CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS

From Consensus to Implementation

22-24 September 2013
Queen Elizabeth II Conference Centre, London

Moving the Ball Down the Court. Perspectives from Vancouver 2013

Julio S.G. Montaner, MD

Prof of Medicine; Chair, AIDS Research &Head, Division of AIDS, University of British Columbia; Director, BC Centre for Excellence in HIV/AIDS, St. Paul's Hospital, Providence Healthcare; Past-President, International AIDS Society (2008-2010).

Impact of HAART Expansion on Morbidity, Mortality and HIV Transmission.

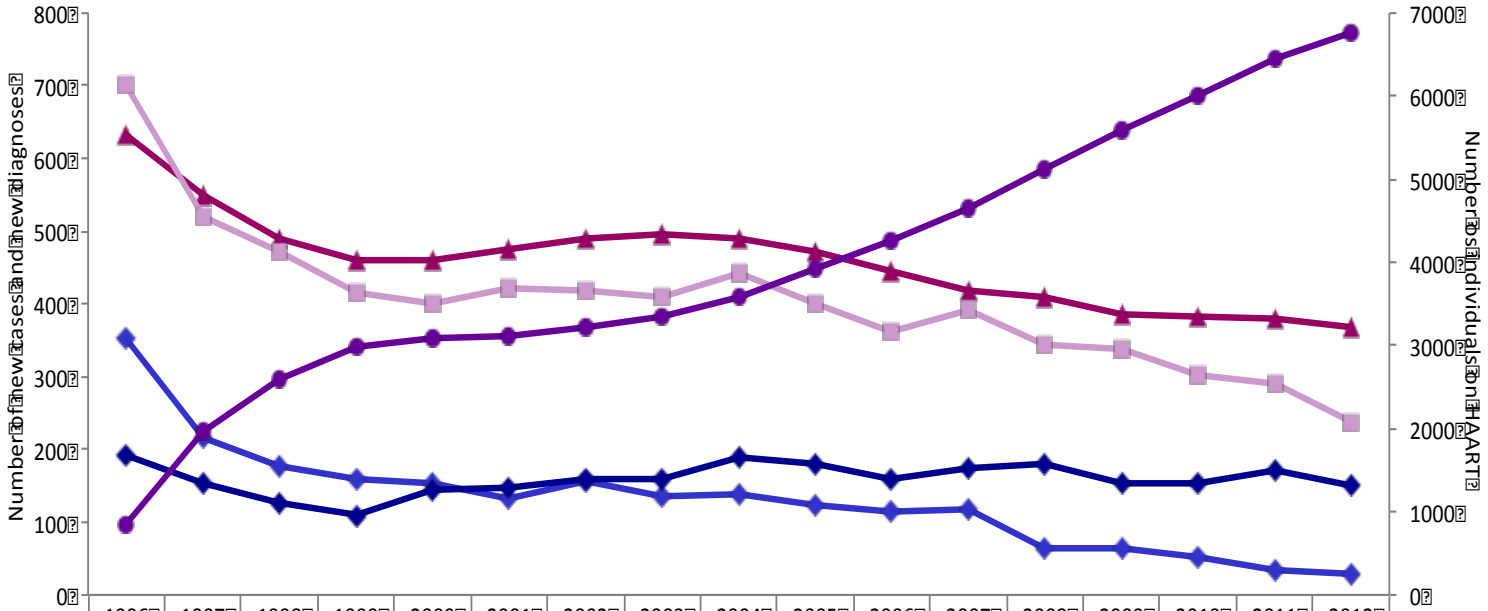
HIV "Treatment as Prevention" in B.C.

J Montaner, V Lima, R Harrigan, L Lourenço, B Yip, B Nosyk, E Wood, T Kerr, K Shannon, D Moore, R Hogg, R Barrios, M Gilbert, M Krajden, R Gustafson, P Daly, P Kendall

Main Funding Sources: BC-Ministry of Health Services, US National Institute on Drug Abuse (Avant-Garde Award No. 1DP1DA026182-01), Michael Smith Health Research Foundation, and Canadian Institutes of Health Research.

Additional research funding: Gilead Sciences, Janssen, Merck and ViiV Healthcare.

HAART USE and HIV Transmission in BC



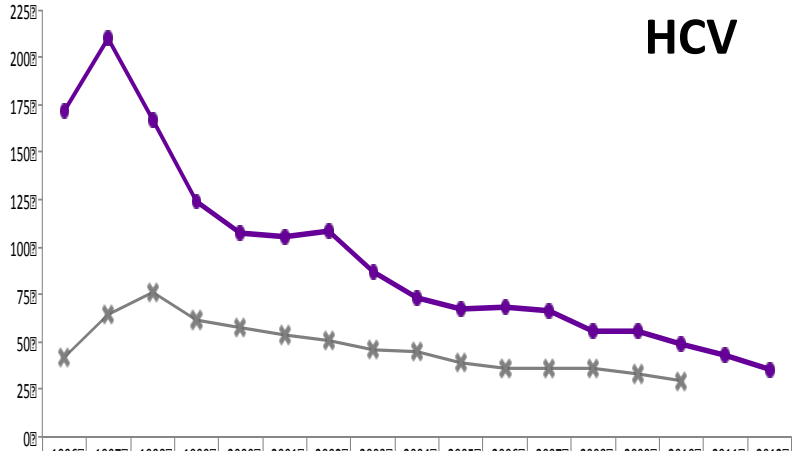
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
HIV Incidence	632	551	490	461	461	476	489	495	490	472	446	418	408	387	382	380	368
New HIV Diagnoses	702	519	471	416	400	420	418	408	442	400	361	391	345	337	301	289	238
New HIV Diagnoses (ever IDU)	352	215	177	159	152	132	156	136	137	125	115	118	65	64	52	34	29
New HIV Diagnoses (MSM)	192	154	126	110	144	147	158	158	188	181	160	173	181	153	153	170	149
Active on HAART	837	1960	2596	2994	3079	3120	3211	3356	3585	3913	4256	4654	5123	5594	5999	6459	6772
HIV Prevalence	7900	8228	8593	8933	9150	9408	9690	9936	10216	10398	10566	10790	11040	11280	11500	11700	11972

Our model suggests that for every 1% increase in the number of individuals suppressed on HAART, the estimated HIV incidence decreased by 1%.

BC Centre for Disease Control
An agency of the Provincial Health Services Authority

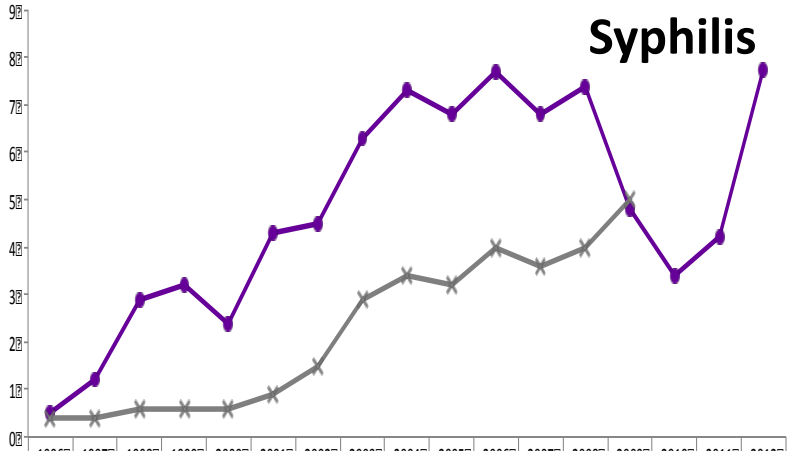
HCV and STIs in BC

HCV



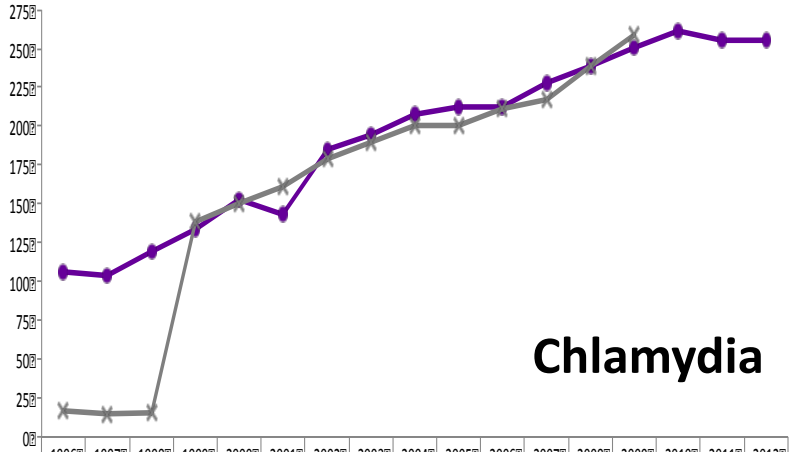
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
BC Hepatitis C Reports	6636	8282	6703	4984	4359	4282	4446	3617	3086	2879	2935	2898	2479	2484	2228	1970	1653
BC Hepatitis C Rate	172.1	210.1	167.2	124.3	107.9	105.0	108.0	87.0	73.4	67.6	67.9	66.2	55.8	55.7	49.2	43.1	35.6
Canadian Hepatitis C Rate	41.8	64.6	76.2	61.7	57.8	54.1	50.7	45.5	45.1	39.3	36.5	35.8	36.1	33.2	29.6		

Syphilis



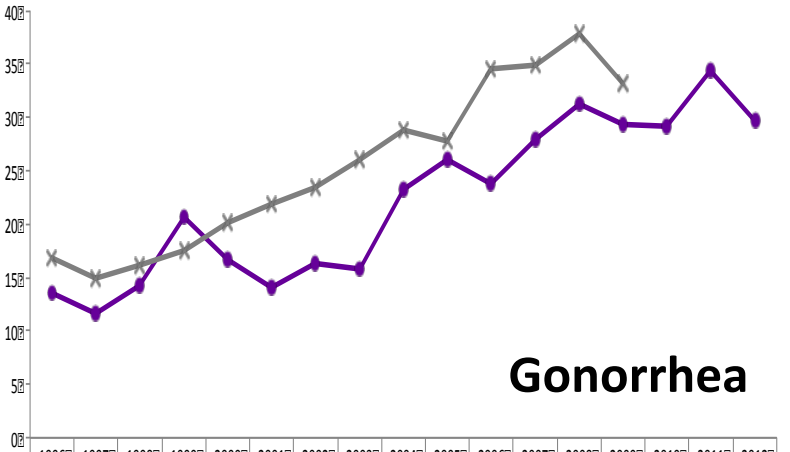
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
BC Syphilis Reports	20	49	115	128	95	176	186	262	305	288	331	300	328	216	154	193	360
BC Syphilis Rate	0.5	1.2	2.9	3.2	2.4	4.3	4.5	6.3	7.3	6.8	7.7	6.8	7.4	4.8	3.4	4.2	7.7
Canadian Syphilis Rate	0.4	0.4	0.6	0.6	0.6	0.9	1.5	2.9	3.4	3.2	4.0	3.6	4.0	5.0			

