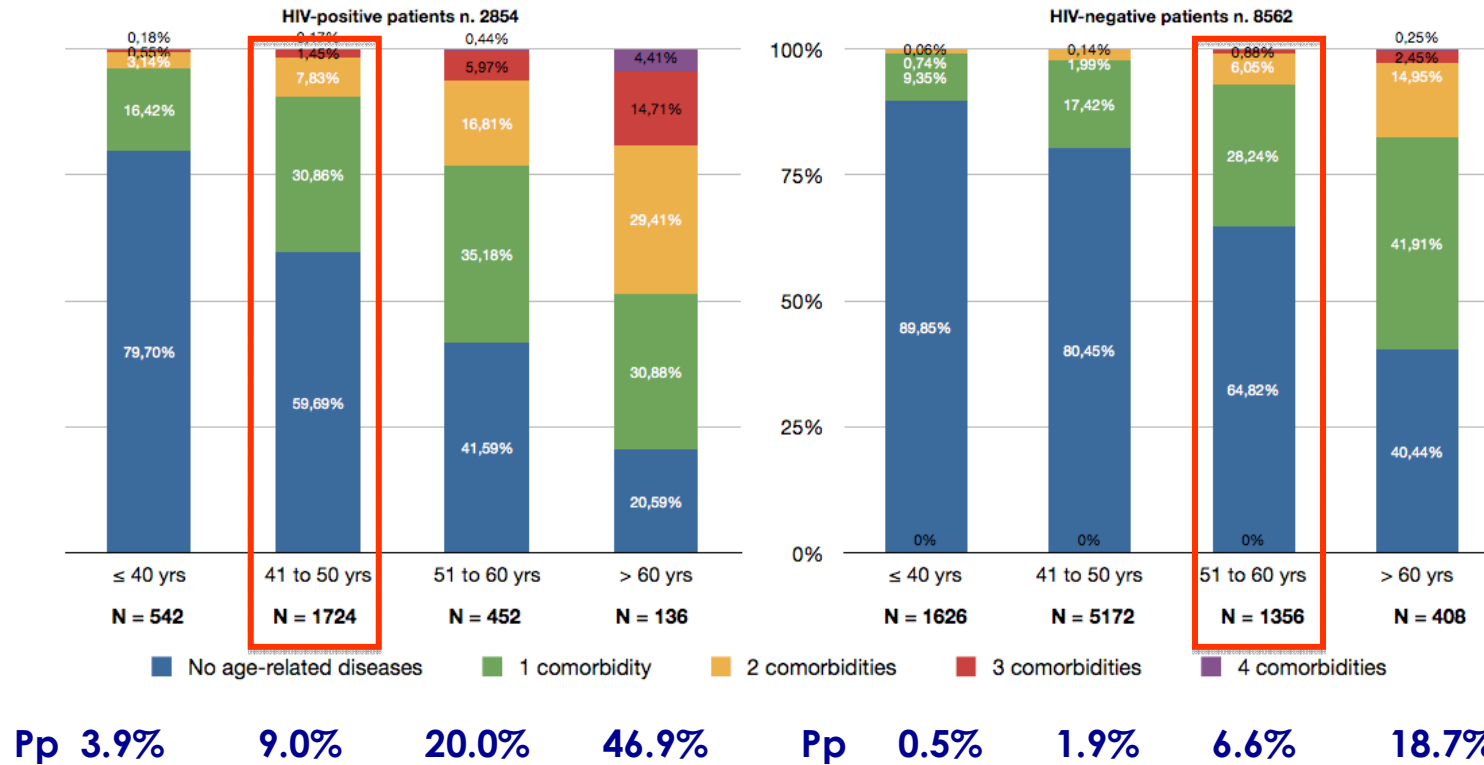
## Result

### Probability of Non Infectious Co-Morbidities (NICM)



*G.Guaraldi 2011 modificato*

## Poly-pathology prevalence in cases and controls, stratified by age categories



Pp prevalence was higher in cases than controls in all age strata (all p-values <0.001)  
Pp prevalence seen cases aged 41-50 was similar to that observed among controls aged 51-60 controls (p=0.282)



