

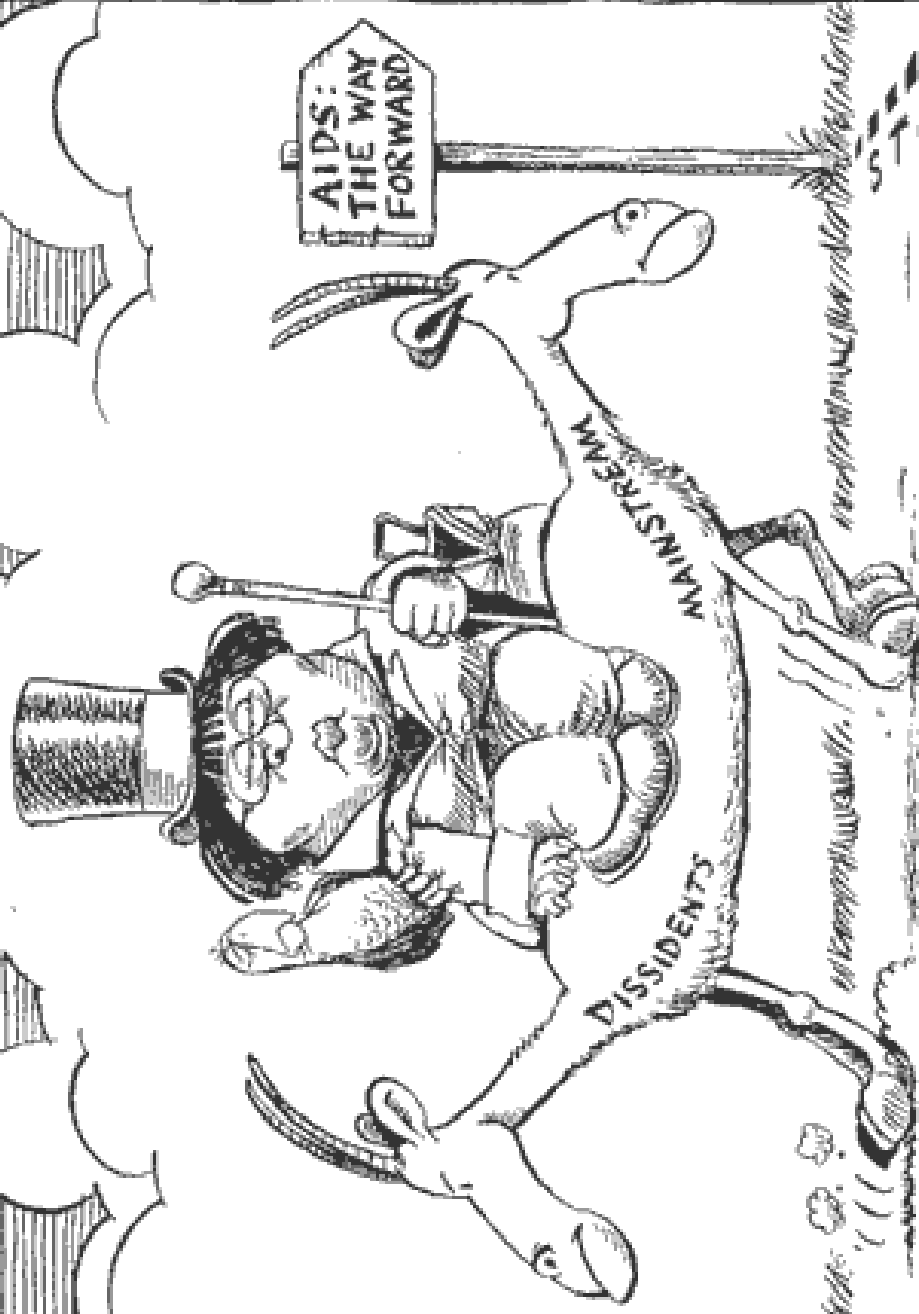
Problems for ARV Implementation in South Africa

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Major Impediments

- Political will
- Scale of the epidemic
- Operational problems
 - When to start
 - What to treat with
 - How to monitor
 - Ensure adherence



R2,5 million into the expedition,
Dr. Dolittle wondered whether
pushmi-pullyu had been the
ideal way to travel.

A Brief History of Antiretrovirals

No therapy	Mono Rx	Dual Rx	Triple Rx
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NRT Inhibitors

