

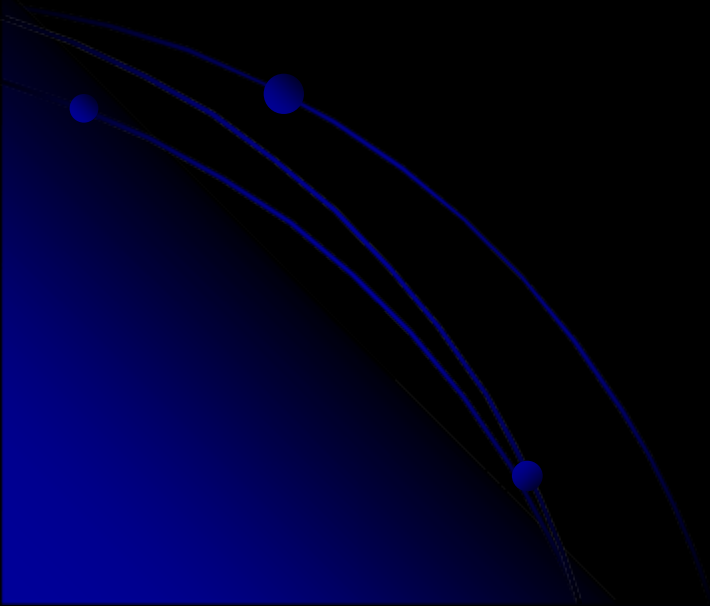
# Observations from Interval and Clinical Cohorts

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# Perspective from Cohorts

- Cohorts are eager to contribute
- Have considerable data to contribute
- Must be taken in their context



# Interval Cohorts – Research Cohorts

- Sparce
  - Several in Europe and North America
  - But also several in low-income settings
  - Post hoc analysis of trial databases
- Characterized by “beyond clinical care ascertainment”
  - Not tied to clinical events – self report, medical record confirmation
  - Include those not in care, non-symptomatic data collection AND those not infected

# Semi-Annual Visit

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- Interview Administered Questionnaires:
  - Behavior
  - Health Services
  - Medical and OB/GYN
  - Demographics/Psychosocial
- Physical and Gynecological Examination
- Lipodystrophy Exam (body measures, BIA)
- Medication use (ART, OI prophylaxis, hepatitis, etc.)
- Participant Samples:
  - Blood (virologic, immunologic, fasting lipodystrophy markers, liver/renal function, etc.)
  - Other (CVL, saliva)
  - Local and National Repositories