Chlamydia



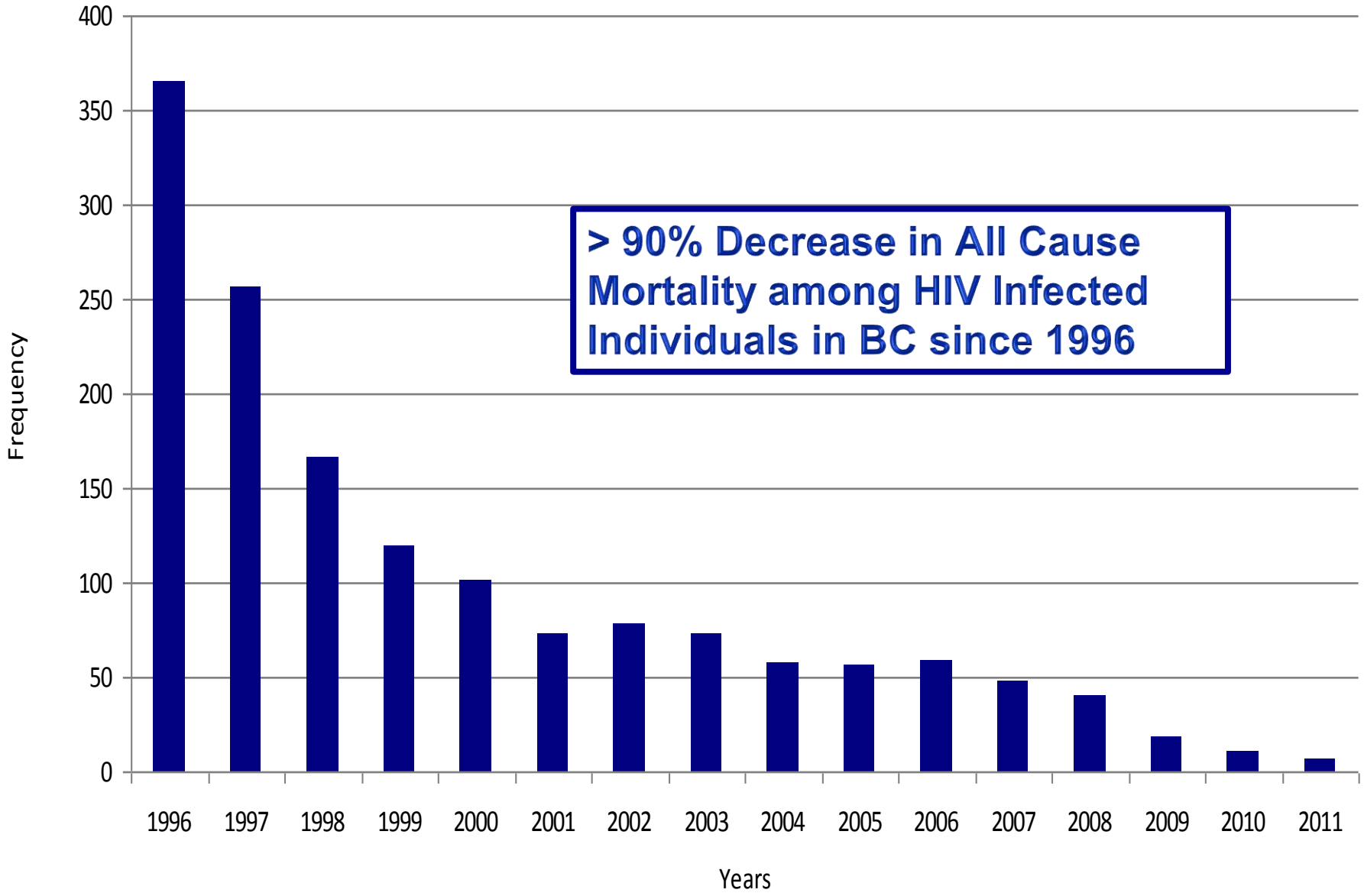
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
BC Chlamydia Reports	4416	4416	4769	5343	6150	5855	7603	8071	8733	9045	9172	9971	10629	11176	11846	11730	11888
BC Chlamydia Rate	106.0	103.9	119.3	133.2	152.3	143.6	184.7	194.2	207.7	212.3	212.3	227.6	239.3	250.9	261.8	255.5	255.9
Canadian Chlamydia Rate	16.9	14.9	16.1	138.2	150.9	161.4	179.4	189.4	200.1	200.4	211.4	217.3	239.3	258.5			

Gonorrhea



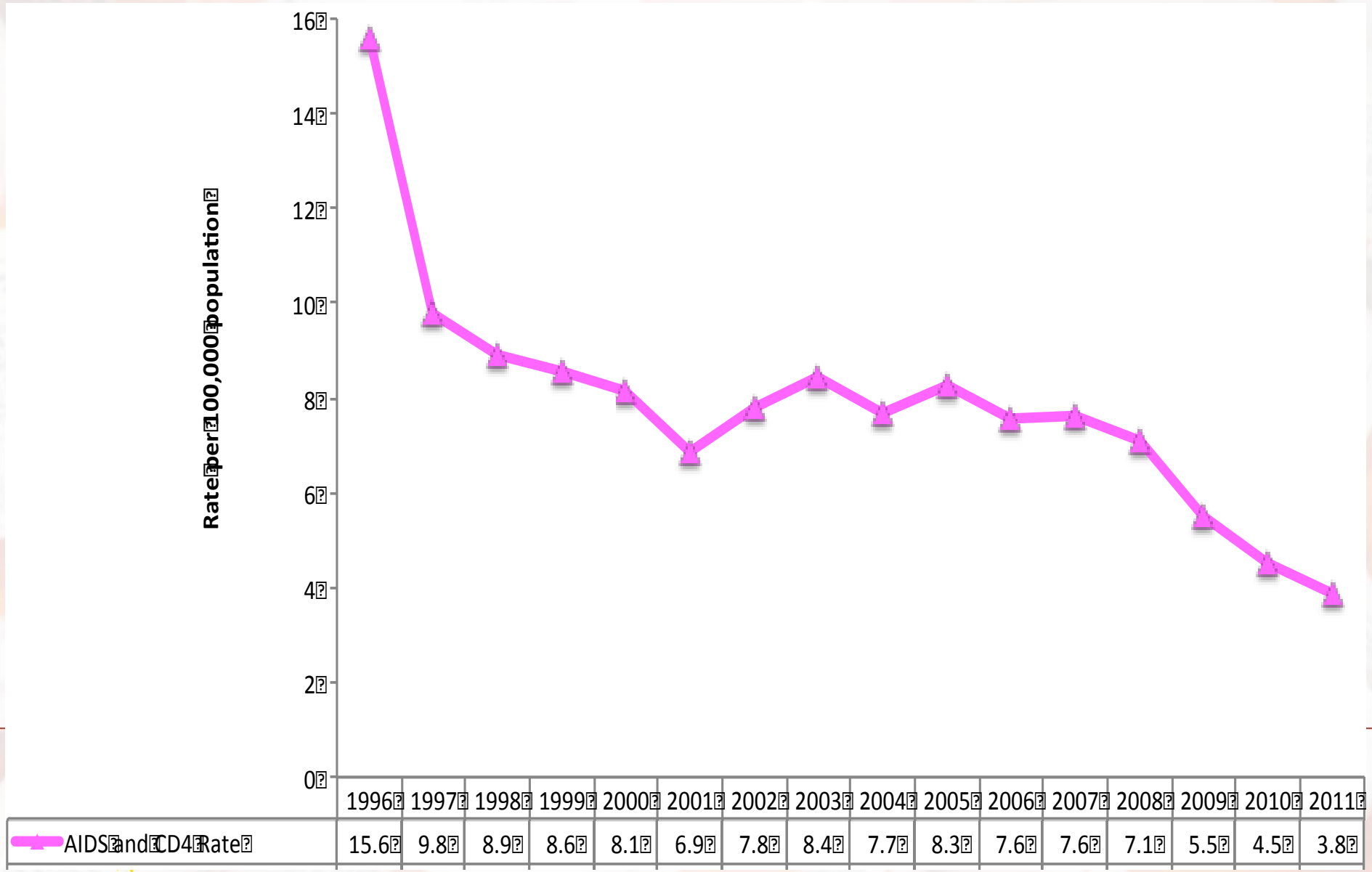
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
BC Gonorrhea Reports	527	458	569	827	675	571	675	656	979	1111	1026	1220	1391	1309	1321	1573	1380
BC Gonorrhea Rate	13.6	11.6	14.2	20.6	16.7	14.0	16.4	15.8	23.3	26.1	23.7	27.9	31.3	29.4	29.2	34.3	29.7
Canadian Gonorrhea Rate	16.9	14.9	16.1	17.6	20.1	21.8	23.5	26.0	28.9	27.8	34.5	34.9	37.8	33.1			

Mortality

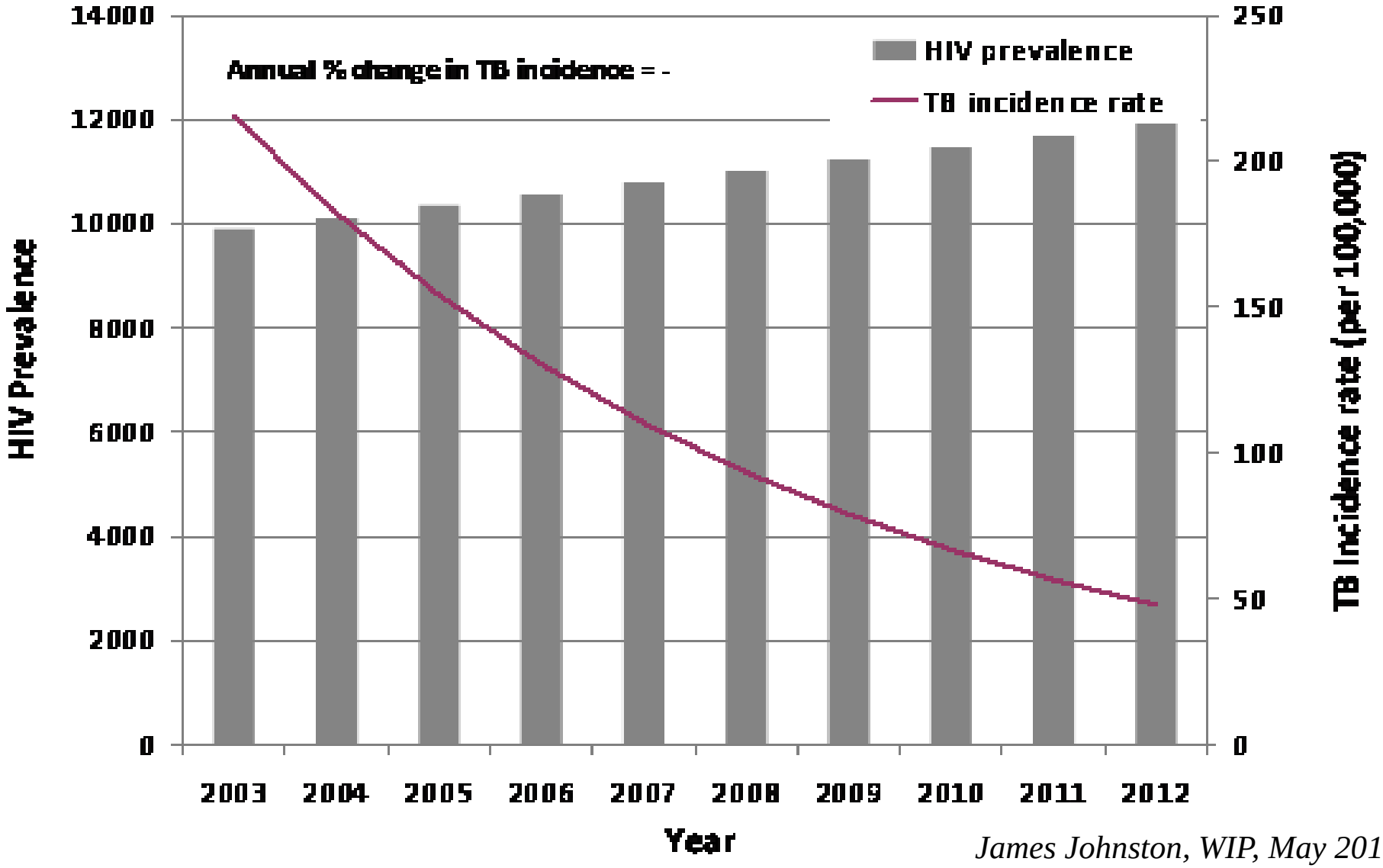


Montaner et al, TasP Workshop, April 2012

New AIDS (ADIs + CD4 <200/mm^3)