AZT	ddI	ddC d4T 3TC	ABC
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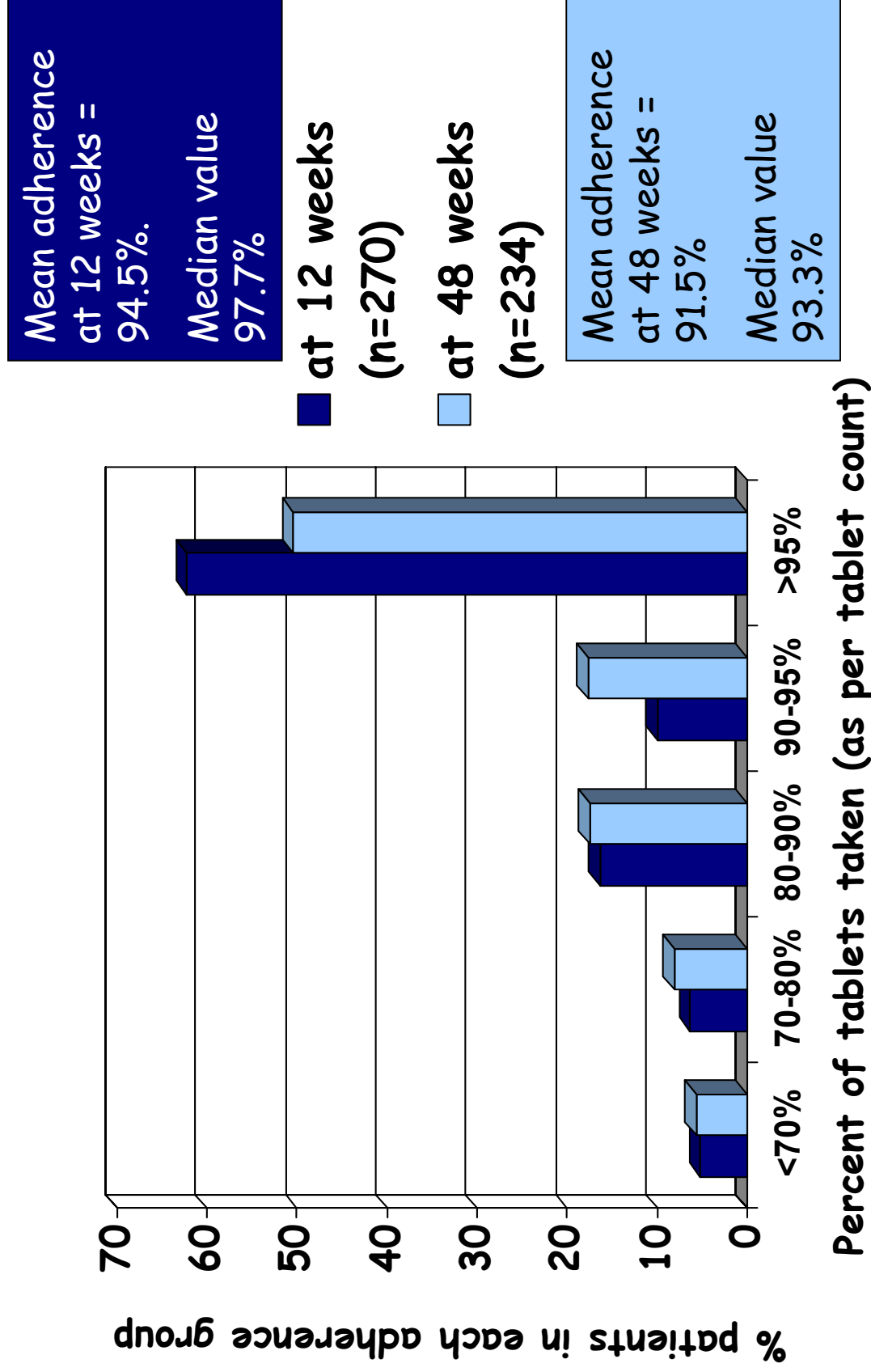
Protease Inhibitors

RTV	SQV	IND	NLV	APV
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Non-nucleoside RT Inhibitors

NVP	DLV	EFV
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Pattern of adherence to therapy at 12 and 48 weeks of treatment