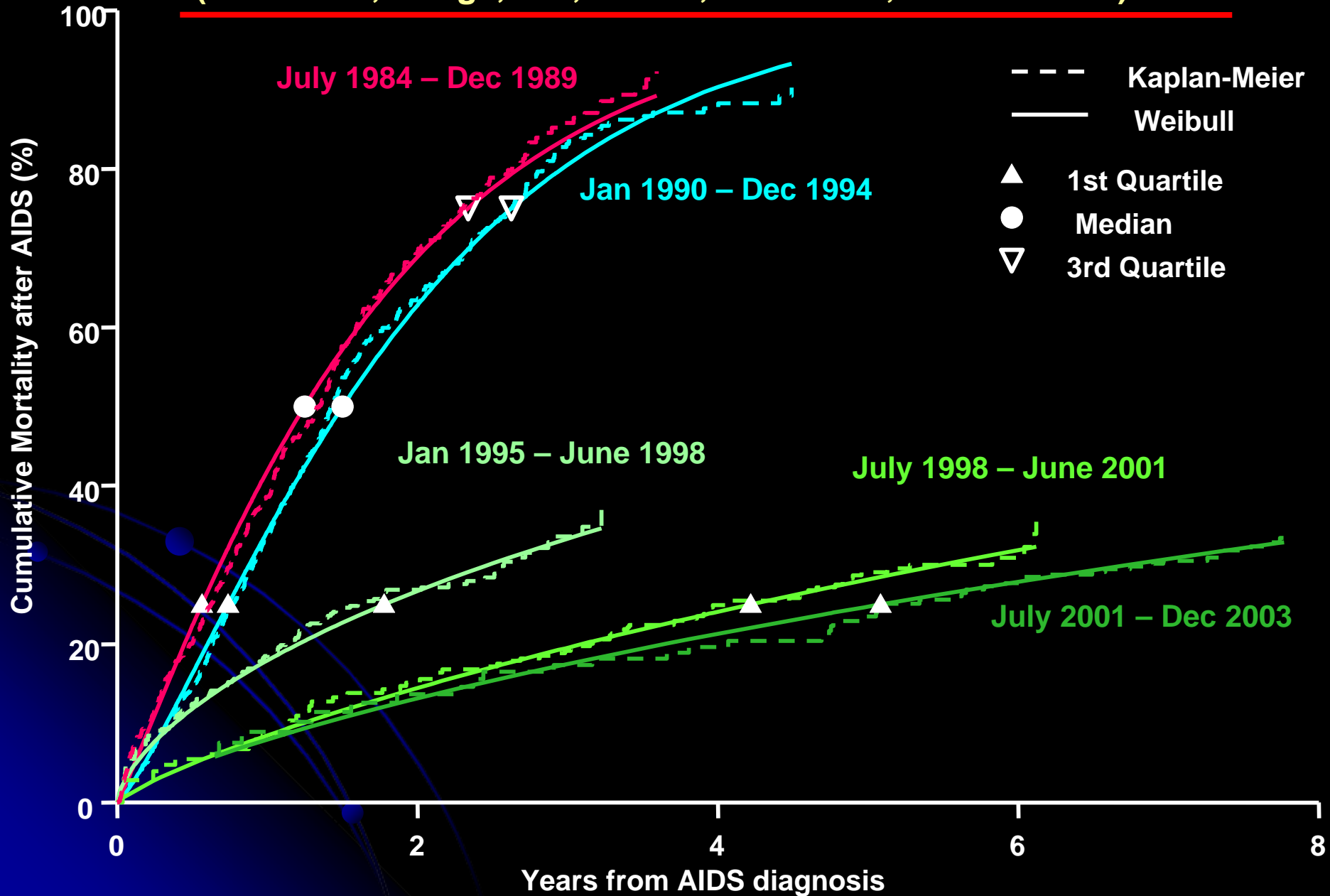
# Continuous Outcome Ascertainment

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- Seroconversion
- Clinical Outcomes:
  - AIDS Diagnoses
  - Malignancies
  - Mortality
  - Tuberculosis
  - Cardiovascular Diagnoses
  - Liver biopsies
  - Hysterectomies
- Sources:
  - Self-report
  - Medical Record Abstraction
  - Registry Match (Cancer, TB)
  - National Death Index

# Cumulative Mortality after AIDS

(Schneider, Gange, . . . , Muñoz, *AIDS* 2005; 19:2009-2018)



# Accident- and Injury-related Causes of Death in MACS and WIHS

(Hessol, Kalinowski, . . . , Cohen, *CID* 2007; 44:287-294)

Cause of Death	MACS			WIHS		
	HIV+	HIV-	ALL	HIV+	HIV-	ALL
Suicide	5 (21)	5 (19)	10 (20)	1 (3)	2 (20)	3 (7)
Poisoning / Drug OD	7 (29)	6 (22)	13 (25)	26 (72)	5 (50)	31 (67)
Drowning	1 (4)	2 (7)	3 (6)	2 (6)	1 (10)	3 (7)
Assault / homicide	3 (13)	6 (22)	9 (18)	5 (14)	1 (10)	6 (13)
Suffocation	1 (4)	1 (4)	2 (4)	0	0	0
Other injury accidents	7 (29)	7 (26)	14 (27)	2 (6)	1 (10)	3 (7)
<b>Total accident / injury</b>	<b>24</b>	<b>27</b>	<b>51</b>	<b>36</b>	<b>10</b>	<b>46</b>
All other causes	1721	58	1779	554	19	573

