



United Nations
Educational, Scientific and
Cultural Organization



UNESCO Chair on Training and Empowering
Human Resources for Health Development
in Resource-Limited Countries
University of Brescia



L'infezione da HIV a 30 (37 per la precisione...) anni dalla prima diagnosi: dalle categorie a rischio ai comportamenti a rischio

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Le Malattie Trasmesse Sessualmente: non solo HIV

**Mercoledì 30 maggio 2018
8.30 - 13.15**

Sala di Rappresentanza ATS di Brescia
Viale Duca degli Abruzzi 15 Brescia

CDC
CENTERS FOR DISEASE CONTROL
AND PREVENTION

MMWRTM

MORBIDITY AND MORTALITY WEEKLY REPORT

June 5, 1981 / Vol. 30 / No. 21

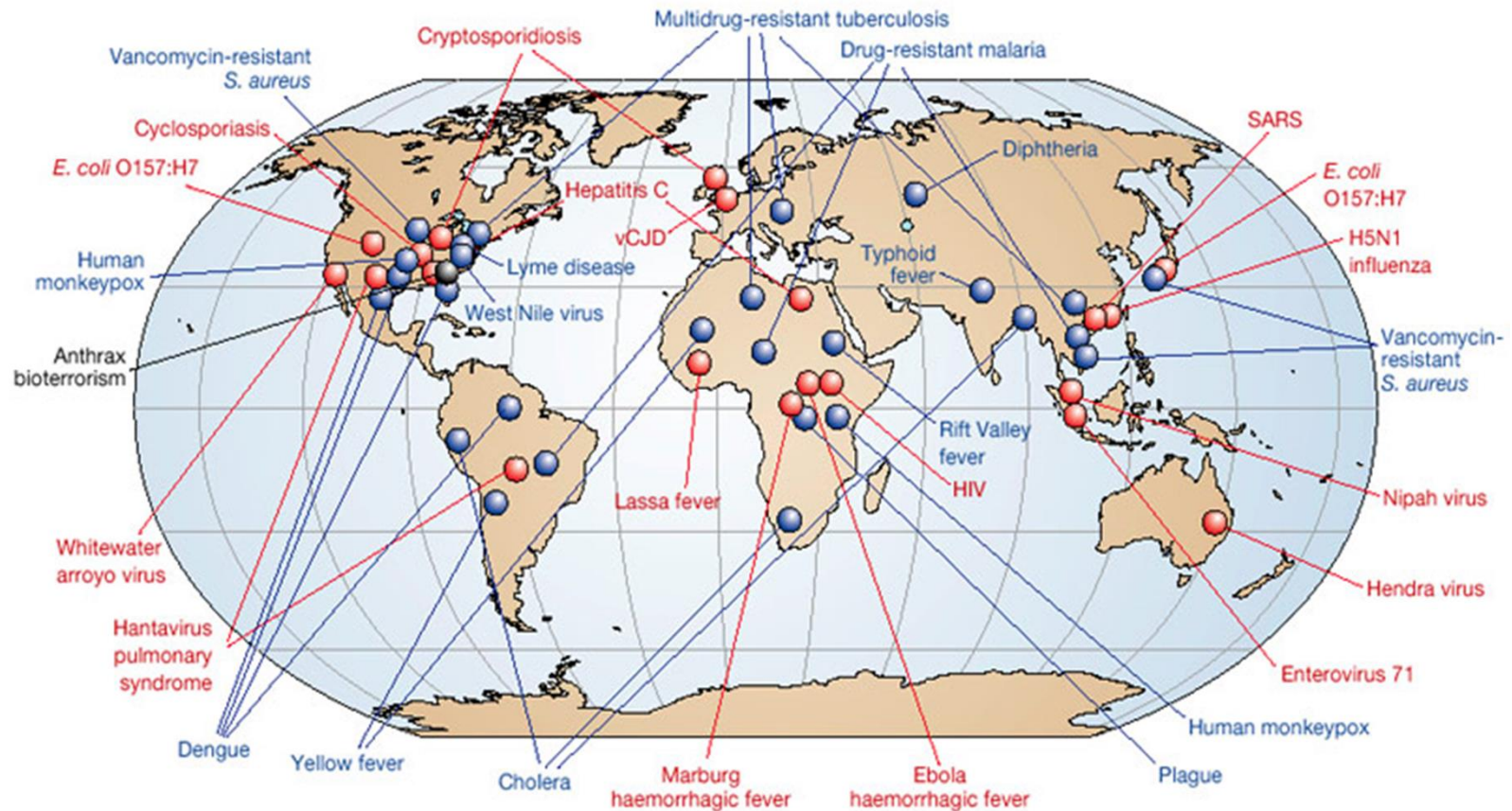
- 249 Dengue Type 4 Infections in U.S. Travelers to the Caribbean
- 250 *Pneumocystis* Pneumonia — Los Angeles
- 252 Measles — United States, Five Weeks
- 253 Risk-Factor-Prevalence Survey
- 259 Surveillance of Childhood Lead Poisoning — United States
- 261 Quarantine Measures

Pneumocystis Pneumonia — Los Angeles

In the period October 1980–May 1981, 5 young men, all active homosexuals treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal infection. Case reports of these patients follow.

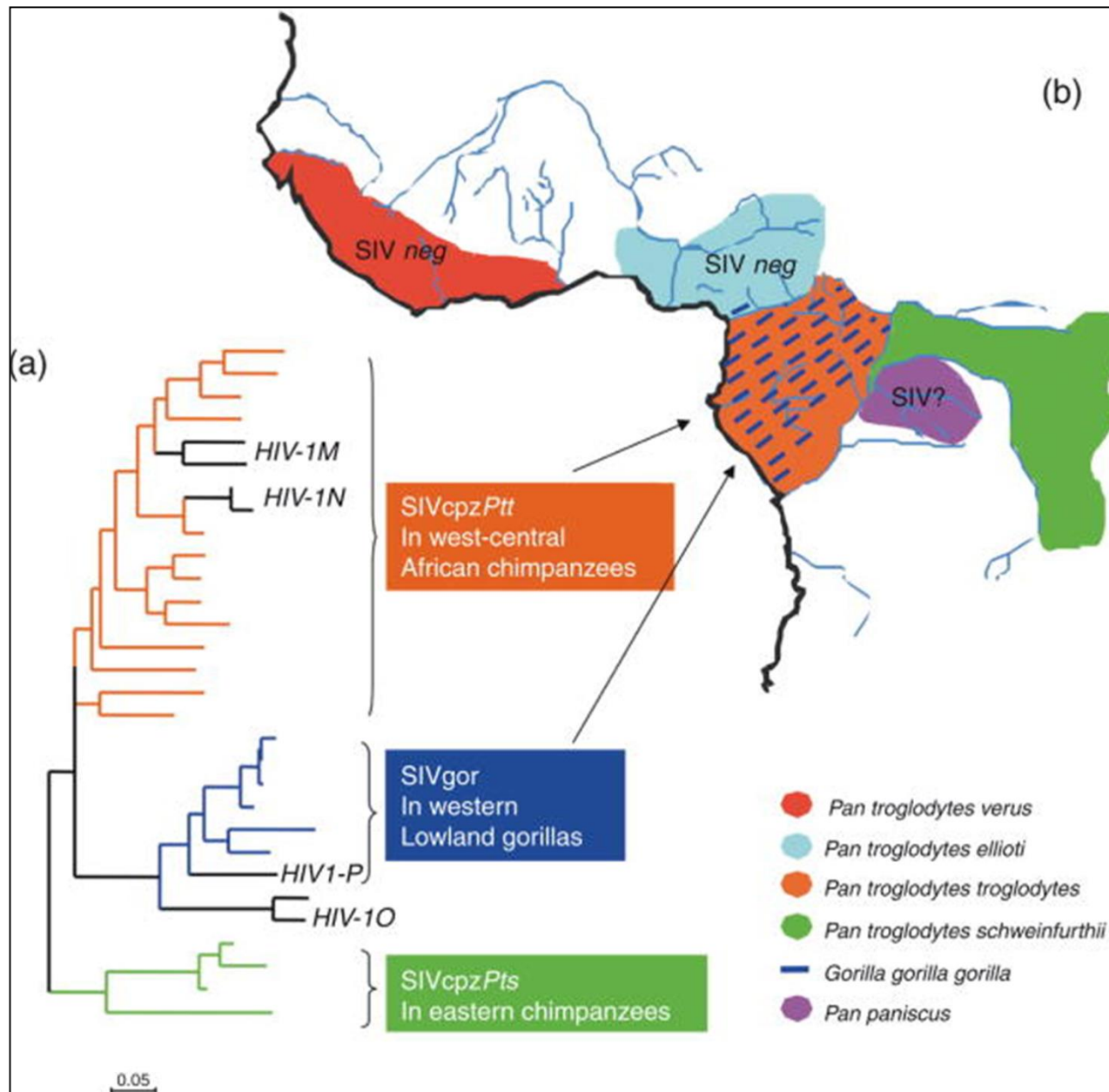
Patient 1: A previously healthy 33-year-old man developed *P. carinii* pneumonia with oral mucosal candidiasis in March 1981 after a 2-month history of fever associated with elevated liver enzymes, leukopenia, and CMV viremia. The serum complement-fixing CMV titer in October 1980 was 256; in May 1981 it was 32. The patient's condition deteriorated despite courses of treatment with trimethoprim-sulfamethoxazole, pyrimethamine, and acyclovir. He died May 3, and postmortem examination confirmed *P. carinii* pneumonia, but no evidence of neoplasia.

Examples of recent emerging diseases

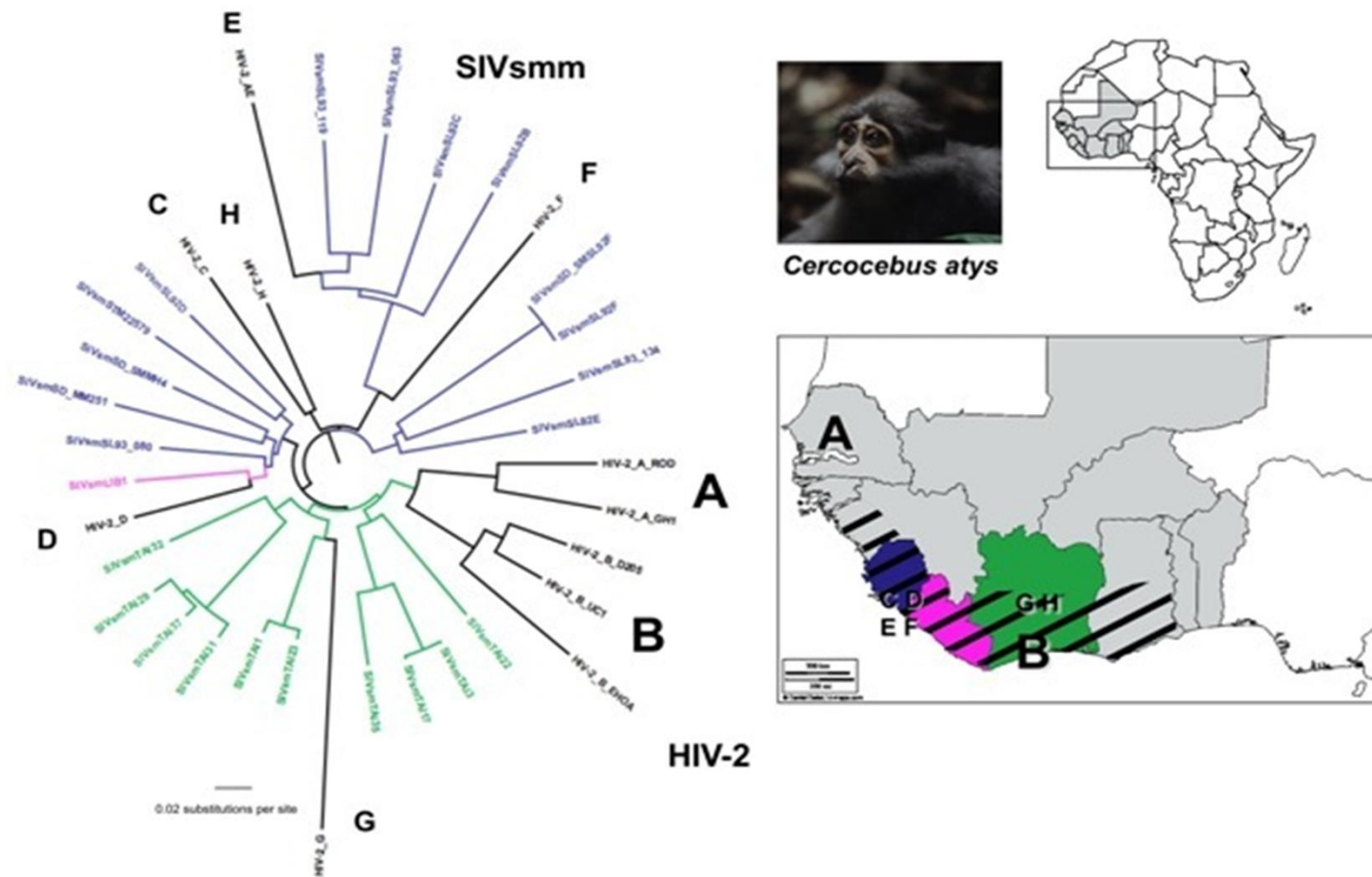


NATURE; Vol 430; July 2004; www.nature.com/nature

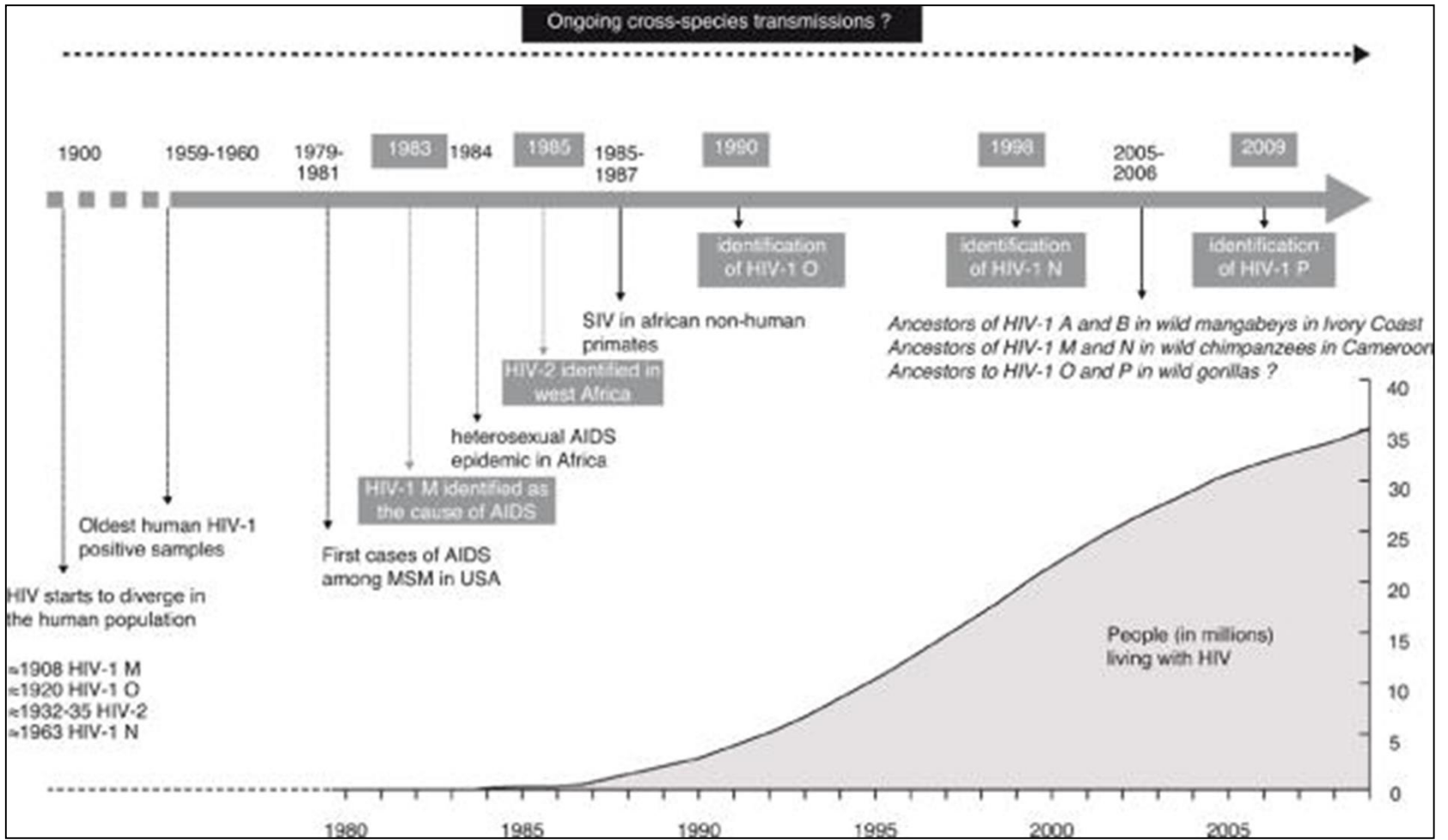
Simian immunodeficiency viruses (SIVs) from chimpanzees and gorillas from west central Africa have crossed the species barrier on at least four occasions, leading to HIV-1 group M, N, O and P in humans



Locatelli, Peeters.
AIDS 2012.