# **Gestione economica**

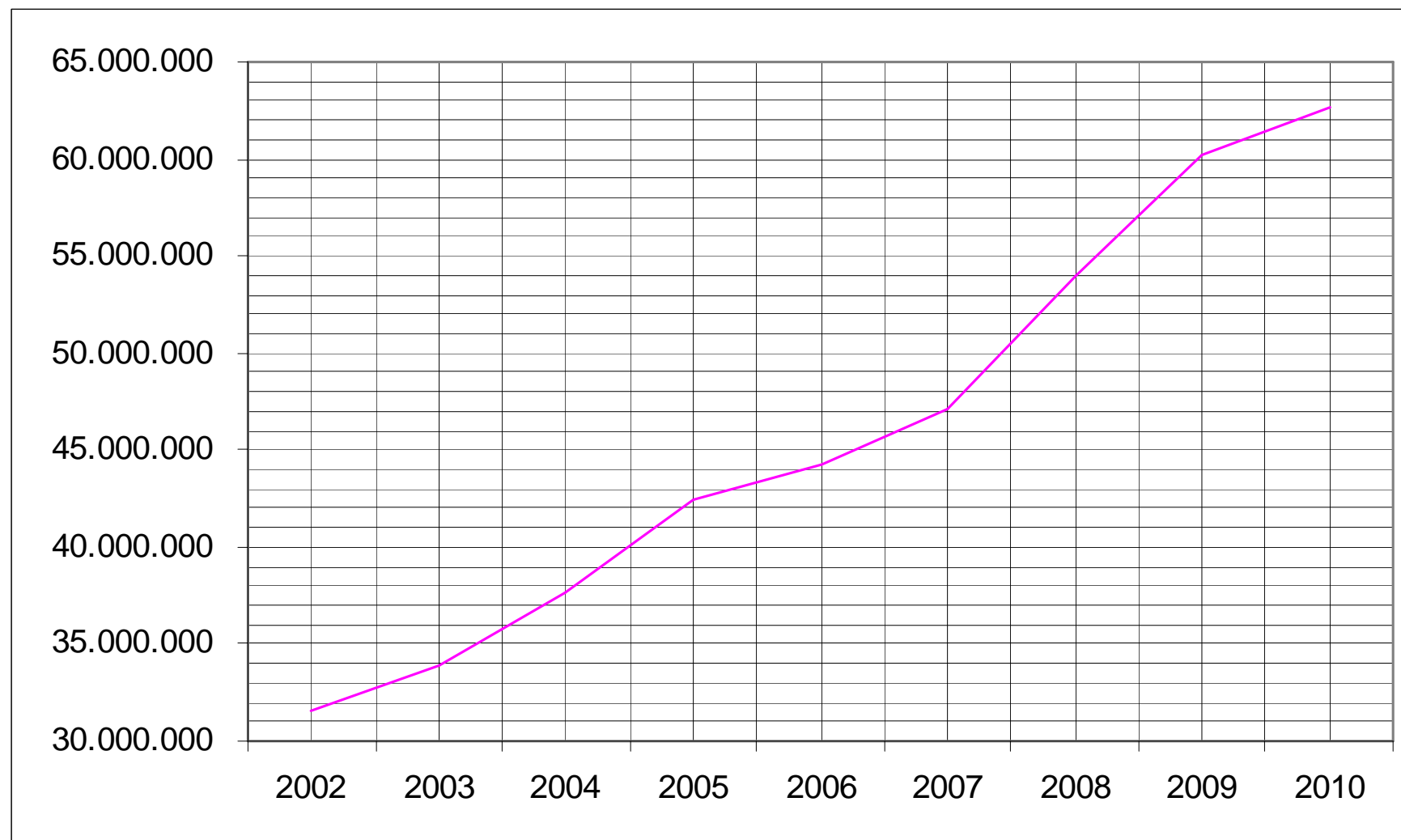
- **Utilizzo delle risorse assistenziali**
- **Terapia cronica**
- **Terapie ad alto costo**



# Gestione economica

- **Utilizzo delle risorse assistenziali**
- **Pre HAART**
  - 70% ricoveri ospedalieri**
  - 10% farmaci
  - 20% assistenza extra-ospedaliera
- **HAART**
  - 40% farmaci**
  - 35% ricoveri ospedalieri
  - 25% ambulatoriale

