

CONTROLLING THE HIV EPIDEMIC WITH
ANTIRETROVIRALS



Having the Courage
of Our Convictions

1 - 2 October 2015 • Paris



Things We Know: What Advances in HIV Treatment Mean in the Context of Ending AIDS?

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International Association of Providers of AIDS Care



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Things we know

- **Treatment works**
- **Treatments are better**
- **Scale up is feasible and it's happening**
- **Price of inaction**
- **Path forward**



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Treatment Works



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The NEW ENGLAND JOURNAL of MEDICINE

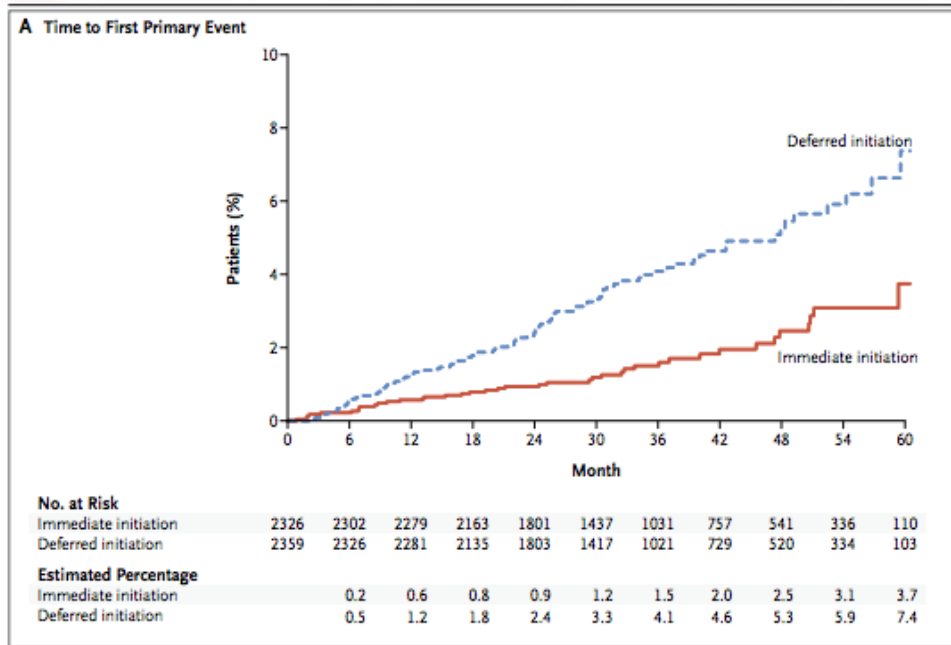
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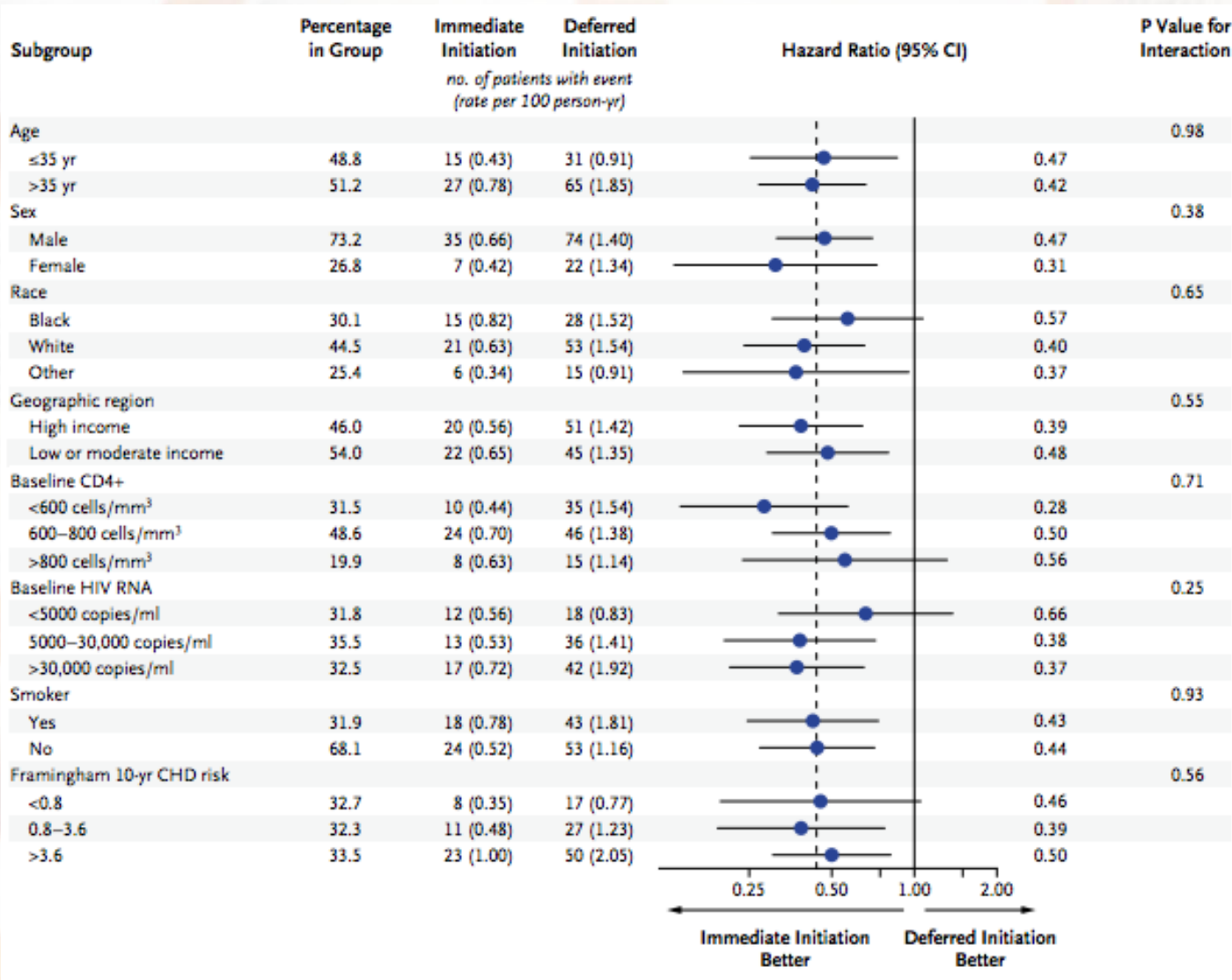
Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection

The INSIGHT START Study Group*



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INSIGHT START study group, NEJM 2015



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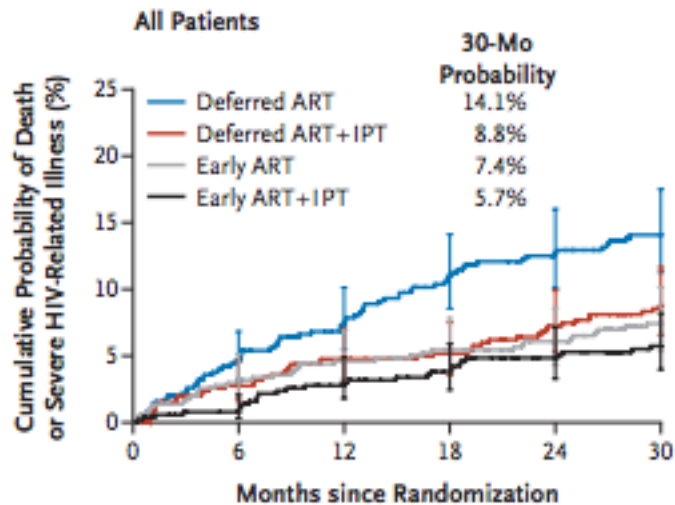
INSIGHT START study group, NEJM 2015