HIV-2 is derived from SIVs circulating in sooty mangabeys from West Central Africa. Evolutionary relationship of HIV-2 groups A to H (black) and SIVsmm (blue, green, and pink according to the country of origin) using the neighbor-joining method on partial env (741 bp) sequences



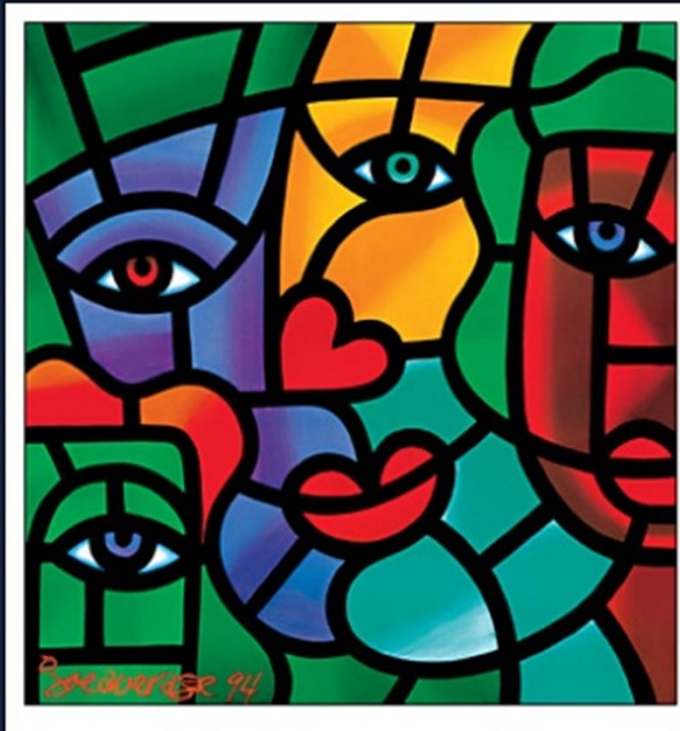
Cross-species transmission of simian retroviruses: how and why they could lead to the emergence of new diseases in the human population.

Locatelli, Peeters. AIDS. 26(6):659-673, March 27, 2012.

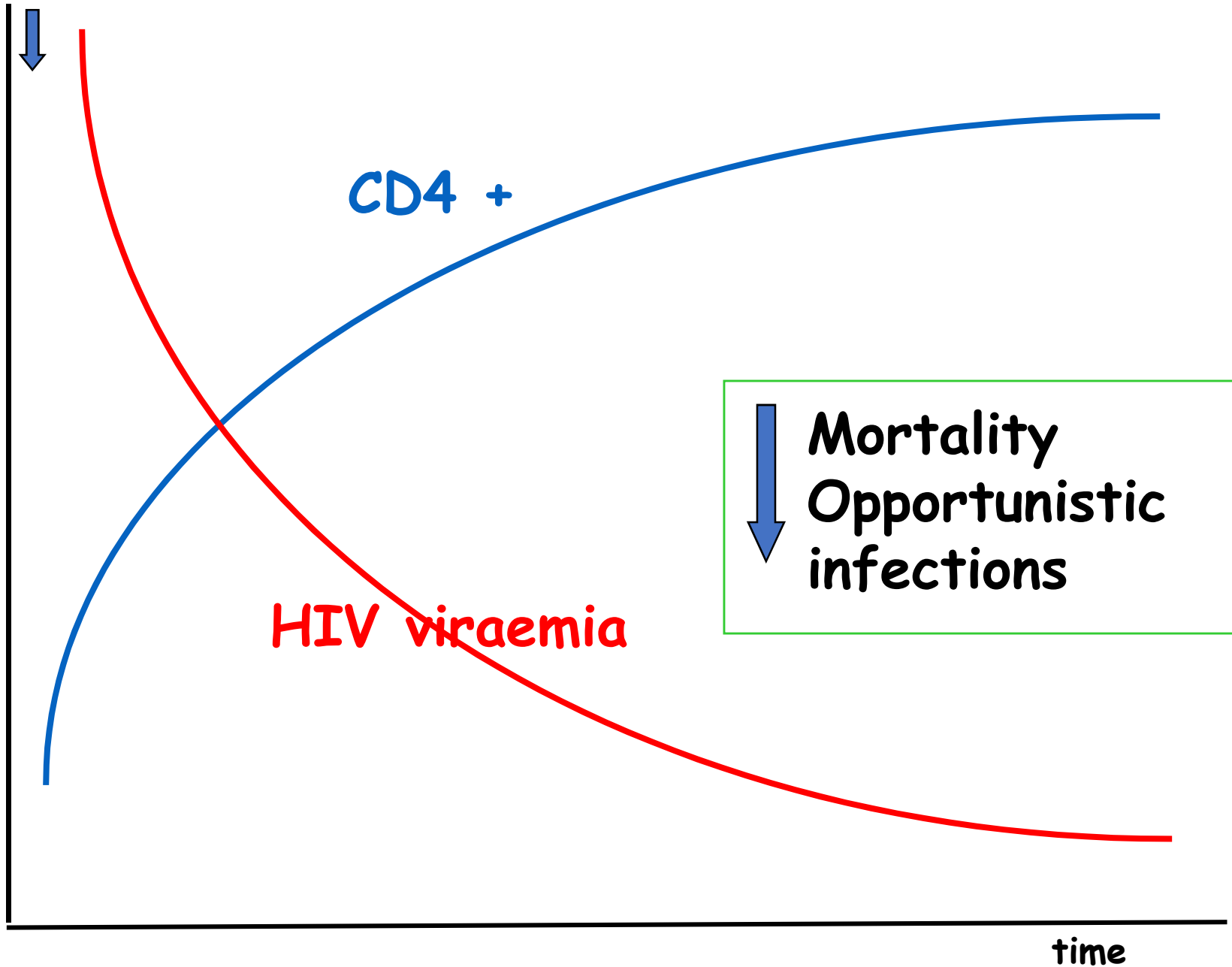
Slim disease



Vancouver 1996
“One World One Hope”



HAART



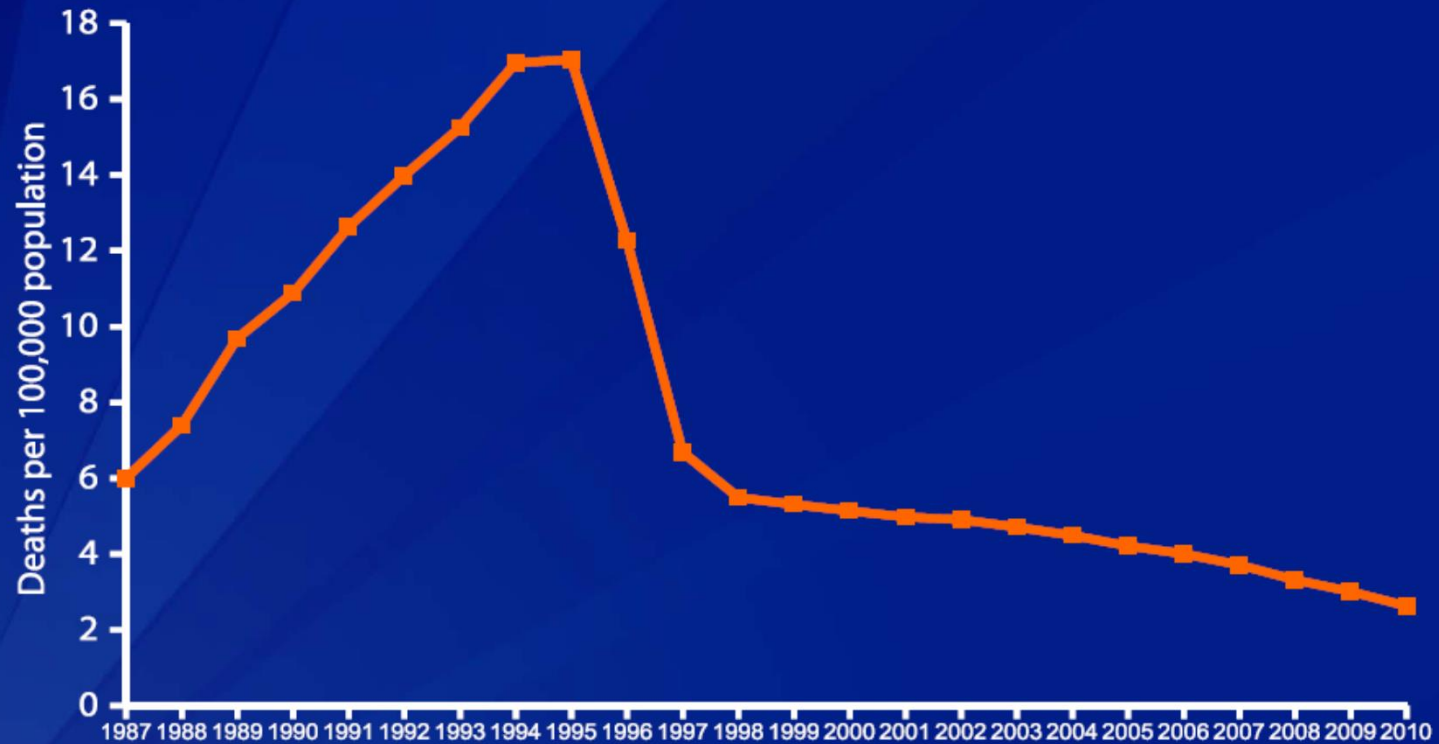
CD4 +

HIV viraemia

Mortality
Opportunistic
infections

time

Trends in Annual Age-Adjusted* Rate of Death Due to HIV Infection, United States, 1987–2010



Note: For comparison with data for 1999 and later years, data for 1987–1998 were modified to account for ICD-10 rules instead of ICD-9 rules.

*Standard: age distribution of 2000 US population

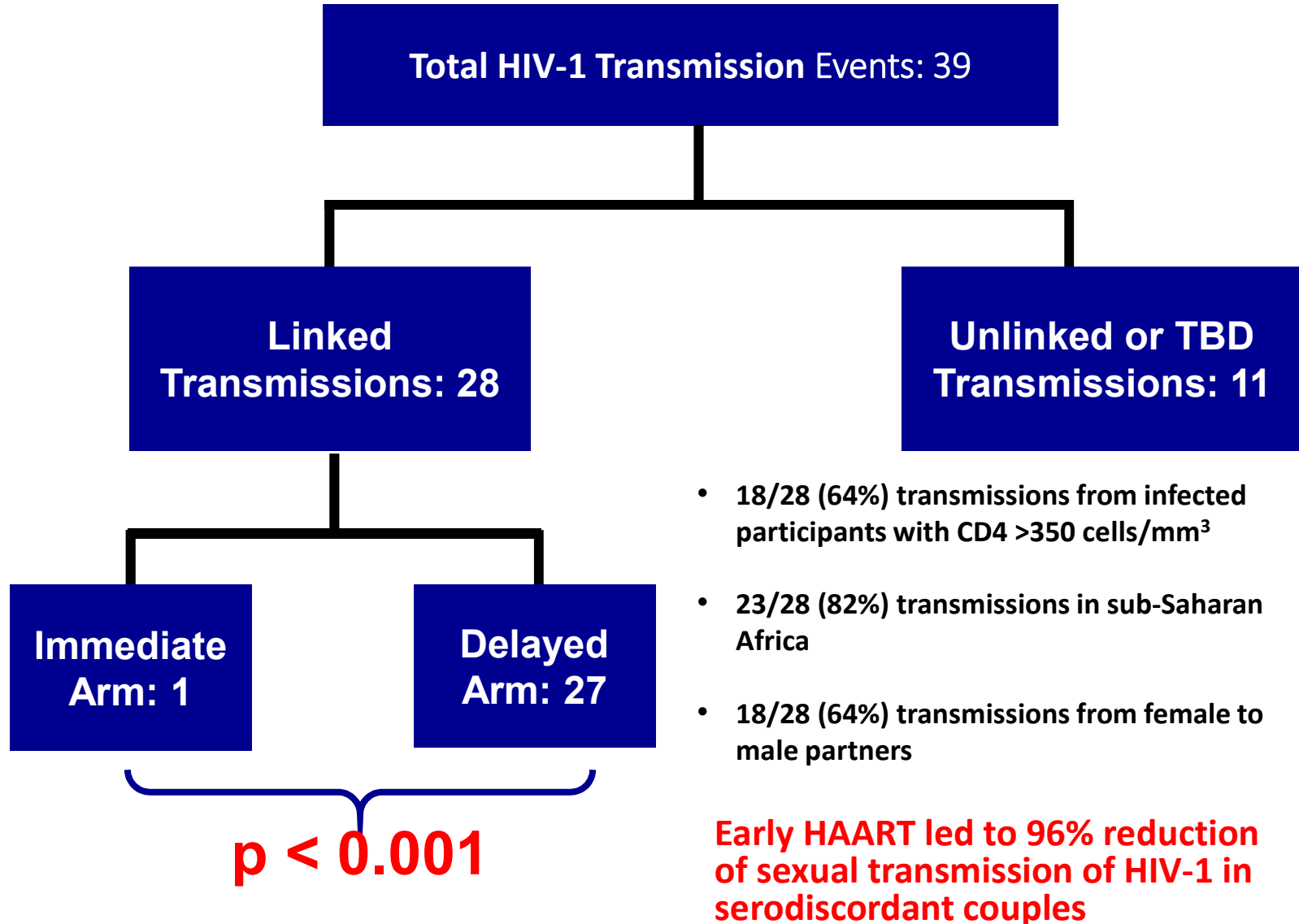






IAS 2011

HPTN 052: HIV-1 Transmission



Global summary of the AIDS epidemic | 2016

Number of people living with HIV

Total	36.7 million [30.8 million–42.9 million]
Adults	34.5 million [28.8 million–40.2 million]
Women (15+ years)	17.8 million [15.4 million–20.3 million]
Children (<15 years)	2.1 million [1.7 million–2.6 million]

People newly infected with HIV in 2016

Total	1.8 million [1.6 million–2.1 million]
Adults	1.7 million [1.4 million–1.9 million]
Children (<15 years)	160 000 [100 000–220 000]

AIDS-related deaths in 2016

Total	1.0 million [830 000–1.2 million]
Adults	890 000 [740 000–1.1 million]
Children (<15 years)	120 000 [79 000–160 000]

5000 new HIV infections (adults and children) a day | 2016

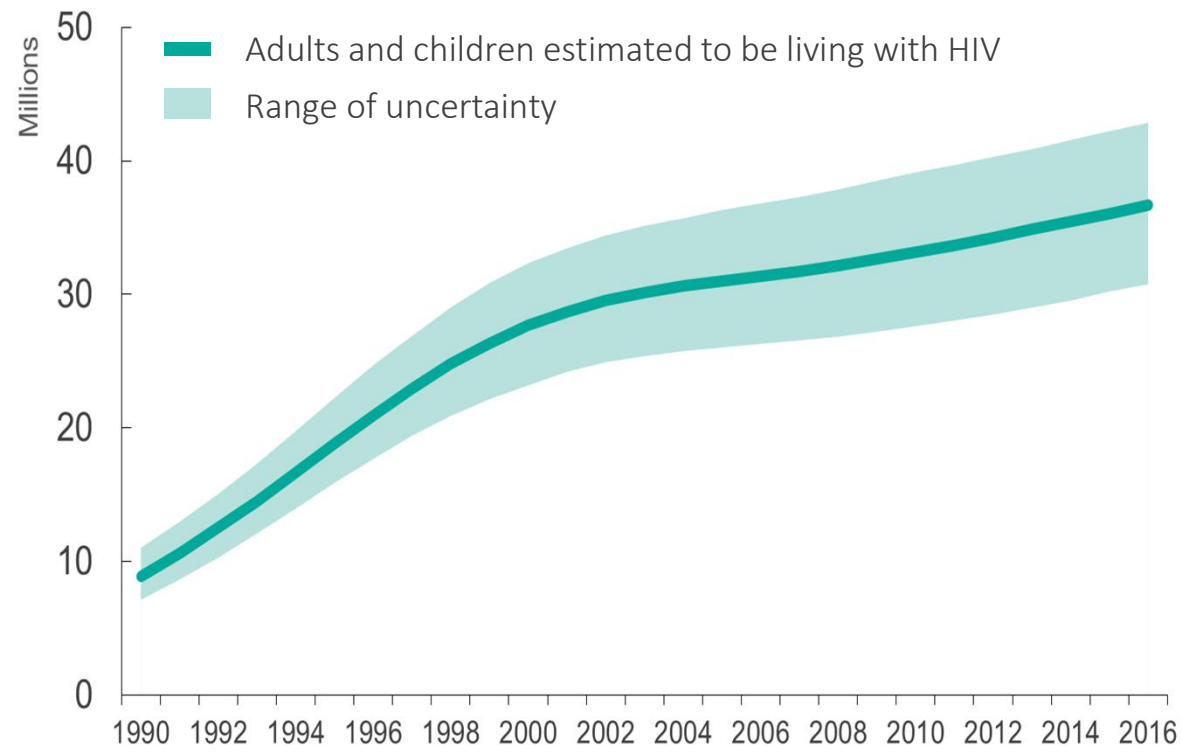
- **About 64% are in sub-Saharan Africa**
- **About 400 are among children under 15 years of age**
- **About 4500 are among adults aged 15 years and older, of whom:**
 - almost 43% are among women
 - about 37% are among young people (15–24)
 - about 22% are among young women (15–24)