## Andamento della spesa per farmaci HIV nella Regione Emilia Romagna (anni 2002-2010)

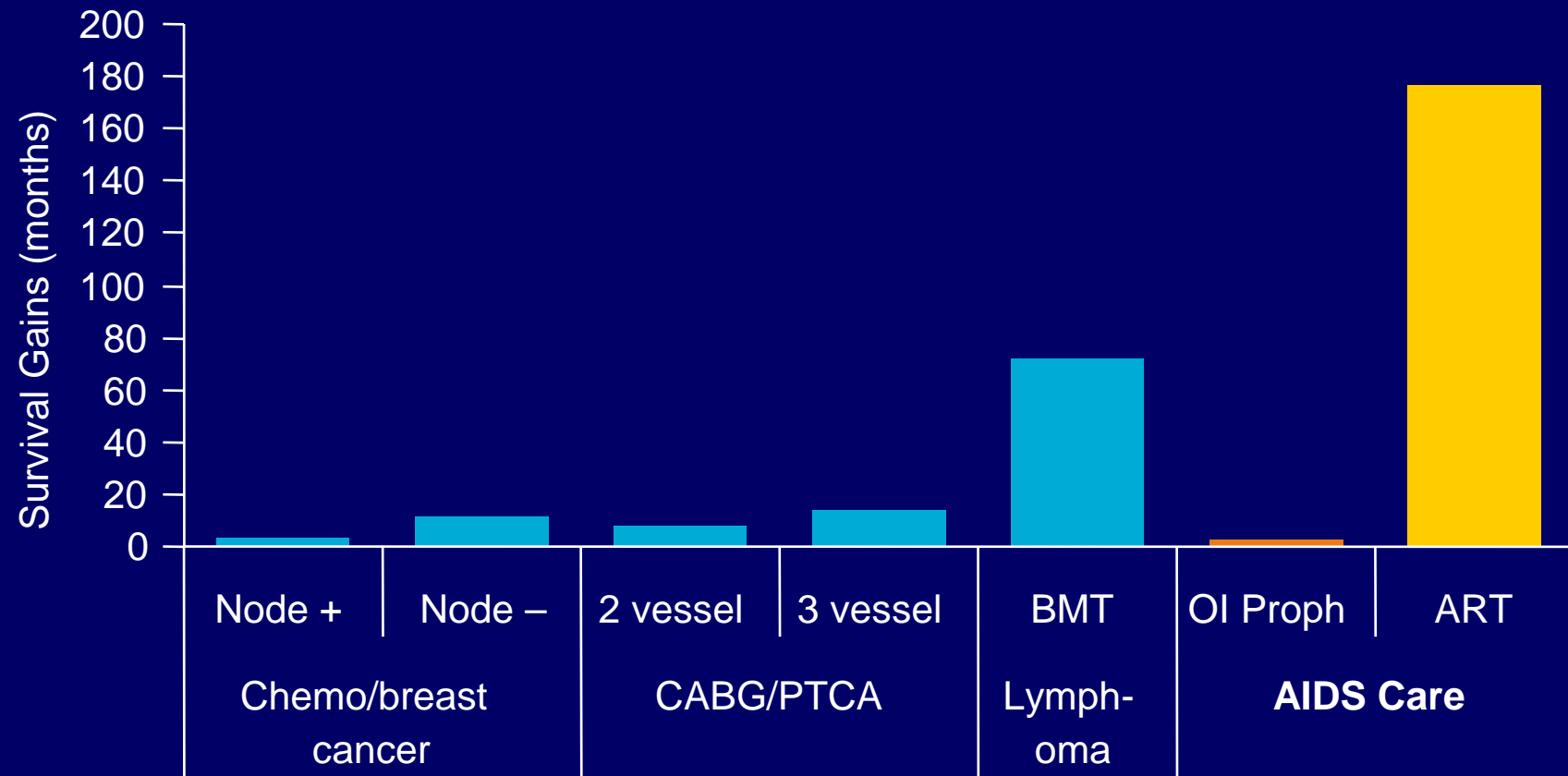


**Stima spesa per paziente trattato in regione Emilia Romagna**

**RER - ANNO 2010 vs anno 2009**

|   |                          |
|---|--------------------------|
| <b>Totale spesa ospedaliera + convenzionata per farmaci HIV anno 2010</b> | <b>62.731.789 (+10%)</b> |
| N° casi trattati anno 2010 presso i Centri RER                            | <b>8.488 (+6%)</b>       |
| Stima di spesa per paziente   | <b>7.391 (4%)</b>        |