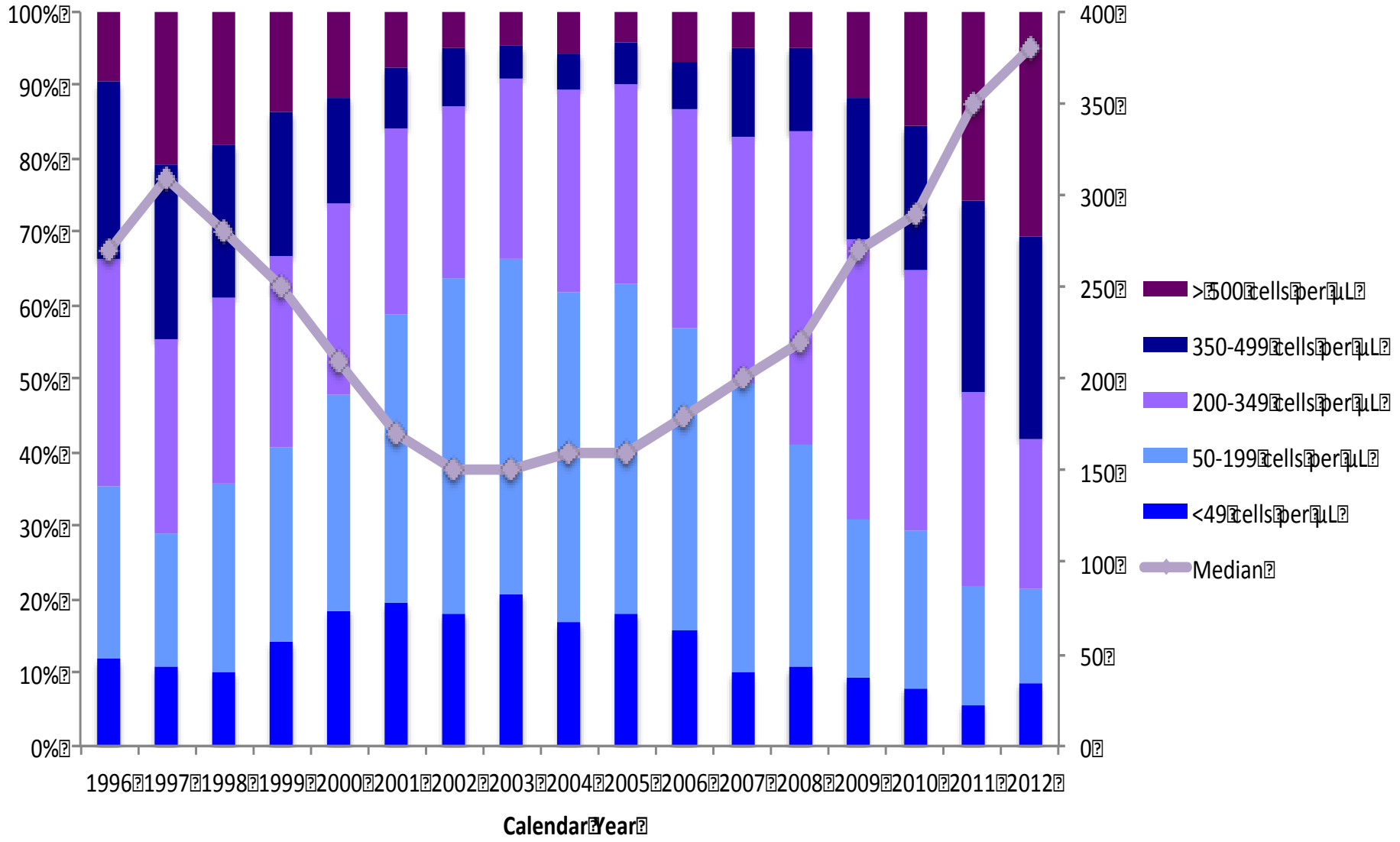


BC: HIV Prevalence and TB Incidence

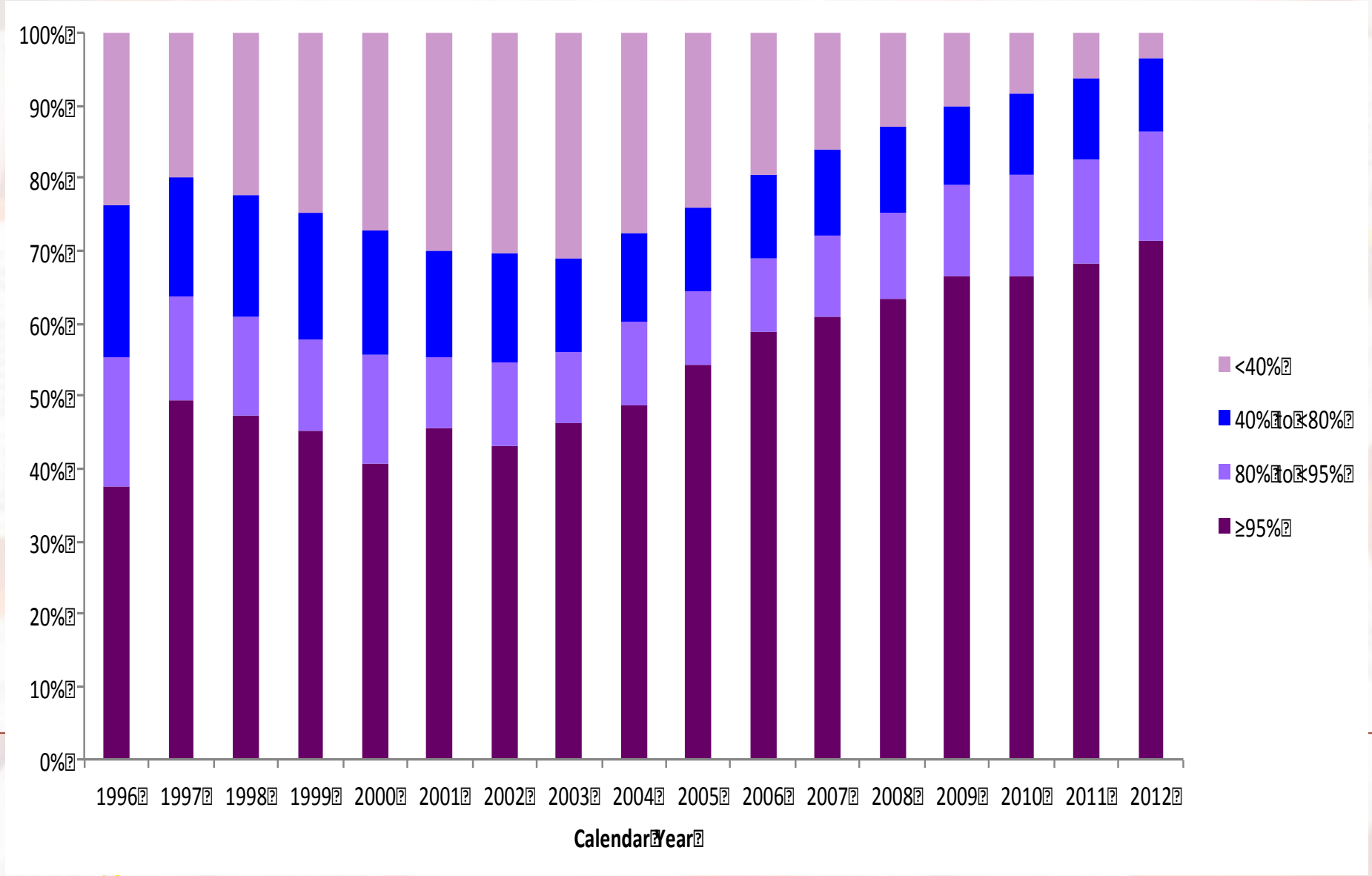


James Johnston, WIP, May 2013

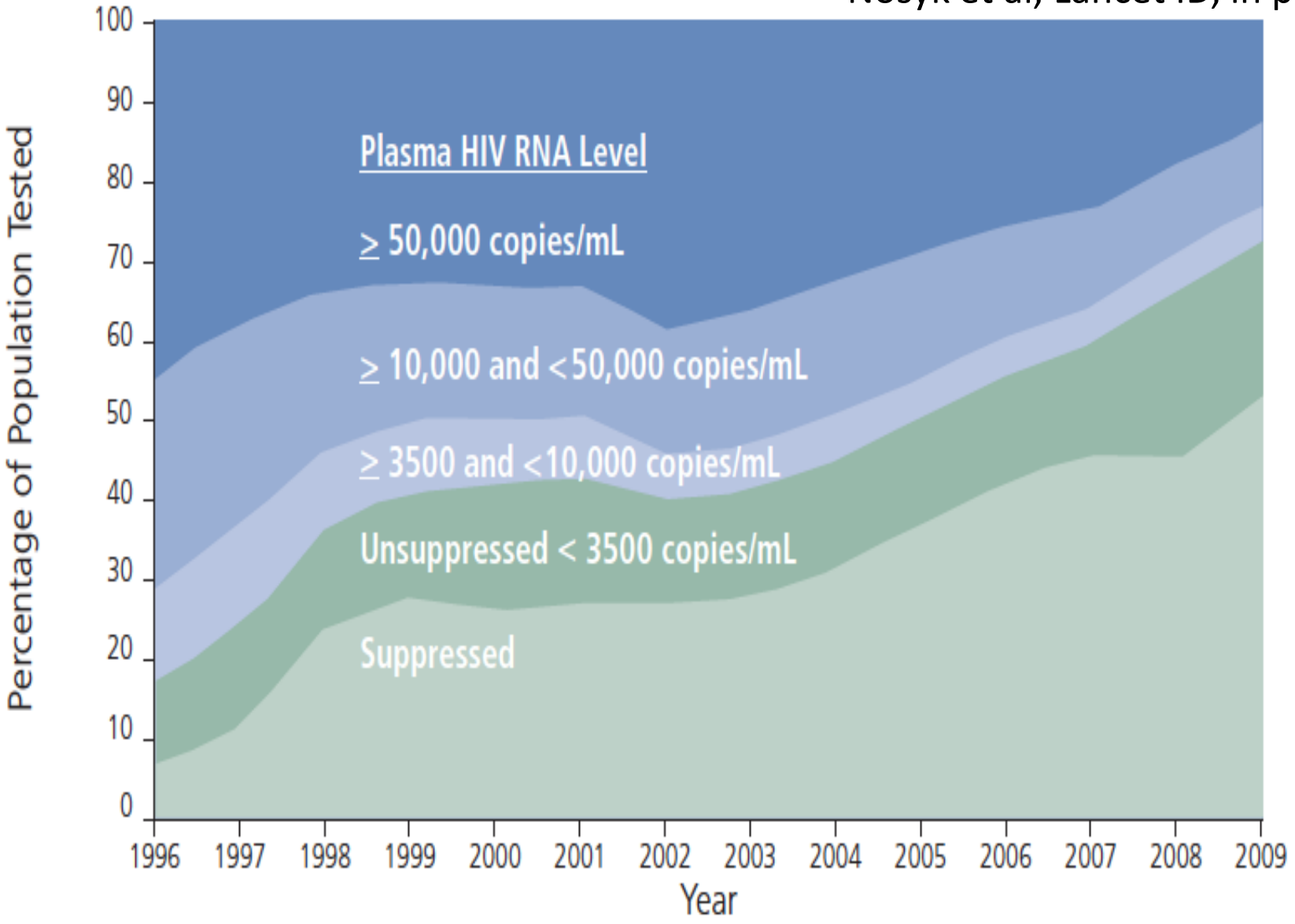
Baseline (pre-HAART) CD4 Counts



Adherence (Refill Compliance)



Nosyk et al, Lancet ID, in press

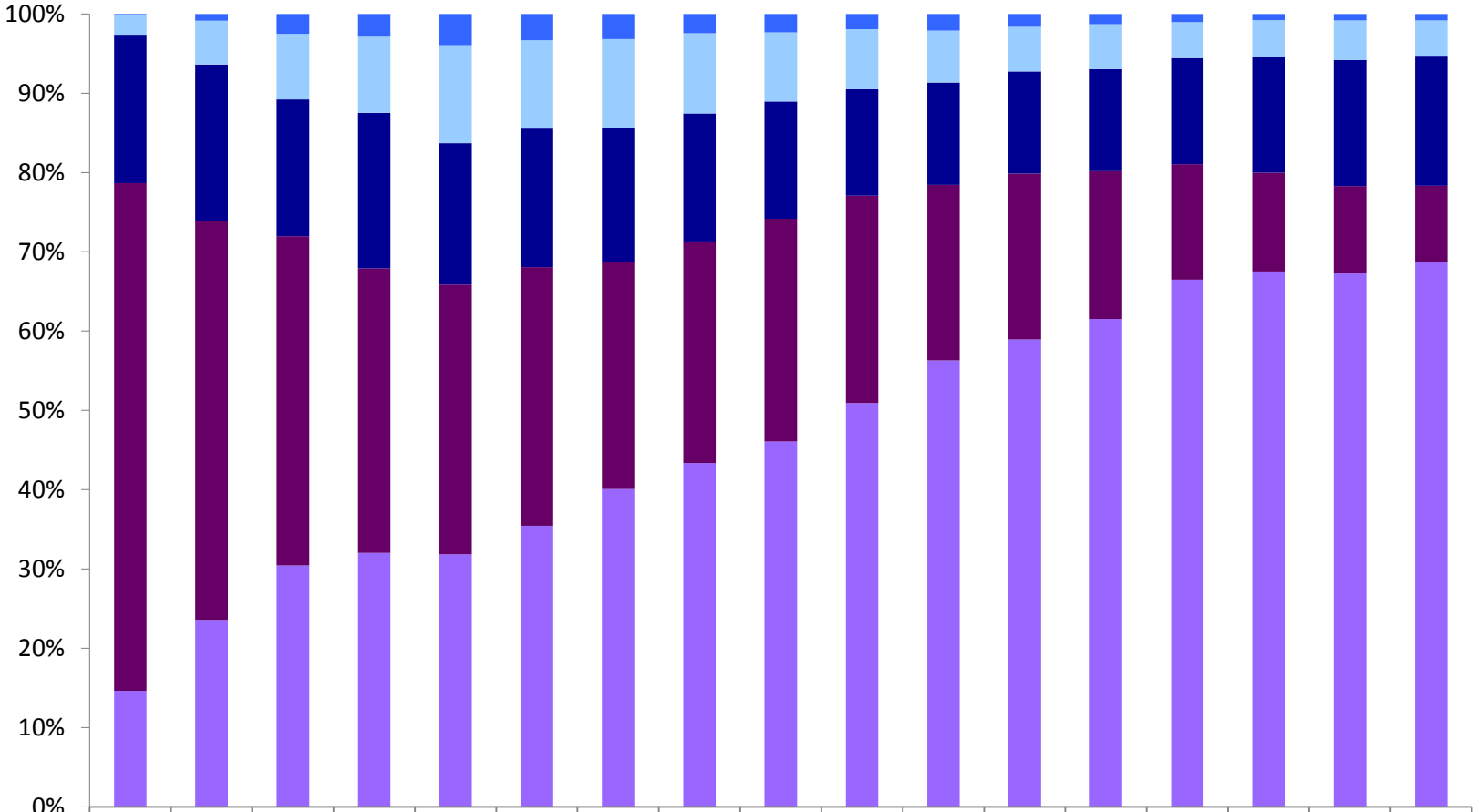


Denominator	2882	3864	4227	4440	4627	4895	5090	5302	5569	5744	5877	6159	6334	6596
Actively on antiretroviral therapy	837	1960	2597	2994	3079	3120	3211	3356	3585	3913	4255	4654	5123	5413
No. of plasma HIV RNA tests	4896	10,803	12,930	14,117	15,888	17,673	19,663	21,259	22,677	23,110	23,815	24,897	26,009	26,818