Regional HIV and AIDS statistics and features | 2016

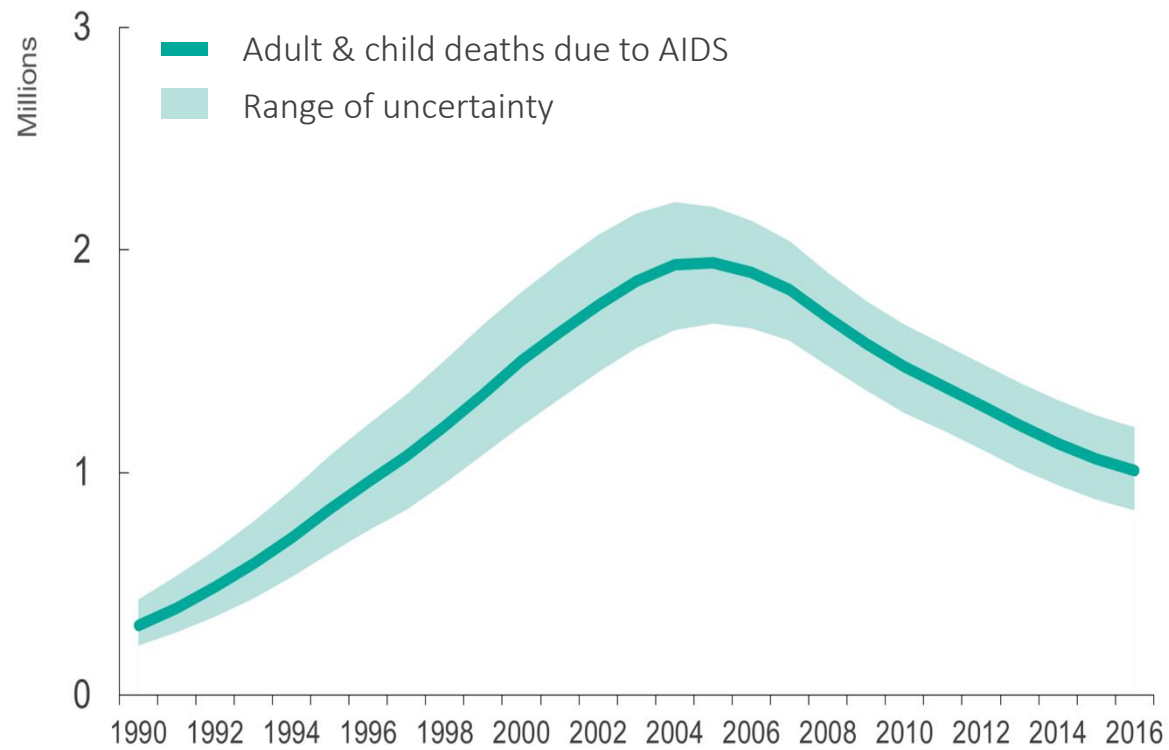
	Adults and children living with HIV	Adults and children newly infected with HIV	Adult & child deaths due to AIDS
Eastern and southern Africa	19.4 million [17.8 million–21.1 million]	790 000 [710 000–870 000]	420 000 [350 000–510 000]
Western and central Africa	6.1 million [4.9 million–7.6 million]	370 000 [270 000–490 000]	310 000 [220 000–400 000]
Middle East and North Africa	230 000 [160 000–380 000]	18 000 [11 000–39 000]	11 000 [7700–19 000]
Asia and the Pacific	5.1 million [3.9 million–7.2 million]	270 000 [190 000–370 000]	170 000 [130 000–220 000]
Latin America	1.8 million [1.4 million–2.1 million]	97 000 [79 000–120 000]	36 000 [28 000–45 000]
Caribbean	310 000 [280 000–350 000]	18 000 [15 000–22 000]	9400 [7300–12 000]
Eastern Europe and central Asia	1.6 million [1.4 million–1.7 million]	190 000 [160 000–220 000]	40 000 [32 000–49 000]
Western and central Europe and North America	2.1 million [2.0 million–2.3 million]	73 000 [68 000–78 000]	18 000 [15 000–20 000]
TOTAL	36.7 million [30.8 million–42.9 million]	1.8 million [1.6 million–2.1 million]	1.0 million [830 000–1.2 million]

The ranges around the estimates in this table define the boundaries within which the actual numbers lie, based on the best available information.

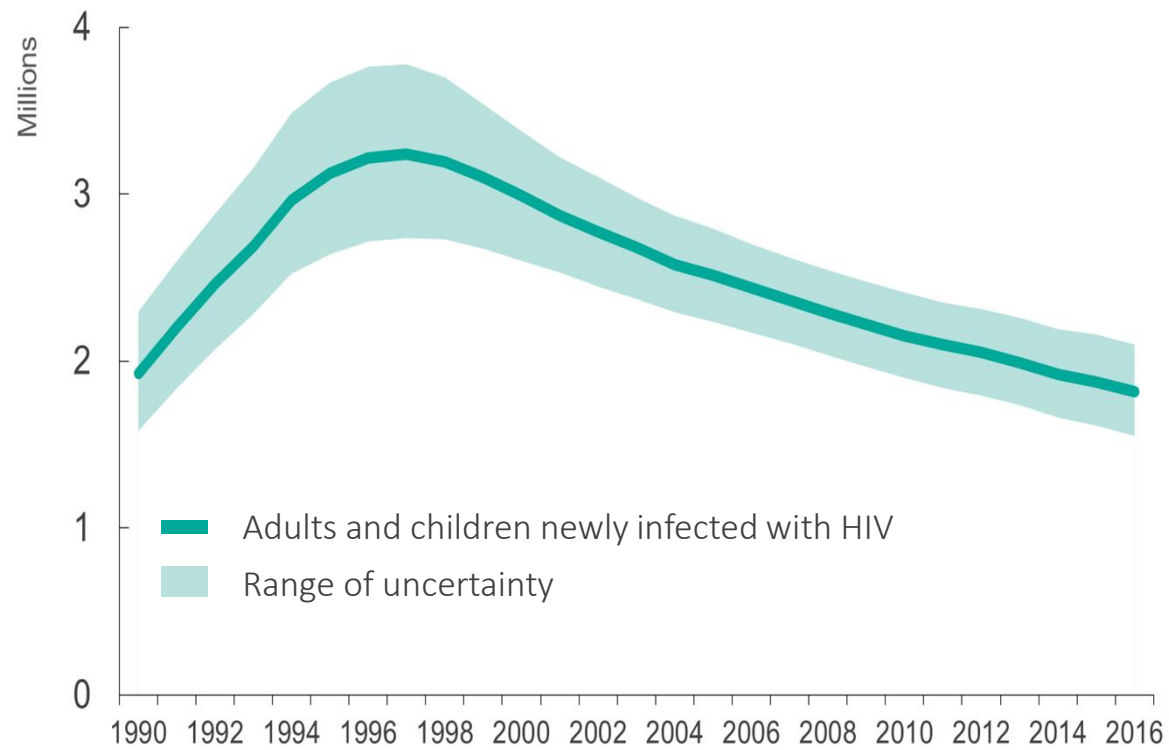
Adults and children estimated to be living with HIV | 1990–2016



Adult & child deaths due to AIDS | 1990–2016



Adults and children newly infected with HIV | 1990–2016



Il mondo "capovolto"



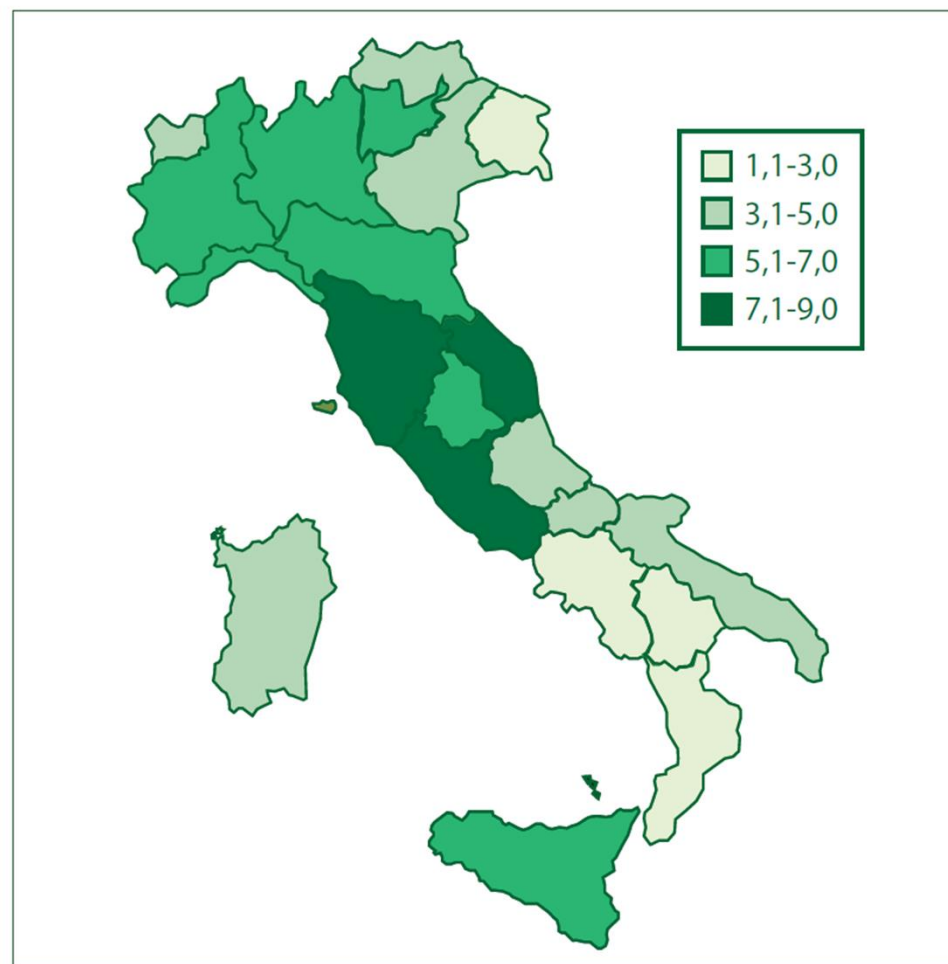


Figura 4 - Incidenza delle nuove diagnosi di infezione da HIV (per 100.000 residenti) per regione di residenza (2016)

Tabella 7 - Numero e incidenza di nuove diagnosi di infezione da HIV per modalità di trasmissione nelle province con numero di diagnosi superiori a 50 (2016)

Province	MSM		Eterosessuali M		Eterosessuali F		IDU		Totale dei casi con modalità riportata	Totale dei casi con modalità non riportata	Totale	Incidenza per 100.000 residenti
	n.	% di riga ^a	n.	% di riga ^a	n.	% di riga ^a	n.	% di riga ^a	n.	n.	n.	
Torino	88	60,3	22	15,1	32	21,9	4	2,7	146	2	148	6,5
Milano	174	60,2	64	22,1	44	15,2	7	2,4	289	24	313	9,8
Bergamo	37	42,5	30	34,5	19	21,8	1	1,1	87	1	88	7,9
Brescia	20	27,4	31	42,5	19	26,0	3	4,1	73	1	74	5,9
Genova	21	40,4	17	32,7	14	26,9	0	0,0	52	9	61	7,1
Bologna	15	34,9	12	27,9	14	32,6	2	4,7	43	14	57	5,7
Firenze	31	50,0	16	25,8	8	12,9	7	11,3	62	9	71	7,0
Roma	120	43,6	94	34,2	57	20,7	4	1,5	275	117	392	9,0
Napoli	45	42,5	31	29,2	25	23,6	5	4,7	106	4	110	3,5
Bari	29	59,2	14	28,6	6	12,2	0	0,0	49	5	54	4,3
Palermo	34	50,0	18	26,5	13	19,1	3	4,4	68	3	71	5,6
Catania	38	52,8	19	26,4	14	19,4	1	1,4	72	2	74	6,6
Totale province selezionate	652	49,3	368	27,8	265	20,0	37	2,8	1.322	191^b	1.513^b	6,9
Totale Italia	1.313	43,0	955	31,3	687	22,5	96	3,1	3.051	400^c	3.451^c	5,7
Percentuale diagnosi nelle 12 province sul totale Italia	49,7		38,5		38,6		38,5				43,8	

(a) Calcolata sul totale dei dati disponibili per modalità di trasmissione; (b) comprende 4 casi di trasmissione verticale e 2 casi di trasmissione per sangue e/o emoderivati; (c) comprende 9 casi di trasmissione verticale e 6 casi di trasmissione per sangue e/o emoderivati

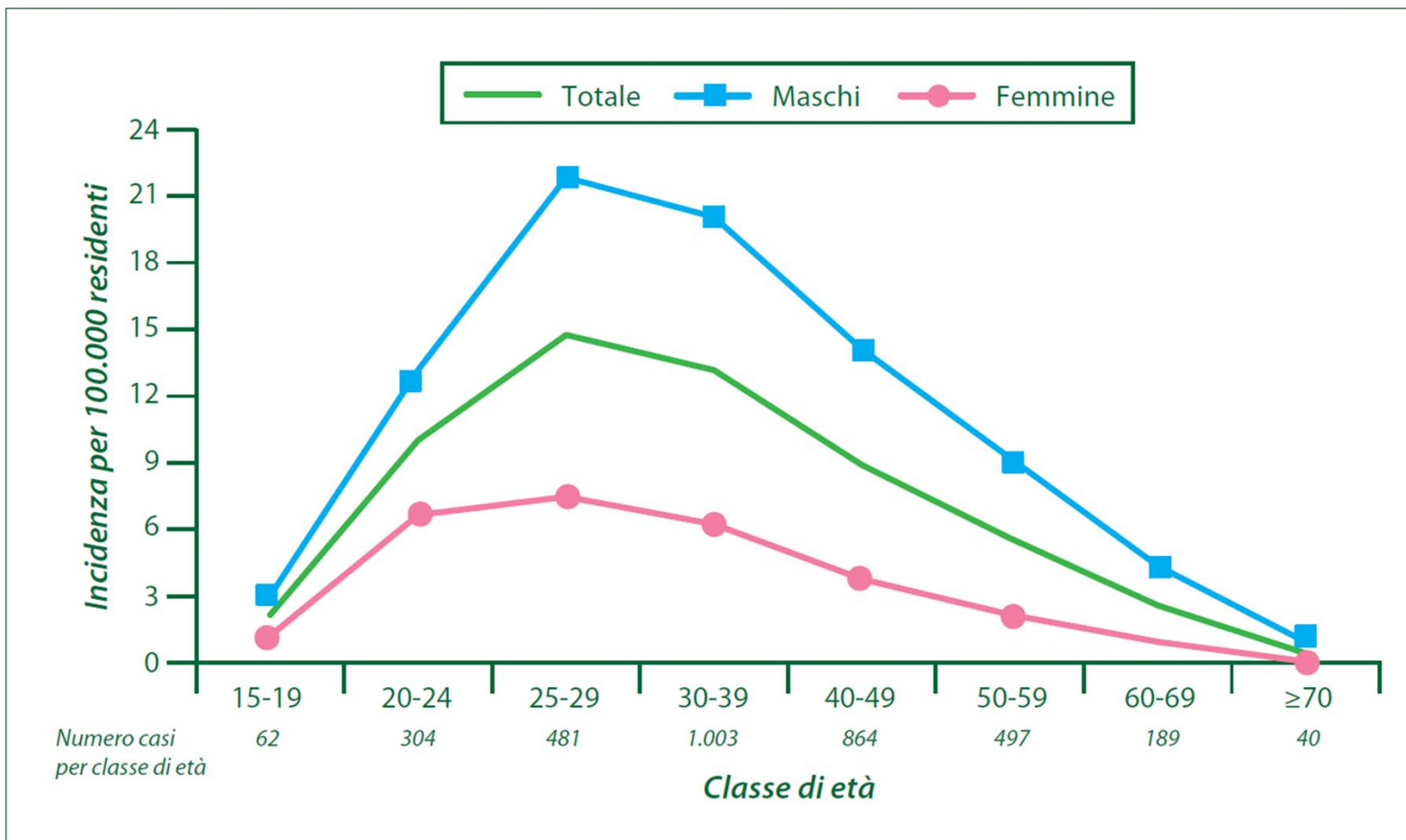
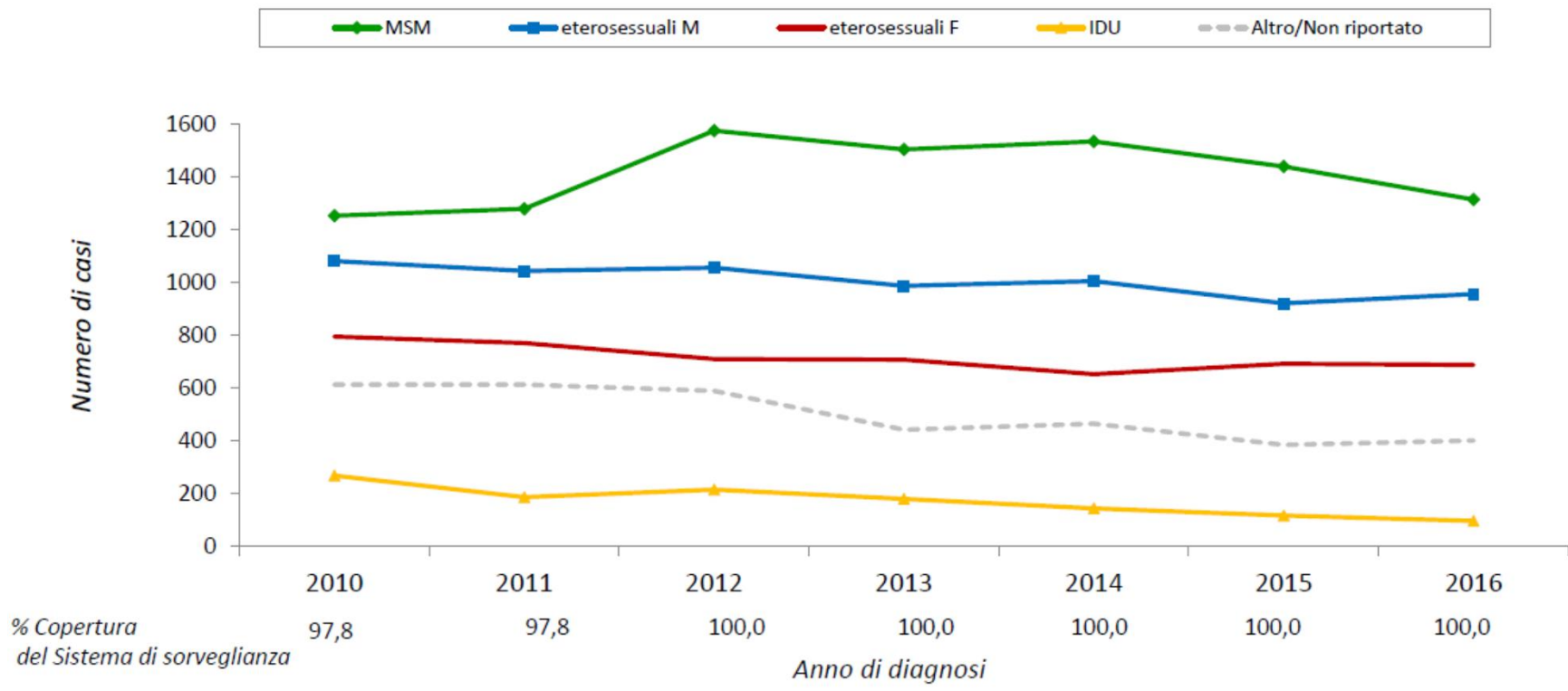