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







## **Controllo diffusione infezione**

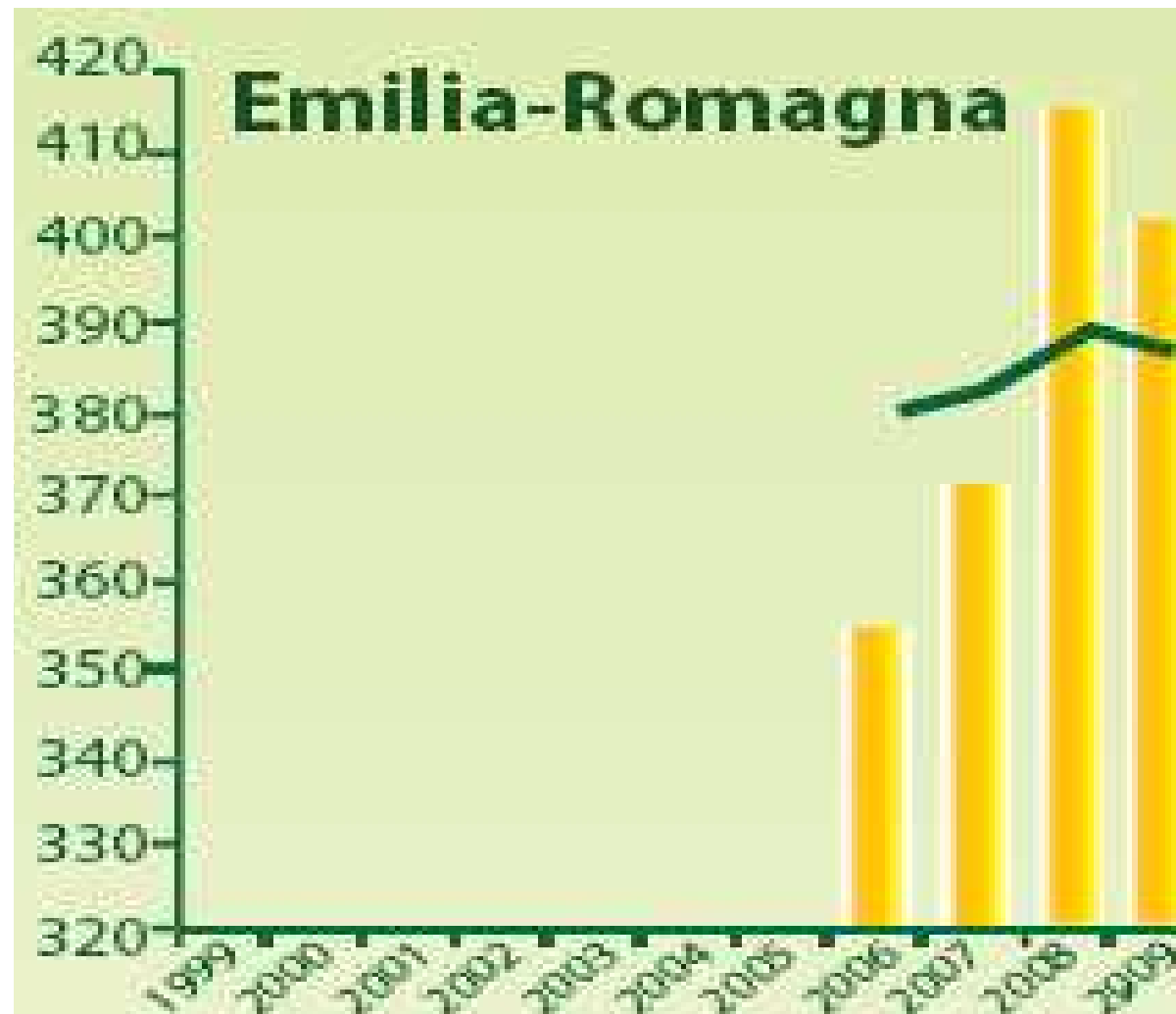
- **Nuove infezioni**  
**Italia: 3000/anno**  
**Regione Emilia Romagna : 400/anno**
- **Ritardo di diagnosi**