ORIGINAL ARTICLE

A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa

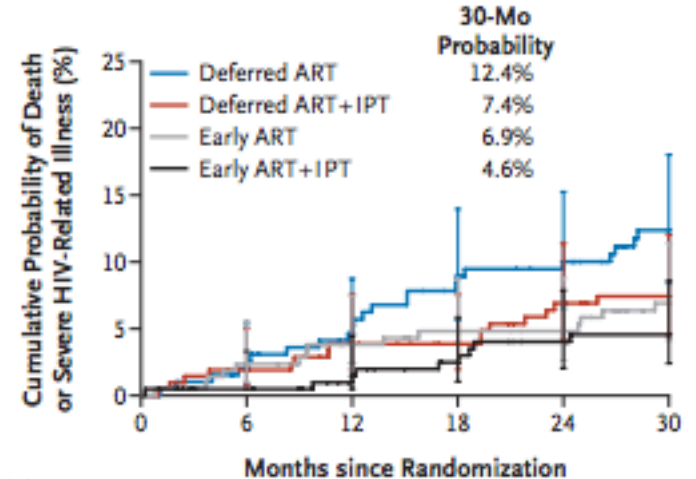
The TEMPRANO ANRS 12136 Study Group*

A Primary Outcome



| No. at Risk | 0 | 6 | 12 | 18 | 24 | 30 |
|------------------|-----|-----|-----|-----|-----|-----|
| Deferred ART | 511 | 473 | 448 | 418 | 400 | 366 |
| Deferred ART+IPT | 512 | 489 | 473 | 459 | 440 | 419 |
| Early ART | 515 | 481 | 463 | 452 | 432 | 403 |
| Early ART+IPT | 518 | 501 | 478 | 459 | 445 | 418 |

Patients with Baseline CD4+ Count $\geq 500/\text{mm}^3$



| No. at Risk | 0 | 6 | 12 | 18 | 24 | 30 |
|------------------|-----|-----|-----|-----|-----|-----|
| Deferred ART | 201 | 190 | 181 | 168 | 162 | 145 |
| Deferred ART+IPT | 212 | 204 | 197 | 191 | 182 | 174 |
| Early ART | 222 | 205 | 193 | 189 | 185 | 171 |
| Early ART+IPT | 214 | 205 | 197 | 190 | 184 | 171 |



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Treatment is Prevention



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Treatment is Prevention



HIV Prevention Trials Network

HPTN 052 - Conclusions

- The benefit of early ART in HIV prevention among HIV-discordant couples is durable
- No index-to-partner (linked) HIV transmissions were observed when the index participant was stably suppressed
- ***ART is highly effective for prevention of sexual transmission of HIV***



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Treatment is Prevention



Partnership for HIV Research

Conclusions

No index-to-partner transmission events were observed when the index was stably suppressed on ART

In the setting of TasP, special efforts should be made to minimize HIV transmission risk before the index is virally suppressed, to achieve durable viral suppression on ART, and to identify and address ART failure



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PEP Works

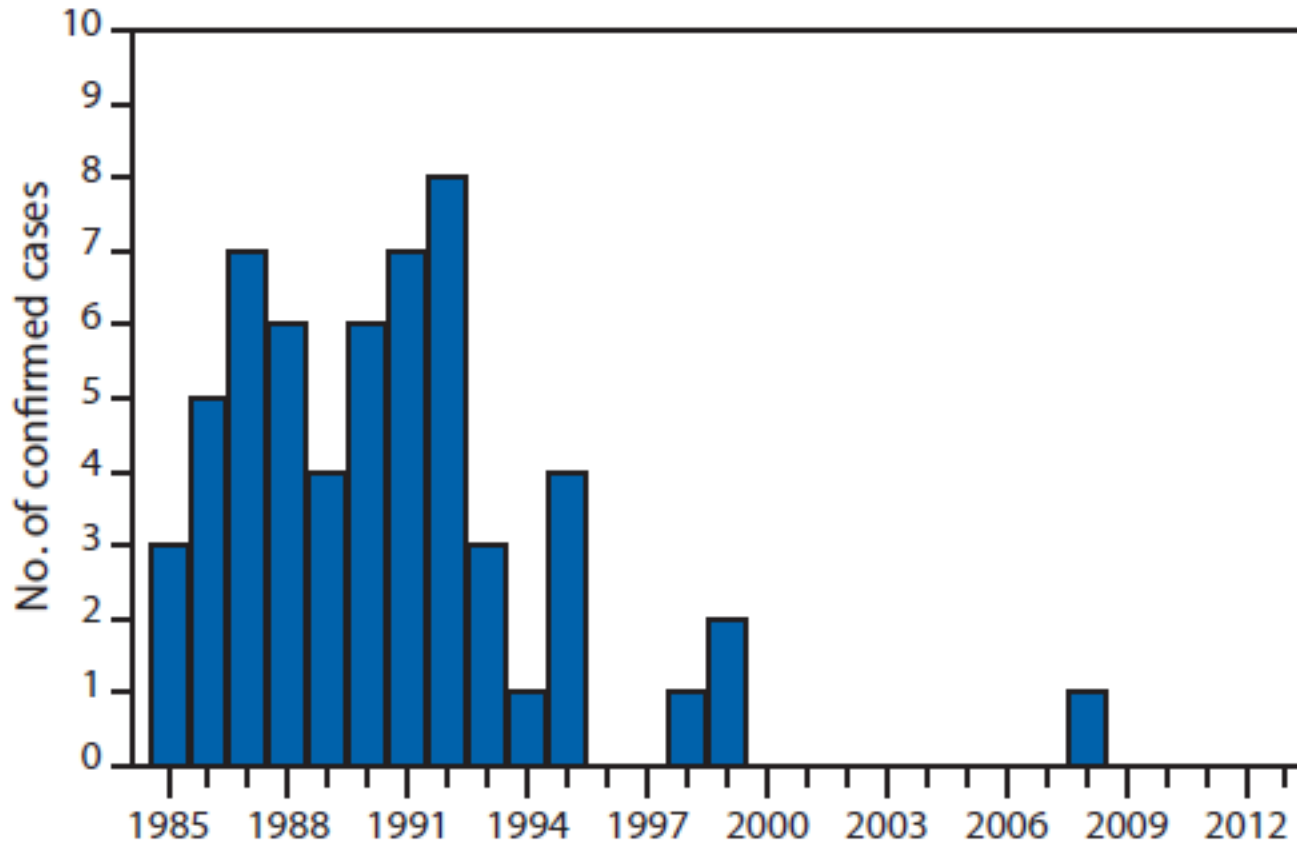


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Notes from the Field: Occupationally Acquired HIV Infection Among Health Care Workers United States, 1985-2013

Weekly

January 9, 2015 / 63(53);1245-1246



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PrEP Works



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No New HIV Infections With Increasing Use of HIV Preexposure Prophylaxis in a Clinical Practice Setting

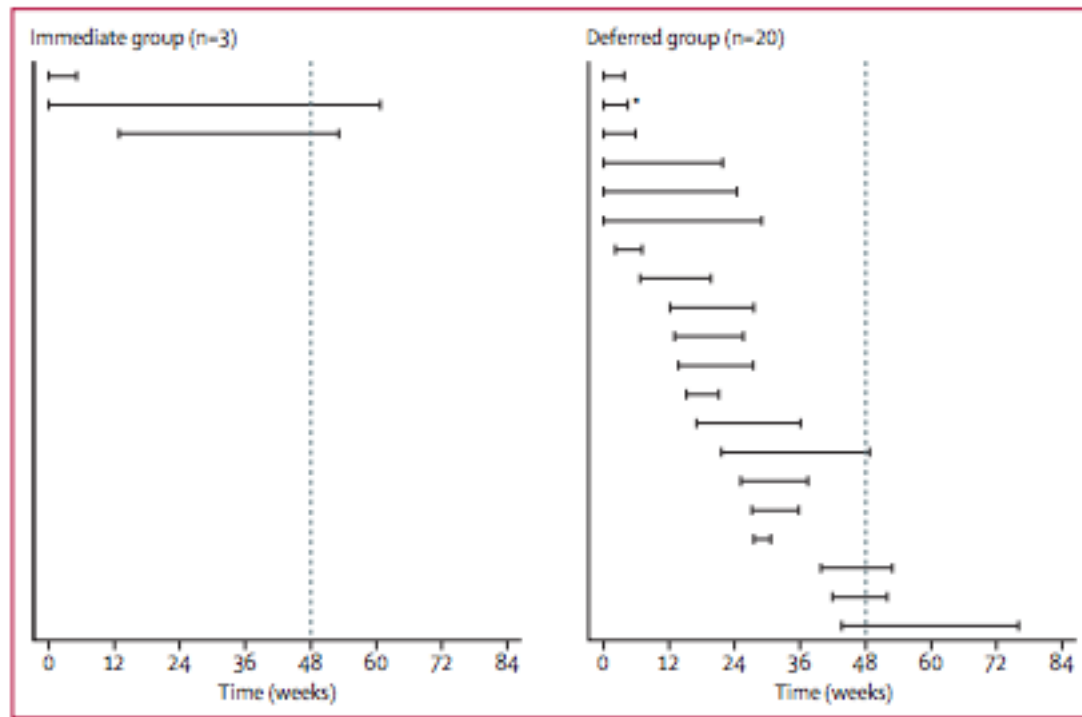
Jonathan E. Volk,¹ Julia L. Marcus,² Tony Phengrasamy,¹ Derek Blechinger,¹ Dong Phuong Nguyen,¹ Stephen Follansbee,¹ and C. Bradley Hare¹

¹Department of Adult and Family Medicine, Kaiser Permanente San Francisco Medical Center, and ²Division of Research, Kaiser Permanente Northern California, Oakland, California

Referrals for and initiation of preexposure prophylaxis (PrEP) for human immunodeficiency virus (HIV) infection increased dramatically in a large clinical practice setting since 2012. Despite high rates of sexually transmitted infections among PrEP users and reported decreases in condom use in a subset, there were no new HIV infections in this population.



Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial

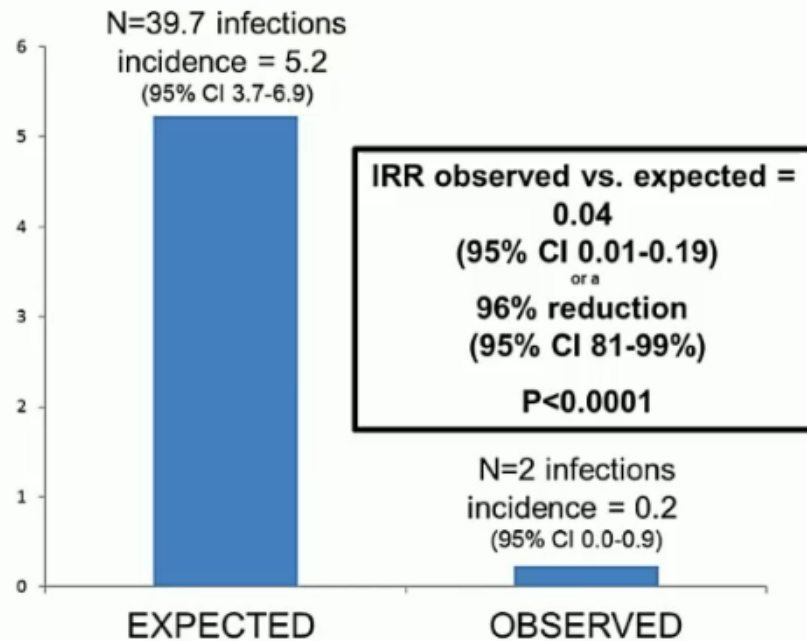


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Near elimination of HIV transmission in a demonstration project of PrEP and ART

HIV incidence

- The observed incidence is a **96% reduction** compared to expected, a result that was highly statistically significant



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Treatments are getting better



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First-line integrase inhibitors vs 3rd agents

| Drug | vs. EFV | vs. PI/r |
|--------------------------------|---------------------------------------|---|
| Raltegravir | Superior* | Superior |
| Elvitegravir/cobicistat | Non-inferior Non-inferior (switch) | Superior (women) Superior (switch) |
| Dolutegravir | Superior | Superior |

*Secondary endpoints, 1 and 5 year data



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Dolutegravir vs Efavirez

Week 144 Treatment-emergent Resistance

| | | DTG + ABC/3TC QD (N=414) | EFV/TDF/FTC QD (N=419) |
|--------------------|---------|-----------------------------|---------------------------|
| Subjects with PDVF | | 39 (9%) | 33 (8%) |
| Primary INI-r | | 0 | 0 |
| Primary NRTI | K65R | 0 | 1 |
| Primary NNRTI | Any | 0 | 6 |
| | K101E | 0 | 1 |
| | K103N | 0 | 2 |
| | K103K/N | 0 | 2 |
| | G190G/A | 0 | 2 |

PDVF definition:

- Confirmed HIV-1 RNA ≥ 50 c/mL at or after Week 24
- PDVF triggered resistance testing for all subjects
- PDVF before week 48 required withdrawal from study
- After week 48, subjects with HIV RNA 50-200 c/mL could remain on study

PDVF: protocol defined virologic failure



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Economic Burden of HIV Antiretroviral Therapy Adverse Events in the United States

Table 6. Differences in Median Total All-Cause Health Care Costs among Matched Event Episodes.

| AE | Episodes with Event of Interest | Episodes without Event of Interest | Difference | P Value ^a |
|--|---------------------------------|------------------------------------|------------|----------------------|
| Depression | US\$677 | US\$0 | US\$677 | <.0001 |
| Diabetes/insulin ^b resistance | US\$14 547 | US\$11 237 | US\$3310 | .0021 |
| Diarrhea | US\$560 | US\$0 | US\$560 | <.0001 |
| Dizziness | US\$521 | US\$0 | US\$521 | <.0001 |
| Hepatic disorders | US\$212 | US\$0 | US\$212 | .0005 |
| Lipid disorders ^b | US\$12 825 | US\$10 033 | US\$2792 | .0004 |
| Nausea/vomiting | US\$772 | US\$0 | US\$772 | <.0001 |
| Rash | US\$390 | US\$0 | US\$390 | <.0001 |
| Renal disorders | US\$1389 | US\$0 | US\$1389 | <.0001 |
| Somnolence/sleep effects | US\$357 | US\$0 | US\$357 | <.0001 |

Abbreviation: AE, adverse event.

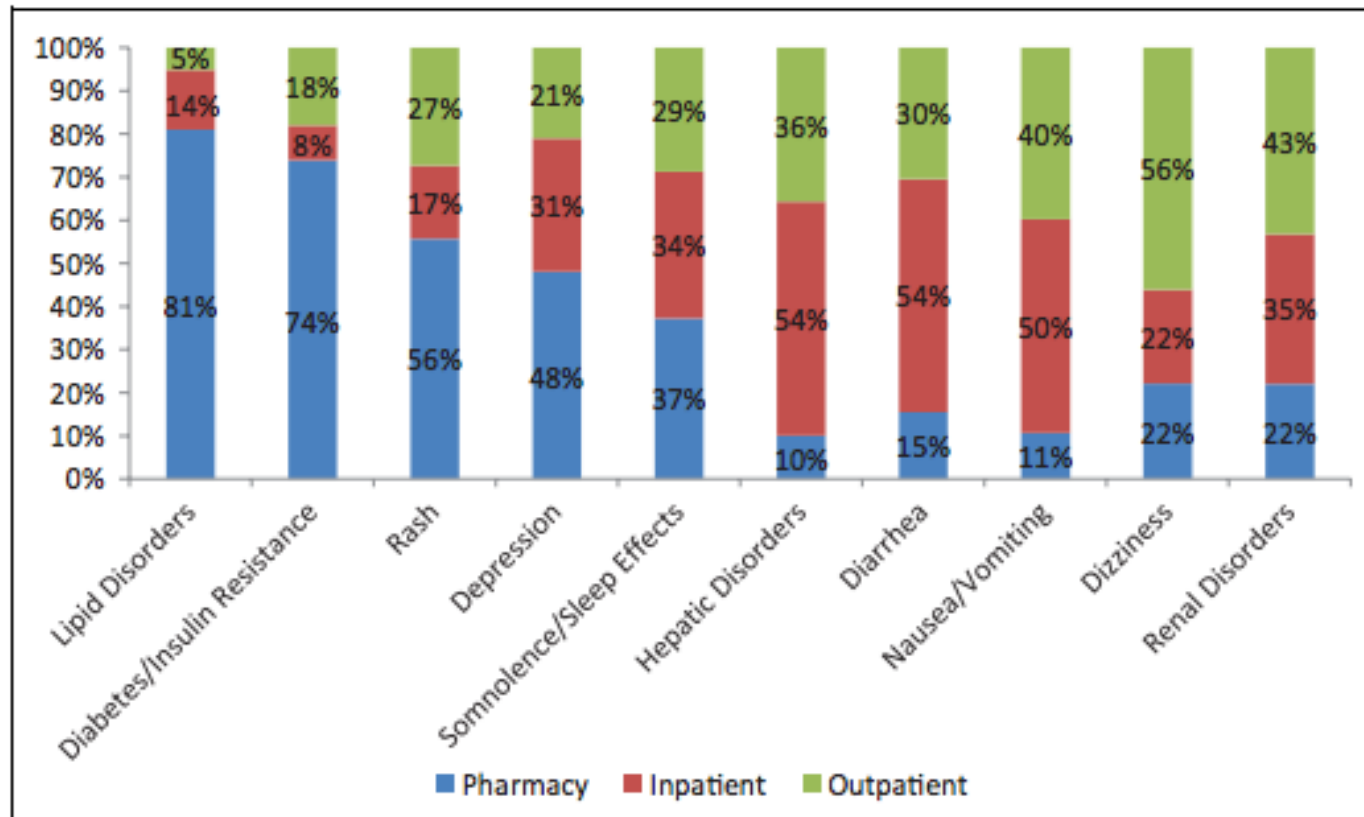
^aWilcoxon signed-rank test was used to compare differences in median total all-cause health care costs.