Figura 6 - Incidenza delle nuove diagnosi di infezione da HIV per classe di età e genere (2016)

Numero delle nuove diagnosi di infezione da HIV per modalità di trasmissione e anno di diagnosi (2010-2016)



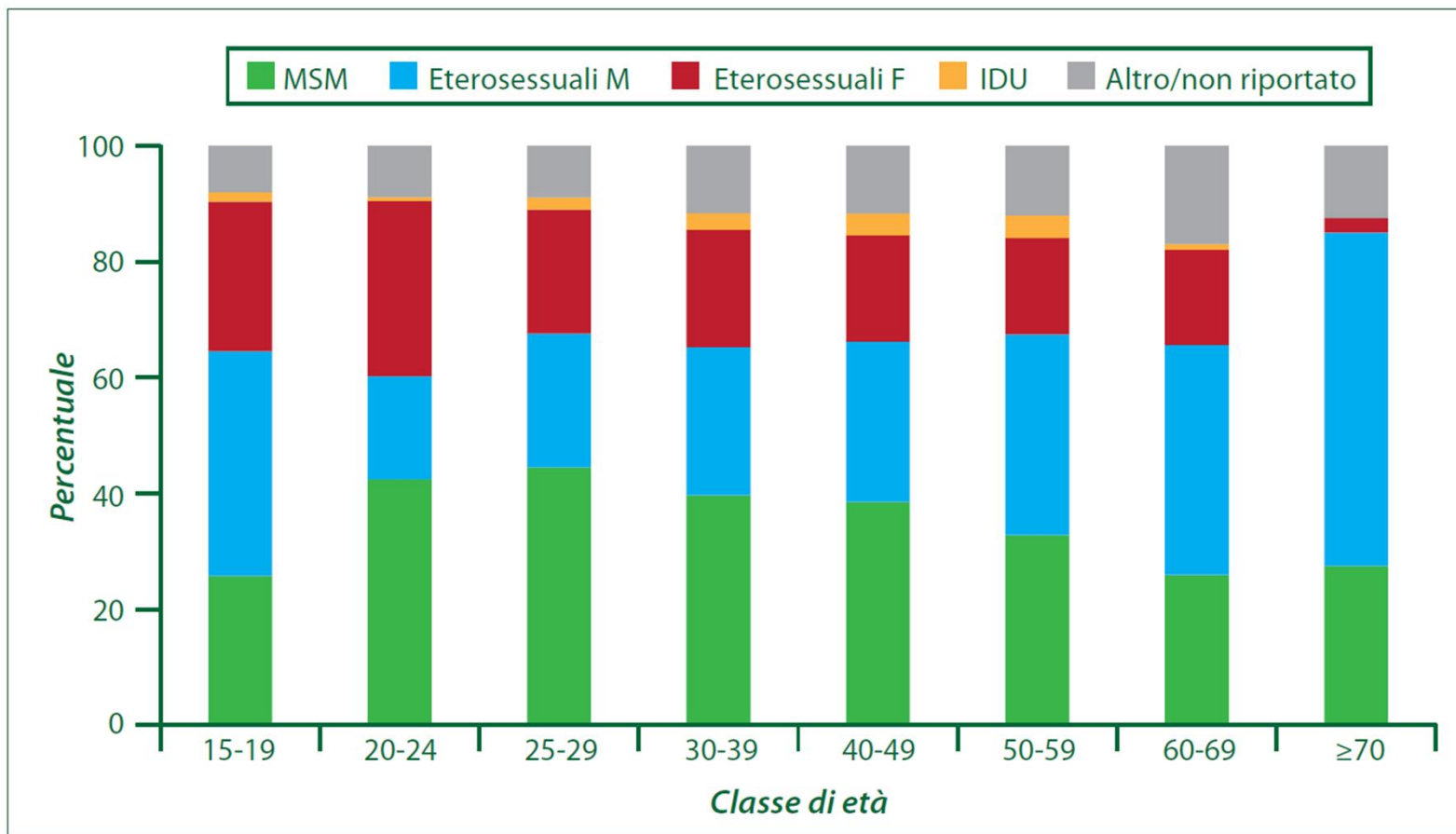


Figura 5 - Proporzione delle nuove diagnosi di infezione da HIV per classe di età e modalità di trasmissione (2016)

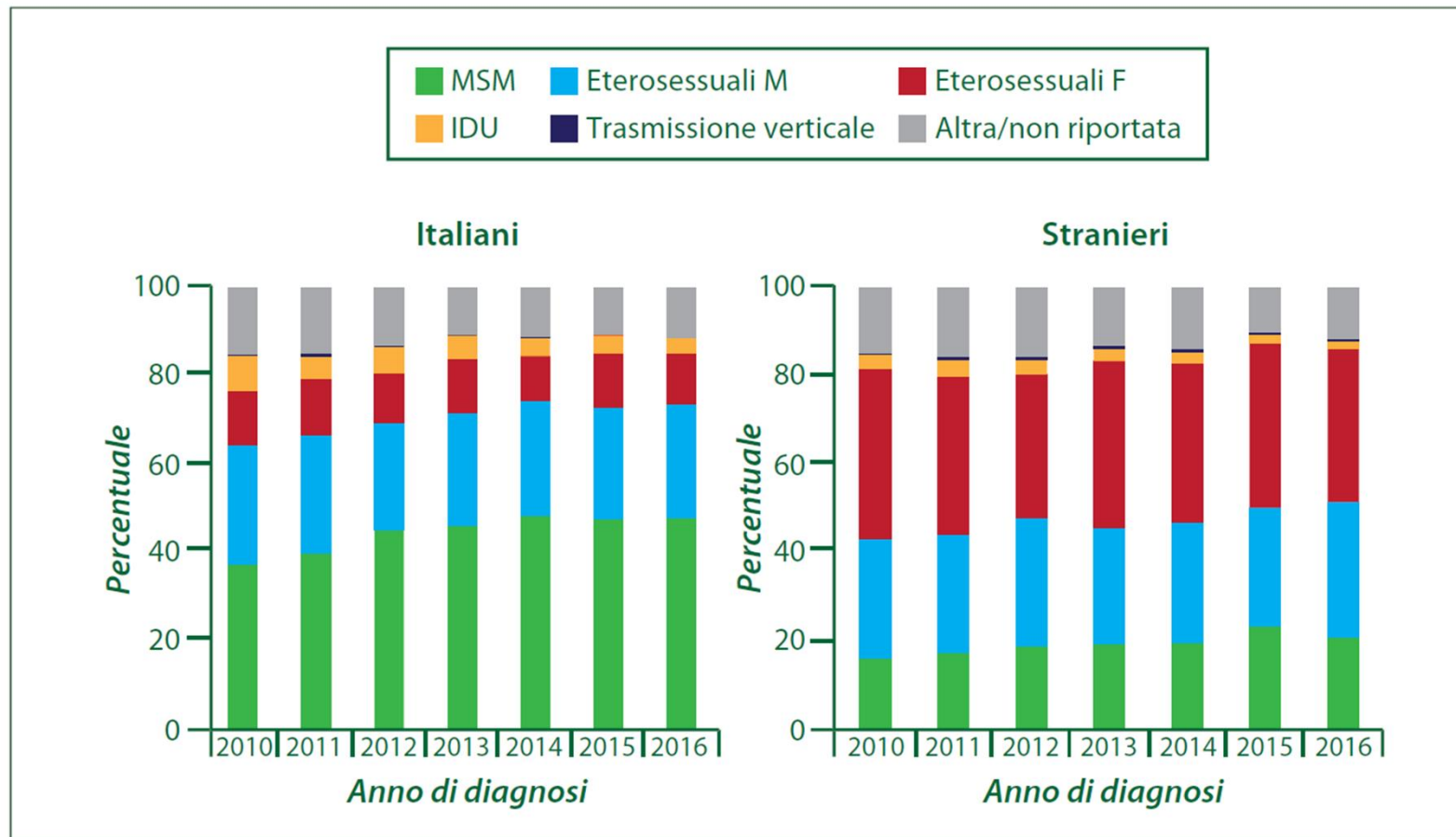


Figura 10 - Distribuzione delle nuove diagnosi di infezione da HIV per nazionalità, modalità di trasmissione e anno di diagnosi (2010-2016)

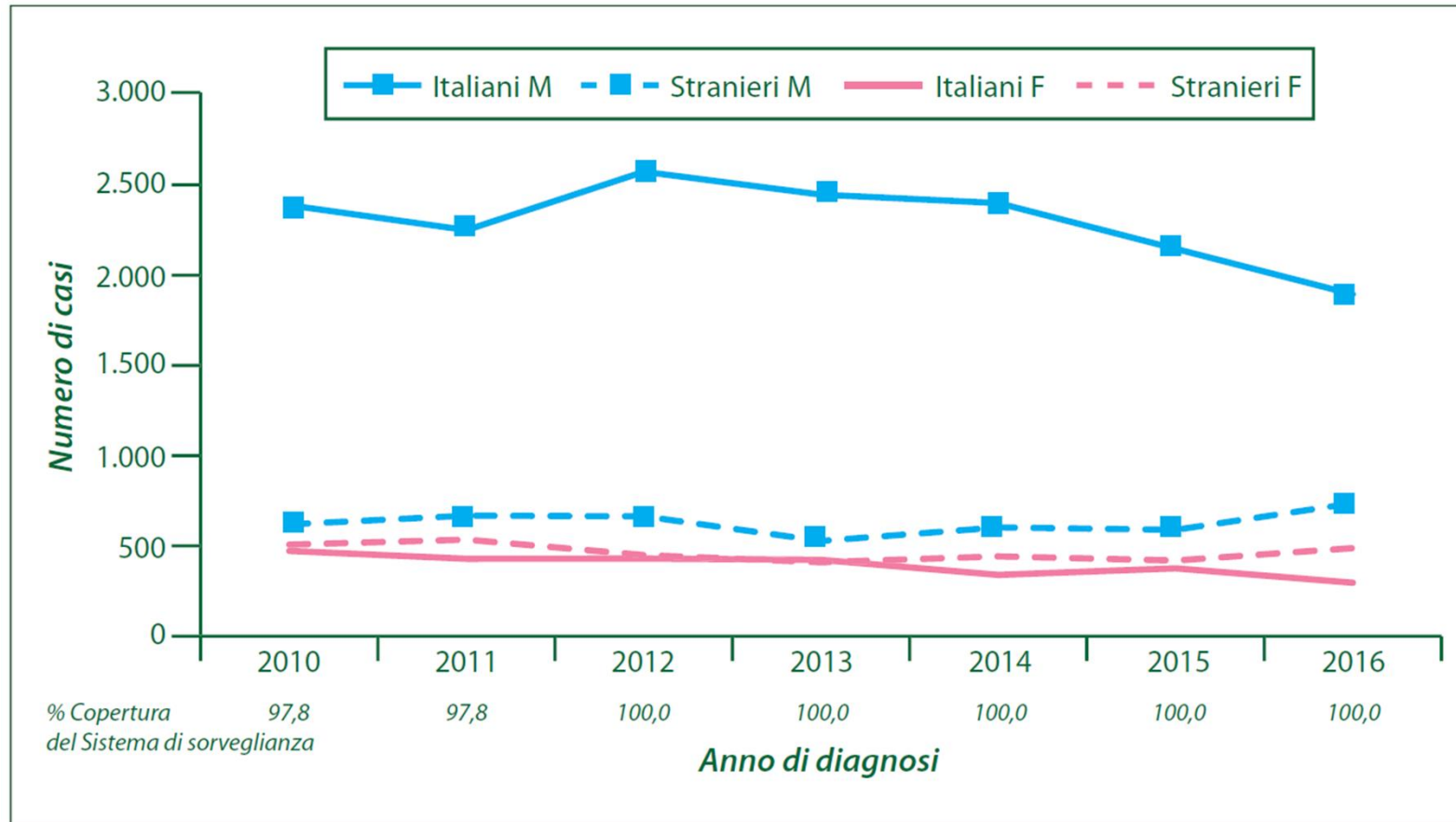
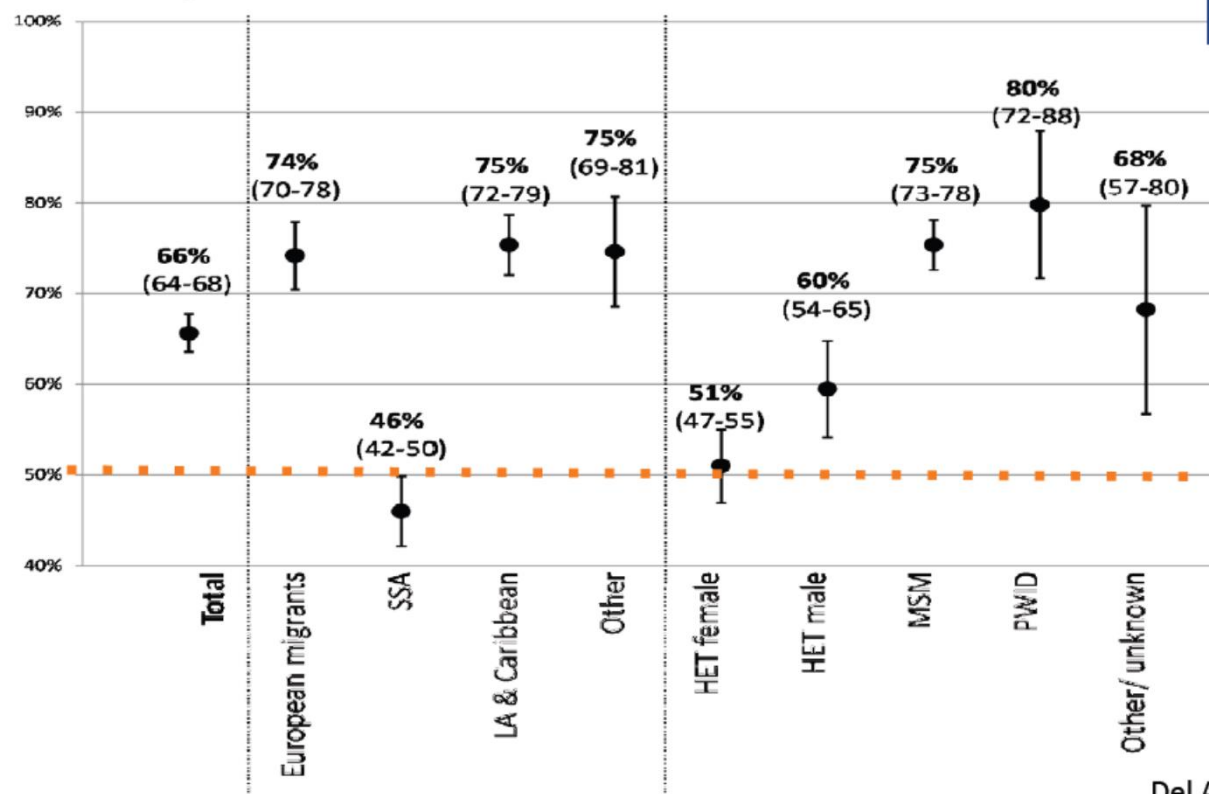