# NUOVE INFEZIONI

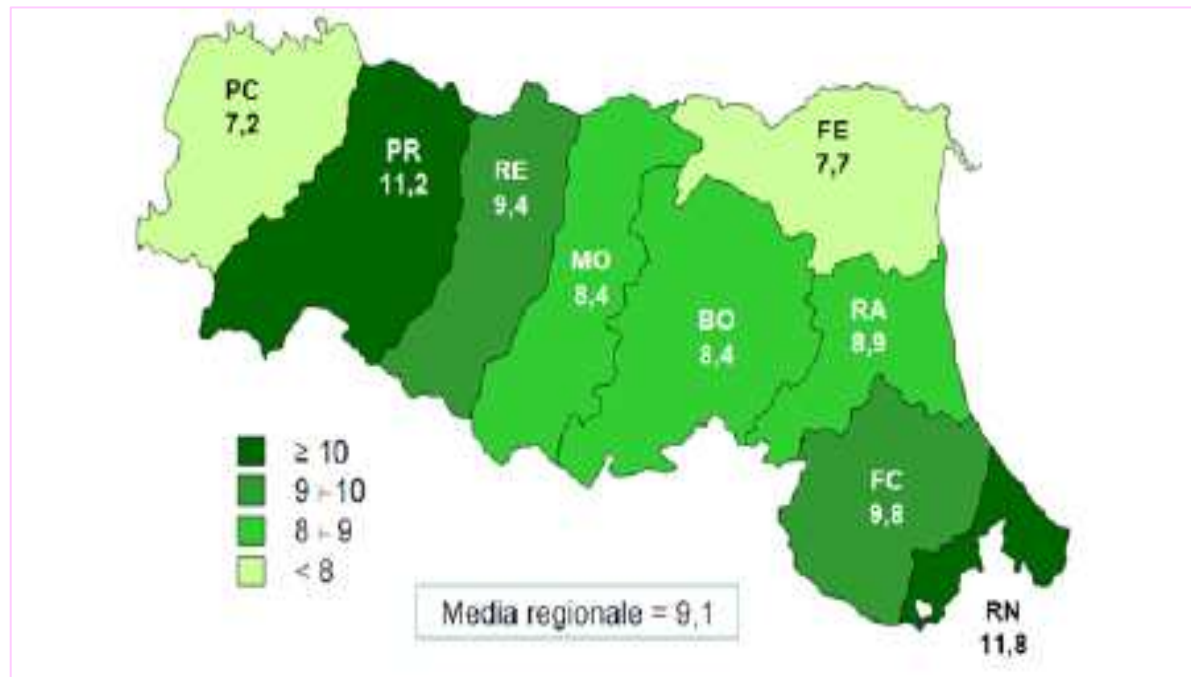
**2198 nuove  
diagnosi**  
2006-2010



11,6% non residenti:  
-Stranieri 44,3%  
-Italiani (Sicilia, Lombardia,  
Puglia, Marche Veneto)