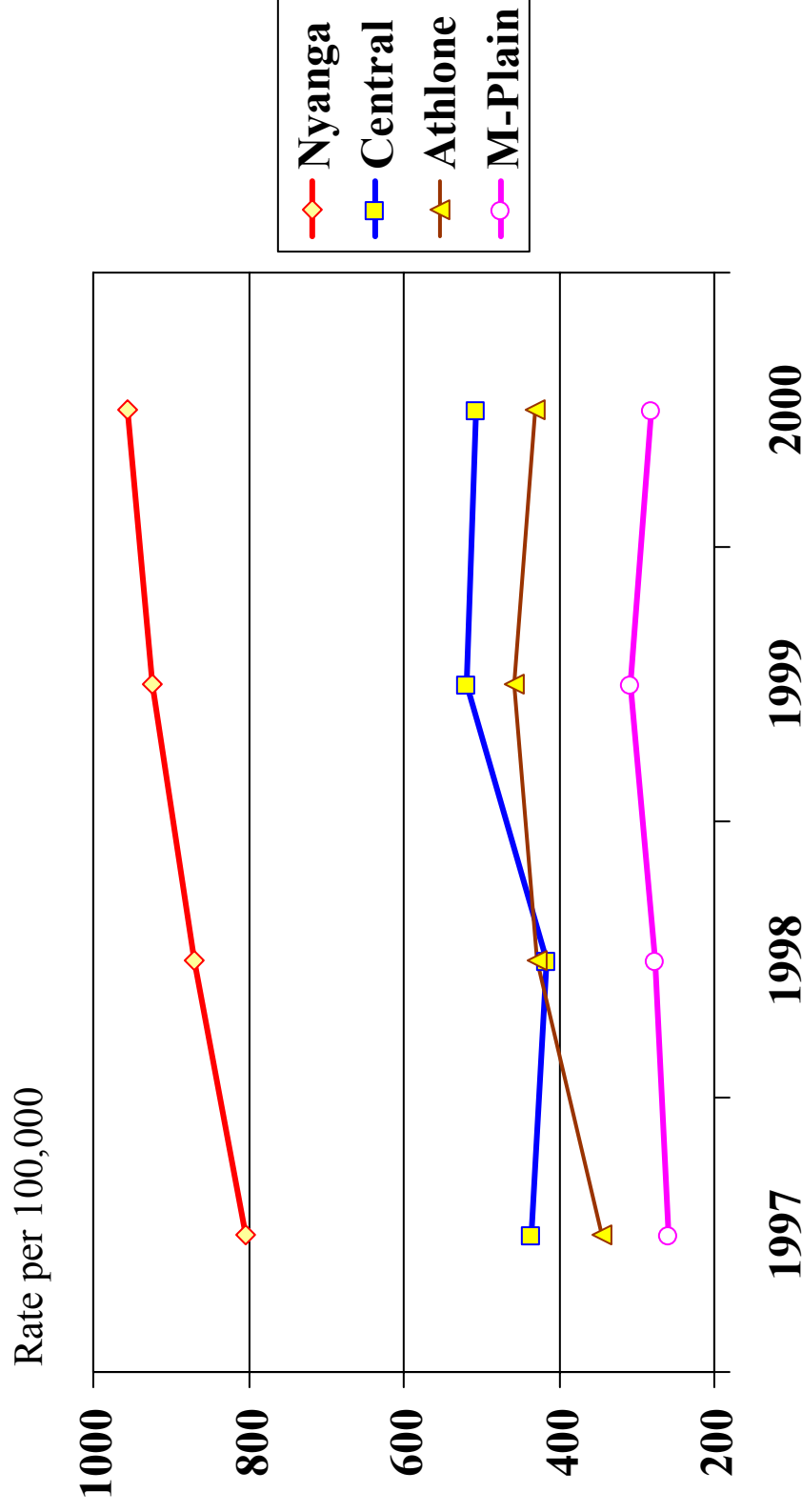


Impact of Antiretroviral Therapy on OI's and Death in SA

	Treated <i>n</i> =450	Naive <i>n</i> =266	
Event	Incidence rate*	Incidence rate*	HR (95% CI)
AIDS	3.2	12.8	0.23 (0.12-0.43)
Death	1.7	14.8	0.09 (0.04-0.20)