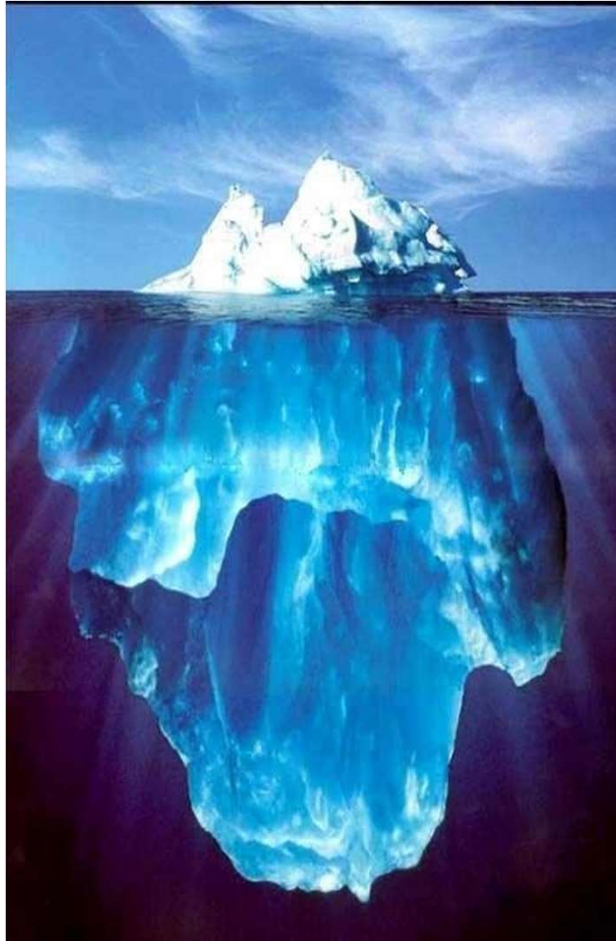
Figura 9 - Numero delle nuove diagnosi di infezione da HIV per nazionalità, genere e anno di diagnosi (2010-2016)

A significant share of HIV-positive migrants living in Europe acquired HIV infection after migration

Percentage of Migrants who acquired HIV infection after migration by Area of Origin and Risk Factor



Del Amo J, 2017



**Soggetti HIV positivi
consapevoli**



**Soggetti HIV positivi
inconsapevoli
(12-15%)**

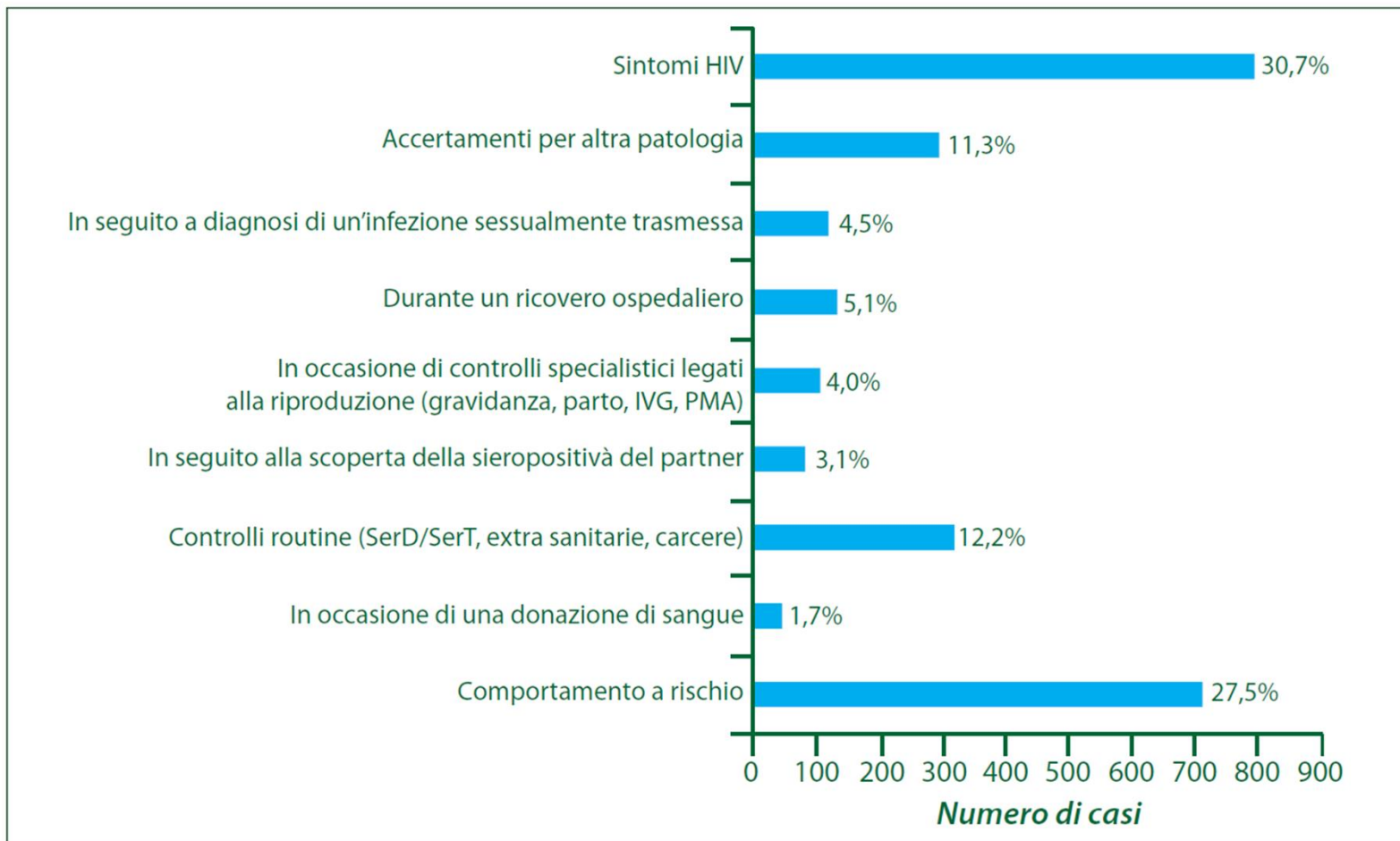


Figura 11 - Motivo di effettuazione del test 2016 (2.592 nuove diagnosi di infezione da HIV che riportano il dato)

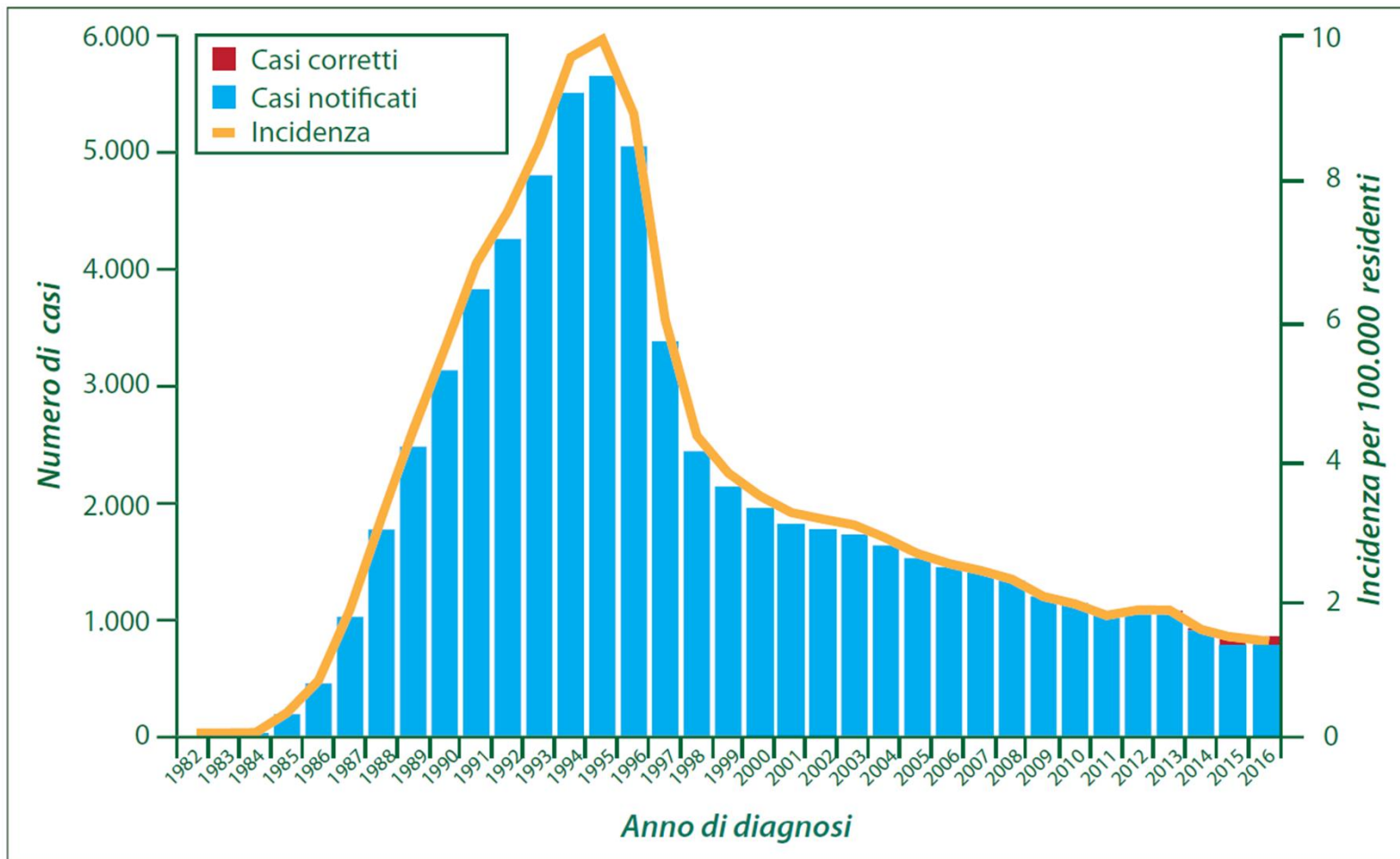


Figura 12 - Numero dei casi di AIDS e incidenza per anno di diagnosi, corretti per ritardo di notifica (1982-2016)

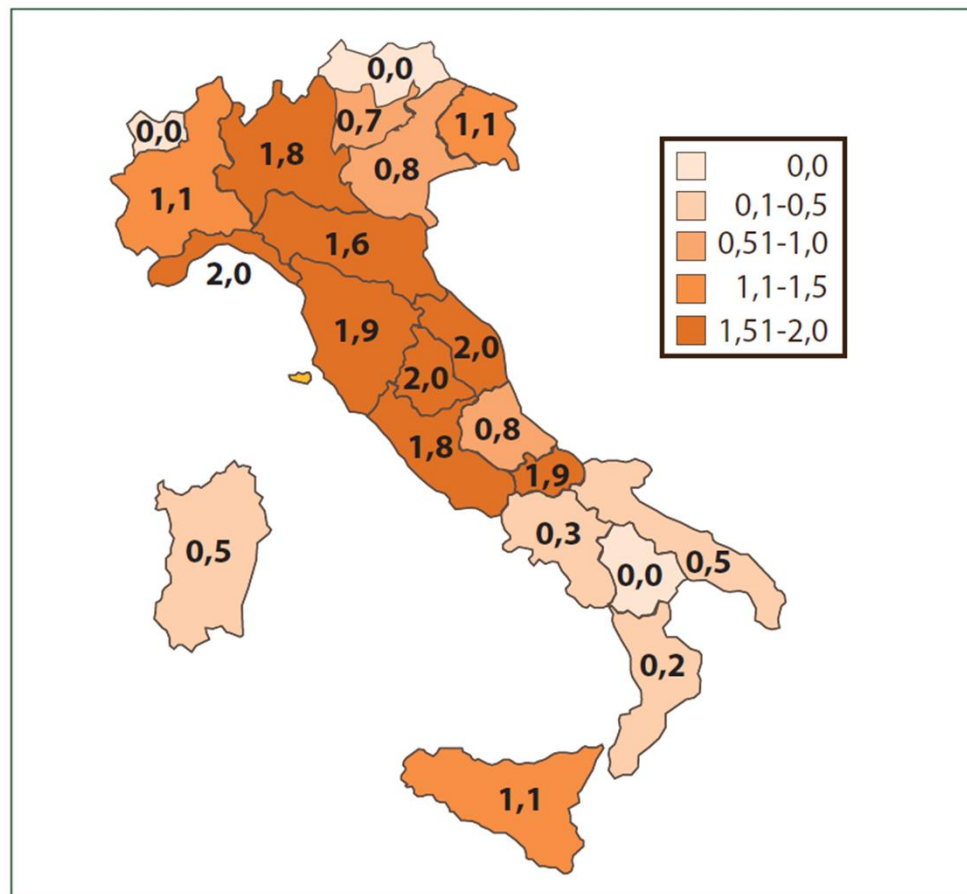
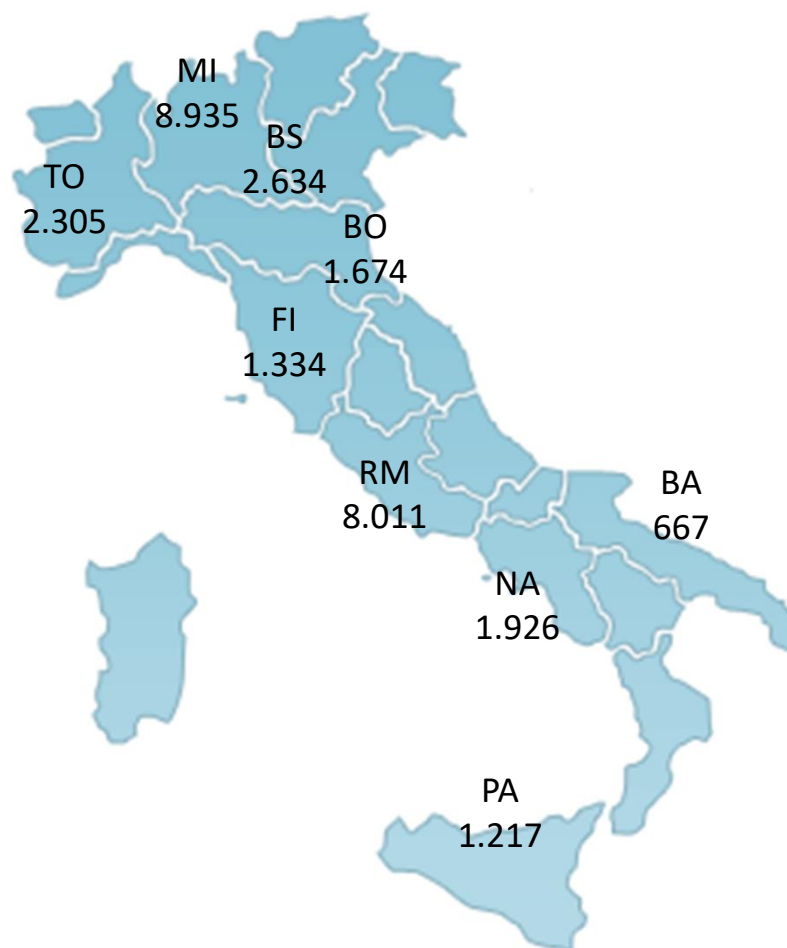


Figura 13 - Incidenza di AIDS (per 100.000 residenti) per regione di residenza (2016)

Tabella 16 - Numero dei casi di AIDS dall'inizio dell'epidemia, per provincia di segnalazione e di residenza, e incidenza per 100.000 residenti (calcolata sui casi diagnosticati nel 2016)