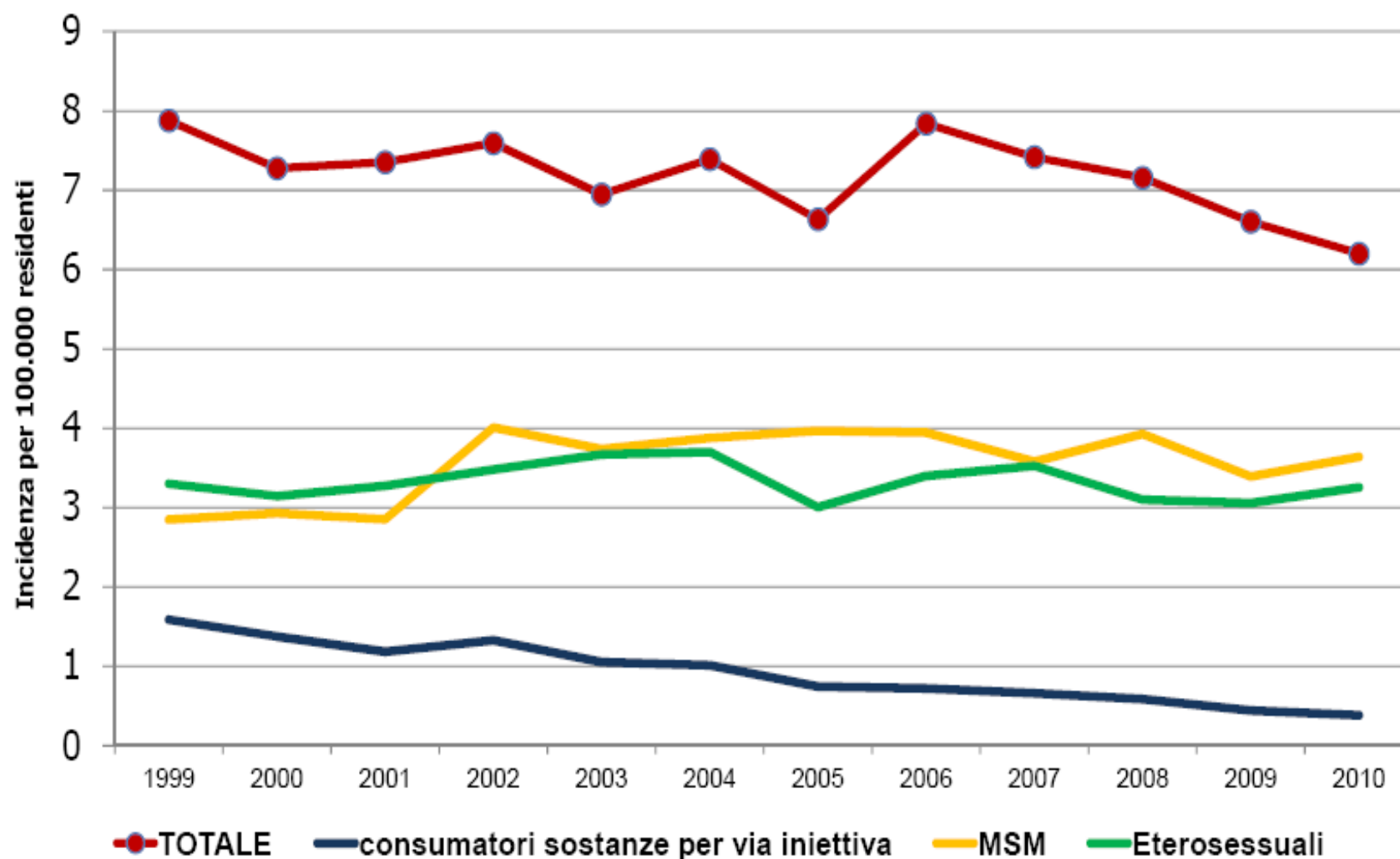
# ***NUOVE INFEZIONI***



**Incidenza  
media nuove  
diagnosi  
2006-2010**

# Incidenza delle nuove diagnosi di infezione da HIV in Italia, per modalità di esposizione, 1999-2010