* Per 100/patient-years

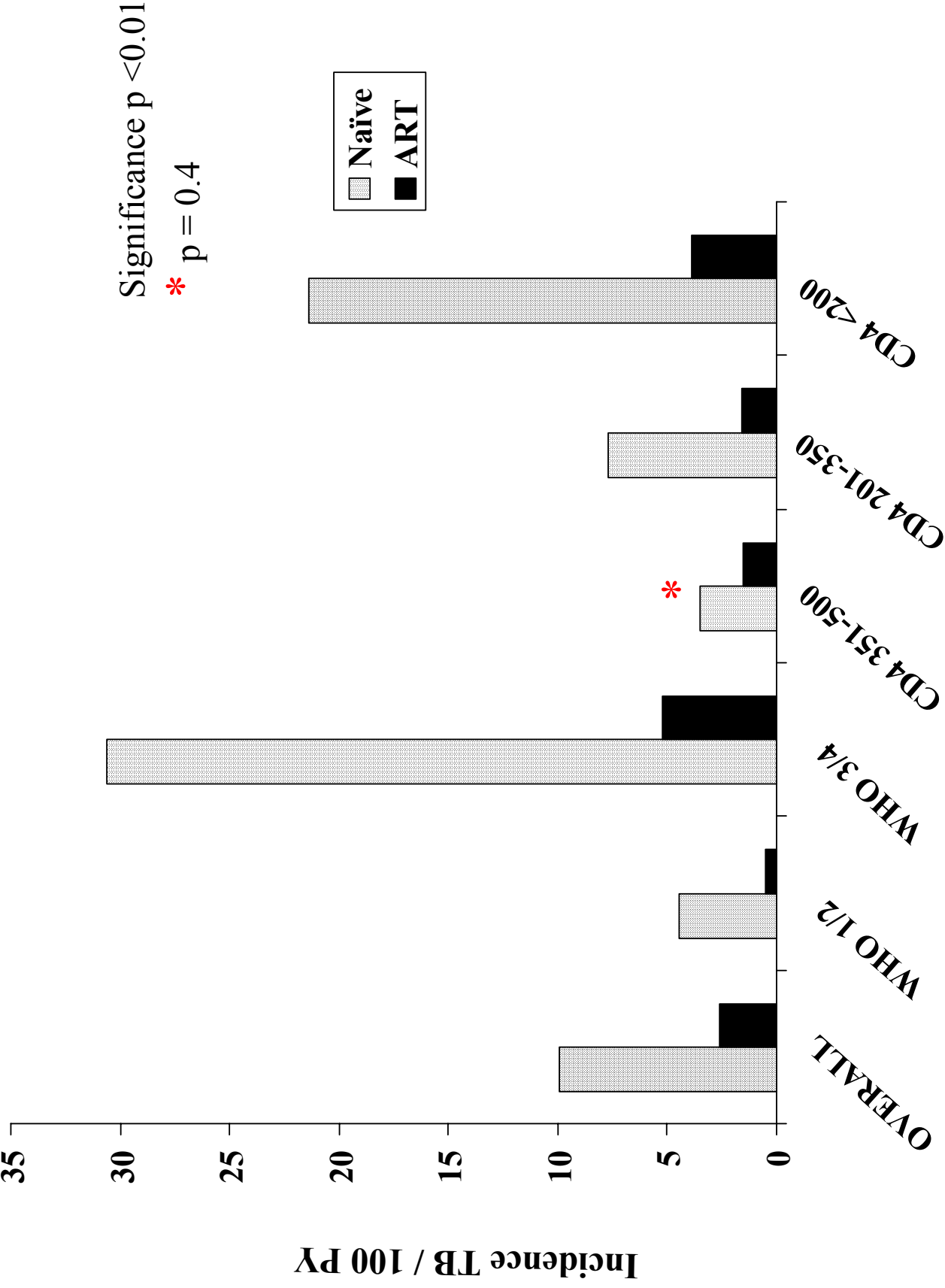
Cape Town TB Incidence Rate



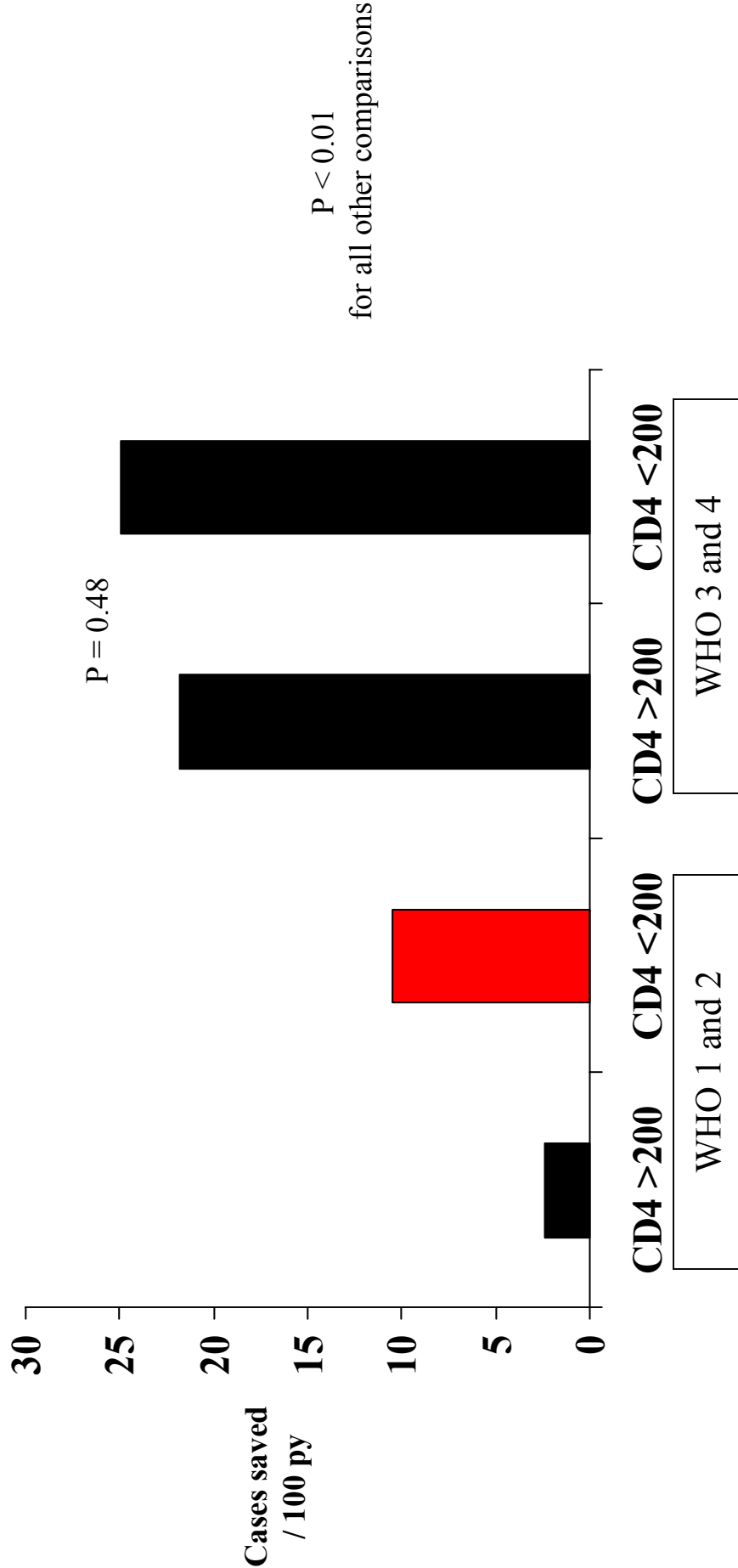
Incidence rate and hazard ratio of TB stratified by baseline CD4 count and WHO stage

Category		Treated	Naive	H R (95% CI)	Cases prevented
Overall	TB cases Patient-years Incidence	10 378.7 2.6	45 454.6 9.9	0.15 (0.08-0.32)	
CD4 count < 200	TB cases Patient-years Incidence	6 150.7 3.9	30 140.3 21.4	0.19 (0.08-0.45)	17.5
WHO Stage 3/4	TB cases Patient-years Incidence	9 173.5 5.2	29 94.9 30.6	0.17 (0.08-0.36)	25.4

Incidence of tuberculosis stratified by WHO stage or CD4 count



Number of cases of tuberculosis prevented per 100 patient years stratified by CD4 count and WHO stage