^bHandled as chronic events, whereby patients can have only 1 "episode".



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Economic Burden of HIV Antiretroviral Therapy Adverse Events in the United States



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It's Beginning to Work



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Addressing the Achilles' Heel in the HIV Care Continuum for the Success of a Test-and-Treat Strategy to Achieve an AIDS-Free Generation

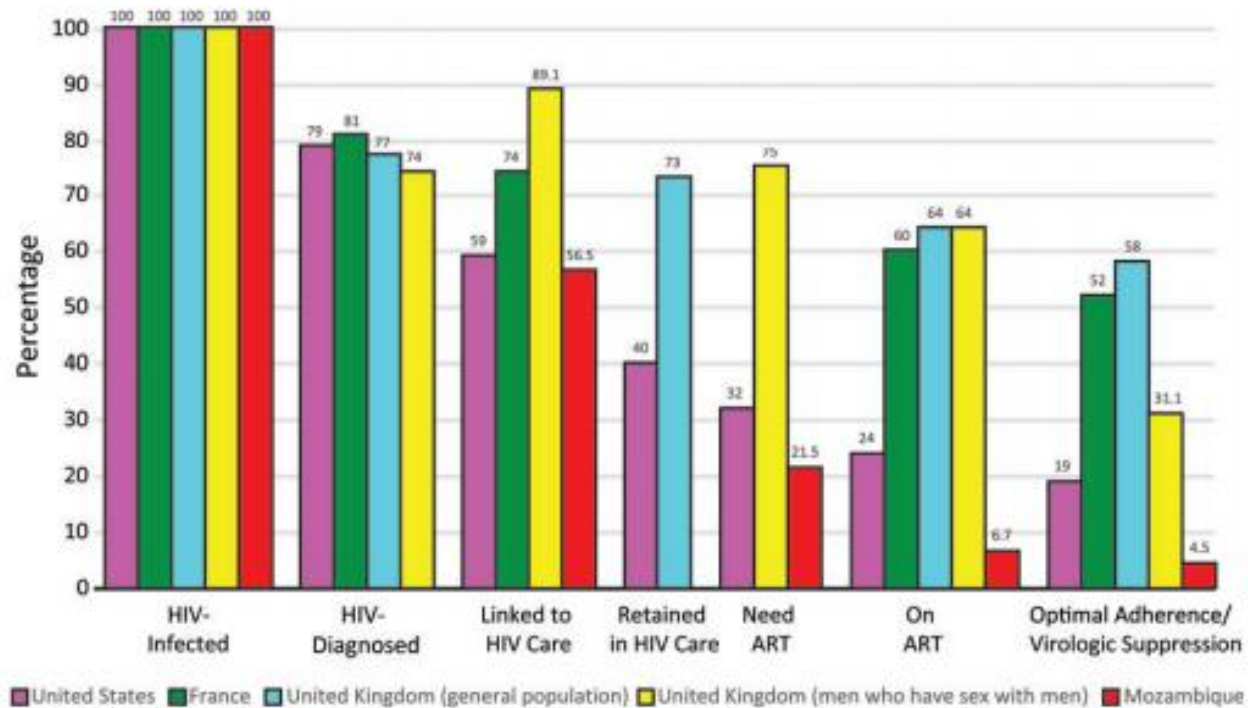


Figure 1. The spectrum of engagement in HIV care in United States, United Kingdom, France and Mozambique traversing from HIV acquisition to achievement of complete viral suppression [5, 7–10].



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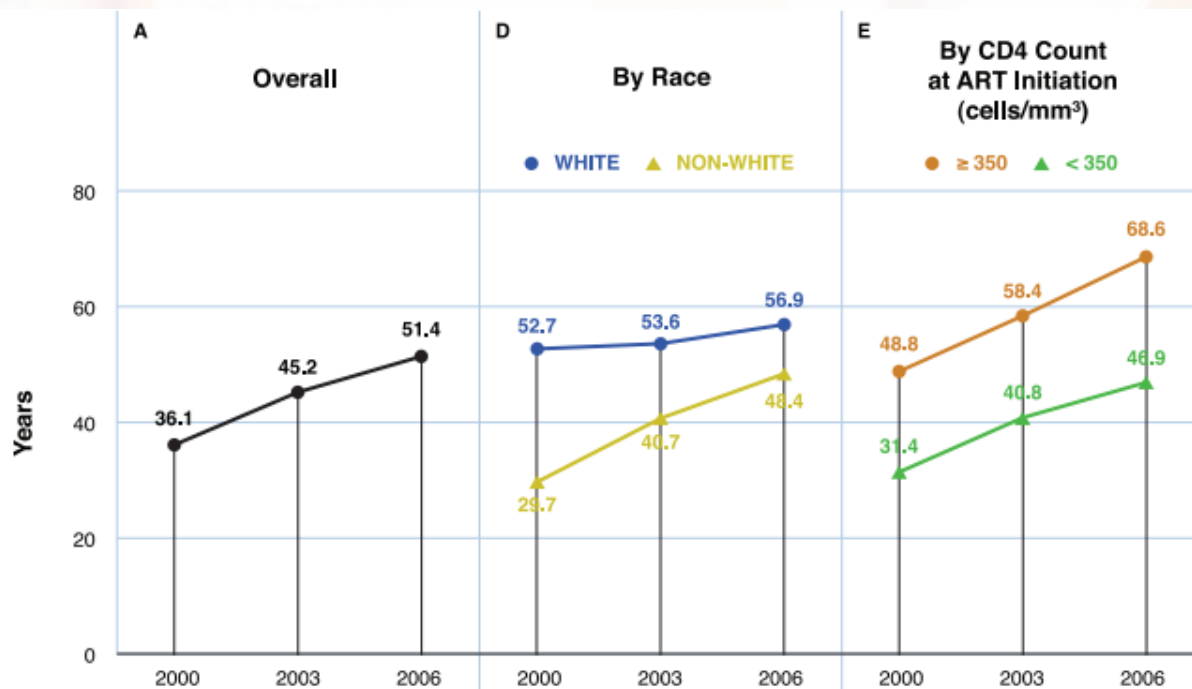
US Cities

- San Francisco¹:
 - 94% tested
 - 84-91% on ART
 - 64% viral suppressed
- Denver²:
 - 90% tested
 - 68% on ART
 - 57% viral suppressed



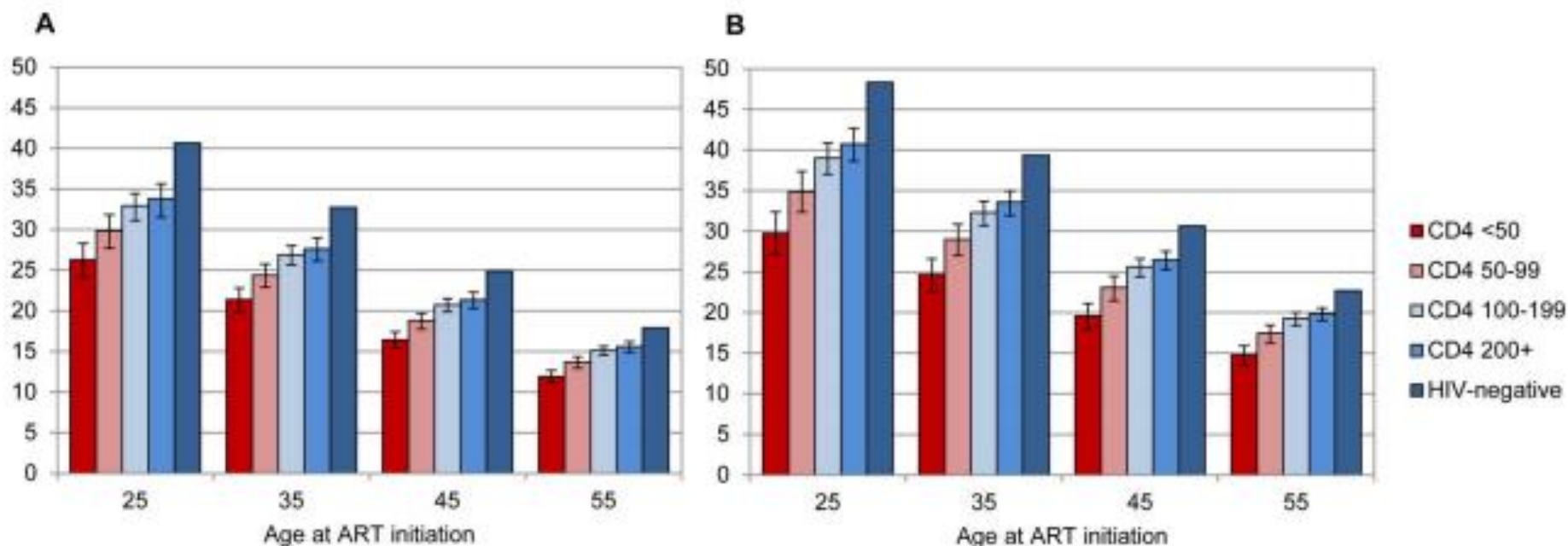
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Closing the Gap: Increases in Life Expectancy among Treated HIV-Positive Individuals in the United States and Canada