**NOTE: Data are number (%) of participants.**

# Standardized Incidence Ratios for Cancer in the HAART and Pre-HAART Eras among 1559 HIV+ Women

(Hessol, Seaberg, . . . , Levine, *JAIDS* 2004; 36:978-985)

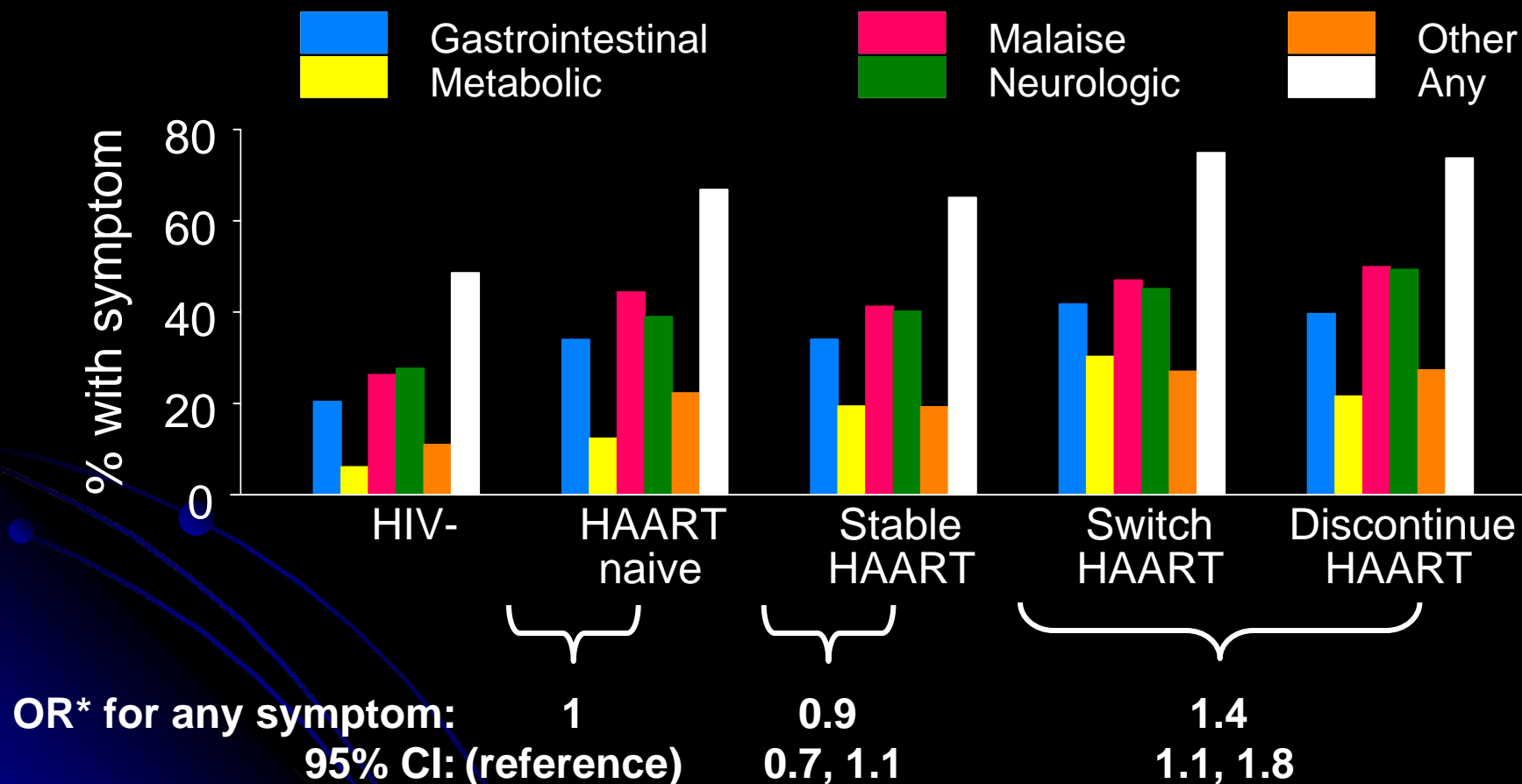
	Years 1994 – 1996			Years 1997 – 2001		
Person-years:	2,492			5,417		
<i>Cancer site/type</i>	<i>Observed</i>	<i>SIR</i>	<i>95% CI*</i>	<i>Observed</i>	<i>SIR</i>	<i>95% CI*</i>
<b>AIDS Cancers</b>	<b>13</b>	<b>23.4</b>	<b>12.5 – 37.7</b>	<b>6</b>	<b>4.4</b>	<b>1.6 – 8.6</b>
NHL	9	53.4	24.4 – 93.6	3	6.4	1.3 – 15.5
KS	4	316.1	86.1 – 692.7	2	189.3	22.9 – 527.3
<b>Non-AIDS Cancers</b>	<b>7</b>	<b>1.4</b>	<b>0.6 – 2.6</b>	<b>15</b>	<b>1.0</b>	<b>0.6 – 1.5</b>
Lung/larynx	2	6.8	0.8 – 18.9	6	6.2	2.3 – 12.1
Breast	1	0.4	0.01 – 1.6	4	0.5	0.1 – 1.2