Cost of CD4 count: ZAR 400.00

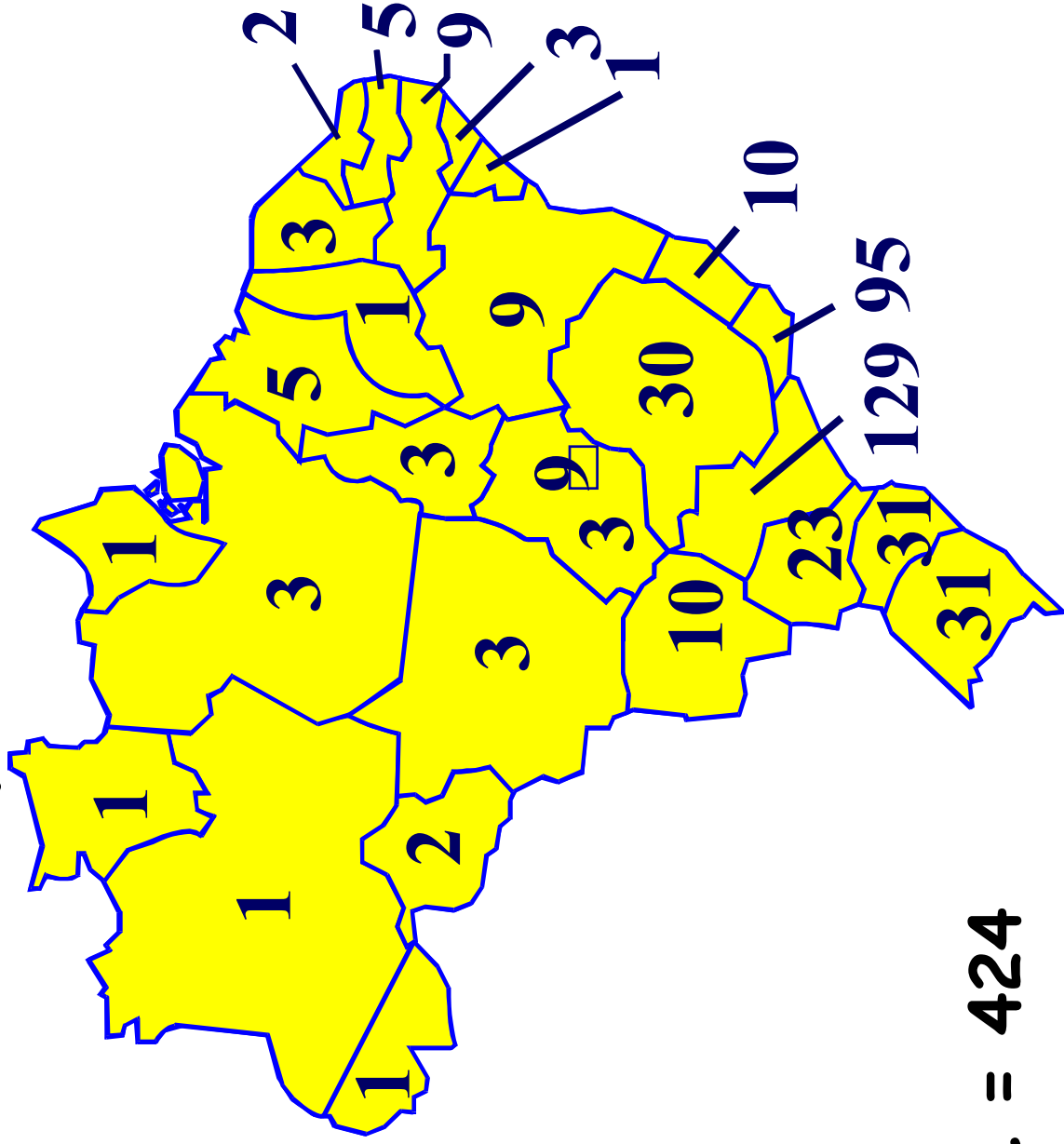


Antiretroviral Therapy in Brazil

- ARV provided free of charge to all who fulfill criteria set by an independent committee
- When to start and what to start with based on risk stratification that includes CD4, viral load and clinical status

Brazil Antiretroviral Dispensaries

- September, 2000



TOTAL = 424

Relative Magnitudes of the HIV Epidemic 1999

	Brazil	South Africa
Total population	168 million	40 million
HIV positive	540,000	4.2 million
AIDS deaths	18,000	250,000

Western Model for ARV

- "Mix & match" drugs
- Complexity of interactions
- High level of expertise needed
- South African private sector
 - Phone support
 - Internet support
 - Expert systems

South African Tuberculosis Program

- Addresses problems of scale
- SA >156,000 cases treated annually
- Network of primary care clinics
- Delivery of a cocktail of toxic drugs
- Standardised regimens ensure uniformity of care

Scheduled Rx Approach

- Simplifies management
- Ensures uniformity of medical care
- Management by nurse practitioners/clinical assistants
- Simplifies drug supply

Schedule Constraints

- Once or twice daily regimens only
- Reasonable toxicity profile
- Pregnancy friendly
- TB Rx compatible
- Can not recycle NNRTI's
- Only 6 NRTI's therefore must recycle
- Recycle early to preserve response

Sizophila Compliance Monitors



Therapy of HIV Infection

"...given the current limitations of antiretroviral therapy, investigators seem unprepared to look beyond guidelines and rise to the challenge of comparing strategies of early, potent antiretroviral therapy with deferred therapy for HIV-1 infection."

