The Implication of Viral Load Measurement in Assessing the Epidemiologic Control of HIV/AIDS

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Summarizing current approach to HIV treatment

• Combination treatment – 2NRTI plus one NRTI/boosted PI / INSTI
• Early treatment – moving away from CD4 guided therapy
• Public health role of effective and early HIV treatment considered
• Shrinking role of CD4 monitoring acknowledged
Natural history of HIV infection with treatment – decrease in viral load at individual level

Viral load measures at population level

Viral Load Measures

<table>
<thead>
<tr>
<th>Component Measures</th>
<th>Population Viral Load</th>
<th>Community Viral Load</th>
<th>In-Care Viral Load</th>
<th>Monitored Viral Load</th>
</tr>
</thead>
<tbody>
<tr>
<td>In care, no VL*</td>
<td>in care with undetectable VL</td>
<td>in care with undetectable VL</td>
<td>in care with detectable VL</td>
<td>in care with detectable VL</td>
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<tr>
<td>Diagnosed but not in care</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Undiagnosed</td>
<td></td>
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</tbody>
</table>

*No VL = missing/unknown, for a variety of reasons (e.g., incomplete reporting)

http://www.cdc.gov/hiv/topics/surveillance/resources/fact_sheets/inc/content/viral_load_table.htm
**Viral load measures at population level**

- **HIV specialist clinic**
  - Patients with viral load records
    - ▶️ Viral load >500/mL
    - ● Viral load ≤500/mL
  - Patients without viral load records
    - ○ Viral load >500/mL (estimated)
    - ○ Viral load ≤500/mL (estimated)

- **Viral load measures**
  - ▶️ Monitored viral load (MVL)
  - ● In-care viral load (ICVL)
  - ○ Community viral load (CVL)
  - □ Population viral load (PVL)

By back-calculation, we estimated each person’s seroconversion time, followed by the construction of viral load curves from seroconversion to diagnosis. Annual full CVL (fCVL), was then estimated by the summation of viral loads of both diagnosed and undiagnosed HIV+ individuals.

MVL = monitored viral load; ICVL = in care viral load; CVL = community viral load; fCVL = “full” community viral load

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**Population viral load cannot be ‘calculated’**

- Viral load of HIV+ patients who were never diagnosed
- Viral load of undiagnosed patients who were eventually diagnosed
- Viral load of patients lost to follow-up

MVL = monitored viral load; ICVL = in care viral load; CVL = community viral load; PVL = population viral load
Conventional epidemic curves -
Hong Kong (DH surveillance data)

Conventional epidemic curves by subpopulation
Population level viral load curves
- overall pattern (QEH & DH-ITC data)

Population level viral load curves
- by subpopulation (heterosexuals) QEH and DH-ITC
Population level viral load curves
- by subpopulation (MSM) QEH and DH-ITC

Viral load suppression in the population
- Treatment %↑, SVL%↑
- time lag between increase of treatment coverage and proportion of patients with SVL
- Treatment % in MSM < heterosexuals

Data from QEH and DH-ITC
Modelling viral load suppression under different scenarios

Data from QEH and DH-ITC for parameters setting
HIV epidemiology from a viral load perspective

- Treatment %↑, SVL%↑, potential of HIV transmission ↓
- Population viral load (fCVL) curve predated incidence curves and unadjusted viral load measures by years
- Further reduction of HIV transmission potential in the population is small if treatment coverage is already optimal
- Reduction of the undiagnosed population is the single most important strategy to achieve effective epidemiologic control
- Non-locally acquired infection, assuming same treatment coverage and timeliness, is unlikely to contribute to the epidemic unless local transmission networks are present
- Epidemiological understanding from viral burden in population per se cannot predict outbreaks.

VL trajectories during HAART
US Military HIV Natural History Study

http://www.plosone.org/article/info:doi/10.1371/journal.pone.0017956
Lifelong cumulative viraemia is associated with a better immunological response following treatment of primary infections

CD4 was highest following early continuous treatment of patients who had the lowest cumulative viraemia. Latest CD4 cell count was not associated with cumulative HIV viraemia in early intermittent vs deferred treatment group. In contrast, patients with high cumulative HIV viraemia (>66th percentile vs. <33rd percentile) were less likely to achieve a CD4/CD8 ratio of more than 1 (26.8 vs. 43.3%, P=0.003), even after controlling for the baseline CD4/CD8 ratio, treatment duration, sex and age..

**CD4/ CD8 ratio**

as a ‘new’ biomarker of HIV infection

Associations of a low ratio

- T cell activation, senescence, and dysfunction and with chronic inflammation
- A higher risk of disease progression, similar to IDU, HCV infection, elderly people
- non-AIDS illnesses usually including cardiovascular, renal, and liver diseases, non-AIDS cancers
- Other infections, for example CMV
- Surrogate of chronic inflammation.

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**Diversifying roles of 2 longstanding HIV markers**

**CD4**

Absolute count for informing urgency of HAART, monitoring response, as outcome measure

**CD4/CD8**

Another outcome measure, morbidity index

**VL**

Marker of response to treatment

**Population VL**

Population risk of transmission

**Cumulative VL**

Lifetime risk of disease progression

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http://www.plosone.org/article/info:doi/10.1371/journal.pone.0017956
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