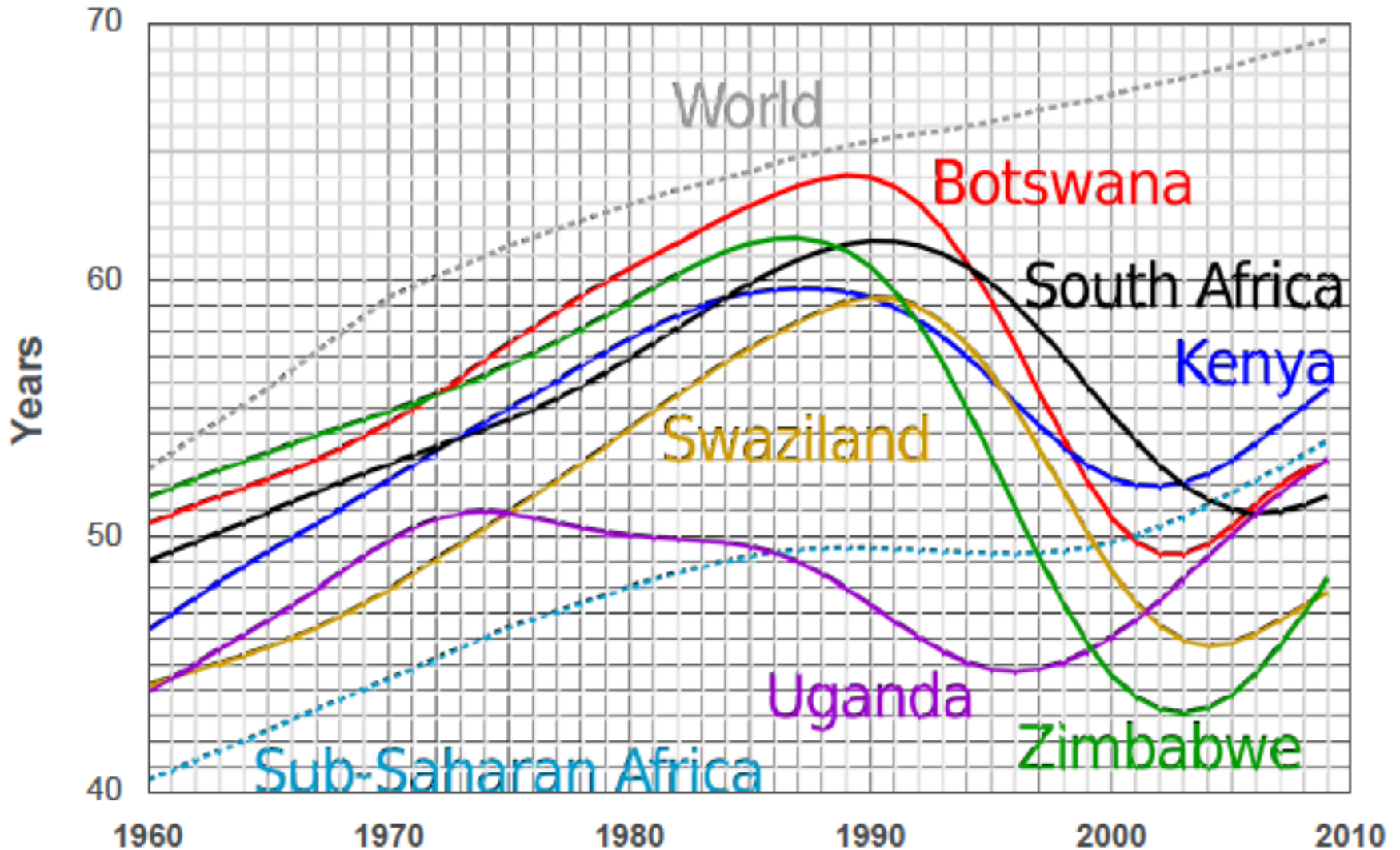
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Life Expectancies of South African Adults Starting Antiretroviral Treatment: Collaborative Analysis of Cohort Studies



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Life expectancy



Concerns



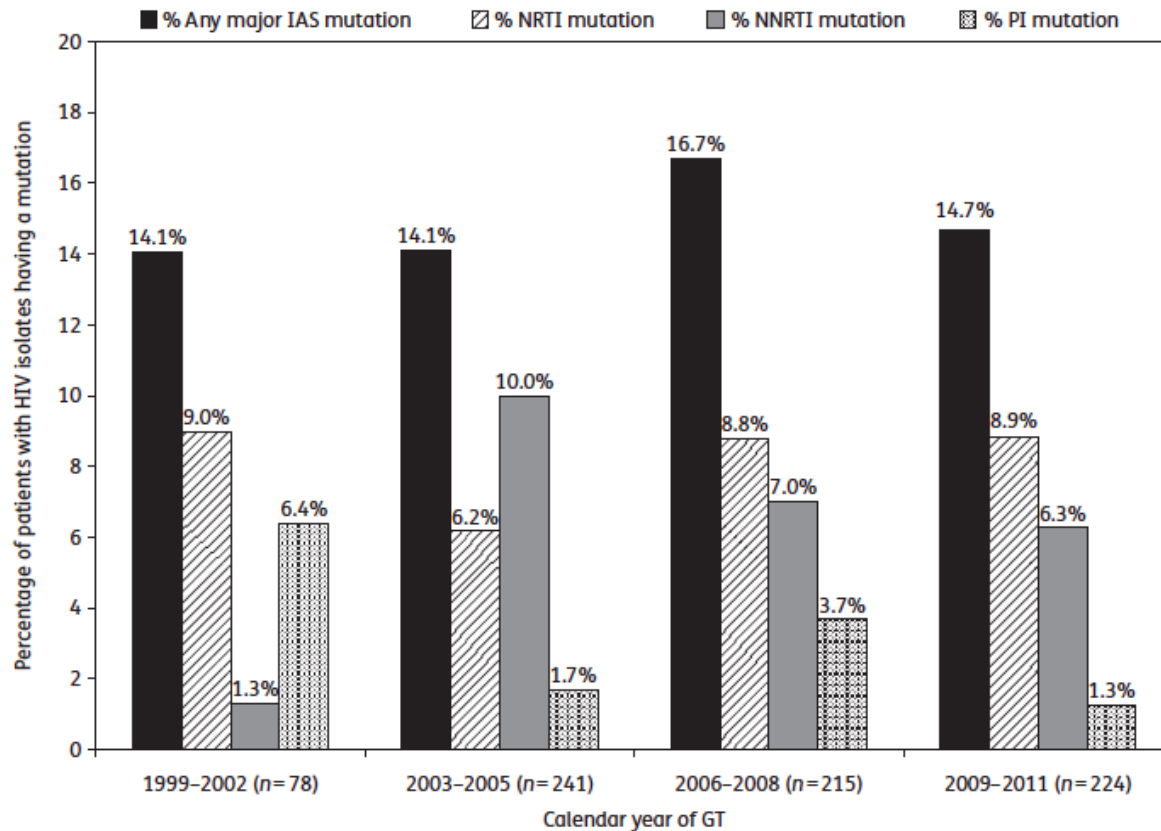
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Concerns about ART scale up

- Stigma
- Coercion, loss of individual rights
- Risk compensation
- Adherence
- ART resistance
- Political theatre, not action