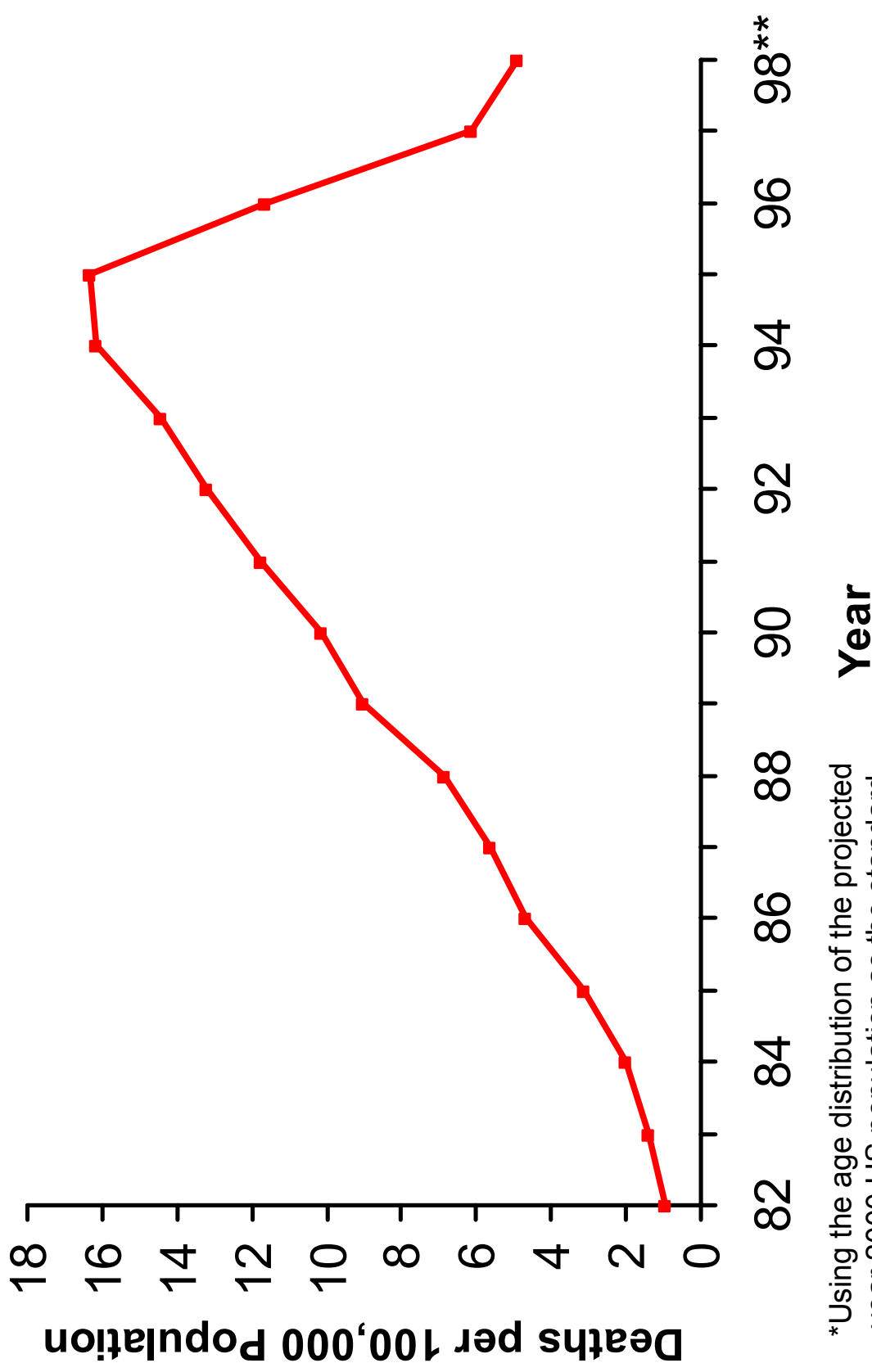
Cooper & Emery, NEJM 1998

National Guidelines

Cook-book of viral load/CD4/Clinical symptoms

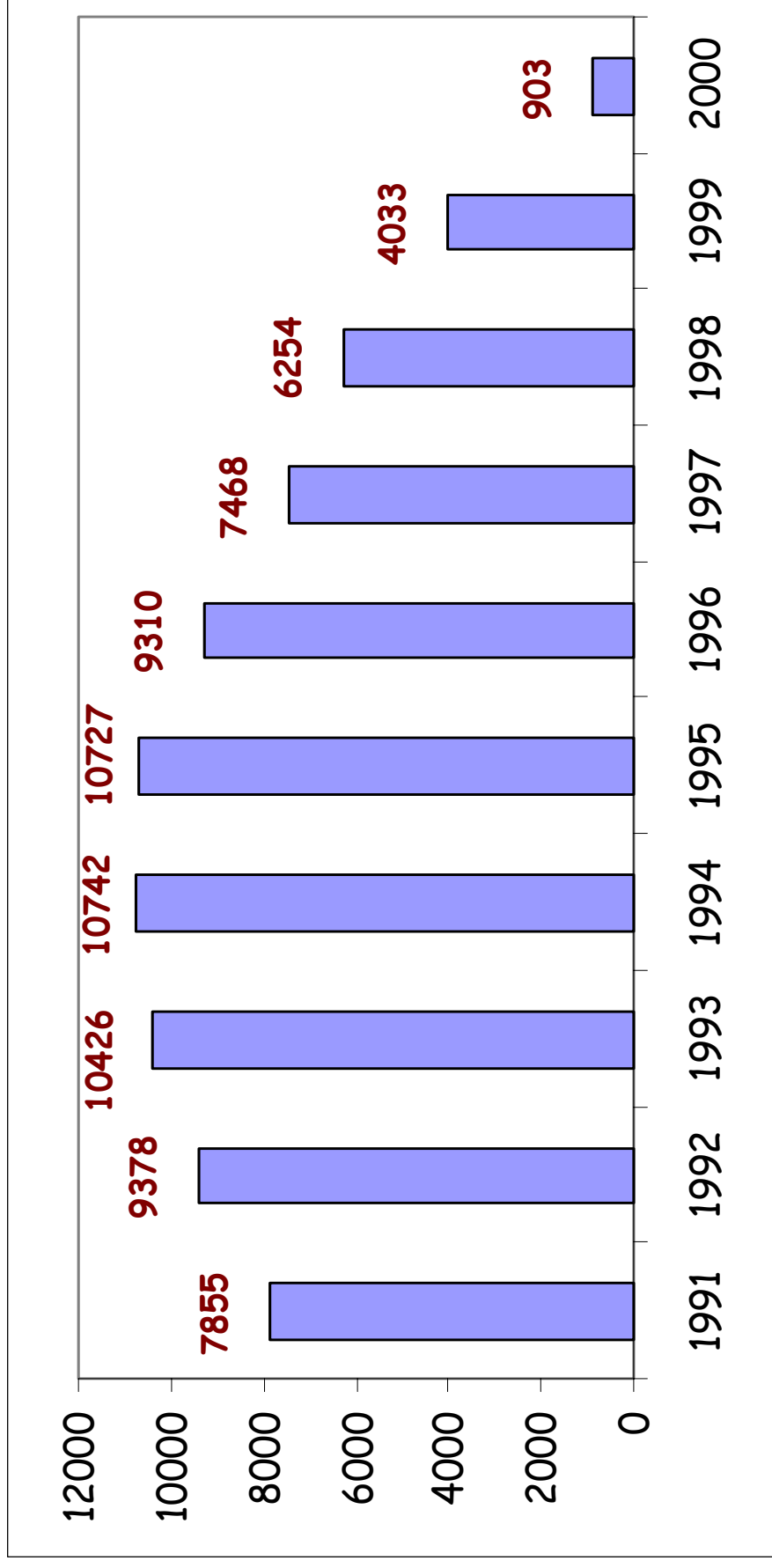
- Viral load
 - 1996 USA-All measurable viral loads
 - 2000 Brazil- Stratify risk by viral load
 - 2001 UK-Viral load not used