\* The 95% confidence intervals (CI) are based on exact statistical methods.



# Prevalence of Clinical Symptoms Associated with HAART

(Silverberg, Gore, . . . , Gange, *Clin Infect Dis* 2004; 39:717-724)

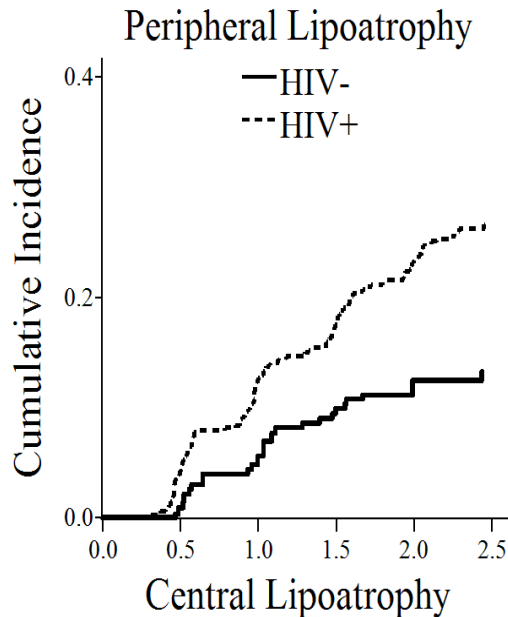


\* Adjusted for age, race, BMI, baseline HIV risk, alcohol, CD4+, HIV RNA, AIDS

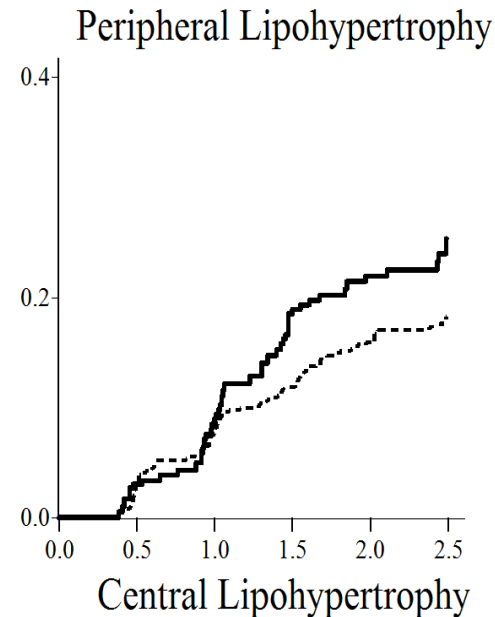
# Incident Lipoatrophy and Lipohypertrophy