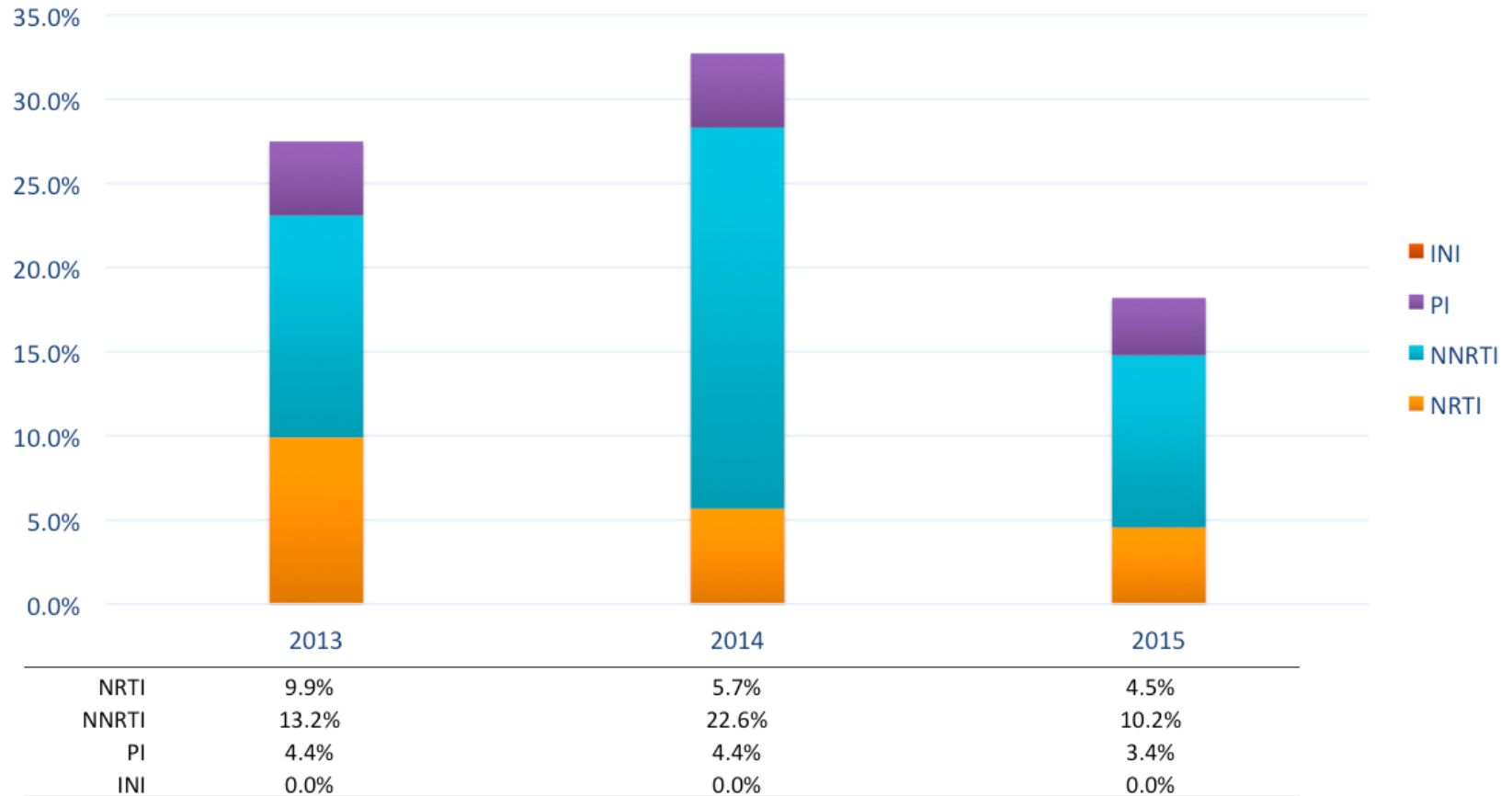


Trends in use of genotypic resistance testing and frequency of major drug resistance among antiretroviral-naïve persons in the HIV Outpatient Study, 1999–2011



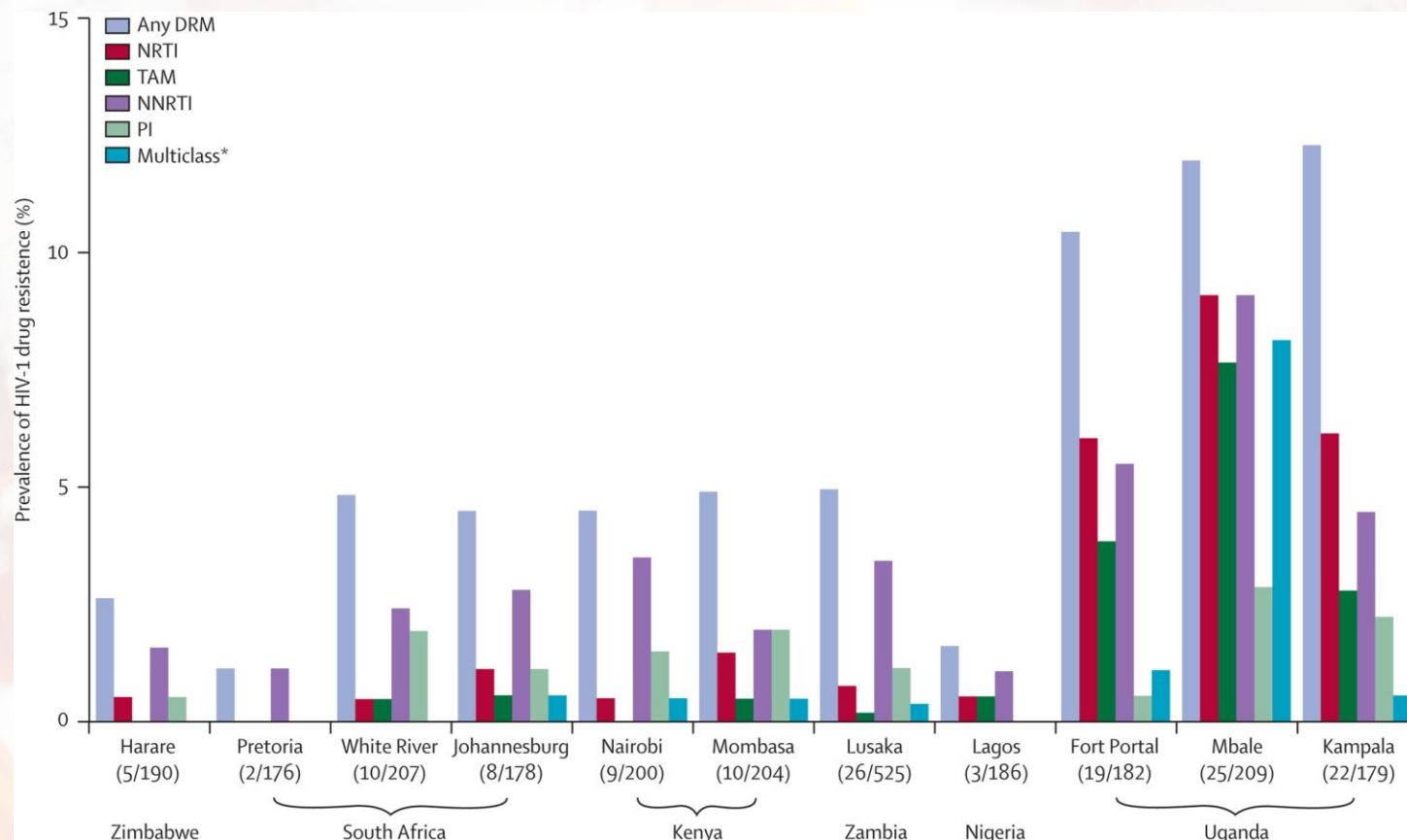
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TDR Prevalence by Class per Year



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HIV-1 drug resistance in antiretroviral-naive individuals in sub-Saharan Africa after rollout of antiretroviral therapy: a multicentre observational study