- CD4-cell counts
 - 1996 USA >500
 - 2000 Brazil >350
 - 2001 UK >200

Trends in Age-Adjusted* Rates of Death due to HIV Infection, USA, 1982-1998

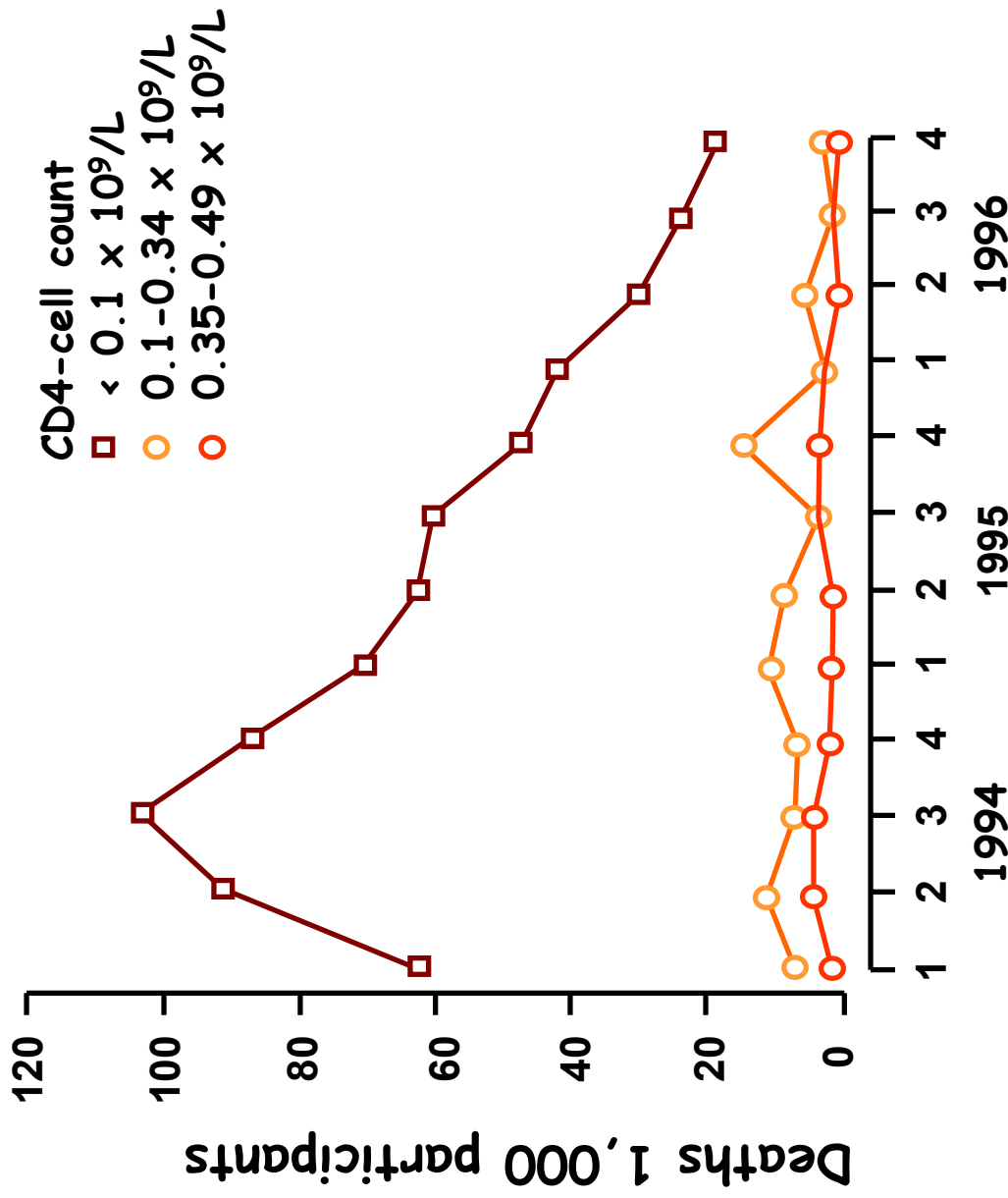


*Using the age distribution of the projected year 2000 US population as the standard.