Provincia	Segnalazione	Residenza	Incidenza 2016	Provincia	Segnalazione	Residenza	Incidenza 2016
Valle d'Aosta				Umbria			
Aosta	98	91	0,0	Perugia	500	444	1,4
Piemonte				Terni	204	168	3,9
Alessandria	427	482	1,6	Marche			
Asti	100	103	0,5	Ancona	682	373	1,3
Biella	274	301	0,6	Ascoli Piceno	64	182	2,9
Cuneo	265	268	0,2	Fermo	160	157	1,7
Novara	574	589	1,9	Macerata	136	205	3,7
Torino	2.538	2.305	1,1	Pesaro e Urbino	213	307	1,1
Verbania	208	286	1,9	Lazio			
Vercelli	161	164	0,6	Frosinone	286	201	1,4
Liguria				Lombardia			
Genova	2.252	2.118	2,0	Bergamo	1.817	1.749	2,7
Imperia	399	439	3,3	Brescia	2.842	2.634	2,1
La Spezia	274	263	1,4	Como	857	870	1,2
Savona	477	467	1,8	Cremona	508	573	1,7
Bologna	1.802	1.674	1,2	Lecco	589	491	4,1
Lombardia				Lodi	378	400	1,3
Bergamo	1.817	1.749	2,7	Mantova	411	446	0,0
Brescia	2.842	2.634	2,1	Milano	8.710	8.935	2,0
Como	857	870	1,2	Monza e della Brianza	560	953	1,3
Cremona	508	573	1,7	Pavia	1.471	884	1,3
Lecco	589	491	4,1	Sondrio	89	152	0,6
Lodi	378	400	1,3	Varese	2.046	1.935	1,5
Mantova	411	446	0,0	Vibo Valentia	48	53	0,0
Milano	8.710	8.935	2,0	Sicilia			
Monza e della Brianza	560	953	1,3	Agrigento	1	145	0,0
Pavia	1.471	884	1,3	Caltanissetta	199	139	0,4
Sondrio	89	152	0,6	Catania	858	714	1,2
Varese	2.046	1.935	1,5	Enna	37	63	2,4
Veneto				Messina	266	299	1,9
Belluno	76	97	1,0	Palermo	1.411	1.217	1,3
Padova	973	707	0,7	Ragusa	85	87	1,2
Rovigo	141	201	0,8	Siracusa	123	193	0,2
Treviso	497	476	0,5	Trapani	63	240	1,4
Venezia	461	643	0,6	Sardegna			
Verona	938	770	1,3	Cagliari	1.381	1.169	0,9
Vicenza	828	902	0,9	Carbonia-Iglesias	0	86	0,8
Friuli Venezia Giulia				Medio Campidano	0	92	1,0
Gorizia	26	57	2,9	Nuoro	70	57	0,0
Pordenone	512	216	1,0	Ogliastra	0	11	0,0
Trieste	208	115	1,3	Olbia-Tempio	3	122	0,0
Udine	145	192	0,6	Oristano	3	64	0,6
Trentino-Alto Adige				Sassari	442	330	0,3
Bolzano - Bozen	320	301	0,0	Residenza estera	-	706	-
Trento	348	360	0,7	Residenza non riportata	-	1.330	-
Emilia-Romagna				Totale	68.982	68.982	
Bologna	1.802	1.674	1,2				
Ferrara	516	549	2,3				
Forlì	486	642	2,5				
Modena	843	789	1,0				
Parma	555	511	2,5				
Piacenza	400	397	2,4				
Ravenna	1.264	954	1,0				
Reggio Emilia	566	513	1,5				
Rimini	780	554	1,2				
Toscana							
Arezzo	213	199	0,6				
Firenze	1.413	1.334	1,6				
Grosseto	297	349	0,4				
Livorno	535	584	3,8				
Lucca	241	484	1,5				
Massa Carrara	295	324	0,0				
Pisa	867	401	2,6				
Pistoia	156	300	3,1				
Prato	349	252	1,2				
Siena	210	193	3,3				

N. assoluto di casi di AIDS al 31 dicembre 2015 per Provincia di Residenza



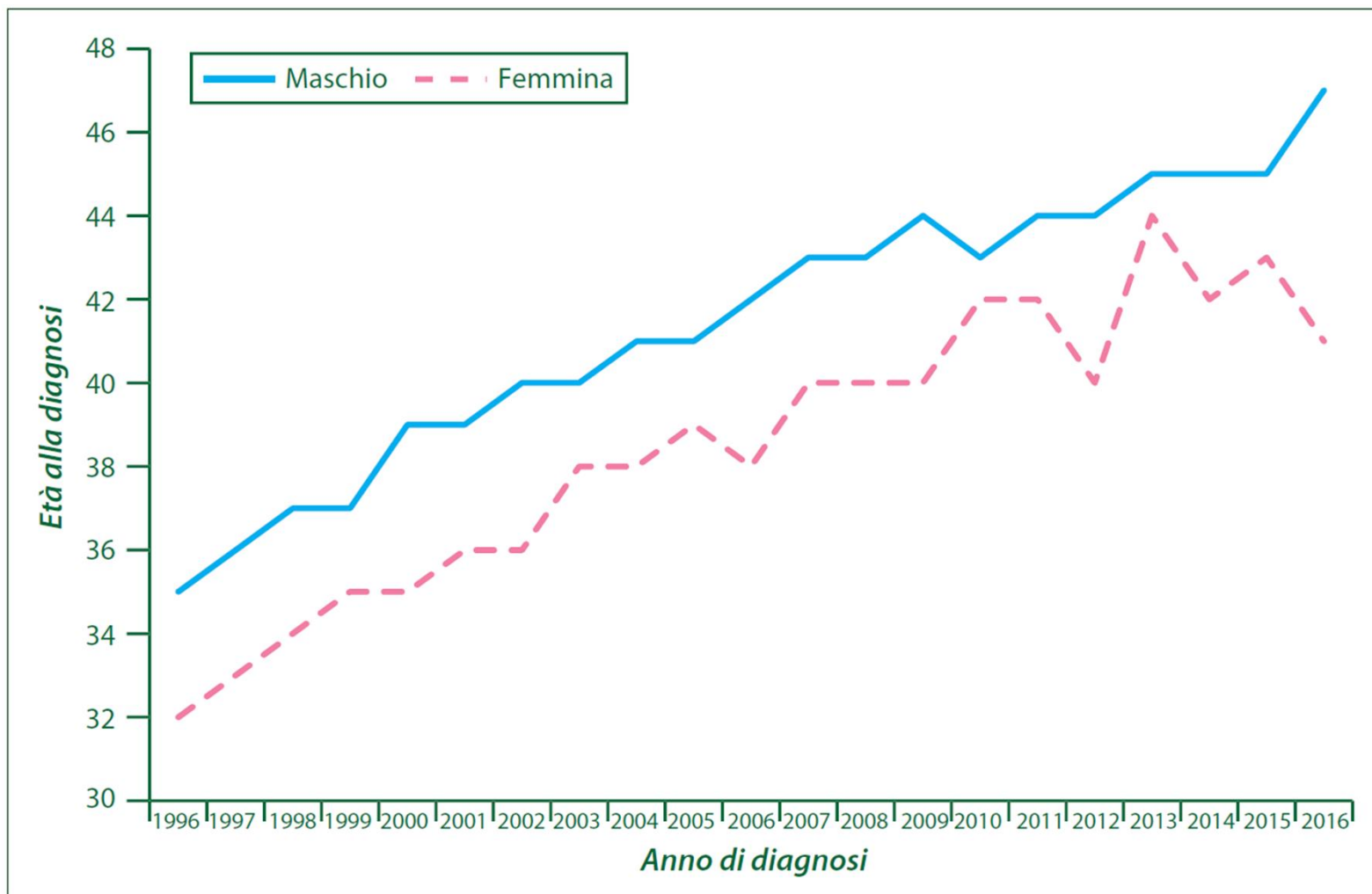


Figura 14 - Età mediana alla diagnosi di AIDS, per genere e anno di diagnosi (1996-2016)

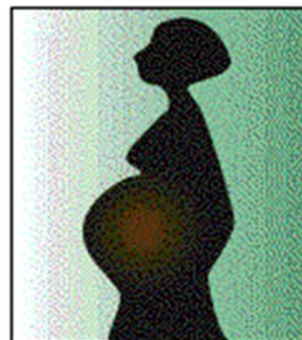
Tabella 22 - Tempo intercorso tra il 1° test HIV+ e la diagnosi di AIDS

Anno di diagnosi	< 6 mesi		≥ 6 mesi	
	n. casi	% di riga	n. casi	% di riga
1996	908	20,5	3512	79,5
1997	1047	33,1	2119	66,9
1998	959	41,2	1367	58,8
1999	973	46,4	1126	53,6
2000	922	48,2	992	51,8
2001	852	47,9	928	52,1
2002	890	51,3	845	48,7
2003	865	51,0	832	49,0
2004	803	51,0	773	49,0
2005	769	52,0	709	48,0
2006	745	53,8	639	46,2
2007	717	55,1	585	44,9
2008	740	58,8	519	41,2
2009	670	60,1	444	39,9
2010	700	66,2	357	33,8
2011	611	62,2	371	37,8
2012	670	66,1	344	33,9
2013	685	68,0	322	32,0
2014	612	71,3	246	28,7
2015	587	74,4	202	25,6
2016	558	76,3	173	23,7

Modalità di trasmissione di HIV

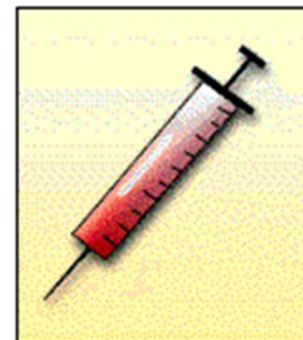


**Unprotected
sexual intercourse
with an infected partner**



**Vertical
transmission**
(from mother
to child)

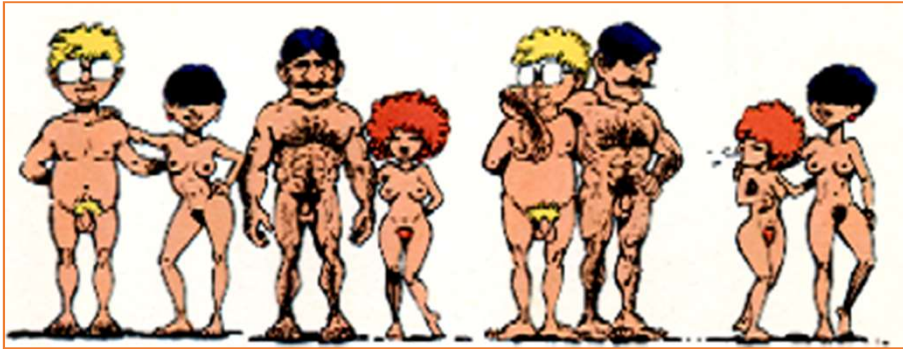
- in utero
- during delivery
- breastmilk



Injection drug use
(rare: infected
blood/blood products)



HIV INFECTION



Trasmissione	Efficienza (%)	Modalità preventive	Efficienza (%)
Sessuale	0.5%	A stinenza B e faithful C ondom D rugs	100% 100% (partner faithful) 99% 93-96%
Parenterale			
Verticale			

HPTN 052: Conclusions

- **Early ART that suppresses viral replication led to 96% reduction of sexual transmission of HIV-1 in serodiscordant couples**

La PreP con TDF/FTC per os: lo Studio iPrEx

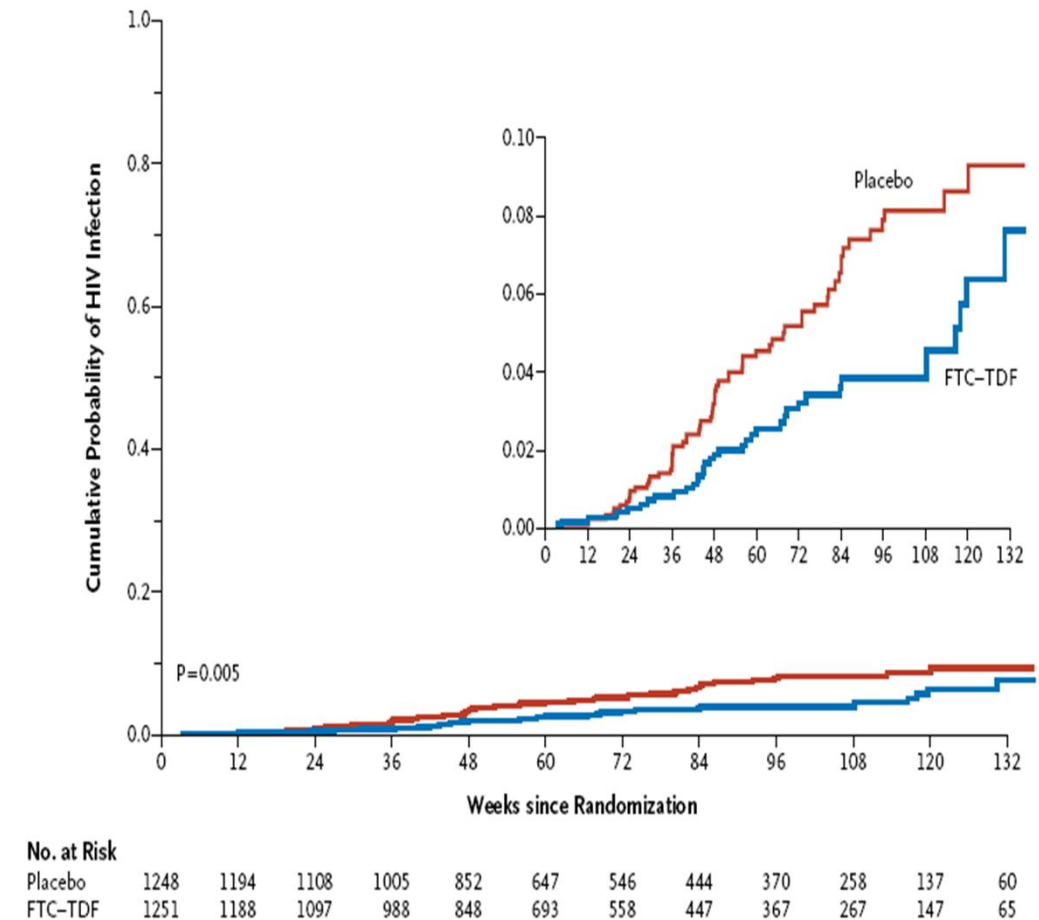
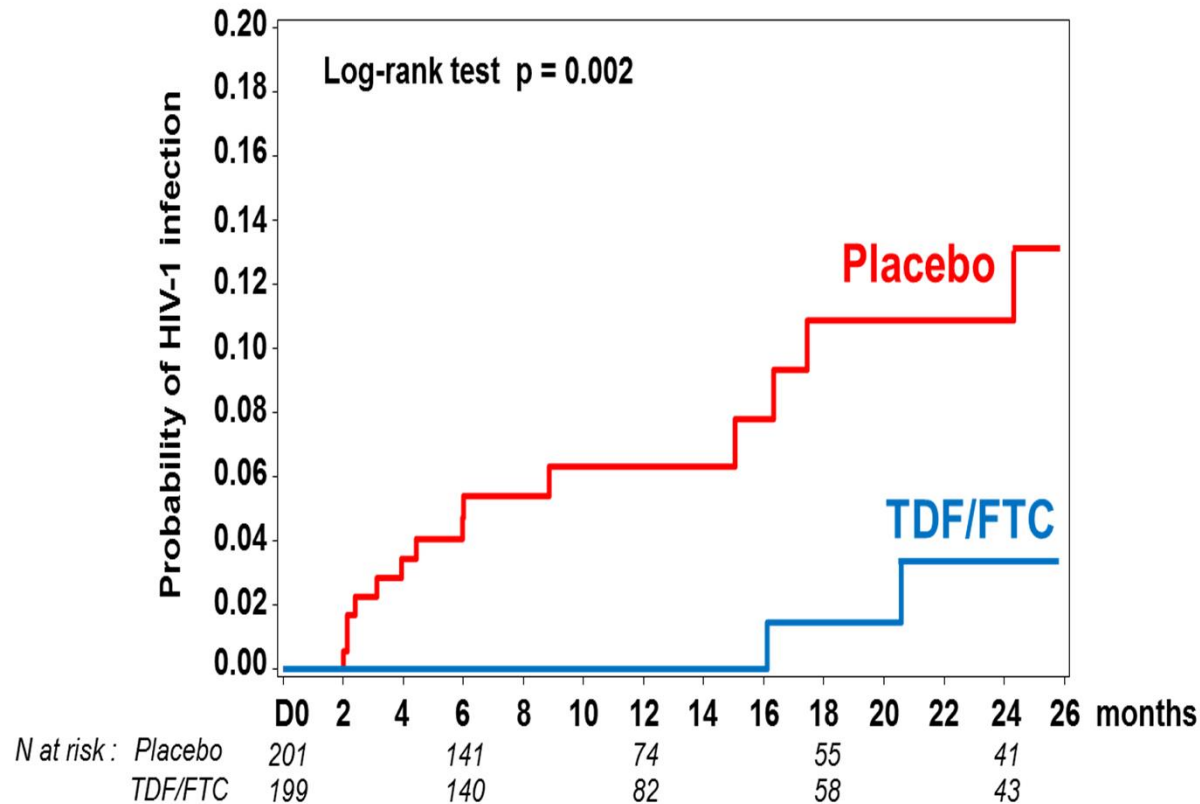


Figure 2. Kaplan–Meier Estimates of Time to HIV Infection (Modified Intention-to-Treat Population).

The cumulative probability of HIV acquisition is shown for the two study groups. The efficacy of preexposure prophylaxis with emtricitabine and tenofovir disoproxil fumarate (FTC–TDF) was 44%, as compared with placebo (P=0.005). The inset graph shows a more detailed version of the overall graph up to a probability of 0.10.

KM Estimates of Time to HIV-1 Infection (mITT Population)



Mean follow-up of 13 months: 16 subjects infected
14 in placebo arm (incidence: 6.6 per 100 PY), **2 in TDF/FTC arm**
 (incidence: 0.94 per 100 PY)

**86% relative reduction in the incidence of HIV-1 (95% CI: 40-99,
 $p = 0.002$)**

Non è tutto oro quel che luccica!