(Tien, Cole, . . . , Grunfeld, *JAIDS* 2003; 34:461- 466)

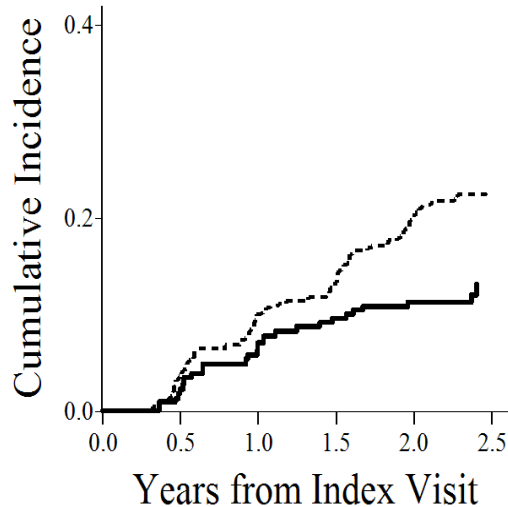
**RH = 2.9**  
**95% CI, 1.4 – 3.2**



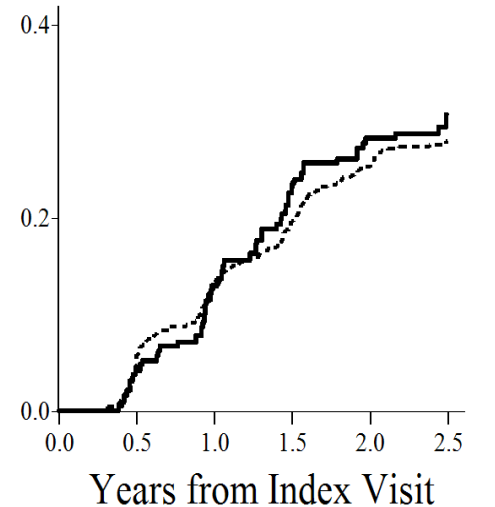
**RH = 0.8**  
**95% CI, 0.6 – 1.1**



**RH = 1.8**  
**95% CI, 1.2 – 2.8**



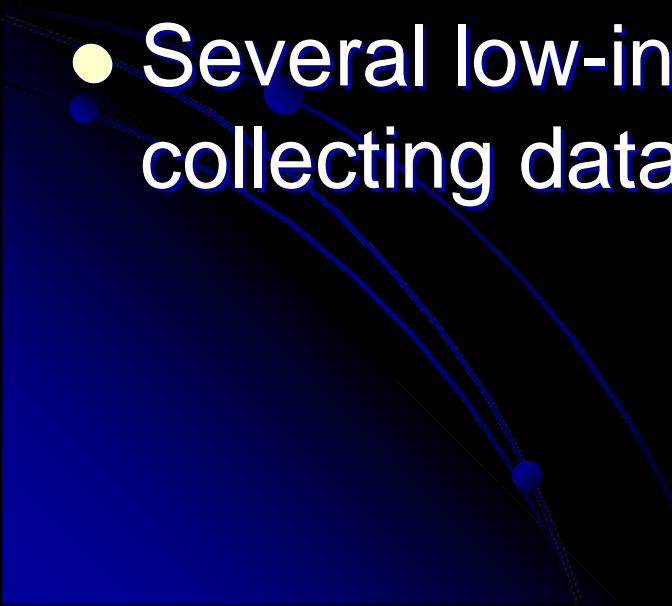
**RH = 1.0**  
**95% CI, 0.7 – 1.3**



# Clinical Cohorts

- Data are being collected everywhere!
  - Good charts are good care
  - Quality is directly proportional to relevance to the collector
- Centered around care events
  - The data is the most dense when something happens
  - Sparse data before an event occurs
  - Standard of care, do not ascertain asymptomatic disease, disease in uninfected