HIV-1-RNA Levels

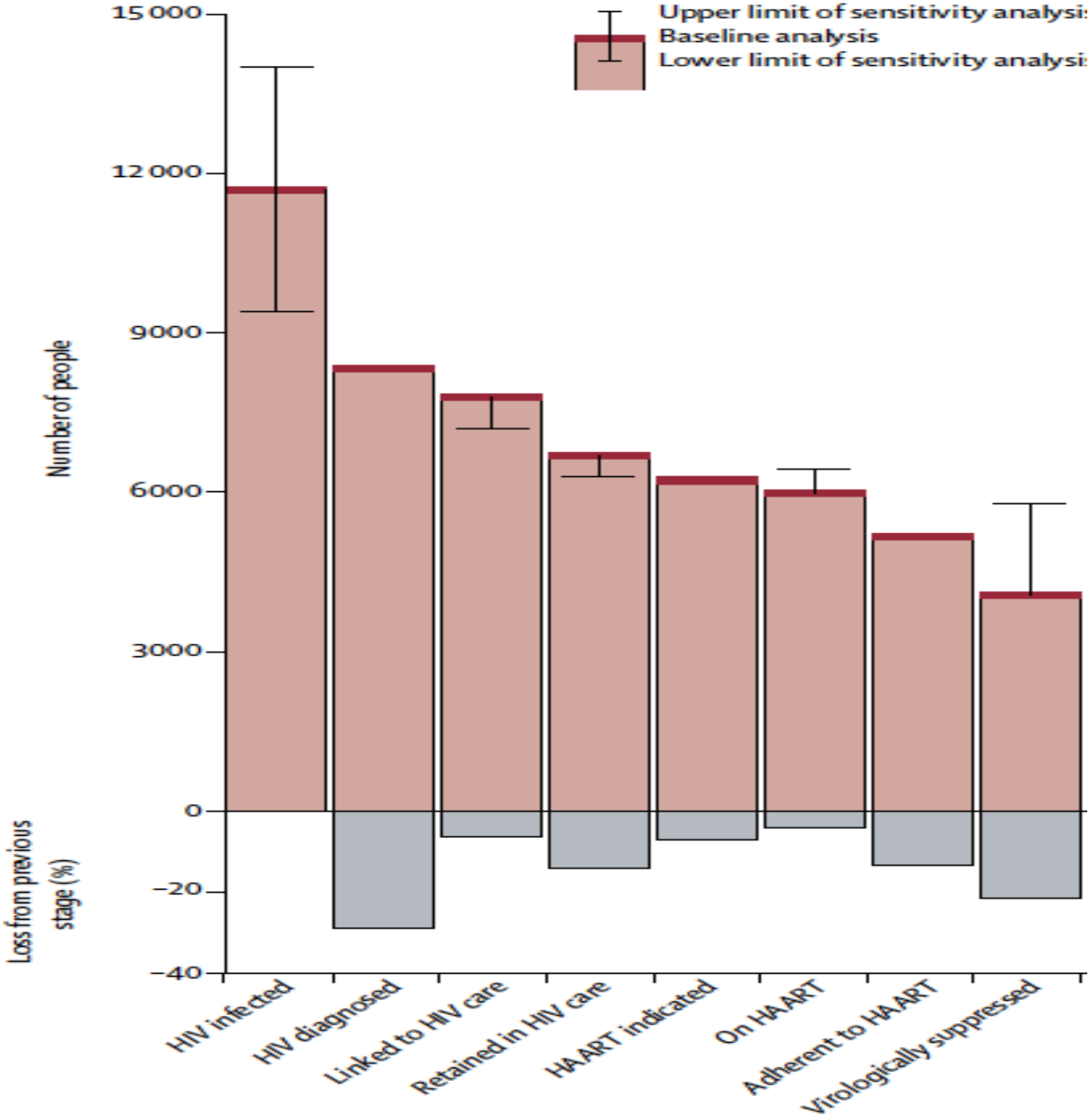
Year	N	Patients with <500 copies/mL (%)	Median HIV-1 RNA plasma concentration (copies per mL; Q1-Q3)	Patients with <50 copies/mL (%)	Median HIV-1 RNA plasma concentration (copies per mL; Q1-Q3)
1996	2924	224 (8%)	35500 (6800 – 100010)	NA (-)	NA (-)
1997	4180	585 (14%)	24000 (3200 – 100010)	NA (-)	NA (-)
1998	4879	1292 (26%)	13000 (499 – 92000)	NA (-)	NA (-)
1999	5443	1755 (32%)	9470 (499 – 84200)	307 (6%)	9470 (359 – 84200)
2000	5931	2052 (35%)	9400 (499 – 85000)	1387 (23%)	9400 (88 – 85000)
2001	6461	2386 (37%)	7700 (499 – 80200)	1693 (26%)	7700 (49 – 80200)
2002	6985	2670 (38%)	10200 (499 – 97000)	1939 (28%)	10200 (49 – 97000)
2003	7437	2902 (39%)	8960 (499 – 86200)	2185 (29%)	8960 (49 – 86200)
2004	7906	3340 (42%)	5035 (499 – 71200)	2577 (33%)	5035 (49 – 71200)
2005	8277	3775 (46%)	2230 (499 – 61600)	3014 (36%)	2230 (49 – 61600)
2006	8552	4195 (49%)	699.5 (499 – 52350)	3431 (40%)	699.5 (49 – 52350)
2007	8868	4621 (52%)	499 (499 – 45350)	3803 (43%)	359 (49 – 45350)
2008	9343	5324 (57%)	499 (499 – 26800)	4033 (43%)	136 (49 – 26800)
2009	9963	6227 (63%)	499 (499 – 14400)	4992 (50%)	49 (49 – 14400)
2010	10548	7060 (67%)	499 (499 – 8514)	5600 (53%)	49 (49 – 8514)
2011	11191	7918 (71%)	499 (499 – 2770)	6237 (56%)	49 (49 – 2770)
2012	11805	8747 (74%)	499 (499 – 755)	7007 (59%)	49 (49 – 755)

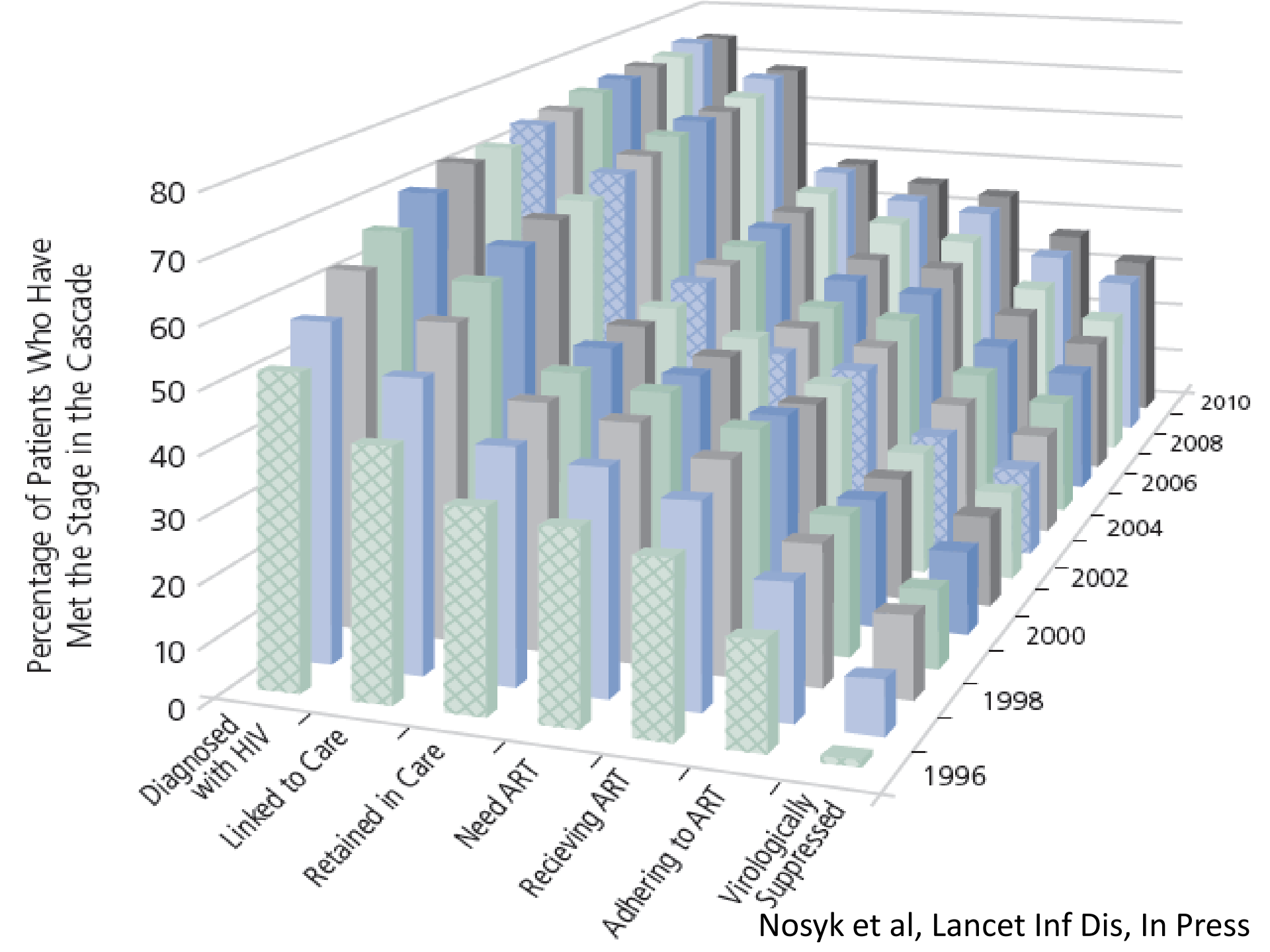
ARV Drug Resistance



	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
3 Classes	3	32	81	123	137	120	119	94	89	69	71	54	45	33	24	25	24
2 Classes	74	207	267	411	426	402	417	387	334	275	221	188	198	141	142	155	130
1 Class	546	740	557	840	617	630	630	617	565	485	435	429	447	420	451	493	481
Never Genotyped	1870	1889	1342	1537	1175	1176	1071	1070	1075	946	746	697	650	457	384	341	282
Wild Type	427	884	983	1371	1100	1278	1497	1659	1762	1842	1898	1965	2142	2084	2081	2084	2014