AIDS-Related Deaths, Brazil 1991-2000



AIDS-Related Deaths, British Columbia



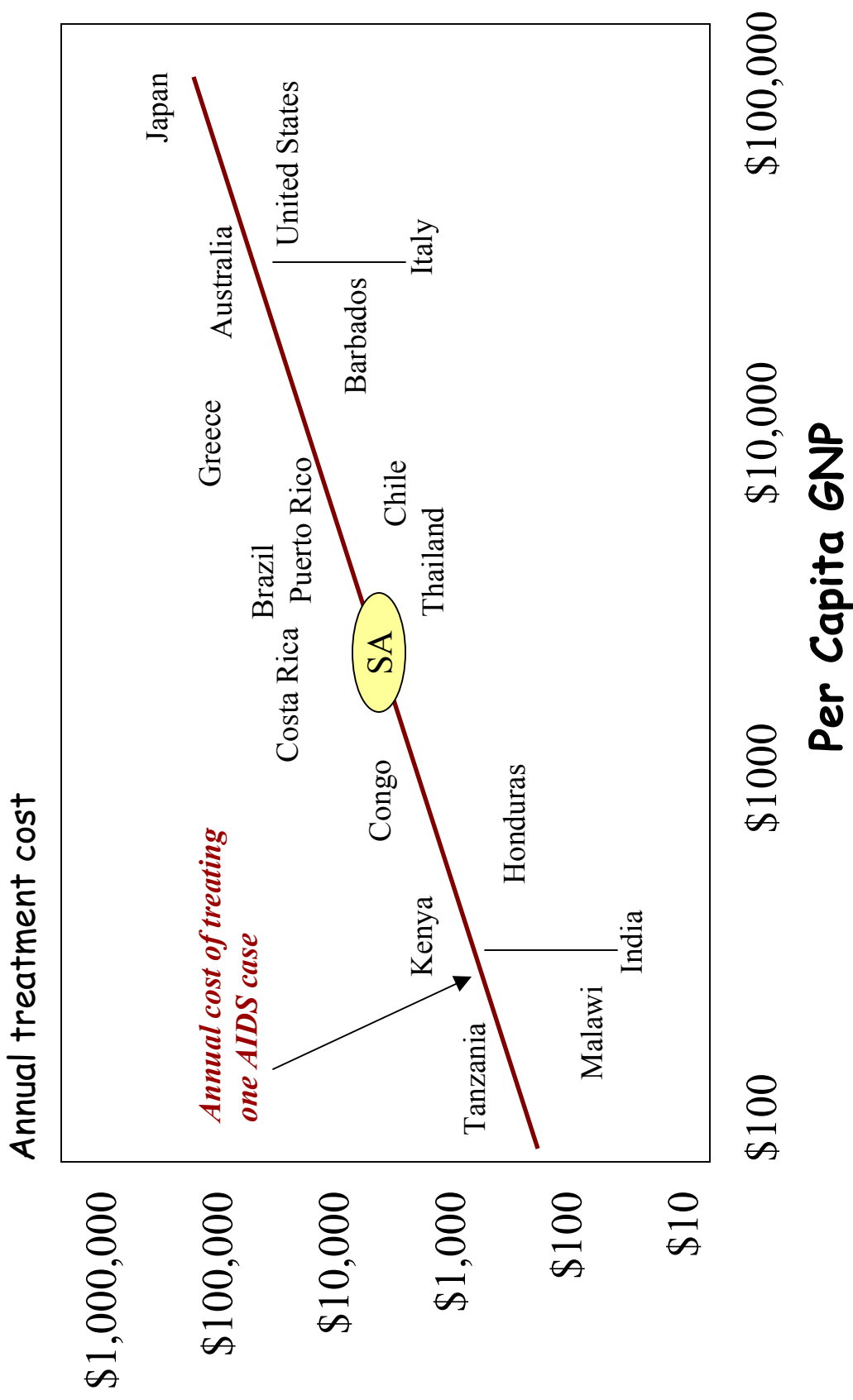
Year and Quarter

Hoggs, Lancet 1997

What can we learn from these Different National Guidelines

- Despite most patients being unaware of their HIV status deaths have plummeted in developed countries
- It must be the similarities between guidelines that impact on AIDS mortality
- "Treating symptomatic patients impacts significantly on AIDS death rates"

Annual Treatment Cost For an Aids Patient



ANAXHOSA FUNERAL UNDERTAKERS

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Conclusions

- Antiretrovirals can be used successfully in SA public sector
- We need political support
- We should avoid looking for unproductive controversies
- Consider other models of care delivery besides western model

The Way Forward

- Political support
- Good costing studies
- Pilot sites
- Avoid unnecessary controversy
- Consider other models of care besides western model