# Strong “global portfolio” of Clinical Cohorts

- European cohort collaborations – extensive and mature research programs
  - CNICS data collection protocol of US Centers for AIDS Research
  - Several low-income country databases are collecting data
- 



•Region 1: North America

- Canada
- United States

Region 5: Australia, India, Pakistan, Asia

- Australia
- Cambodia
- India
- Indonesia
- Japan
- China
- Malaysia
- Singapore
- Thailand

Region 2: Latin America & Caribbean

- Argentina
- Brazil
- Chile
- Haiti
- Honduras
- Mexico
- Peru

Region 8: East Africa

- Kenya
- Tanzania
- Uganda

Region 8: Central Africa

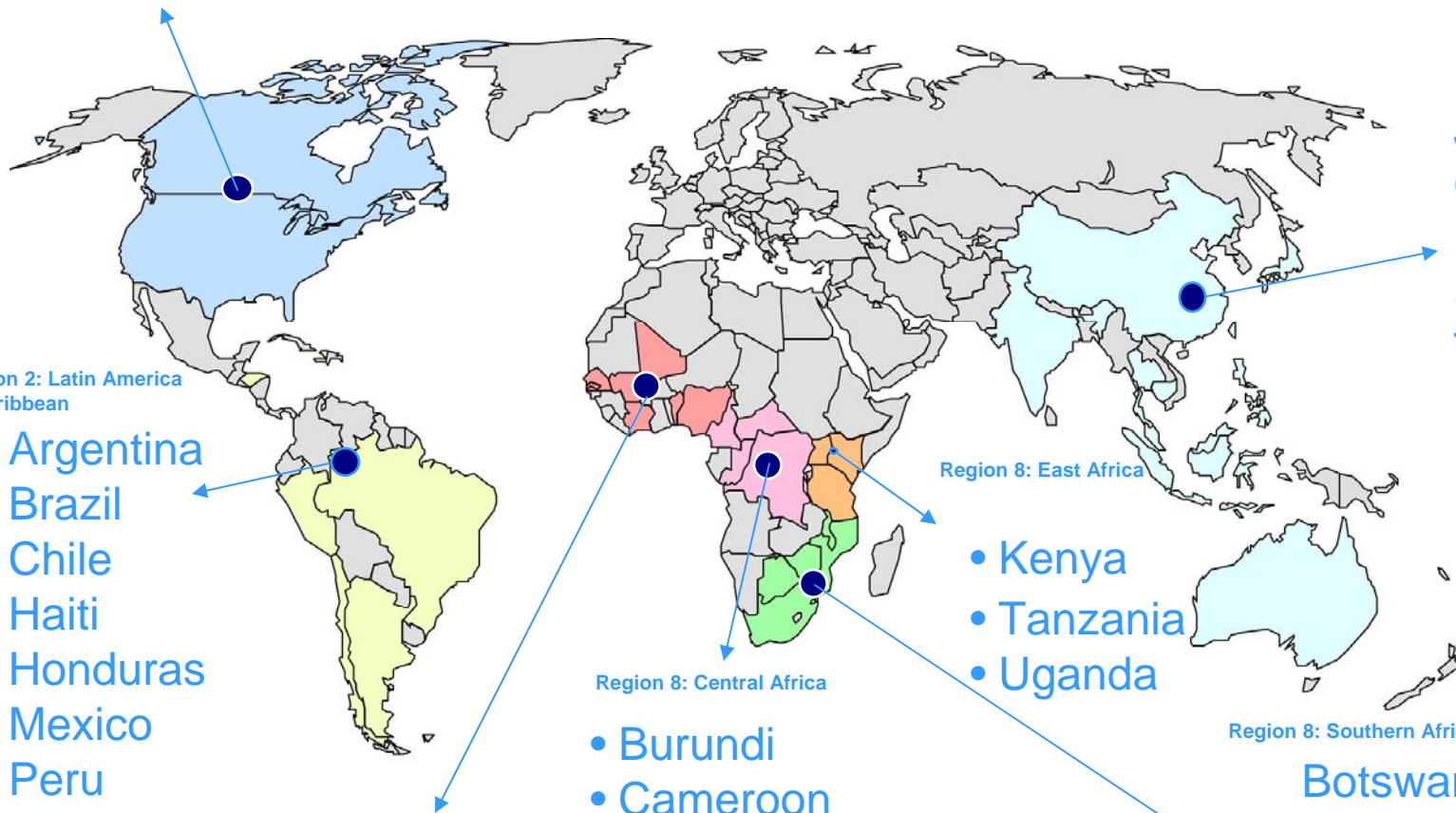
- Burundi
- Cameroon
- Central African Republic
- Congo, Dem. Rep. of (Zaire)
- Congo, Republic of
- Rwanda