(Piemonte, Veneto, Friuli Venezia-Giulia, Modena, Trento, Bolzano, Lazio)\*





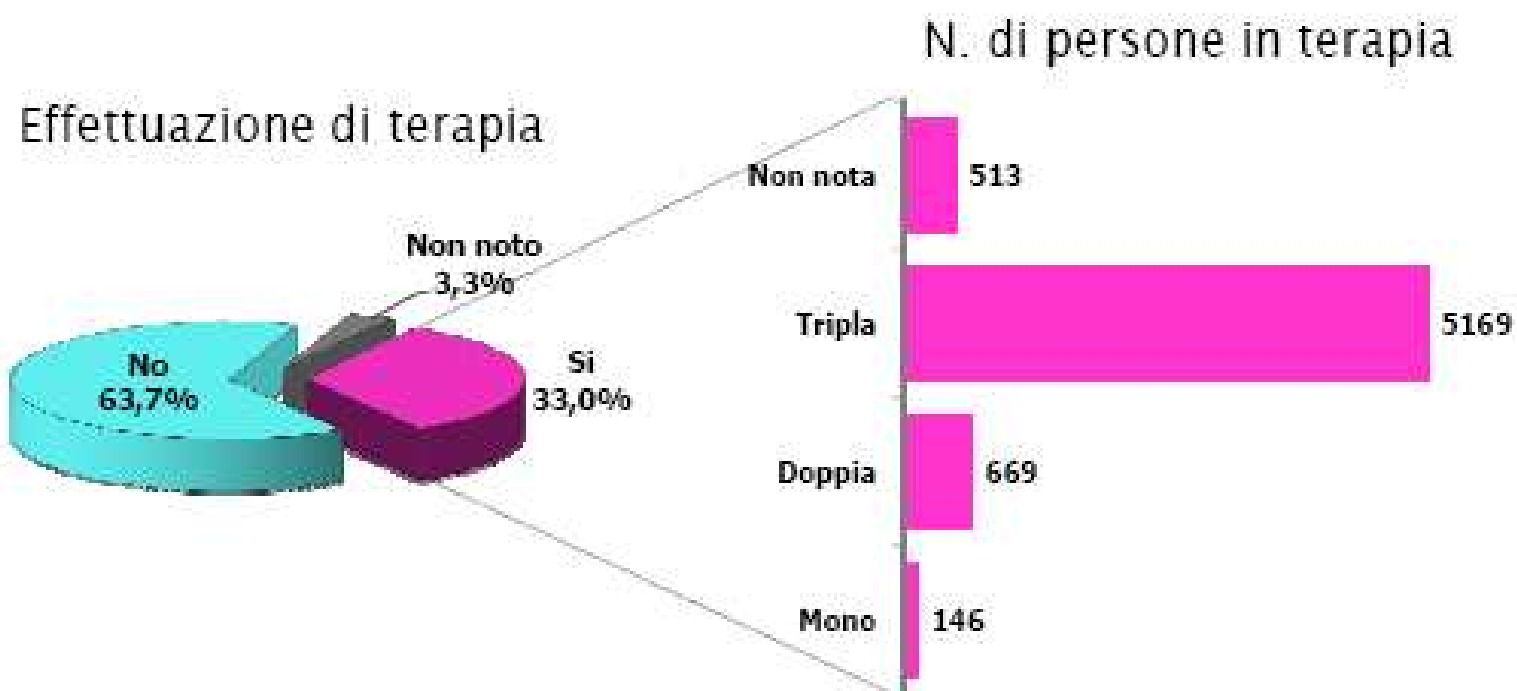
# Problemi attuali

---

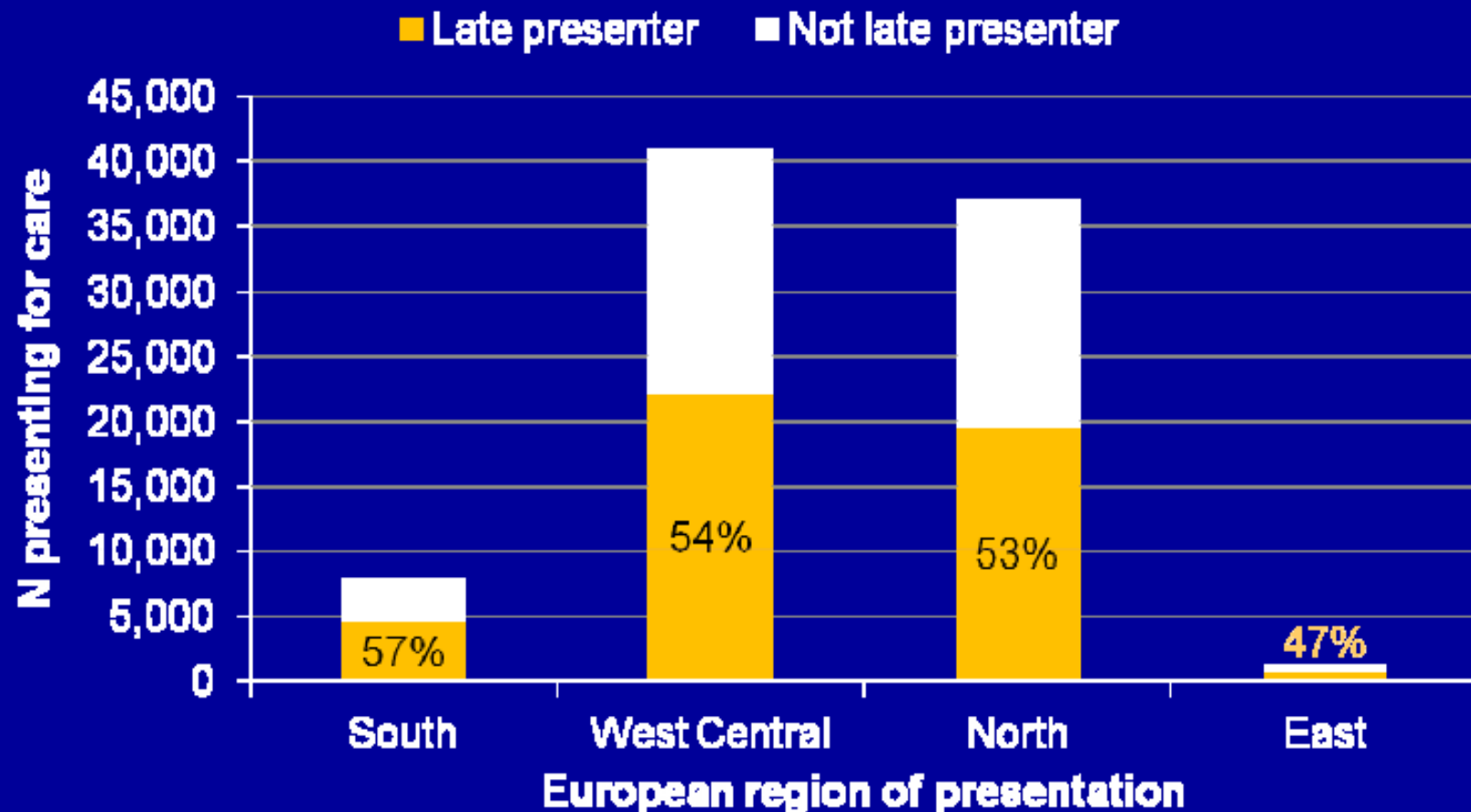
- Nuove infezioni
- **Ritardo di diagnosi**

