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

- **Sparse**
  - 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

- **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

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


<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>MACS</th>
<th>WIHS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV+</td>
<td>HIV-</td>
</tr>
<tr>
<td>Suicide</td>
<td>5 (21)</td>
<td>5 (19)</td>
</tr>
<tr>
<td>Poisoning / Drug OD</td>
<td>7 (29)</td>
<td>6 (22)</td>
</tr>
<tr>
<td>Drowning</td>
<td>1 (4)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Assault / homicide</td>
<td>3 (13)</td>
<td>6 (22)</td>
</tr>
<tr>
<td>Suffocation</td>
<td>1 (4)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Other injury accidents</td>
<td>7 (29)</td>
<td>7 (26)</td>
</tr>
<tr>
<td><strong>Total accident / injury</strong></td>
<td><strong>24</strong></td>
<td><strong>27</strong></td>
</tr>
<tr>
<td><strong>All other causes</strong></td>
<td>1721</td>
<td>58</td>
</tr>
</tbody>
</table>

**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)

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<thead>
<tr>
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</thead>
<tbody>
<tr>
<td></td>
<td>Person-years:</td>
<td></td>
<td></td>
<td>Person-years:</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>2,492</td>
<td></td>
<td></td>
<td>5,417</td>
<td></td>
<td></td>
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<tr>
<td>AIDS Cancers</td>
<td>Observed</td>
<td>SIR</td>
<td>95% CI*</td>
<td>Observed</td>
<td>SIR</td>
<td>95% CI*</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>23.4</td>
<td>12.5 – 37.7</td>
<td>6</td>
<td>4.4</td>
<td>1.6 – 8.6</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>53.4</td>
<td>24.4 – 93.6</td>
<td>3</td>
<td>6.4</td>
<td>1.3 – 15.5</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>316.1</td>
<td>86.1 – 692.7</td>
<td>2</td>
<td>189.3</td>
<td>22.9 – 527.3</td>
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<tr>
<td>NHL</td>
<td>7</td>
<td>1.4</td>
<td>0.6 – 2.6</td>
<td>15</td>
<td>1.0</td>
<td>0.6 – 1.5</td>
</tr>
<tr>
<td>KS</td>
<td>2</td>
<td>6.8</td>
<td>0.8 – 18.9</td>
<td>6</td>
<td>6.2</td>
<td>2.3 – 12.1</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>0.4</td>
<td>0.01 – 1.6</td>
<td>4</td>
<td>0.5</td>
<td>0.1 – 1.2</td>
</tr>
</tbody>
</table>

* 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)

OR* for any symptom: 1
95% CI: (reference) 0.9
0.7, 1.1
1.4
1.1, 1.8

* 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)*

- **Peripheral Lipoatrophy**
  - RH = 2.9
  - 95% CI, 1.4 – 3.2

- **Peripheral Lipohypertrophy**
  - RH = 1.0
  - 95% CI, 0.7 – 1.3

- **Central Lipoatrophy**
  - RH = 0.8
  - 95% CI, 0.6 – 1.1

- **Central Lipohypertrophy**
  - RH = 1.8
  - 95% CI, 1.2 – 2.8
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
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
    - 1,930 with viral load
    - 2,272 SGPT, 1,552 SGOT for liver function
    - 1,790 Creatinine
    - ~1,679 Lipid measurements including triglycerides
    - 152 lactic acid

<table>
<thead>
<tr>
<th>CD8</th>
<th>Glucose</th>
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<tbody>
<tr>
<td>Total lymphocyte</td>
<td>Amylase</td>
</tr>
<tr>
<td>Weight</td>
<td>Lipase</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Alkaline</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>Bilirubin</td>
</tr>
</tbody>
</table>
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
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