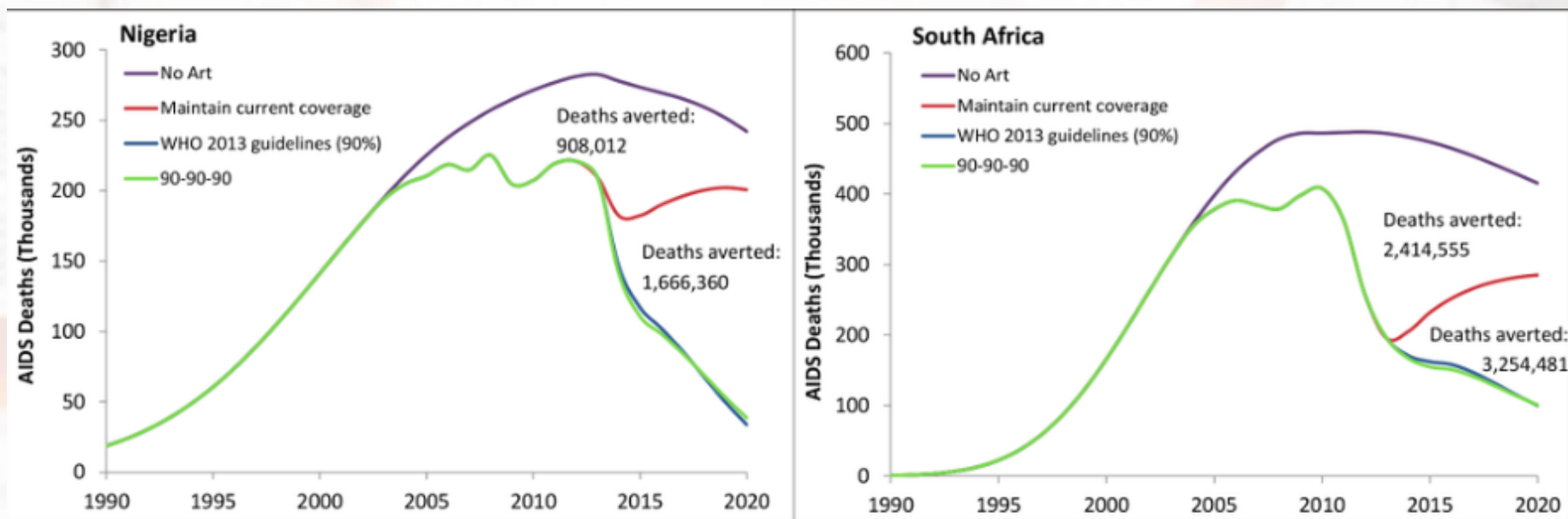
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Price of Inaction

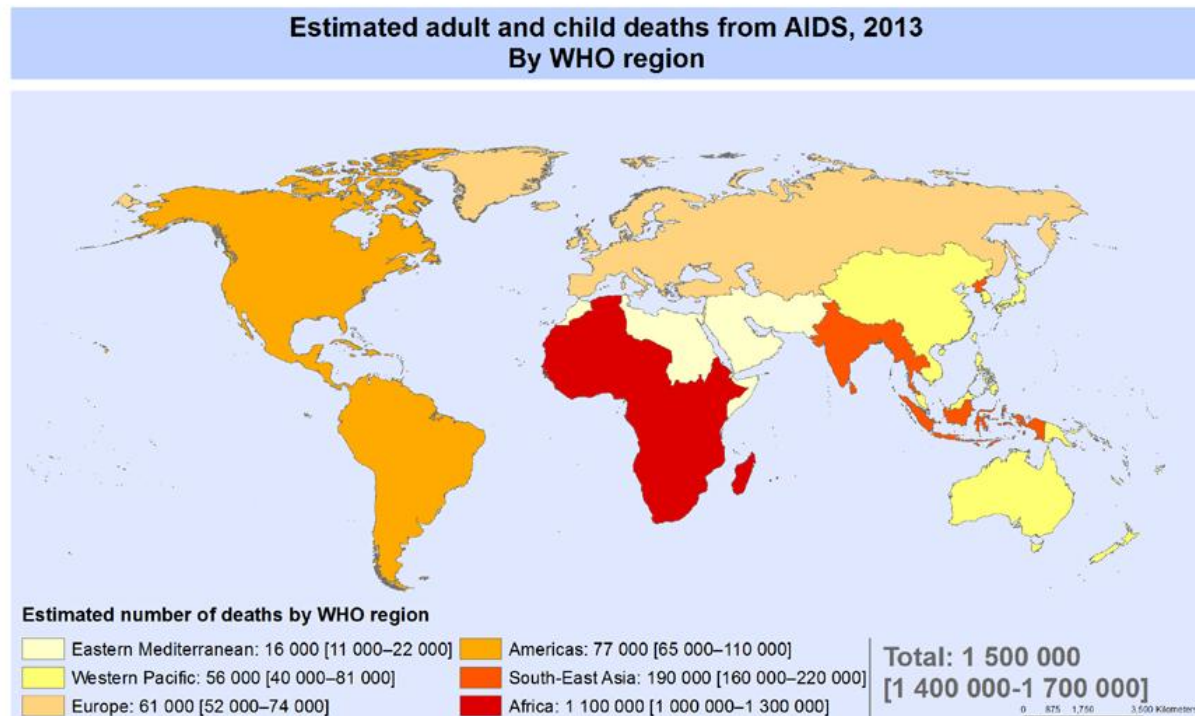


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Trends in AIDS Deaths, New Infections and ART Coverage in the Top 30 Countries with the Highest AIDS Mortality Burden; 1990–2013



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- 47 days since publication of START
 - 4100 AIDS-related deaths per day
 - 193,000 preventable deaths



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Making it Happen



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IAPAC GUIDELINES FOR OPTIMIZING THE HIV CARE CONTINUUM FOR ADULTS AND ADOLESCENTS

- **Optimizing the care environment**
- **Increasing HIV testing coverage and linkage to care**
- **Increasing HIV treatment coverage**
 - The immediate offer of ART after HIV diagnosis, irrespective of CD4 count or clinical stage, is recommended
 - Viral load testing at least every six months is recommended as the preferred tool for monitoring ART response
- **Increasing retention in care, ART adherence and viral suppression**
- **Metrics for monitoring the HIV care continuum**



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GUIDELINES

GUIDELINE ON WHEN TO START ANTIRETROVIRAL THERAPY AND ON PRE-EXPOSURE PROPHYLAXIS FOR HIV

SEPTEMBER 2015

- ART should be initiated in all adults living with HIV at any CD4 cell count
- Oral PrEP should be offered as an additional prevention choice for people at substantial risk of HIV infection



DHHS 28 Jul 2015:

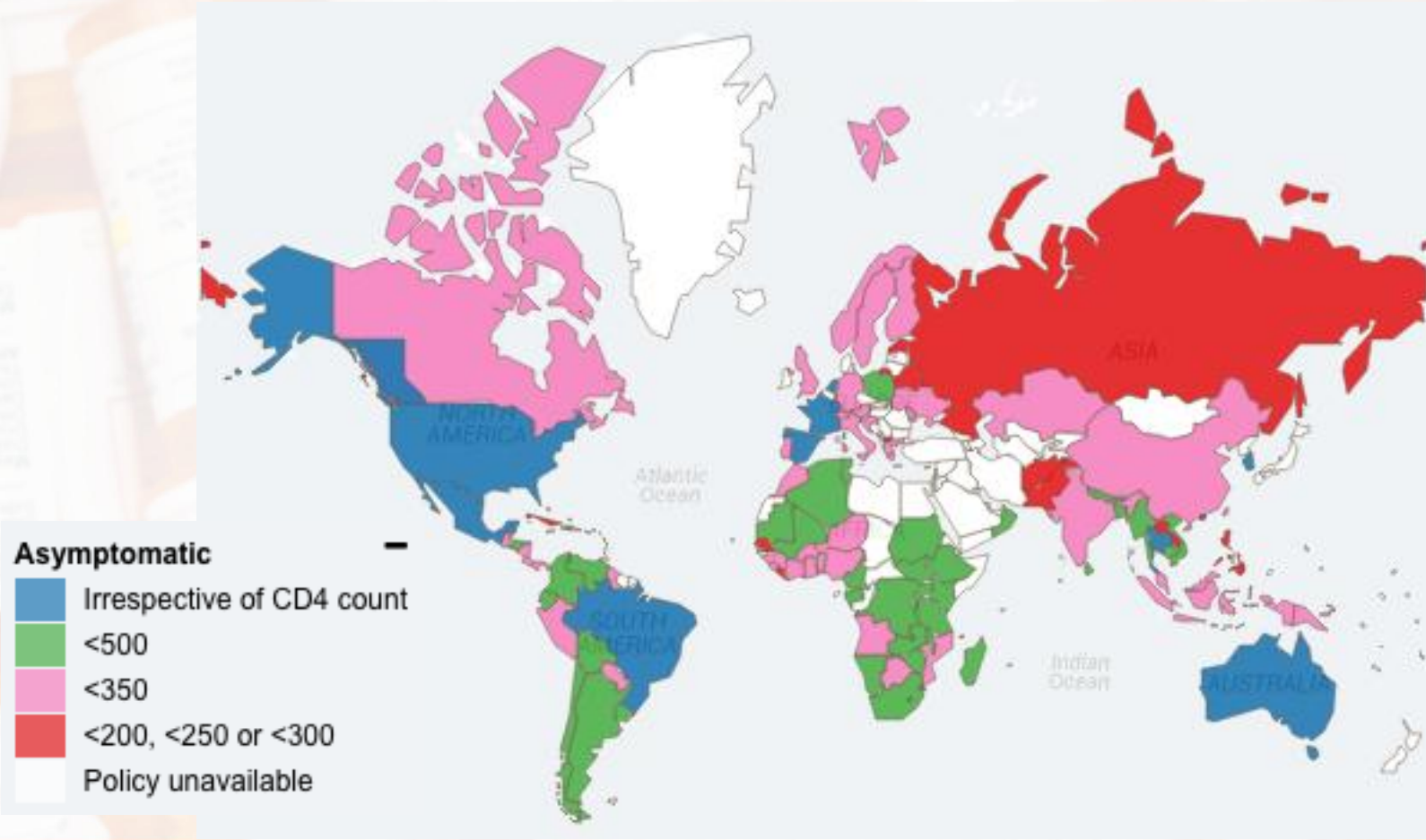
ART is recommended for HIV-infected patients regardless of pre-treatment CD4 count level (A1)