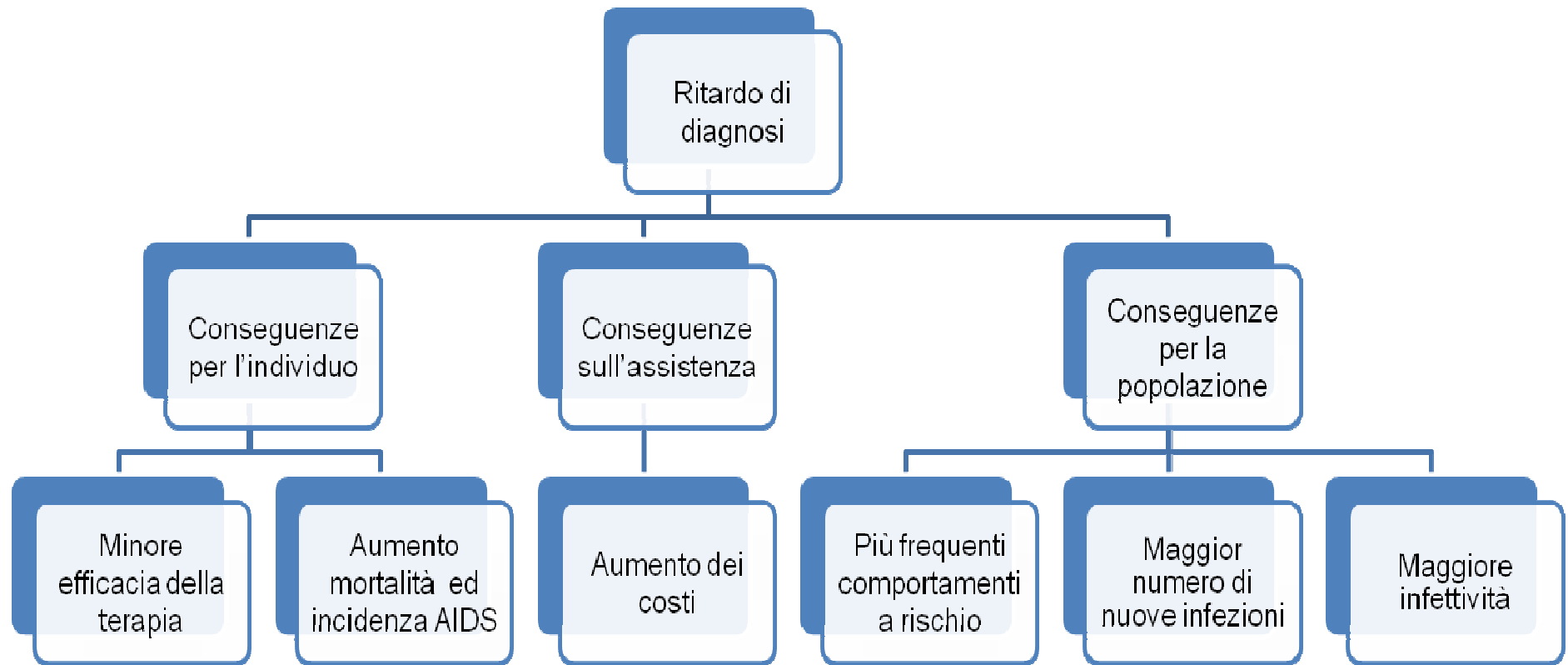


## Uso di terapie antiretrovirali e regime terapeutico pre-AIDS in Italia, 1996-2011



## Total individuals presenting for care by European region of presentation







## Fattori favorevoli il ritardo di diagnosi

### Paziente

- Scarsa percezione del rischio
- Negazione
- Paura dello stigma e della discriminazione
- Difficoltà ad accedere ai servizi

### Medico

- Scarsa percezione del rischio
- Difficoltà nel rapporto medico-paziente
- Difficoltà nella discussione di rischi comportamentali



## **COSA FARE ?**

- Prevenzione dei comportamenti a rischio**
  
- Favorire l'accesso al test**
  - Test a tutti?**
  - Test a tutti i ricoverati?**



**HIV in Europe**

Working Together for Optimal  
Testing and Earlier Care

Copenhagen 2012 Conference

# Indicator conditions

1. AIDS-defining conditions (ADC)
2. Conditions associated with increased HIV prevalence (>0.1%)
3. Conditions where failure to diagnose HIV infection may have severe consequences for person's health



## 1. AIDS-defining conditions (ADC)

- Opportunistic infections
  - Fungal
    - E.g. *Pneumocystis jiroveci*, cryptococcosis, histoplasmosis, candidiasis (oesophageal, tracheal, pulmonary)
  - Bacterial
    - E.g. Tuberculosis (TB), disseminated *Mycobacterium avium*, recurrent pneumonia or salmonella septicaemia
  - Parasitic
    - E.g. cerebral toxoplasmosis, cryptosporidiosis, microsporidiosis
  - Viral
    - E.g. CMV retinitis, PML, persistent HSV
- Neoplasms
  - Non-Hodgkin's lymphoma, Kaposi's sarcoma, cervical carcinoma

## 2a Strongly recommend testing (HIV prevalence >0.1%)



**HIV in Europe**

Working Together for Optimal  
Testing and Earlier Care

Copenhagen 2012 Conference

- Sexually transmitted infections (4.06%)<sup>1</sup>
- Lymphoma (0.29%)<sup>1</sup>
- Anal cancer/dysplasia (2.90%)<sup>1</sup>
- Cervical/anal dysplasia (0.37%)<sup>1</sup>
- Herpes zoster (2.89%)<sup>1</sup>
- Hepatitis B or C (0.36%)<sup>1</sup>
- Mononucleosis-like illness (3.85%)<sup>1</sup>
- Unexplained leucopaenia or thrombocytopaenia, >4 weeks (3.19%)<sup>1</sup>
- Seborrhic dermatitis or exanthema (2.06%)<sup>1</sup>
- Unexplained oral candidiasis (6-23%)
- Invasive pneumococcal disease (2.4%)
- Unexplained chronic fever (3%)
- Unexplained chronic diarrhoea (10-12%)
- Pregnancy (0.17%)<sup>2</sup>

1. HIDES, EACS Belgrade 2011.
2. National Antenatal Infections Screening Monitoring. HPA.



**HIV in Europe**

Working Together for Optimal  
Testing and Earlier Care

Copenhagen 2012 Conference

### **3. Conditions where failure to diagnose HIV infection may have severe consequences for person's health**

- Prior to initiating aggressive immuno-suppressive therapy
  - Malignancy
  - Transplantation
  - Auto-immune disease
- Primary space occupying lesion of the brain

**HIV trent'anni dopo**

***“Far emergere il sommerso”***



***Grazie per l'attenzione***