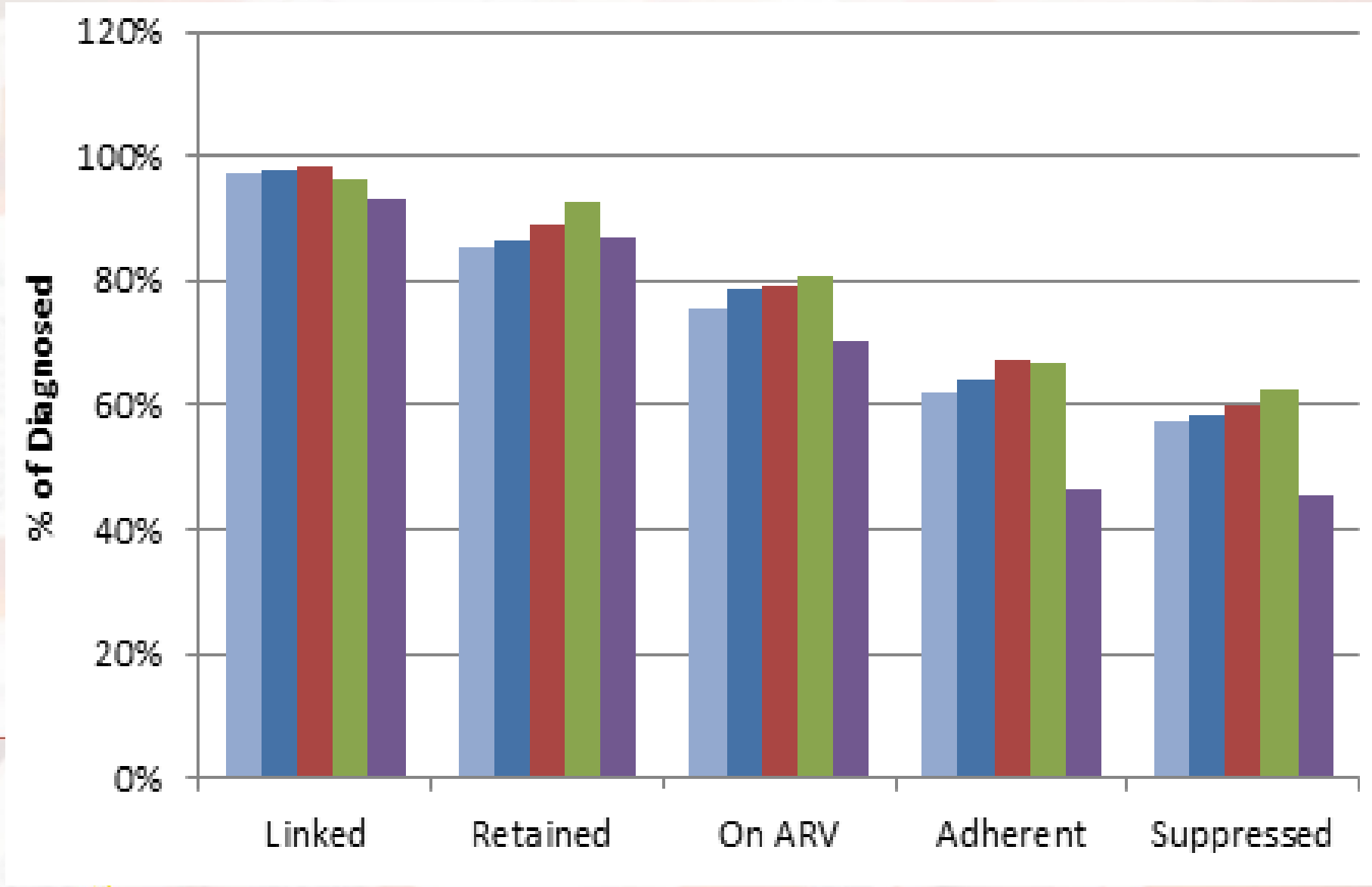
The Cascade of Care

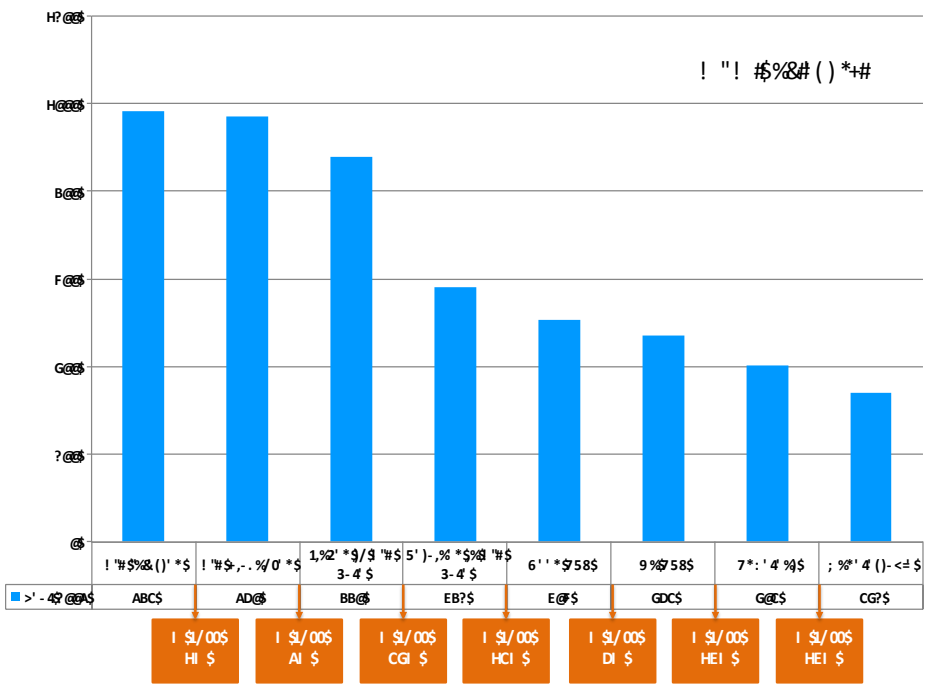

Upper limit of sensitivity analysis
Baseline analysis
Lower limit of sensitivity analysis
15 000
12 000
9000
6000
3000
0
−20
−40
Number of people
Loss from previous stage (%)
HIV infected
HIV diagnosed
Linked to HIV care
Retained in HIV care
HAART indicated
On HAART
Adherent to HAART
Virologically suppressed

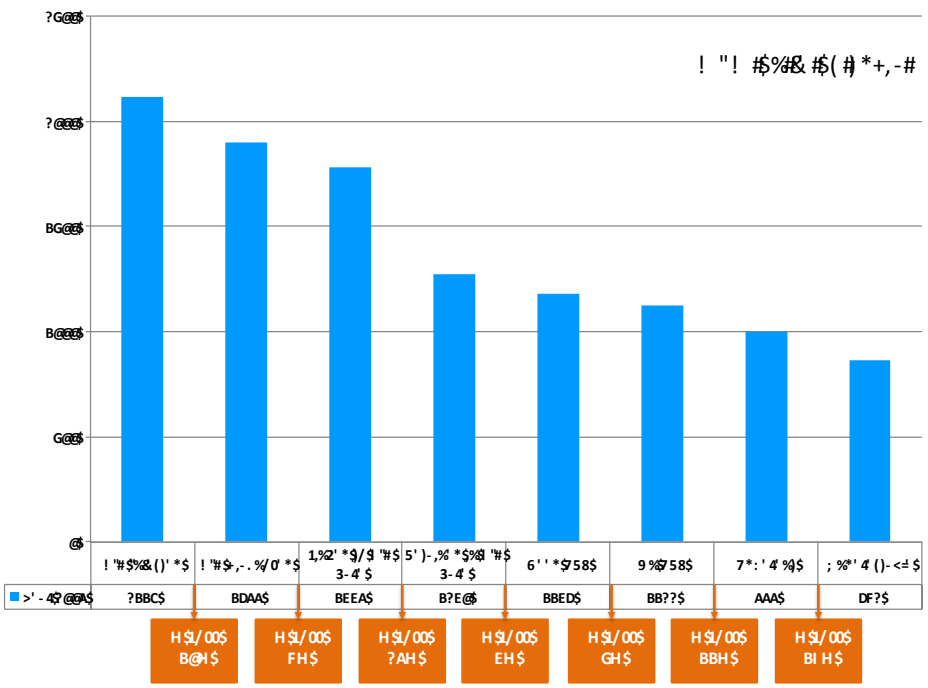


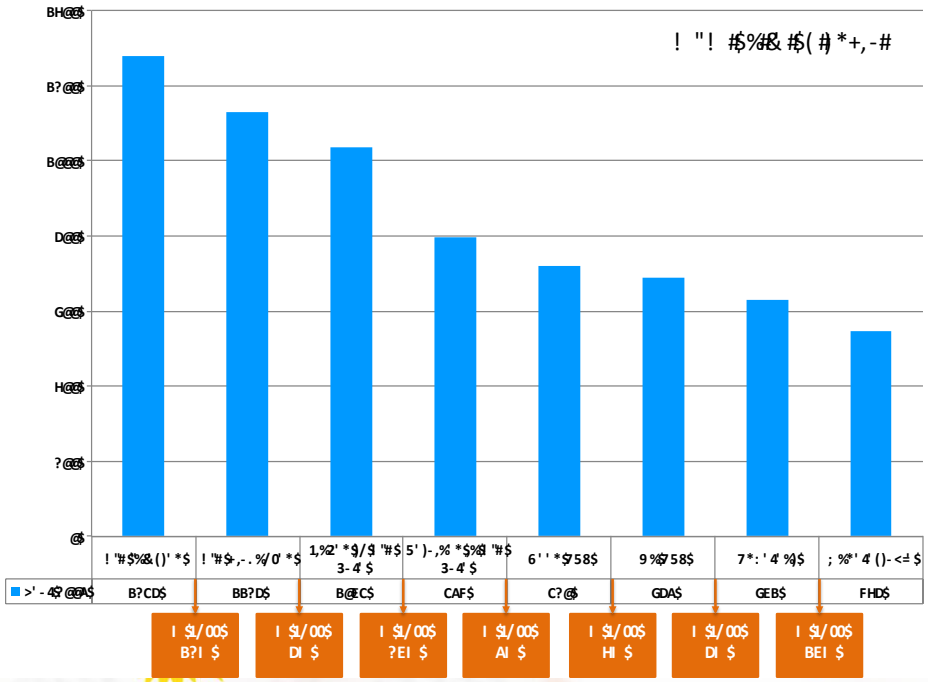
Nosyk et al, Lancet Inf Dis, In Press

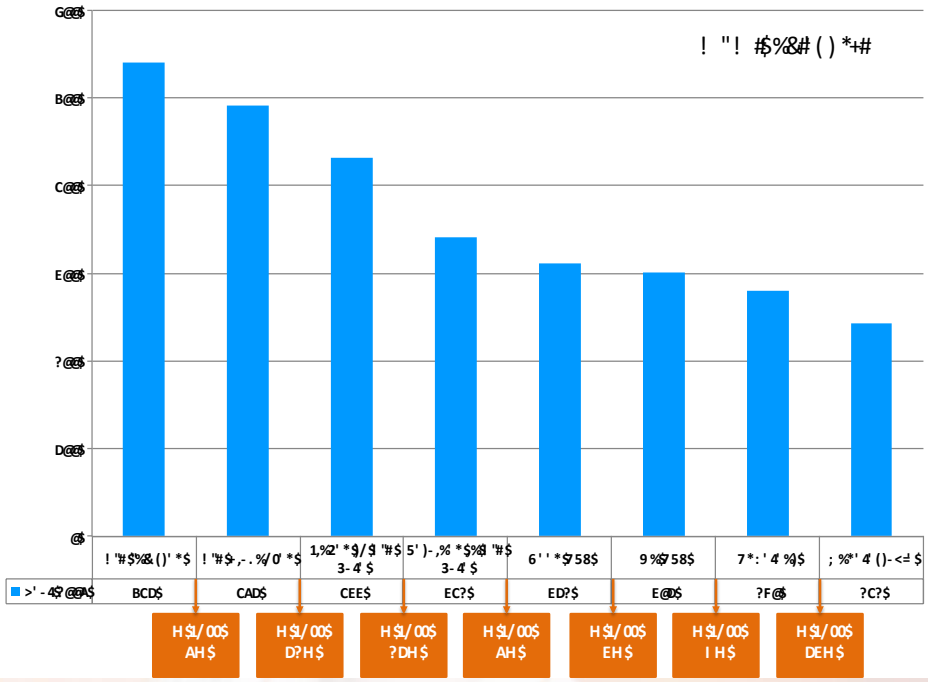
Cascade of Care by HA, June 2012











Lima et al, Int TasP Workshop, 2013

Programatic Compliance Score

Programmatic Compliance Score

Assesses the impact of non-compliance with HIV treatment guidelines on all-cause mortality

PCS components include:

- Baseline CD4 > 200/mm3
- Three CD4 in 1st year
- Three VL in 1st year
- Baseline resistance
- Recommended HAART
- Undetectable pVL at 9 months