Region 8: Southern Africa

- Botswana
- Malawi
- Mozambique
- South Africa
- Zambia
- Zimbabwe

Region 8: West Africa

- Benin
- Cote d'Ivoire
- Gambia
- Mali
- Nigeria
- Senegal





- Formal gathering of data
  - Iterative improvements – feedback loops
  - Interaction with data collectors improve relevance of data collected
  - Specific studies improve definitions of conditions
  - Extremely large datasets
- Coalition of the willing
  - Primary to REFERRAL
  - Not representative of all clinics in a region
- Predominately standard of care
  - Based on patient encounters
  - Some pre-ARV data at some sites
  - No data on HIV-s outside of NA-ACCORD



# Capacity to Diagnose AE

- Regional database query
- Site level data query
- Meta-data on site level characteristics
  - Numbers of patients
  - Contents of database, pre and post ARVs
  - AE ascertainment
    - Health practitioner level
    - Laboratory capacity
    - Visit schedules, testing schedules



# Regional Responses

- NA-ACCORD 50,000 patients
- West Africa 16,945 adults, 2,204 pediatric
- Central Africa 872 adults
- Australia/Asia 2,947 adults
- Caribbean, Central America S. America ~ 50,000
- East Africa ~150,000
- Southern Africa ~ 100,000





# Regional Responses

- Australia/Asia – more intensive data collection system
  - 2,645 patients in database with CD4
    - 1930 with viral load
    - 2,272 SGPT, 1,552 SGOT for liver function
    - 1,790 Creatinine
    - ~1,679 Lipid measurements including triglycerides
    - 152 lactic acid

CD8  
Total lymphocyte  
Weight  
Blood pressure  
Haemoglobin

Glucose  
Amylase  
Lipase  
Alkaline  
Bilirubin



# Regional Responses

- West Africa – 16,945
  - 11,114 patients in database with CD4
    - 1,749 with viral load
    - 9,444 with liver function
    - 10,472 with Hemoglobin
    - 5,390 with neutrophil count
  - 1,663 pediatric patients with CD4
    - 376 viral loads
    - 338 liver function
    - 305 Creatinine
    - 611 lymphocyte count
    - 1,651 Hemoglobin
    - 77 Uremia



# Regional Responses

Central Africa 872 prospectively collected

- 872 patients in database with CD4
  - 0 viral load
  - 872 CBC
  - 872 liver function
  - 872 Creatinine
  - 0 lactic acid
  - 872 glycemia



# Regional Responses

- Central Africa – diagnoses in database
  - Laboratory based
    - 1,120 anemia
    - 1,950 neutropenia
    - 2, 286 lymphopenia
    - 2,307 thrombocytopenia
  - Patient report
    - 64 nausea, 99 diarrhea, 23 vomiting
    - 144 fatigue
    - 315 nightmares, 86 abnormal dreams
  - Clinical exam
    - 262 peripheral neuropathy
    - 14 KS, 1 cervical cancer

# Summary

- Interval Cohorts
  - Beyond standard of care
  - Comparison to negatives, asymptomatics
- Clinical cohorts
  - Can only see at the “standard of care”
  - Will improve as expectations of monitoring change