WHO: 30 Sep 2015

| Recommendation 1: When to start ART among people living with HIV | | | |
|--|---|--------------------------------|-------------------------------|
| Target population | Specific recommendation | Strength of the recommendation | Quality of the evidence |
| Adults ^a (>19 years) | ART should be initiated in all adults living with HIV at any CD4 cell count | <i>Strong</i> | <i>Moderate</i> NEW |
| | As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and individuals with CD4 count ≤ 350 cells/mm ³ | <i>Strong</i> | <i>Moderate</i> |

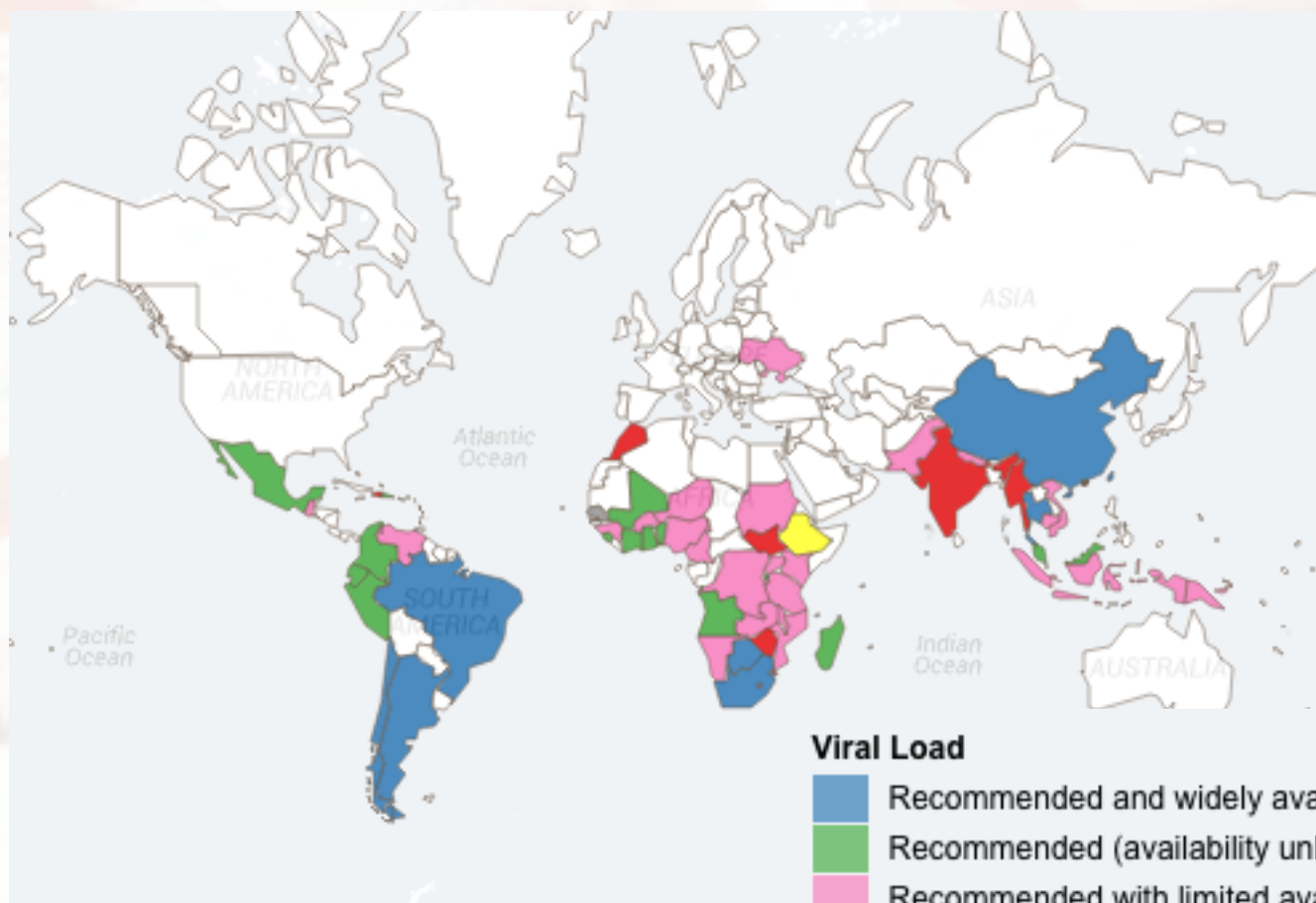


HIVpolicywatch.org



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Viral Load

- Recommended and widely available
- Recommended (availability unknown)
- Recommended with limited availability
- Recommended only for monitoring treatment failure
- Not recommended
- No recommendation
- Recommendation unavailable



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Current Fast-Track Cities

| AFRICA | | LATIN AMERICA/CARIBBEAN |
|-------------------|----------------|-------------------------|
| 1. Abidjan | 16. Durban | 30. Buenos Aires |
| 2. Accra | 17. Kinshasa | 31. Curitiba |
| 3. Algiers | 18. Lagos | 32. Kingston |
| 4. Atakpamé | 19. Libreville | 33. Port-au-Prince |
| 5. Bamako | 20. Lilongwe | 34. Salvador de Bahia |
| 6. Bamenda | 21. Lomé | 35. Santa Fe |
| 7. Bangui | 22. Lubumbashi | 36. Santiago |
| 8. Blantyre | 23. Lusaka | 37. San Miguelito |
| 9. Casablanca | 24. Maputo | |
| 10. Cotonou | 25. Mbujimayi | |
| 11. Dakar | 26. Nairobi | |
| 12. Dar es Salaam | 27. Ouessou | |
| 13. Djibouti | 28. Windhoek | |
| 14. Djougou | 29. Yaounde | |
| 15. Douala | | |
| EUROPE | ASIA | NORTH AMERICA |
| 38. Amsterdam | 43. Bangkok | 46. Atlanta |
| 39. Brussels | 44. Delhi | 47. Denver |
| 40. Bucharest | 45. Mumbai | 48. Miami |
| 41. Geneva | | 49. San Francisco |
| 42. Paris | | |



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IAPAC African Regional Capacity Building Hub



- Mission to strengthen clinician capacity on HIV, HBV and HCV clinical management.
- Help to integrate and implement WHO and other normative guidance



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“We scientists don’t communicate well”

- To communicate to public more efficiently:
 - There is clear consensus
 - Impact is already happening
 - The risks are acceptable because the consequences are serious
 - We can do something about this at a reasonable cost



Mario Molina, PhD
Nobel Prize, 1995



What must be done?

- Guidelines and proclamations must not just be signatures on paper
- Support bold leadership and targets with action
- Demand non-judgmental testing, care and treatment must match the magnitude of preventable death
- We must not forget the need to support cadres of well-trained care providers
- We must not forget that every data point is a human being



Things we know

- HIV treatments work.
 - Prevent disease, death and transmission
- Treatments are even getting better
- The risks of not acting outweigh the risks of implementing
- ART impact is already happening
- Thousands are at risk every day. We must have the courage to act now.



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