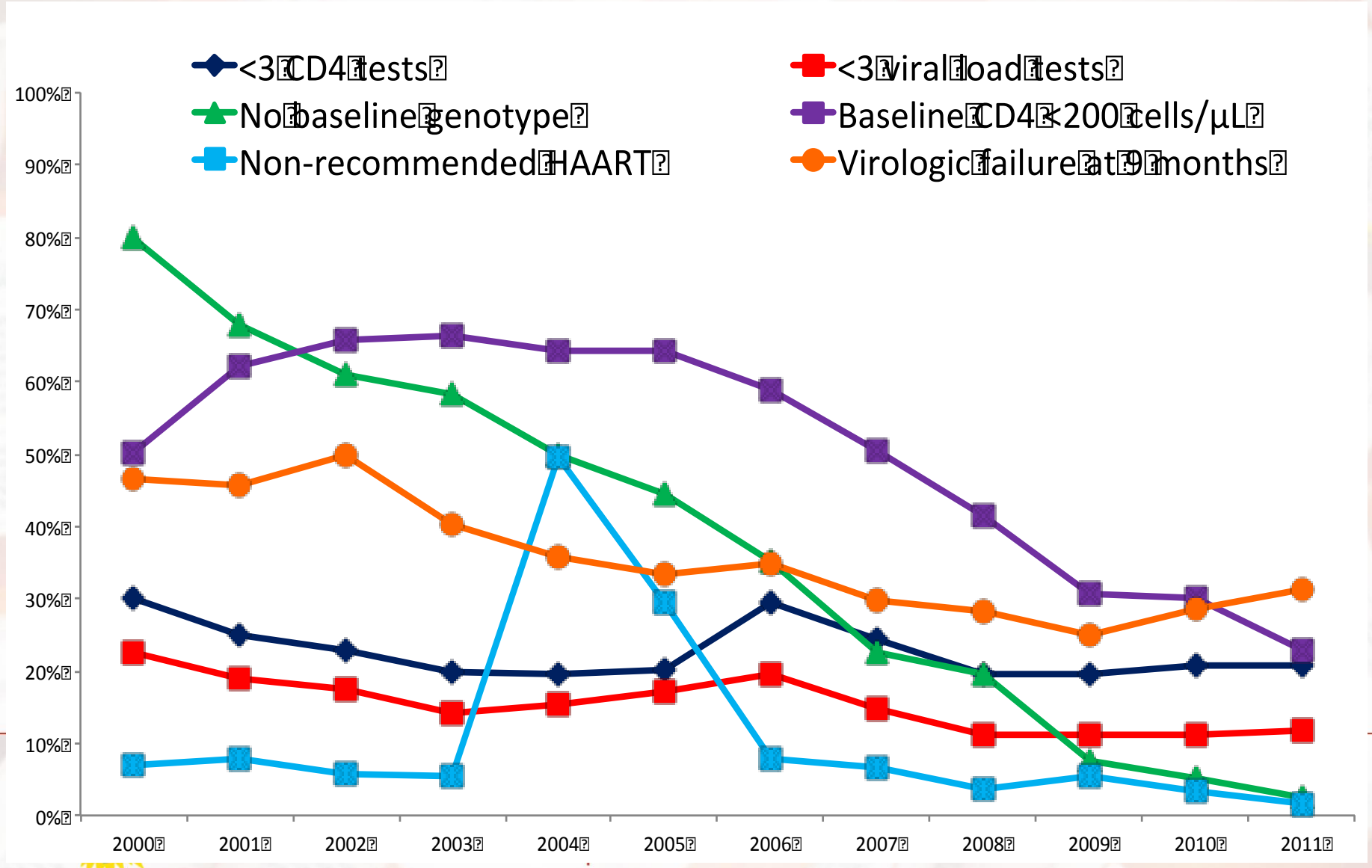
Failure to meet a given component add one to the score

PCS predicts **mortality**

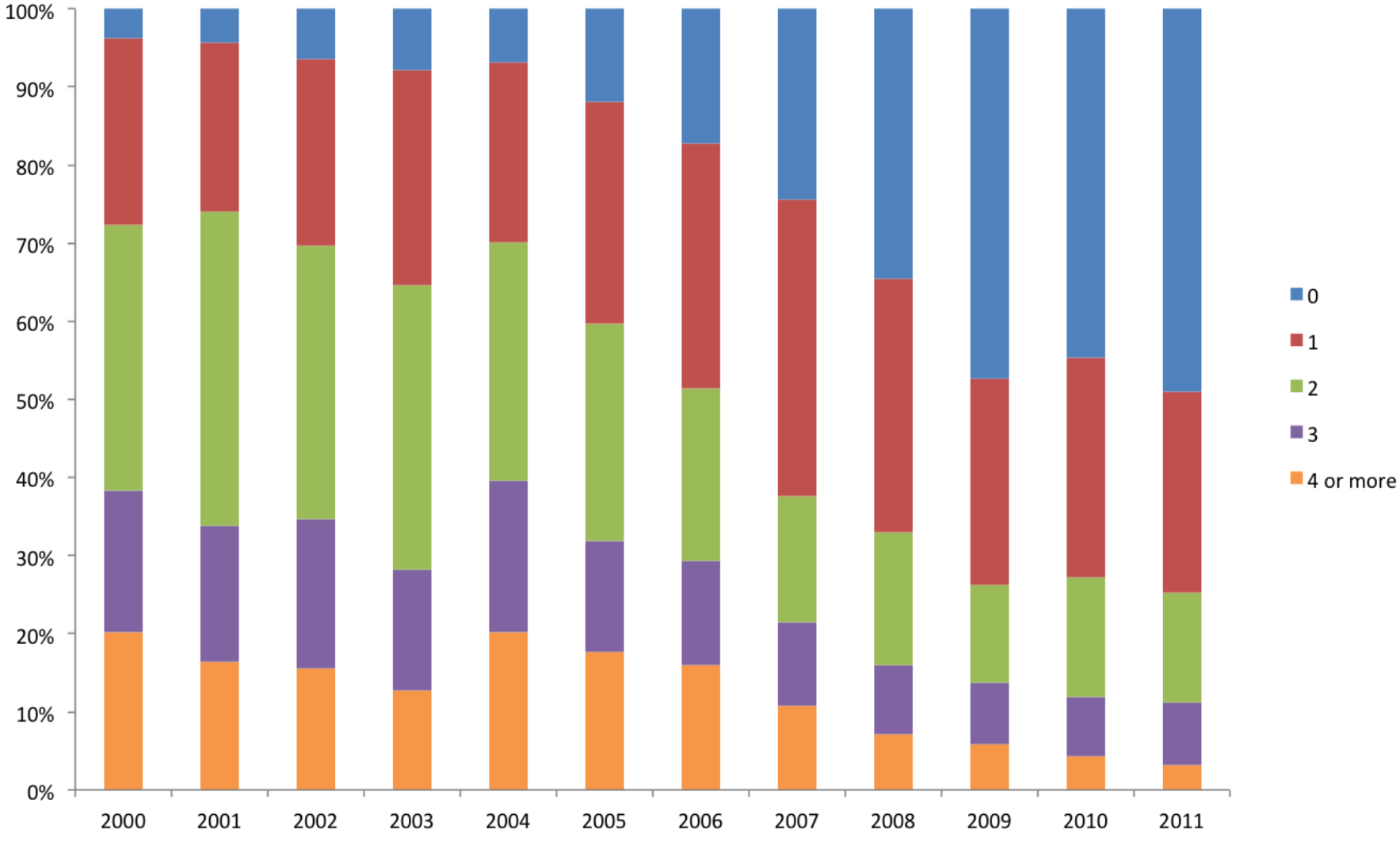
Lima et al. PLoS ONE 7(11): e47859. 2012

Programmatic Compliance Score	Odds Ratio (95% Confidence Interval)	Type III P-value
0	1 (-)	<0.0001
1	3.81 (1.73–8.42)	
2	7.97 (3.70–17.18)	
3	11.51 (5.28–25.08)	
4 or more	22.37 (10.46–47.84)	

Programmatic Compliance Score



Programmatic Compliance Score

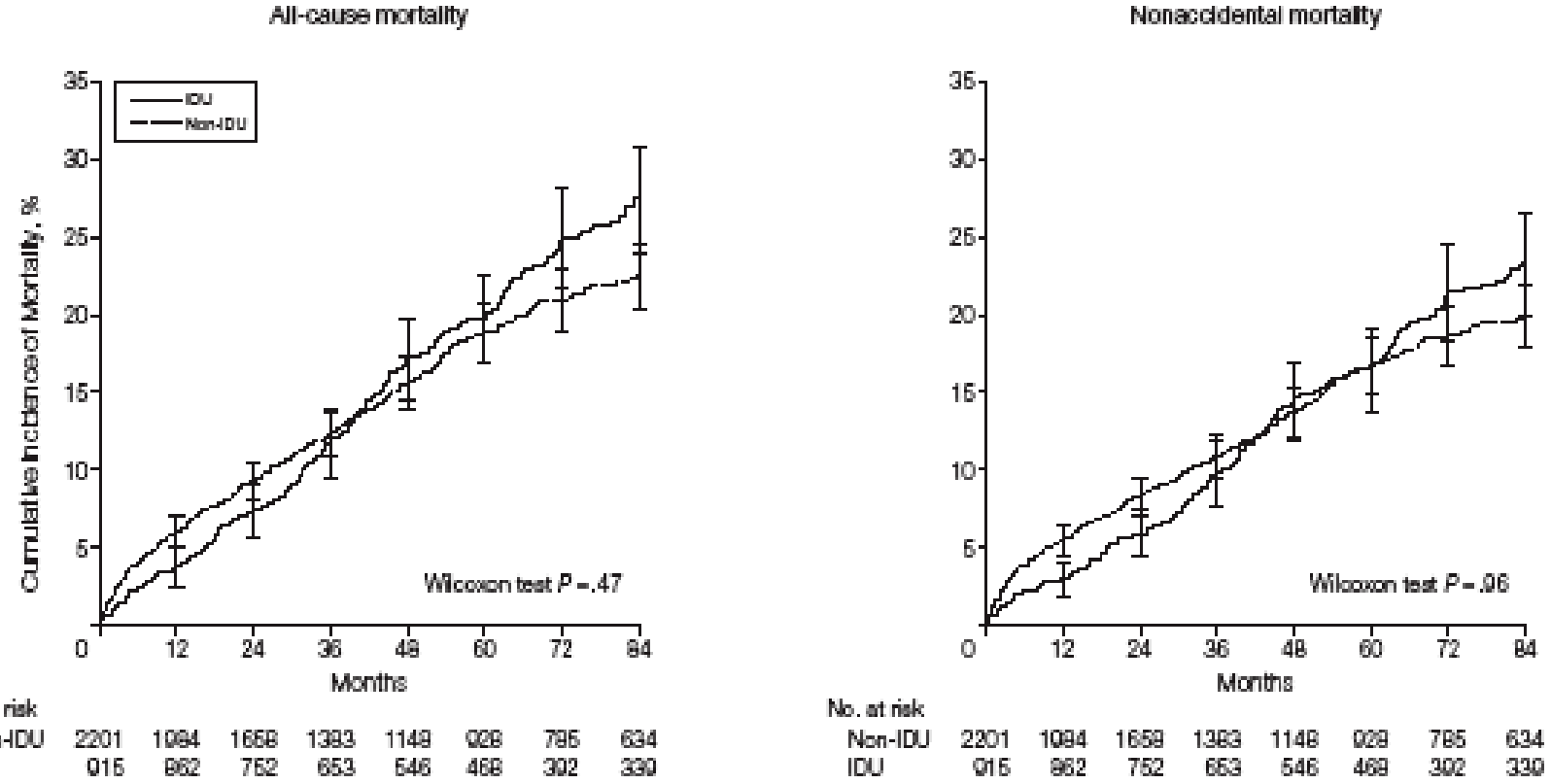


TasP in MARPs

- IDU
- MSM

Highly Active Antiretroviral Therapy and Survival in HIV-Infected Injection Drug Users