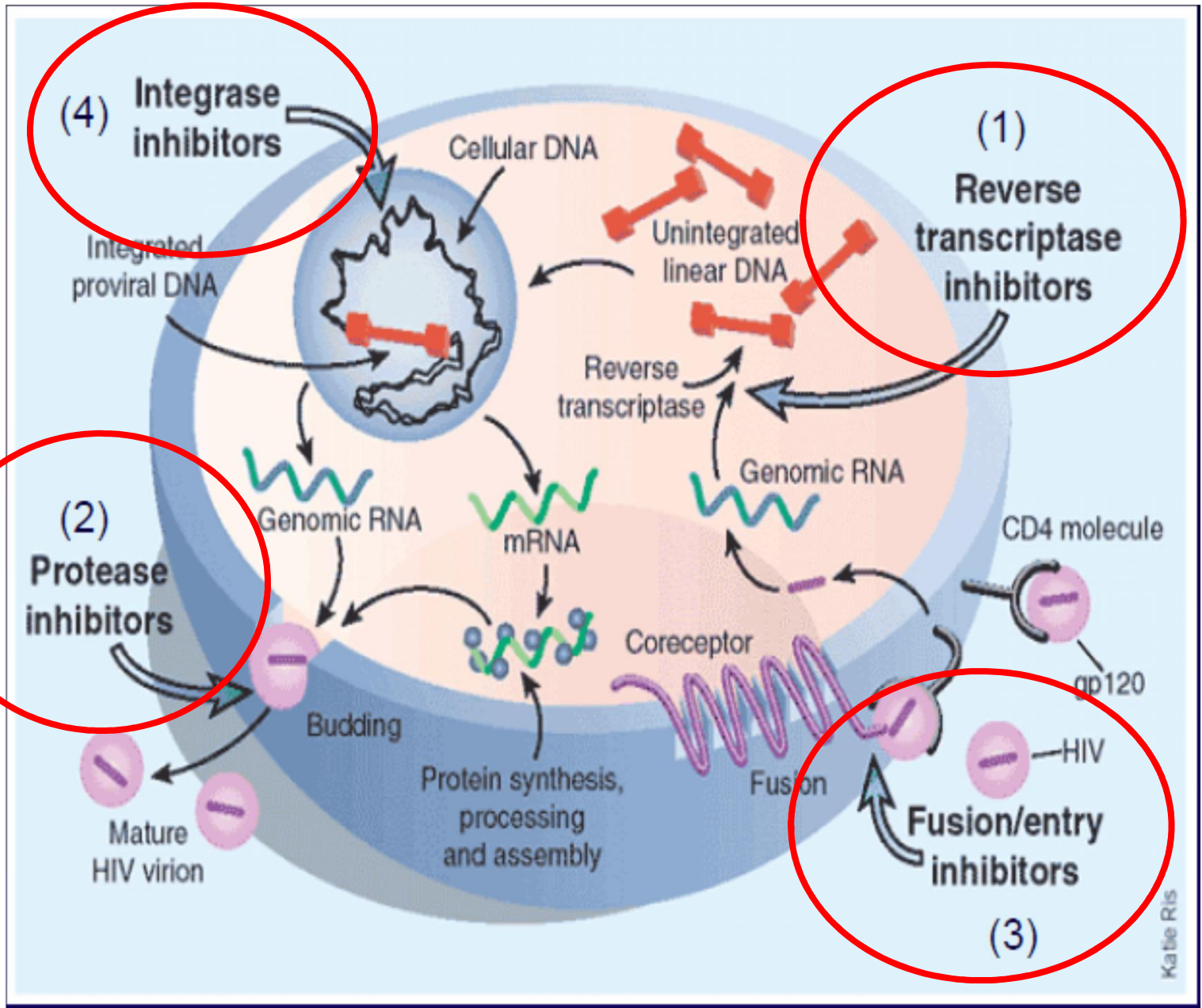
Table 1. Ongoing human efficacy trials of topical and oral preexposure prophylaxis					
Study name (location)	Sponsor/funder	Population	N	PrEP agent	Status
CAPRISA 004 (South Africa Department of Science and Technology)	USAID, South Africa, CONRAD, FHI	Women	889	Vaginal tenofovir gel (coitally associated use)	39% efficacy [15 ^{***}]
iPrEx (Brazil, Ecuador, Peru, South Africa, Thailand, USA)	NIH/BMGF	MSM and transgender women	2499	FTC/TDF	44% efficacy [16 ^{***}]
FEM-PrEP (Kenya, South Africa, Tanzania)	USAID/FHI	Higher risk women	1950	FTC/TDF	Stopped in April 2011 for lack of efficacy [17]
Partners PrEP Study (Kenya, Uganda)	UW/BMGF	HIV serodiscordant couples	4758	TDF, FTC/TDF	63% efficacy for TDF 73% efficacy for FTC/TDF [18]
TDF2 Study (Botswana)	CDC	Heterosexual men and women, ages 18–39 years	1200	FTC/TDF	62% efficacy [19]
VOICE/MTN 003 (South Africa, Uganda, Zimbabwe)	MTN/NIH	Women	5021	TDF, FTC/TDF, vaginal tenofovir gel (daily)	Oral TDF stopped for lack of efficacy September 2011 [20]
Bangkok Tenofovir Study (Thailand)	CDC	Injection drug users	2400	TDF	Ongoing [21]
FACTS 001 (South Africa Department of Science and Technology)	CONRAD, South Africa, USAID, BMGF	Women	2600	Vaginal tenofovir gel (coitally associated use)	Initiated October 2011



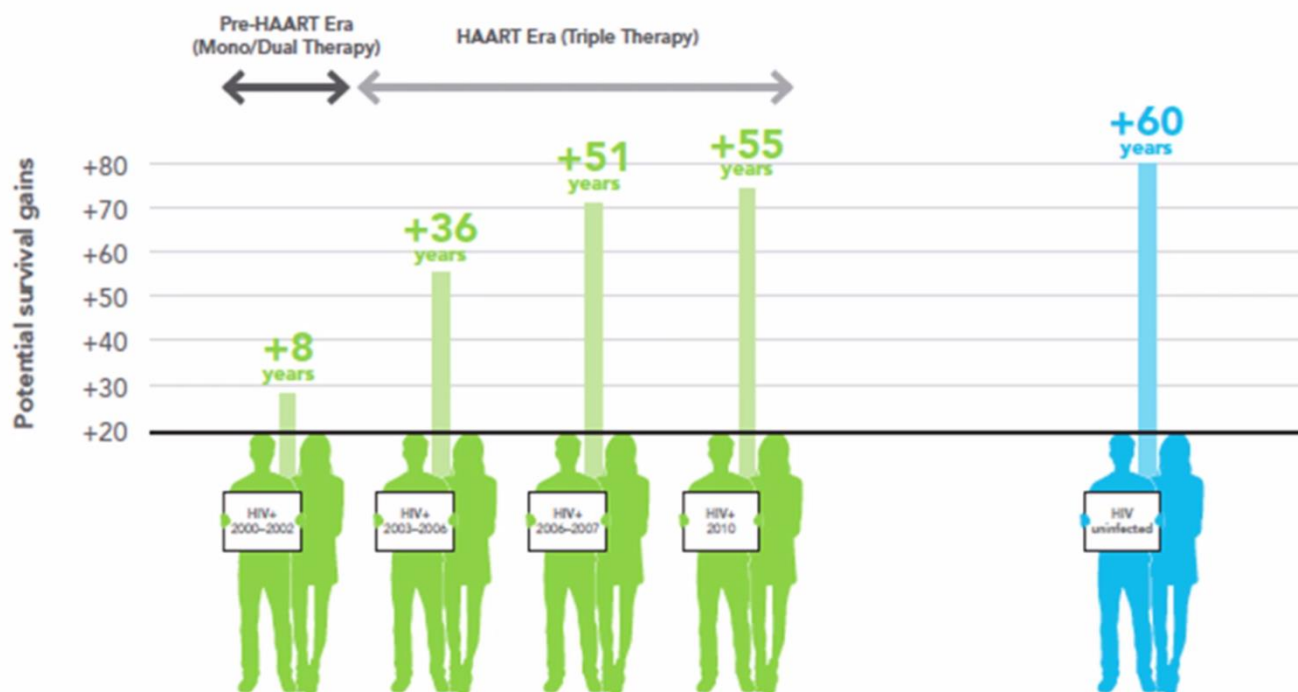
Trasmissione	Efficienza (%)	Modalità preventive	Efficienza (%)
Sessuale	0.5%	Astinenza Be faithful Condom Drugs	100% 100% (partner faithful) 99% 93-96%
Parenterale	0.3%	Precauzioni universali	~ 100%
	99%	Test unità sangue	~ 100%
Verticale			



Trasmissione	Efficienza (%)	Modalità preventive	Efficienza (%)
Sessuale	0.5%	Astinenza Be faithful Condom Drugs	100% 100% (partner faithful) 99% 93-96%
Parenterale	0.3%	Precauzioni universali	100%
	99%	Blood bank	100% (...)
Verticale	20-40%	Terapia Parto cesareo Non allattamento	} > 90%



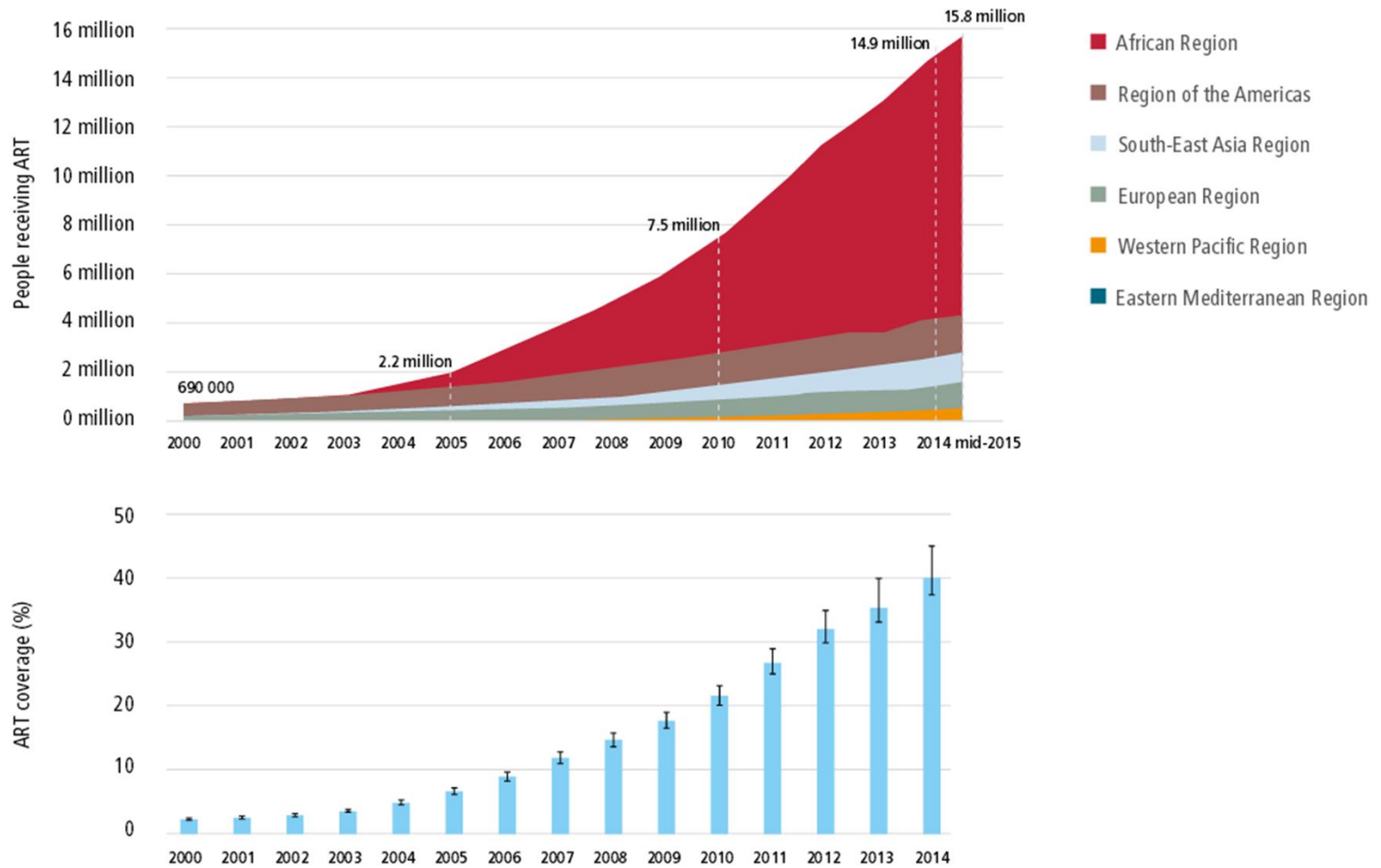
HIV TREATMENT CAN NORMALIZE SURVIVAL



Expected impact of HIV treatment in survival of a 20 years old person living with HIV in a high income setting (different periods)

Source: Samji H et al., PLoS ONE, 2013.

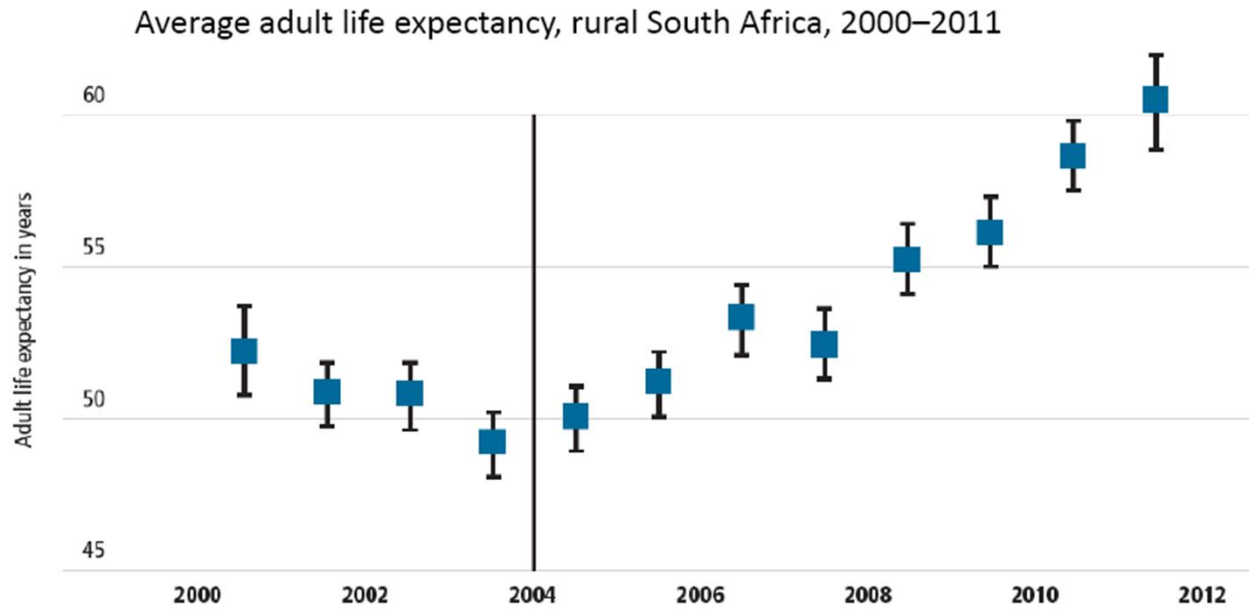
Estimated numbers of people receiving antiretroviral therapy globally and by WHO Region and percentage coverage globally, 2000–2015



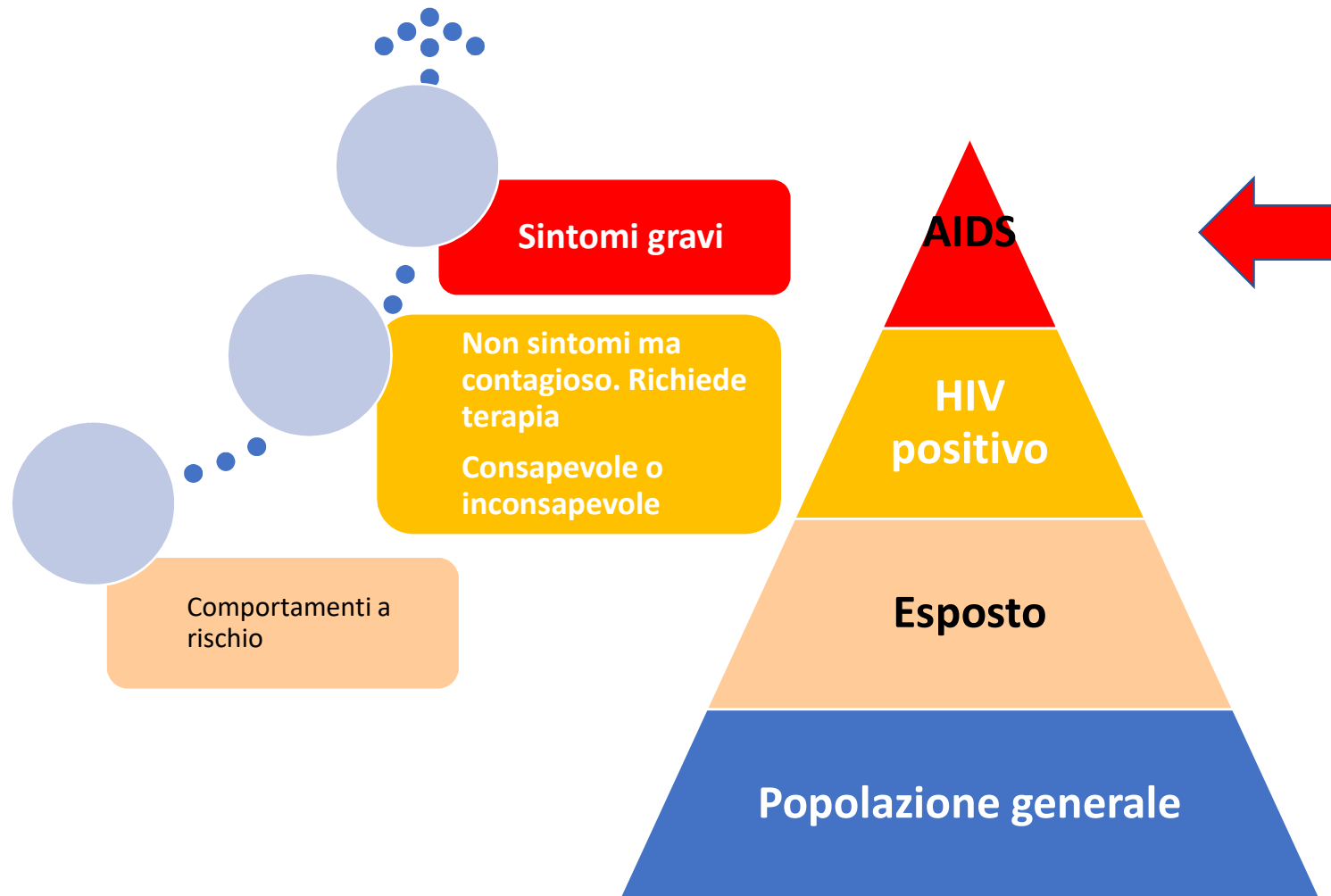
Source: Global AIDS Response Progress Reporting (UNAIDS/UNICEF/WHO) and UNAIDS/WHO estimates.