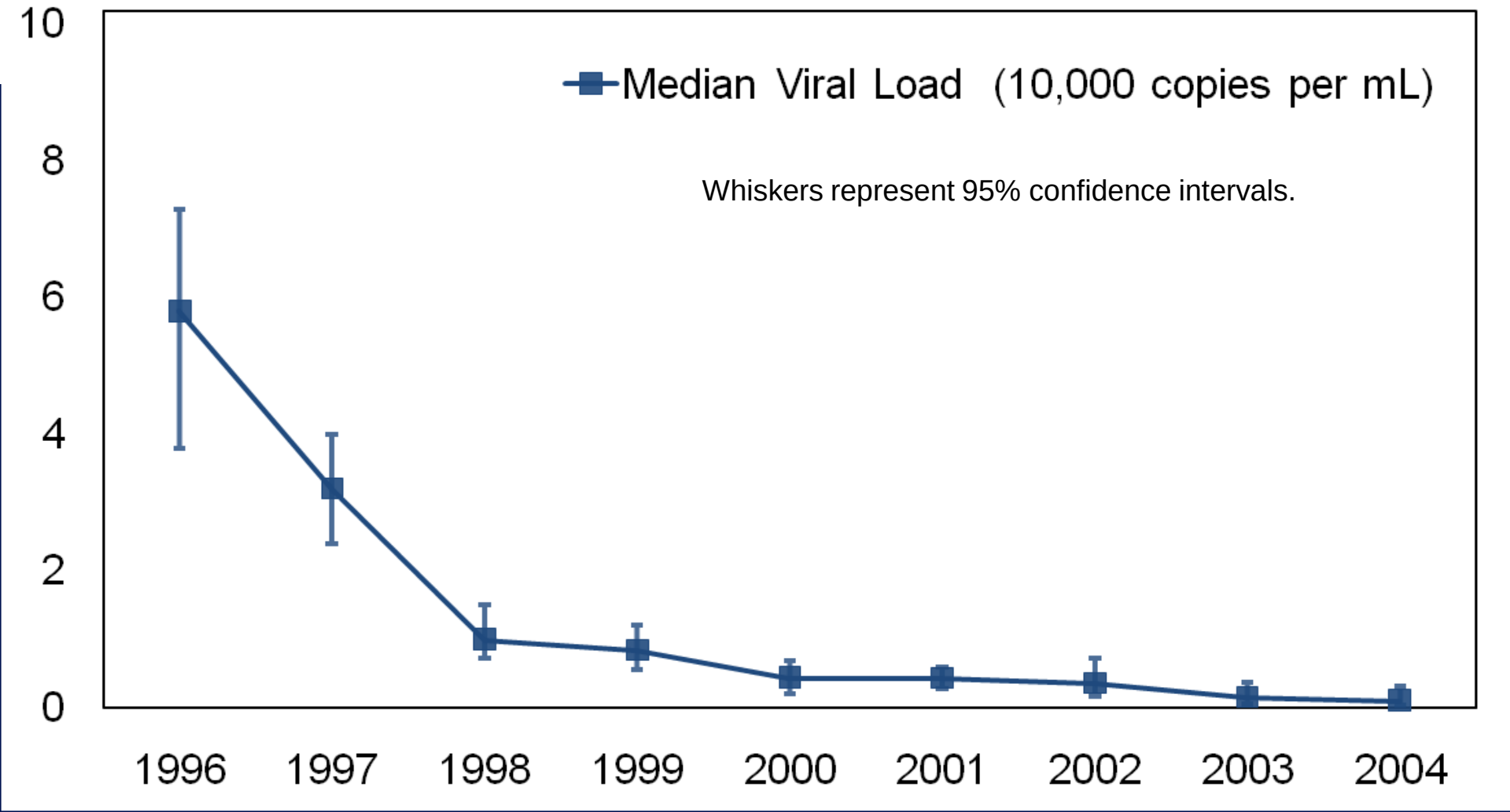
Figure. Mortality Rate Among 3116 Antiretroviral-Naive Patients Initiating HAART



Overall, there were 622 deaths and the analysis of nonaccidental mortality censored 87 deaths (14.0%) as nonevents among which 62 deaths (71.2%) were accidental poisonings, 16 were suicides (18.3%), 6 were traumas (<0.1%), and 3 were classified as other (<0.1%). Survival curves were compared using the Wilcoxon test and all follow-up data for all participants. Error bars indicate 95% confidence intervals; HAART, highly active antiretroviral therapy; IDU, injection drug user.

Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: prospective cohort study

BMJ | 16 MAY 2009 | VOLUME 338



Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: prospective cohort study

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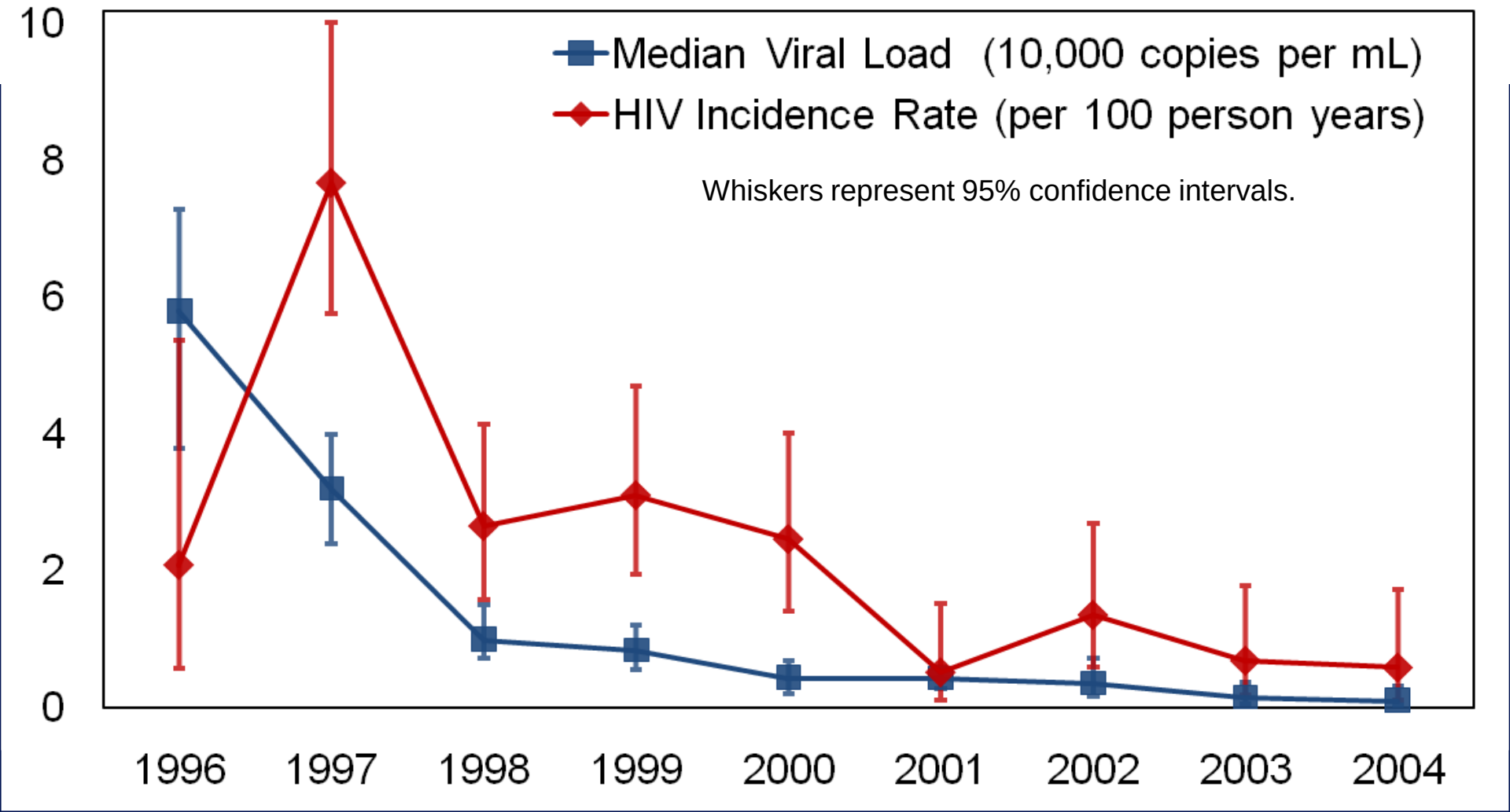


HAART Reduces HIV incidence in IDUs

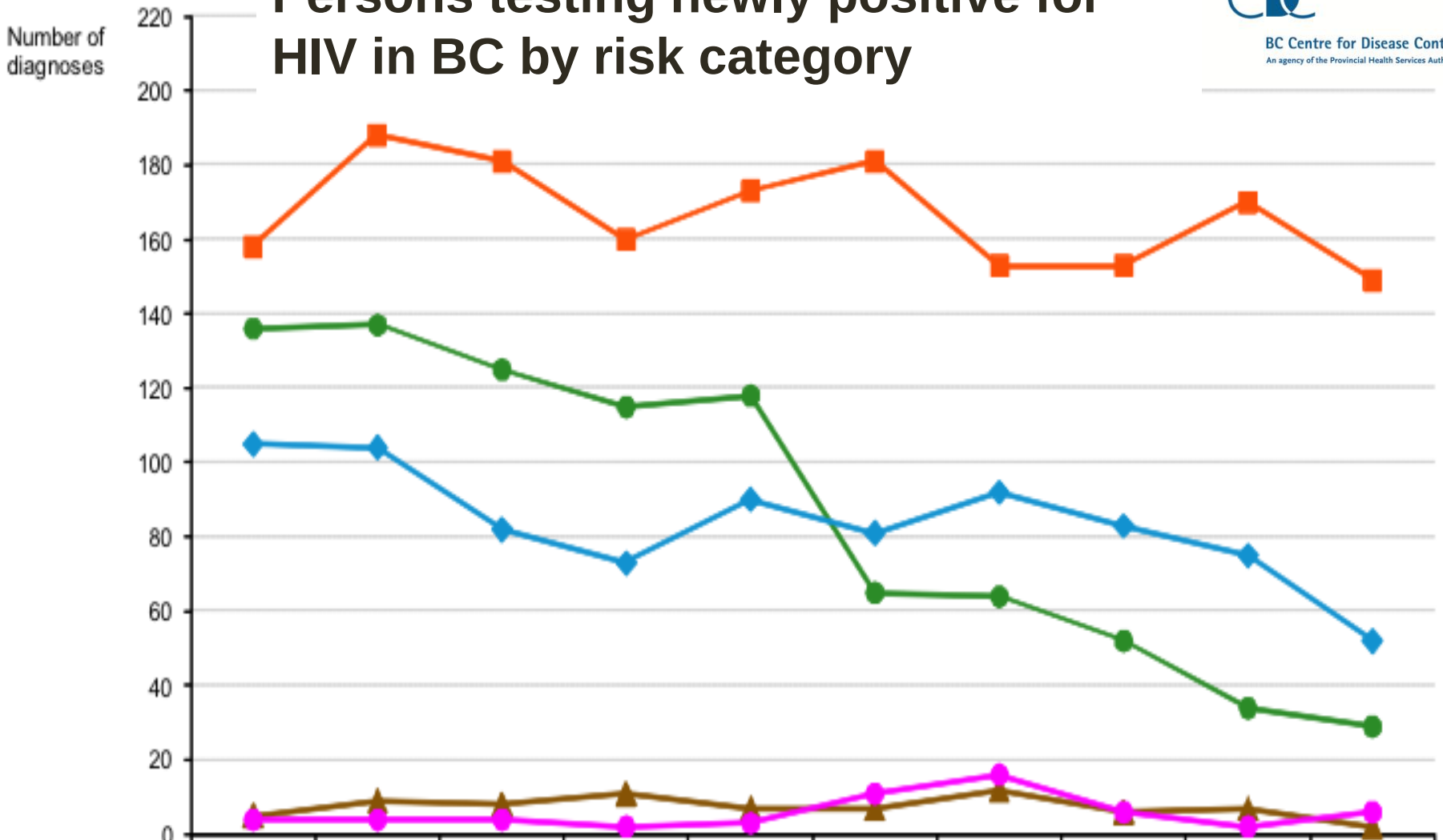
- From 1997, HIV incidence decreased by 74% for each log decline in community HIV viral load

- In a separate model, HIV incidence decreased by 5% for each 1% increase in HAART coverage

Modified from G Kirk et al, for the Alive Cohort, CROI 2011

Persons testing newly positive for HIV in BC by risk category

BC Centre for Disease Control
An agency of the Provincial Health Services Authority



	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
MSM	158	188	181	160	173	181	153	153	170	149
IDU	136	137	125	115	118	65	64	52	34	29
HET	105	104	82	73	90	81	92	83	75	52
Other	5	9	8	11	7	7	12	6	7	2
NIR/UNK	4	4	4	2	3	11	16	6	2	6

Mark Gilbert, April 26, 2013

Syphilis and neurosyphilis increase to historic levels in BC

R Lester, M Morshed, and M Gilbert, BCMJ, May 4th 2013

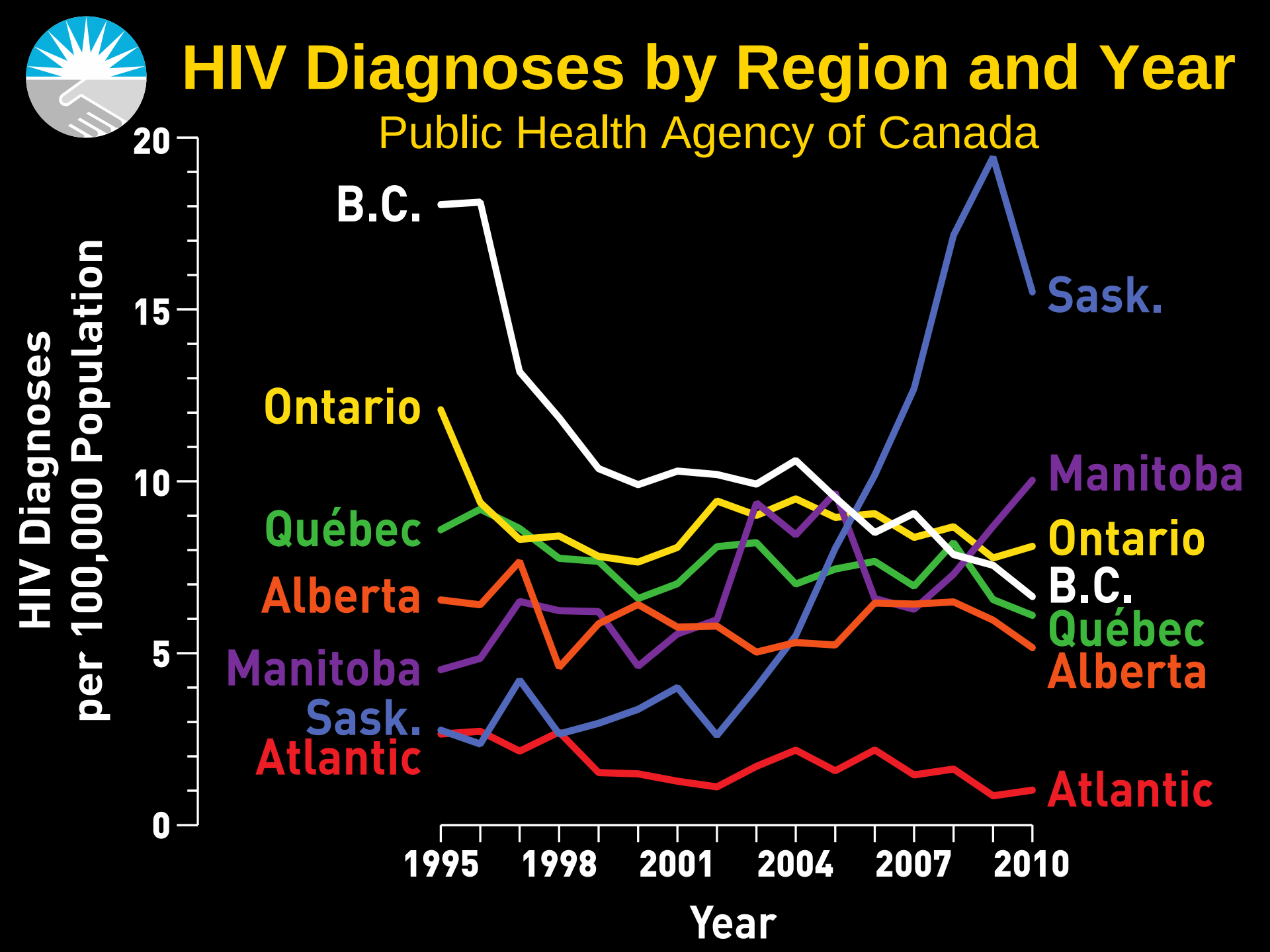
BC Centre for Disease Control
An agency of the Provincial Health Services Authority

Other Jurisdictions

- Canada
- KuaZulu-Natal

HIV Diagnoses by Region and Year

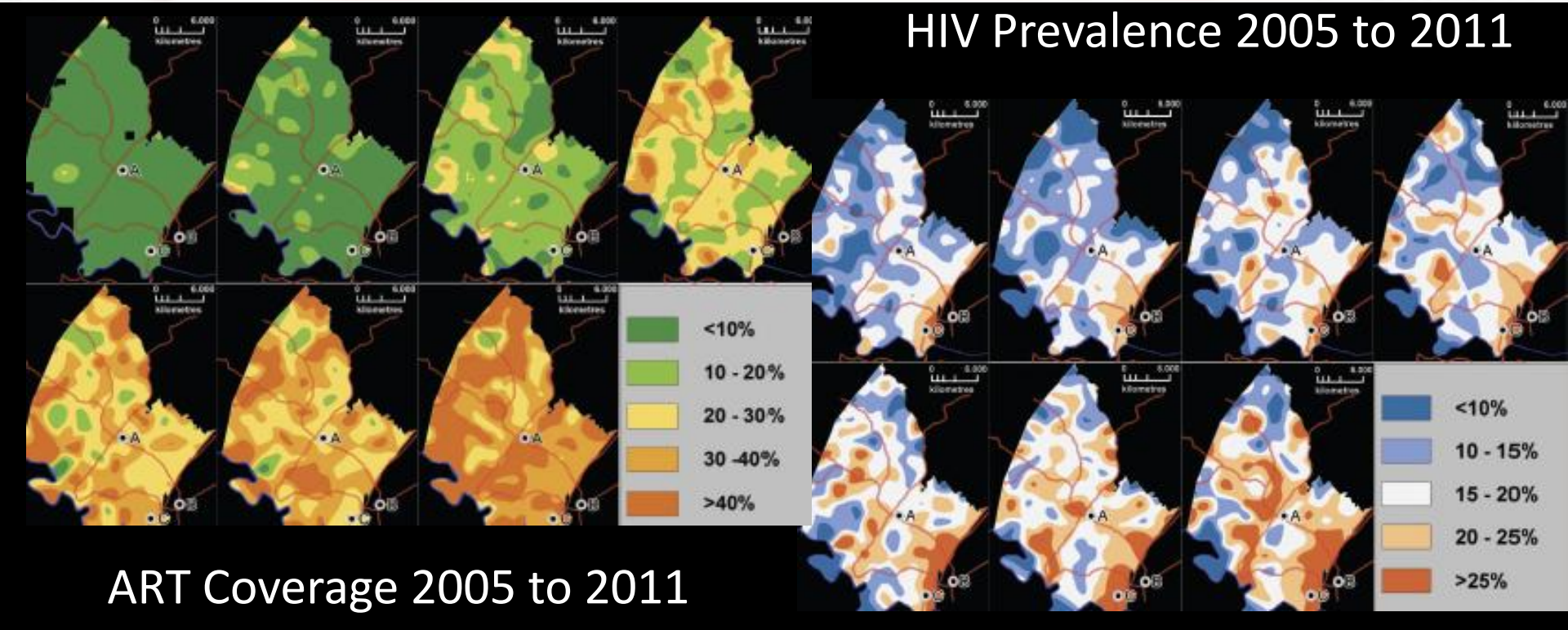
Public Health Agency of Canada



High Coverage of ART Associated with Decline in Risk of HIV Acquisition in Rural KwaZulu-Natal, South Africa

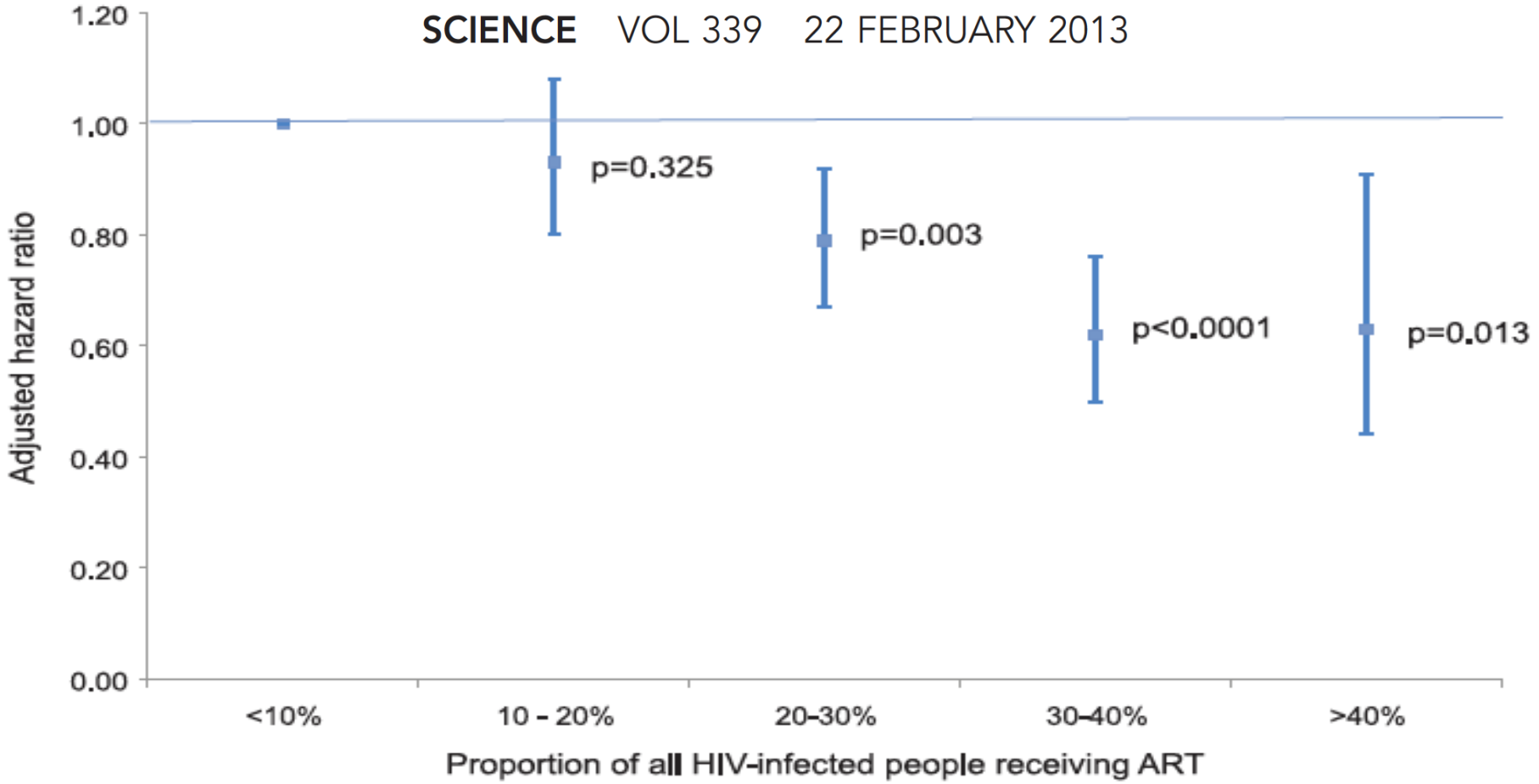
Frank Tanser,[1*] Till Bärnighausen,[1,2] Erofili Grapsa,[1] Jaffer Zaidi,[1] Marie-Louise Newell[1,3]

SCIENCE VOL 339 22 FEBRUARY 2013



High Coverage of ART Associated with Decline in Risk of HIV Acquisition

SCIENCE VOL 339 22 FEBRUARY 2013



Holding other key HIV risk factors constant, individual HIV acquisition risk declined significantly with increasing ART coverage in the surrounding local community. For example, an HIV-uninfected individual living in a community with high ART coverage (30 to 40% of all HIV-infected individuals on ART) was 38% less likely to acquire HIV than someone living in a community where ART coverage was low (<10% of all HIV-infected individuals on ART).

ARV Guidelines

Current Guidelines for Initiating ART

	Sympt. or AIDS	CD4 <200	CD4 200-350	CD4 350-500	CD4 >500
DHHS (2/2012)	Yes	Yes	Yes	Yes	Yes
IAS-USA (7/2012)	Yes	Yes	Yes	Yes	Yes
WHO (7/2010)	Yes	Yes	Yes	Yes	Consider

When to start: Potential scenarios

Estimated millions of people eligible for ART in lower & middle-income countries in 2011

11 | **15** | **23** | **>25** | **32**

1. *CD4 ≤ 200*
   Recommended Since 2002
2. *CD4 ≤ 350 +*
3. *CD4 ≤ 350 +*
   Expanded CD4 independent conditions
4. *CD4 ≤ 500*
   TB/HIV
   HBV/HIV
   ART regardless of CD4 count for:
   - HIV-SD couples
   - Pregnant women
5. "Test and treat"
   All HIV+

Modified from Meg Doherty, et al. 3rd International TasP Workshop, Vancouver 2013

INTERNATIONAL

HIV TREATMENT AS PREVENTION

WORKSHOP

Proceedings from the 3rd International HIV Treatment as Prevention Workshop

http://www.treatmentaspreventionworkshop.org/wp-content/uploads/2013/06/TasP-Report-2013-FINAL.pdf

4th Intl **HIV TREATMANT AS PREVENTION** Workshop
April 1st to 4th 2014 - Vancouver, BC, Canada.

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in HIV/AIDS

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In Collaboration with PHC, VCHA, NHA, FHA, IHA, VIHA, PHSA, FNHA, Community, and BC-MoH

Providence HEALTH CARE
How you want to be treated.

Supported by the MoH, Gov of British Columbia, plus research grants, including $5M 10 year Award from the National Institute for Drug Abuse (NIDA) at the NIH, $5M from Genome Canada/BC and from Pharmaceutical Industry, including Merck, Gilead, ViiV and BMS