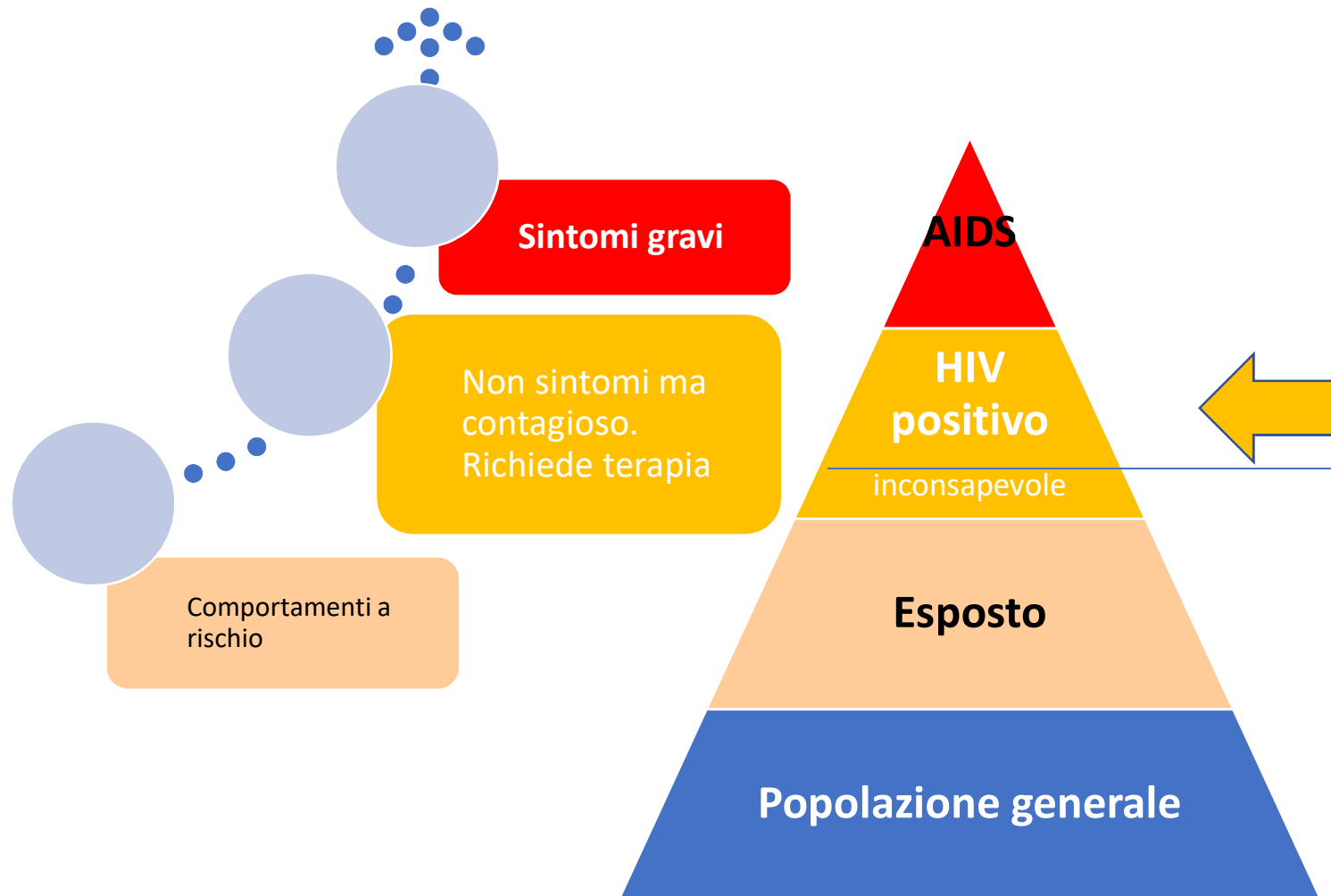


02 | Impact: Life expectancy increase in rural South Africa

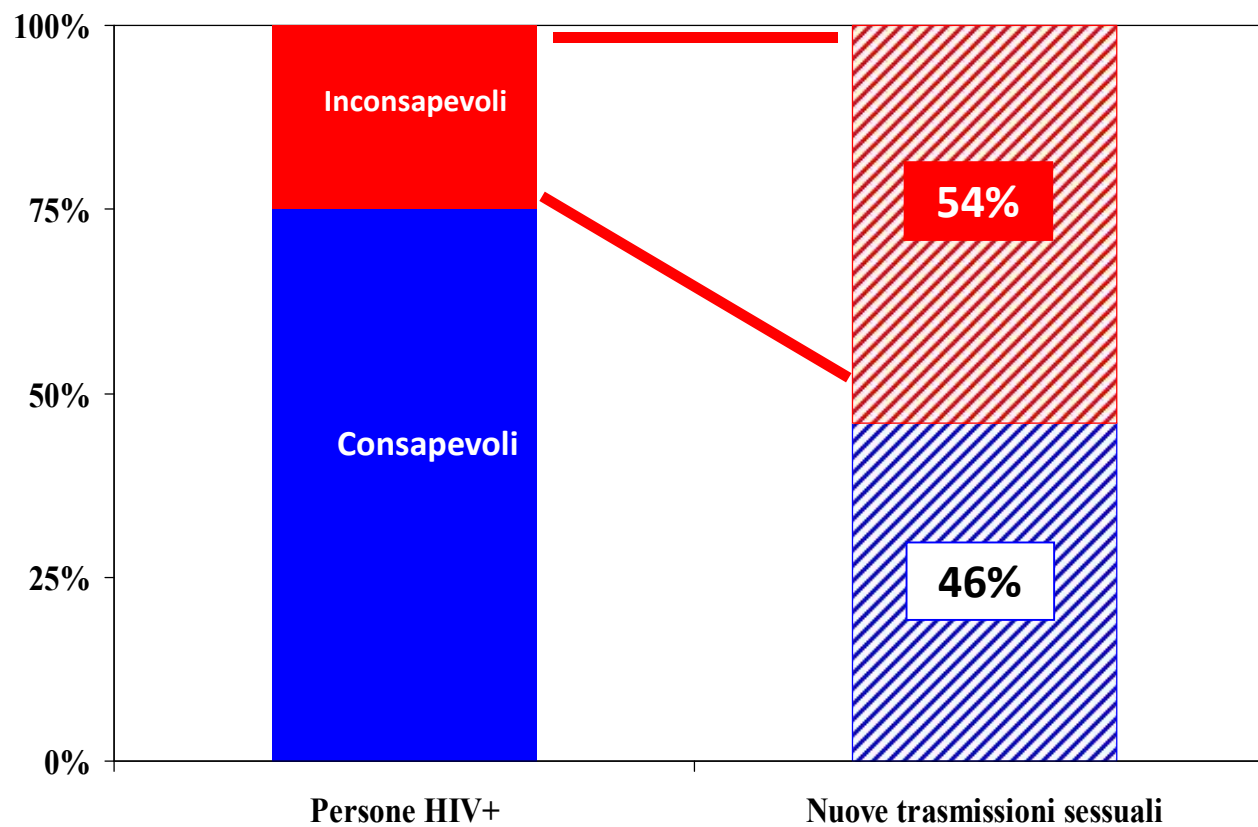


Source: Bor et al. (18). Increases in adult life expectancy in rural South Africa: valuing the scale-up of HIV treatment. *Science*, 2013, 339:961–965.





Il tasso di trasmissione dell'infezione da HIV è correlato con la consapevolezza dell'infezione

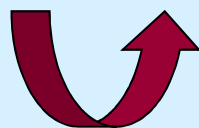


La trasmissione sessuale potrebbe essere ridotta del 31% se tutti i soggetti fossero consapevoli del loro sierostato

Strategie di testing



Italia

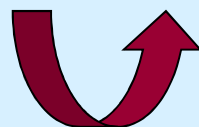


Strategia OPT-IN:

test solo se consenso espresso esplicitamente
(accompagnato da *counseling*), *risk driven*
(popolazioni a rischio o *trigger* clinici di infezione)



USA



Strategia OPT-OUT:

test di *routine* in tutti i soggetti di età compresa tra 13 e 64 anni, che afferiscono a strutture sanitarie (se il soggetto non lo rifiuta esplicitamente).

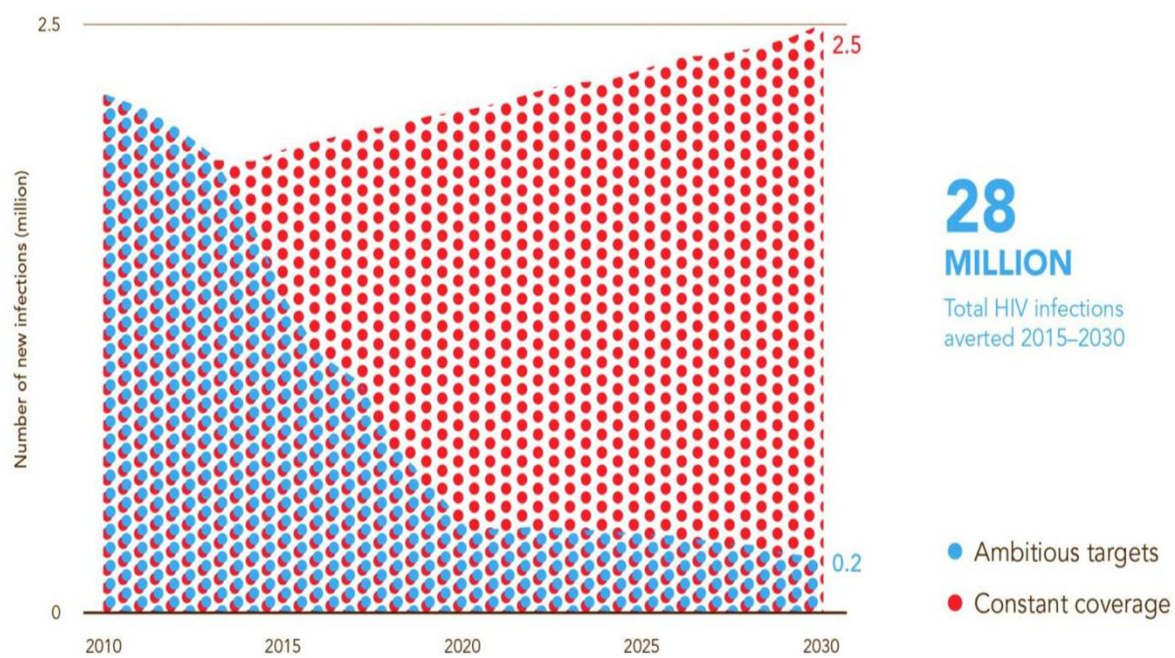
GOAL 3: Ensure healthy lives and promote well-being for all at all ages

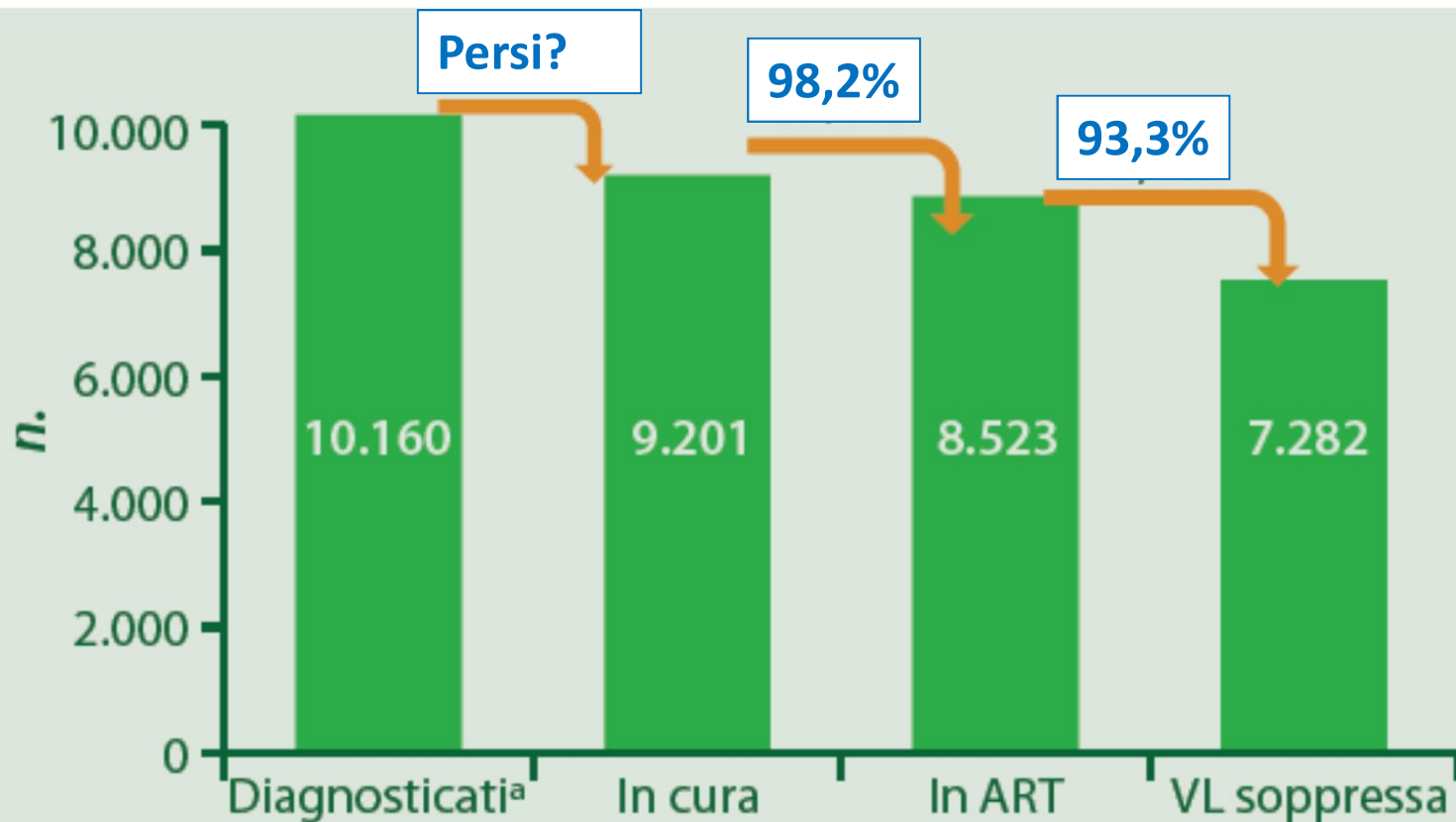
3.3 By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases

TARGETS FOR ENDING THE AIDS EPIDEMIC:

by 2020	90-90-90	by 2030	95-95-95
	Treatment		Treatment
	500 000		200 000
	New infections among adults		New infections among adults
	ZERO		ZERO
	Discrimination		Discrimination

New HIV infections in low- and middle-income countries, 2010–2030, with achievement of ambitious Fast-Track Targets, compared to maintaining 2013 coverage





(a) Diagnosticati presso i centri clinici che hanno avuto accesso almeno una volta

HIV *continuum of care* in 12 centri clinici di malattie infettive in Italia, 2013

Totale pazienti regolarmente seguiti presso ASST Spedali Civili Brescia = 3.822

Totale pazienti in trattamento = 98.2%

Totale pazienti in trattamento con viremia non rilevabili = 93.3%



David Kirby's Final Moments - Benetton Advertisement

Photo © 1990 Therese Frare

1990

1989



E poi...?



Take home messages

- Nel mondo, HIV/AIDS rappresenta ancora priorità di sanità pubblica;
- Nei Paesi industrializzati i progressi terapeutici consentono una aumentata sopravvivenza ed una buona qualità di vita
- Proporzione significativa (12-15%) non consapevole della infezione
 - progressione di malattia
 - trasmissione nella comunità
- Diminuzione della consapevolezza del rischio di infezione
- Modalità di infezione prevalente è sessualità promiscua (etero/MSM)