The PEPFAR Approach to Advanced HIV Disease

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17 YEARS OF SAVING LIVES THROUGH AMERICAN GENEROSITY AND PARTNERSHIPS
PEPFAR’s Approach to CD4 Testing

• Supported to identify individuals with advanced disease; not for monitoring response to ART
  • Persistent viremia in individuals older than 5. Persistent viremia defined as documented viremia ≥ 1 year.
  • Individuals initiating ART in geographic regions where the documented (or suspected) prevalence of advanced disease is >15%
  • Geographic prevalence can include SNUs, specific populations and high volume sites implementing advanced disease
  • Individuals off therapy for a year or more could potentially be considered a population at risk for advanced disease

• CD4 Testing networks need to be optimized:
  • Health facility and test location inventories; priority on places that have capacity for treating advanced disease
  • Testing volumes
Trends in Prevalence of Advanced Disease

(IeDEA Collaboration, Zaniewski E et al, JAIDS, 2020)
Burden of Disease in PEPFAR countries

Zimbabwe PHIA
AFRICOS
Using the Pepfar mortality as a surrogate marker for advanced disease.
Zimbabwe PHIA 2015-2016

Table 1. Characteristics of ZIMPHIA 2015–16 HIV-positive study population disaggregated by CD4 count.

<table>
<thead>
<tr>
<th></th>
<th>CD4 &lt; 200 cells/mm³</th>
<th>CD4 ≥ 200 cells/mm³</th>
<th>p-value</th>
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<tbody>
<tr>
<td></td>
<td>n</td>
<td>weighted%</td>
<td>95% CI</td>
</tr>
<tr>
<td>Sex</td>
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<tr>
<td>Female</td>
<td>252</td>
<td>39.5</td>
<td>(34.5–44.4)</td>
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<tr>
<td>Male</td>
<td>290</td>
<td>60.5</td>
<td>(55.6–65.5)</td>
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<td>Age</td>
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<tr>
<td>15–24</td>
<td>41</td>
<td>8.9</td>
<td>(6.0–11.9)</td>
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<td>25–34</td>
<td>117</td>
<td>23.8</td>
<td>(19.5–28.1)</td>
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<td>35–49</td>
<td>255</td>
<td>47.1</td>
<td>(42.2–52.1)</td>
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<td>50+</td>
<td>129</td>
<td>20.1</td>
<td>(16.1–24.1)</td>
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</tbody>
</table>

Balachandra et al. 2020
Mortality in Select PEPFAR Countries — 2020 Q2

- **Asia Regional Region:**
  - Cameroon
  - Côte d’Ivoire
  - Ethiopia
  - Kenya
  - Malawi
  - Mozambique
  - Namibia
  - Nigeria
  - Tanzania
  - Uganda

- **Western Hemisphere Region:**
  - Zambia
  - Zimbabwe

- **South Africa**

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**Legend:**
- Total number of patients with no clinical contact
- Number of patients found dead on follow-up
## Estimates of mean VLS, and VLS-adjusted mortality proportion

<table>
<thead>
<tr>
<th>Country</th>
<th>n</th>
<th>N</th>
<th>VLS%</th>
<th>95% CI</th>
<th>n</th>
<th>N</th>
<th>Mortality per 1000 persons</th>
<th>VLS-adjusted Mortality</th>
<th>95% CI</th>
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<td><strong>Model 1 a</strong></td>
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<tr>
<td>Angola</td>
<td>21,924</td>
<td>29,259</td>
<td>75.3</td>
<td>69.2, 81.5</td>
<td>35</td>
<td>22,961</td>
<td>1.58</td>
<td>0.70, 3.56</td>
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<tr>
<td>Botswana</td>
<td>282,699</td>
<td>287,792</td>
<td>98.7</td>
<td>96.3, 1.01</td>
<td>165</td>
<td>154,413</td>
<td>1.30</td>
<td>0.91, 1.84</td>
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<tr>
<td>Cote d'Ivoire</td>
<td>301,129</td>
<td>374,083</td>
<td>80.7</td>
<td>78.8, 82.6</td>
<td>1,371</td>
<td>253,799</td>
<td>7.67</td>
<td>6.41, 9.18</td>
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<tr>
<td>Mozambique</td>
<td>850,654</td>
<td>1,040,90</td>
<td>81.7</td>
<td>80.7, 82.7</td>
<td>6,398</td>
<td>1,037,320</td>
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<td>6.65, 10.09</td>
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<td>South Africa</td>
<td>4,859,363</td>
<td>5,198,880</td>
<td>93.9</td>
<td>93.4, 94.5</td>
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<td>4.50, 7.30</td>
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<td>1,053,868</td>
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<td>90.5</td>
<td>89.5, 91.5</td>
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<td>935,829</td>
<td>5.05</td>
<td>4.05, 6.31</td>
<td>5.73</td>
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### Age group

<table>
<thead>
<tr>
<th>Age group</th>
<th>n</th>
<th>N</th>
<th>VLS%</th>
<th>95% CI</th>
<th>n</th>
<th>N</th>
<th>Mortality per 1000 persons</th>
<th>VLS-adjusted Mortality</th>
<th>95% CI</th>
</tr>
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<tbody>
<tr>
<td>15-49</td>
<td>5,859,888</td>
<td>6,488,701</td>
<td>85.1</td>
<td>83.9, 86.3</td>
<td>20,857</td>
<td>5,857,818</td>
<td>3.16</td>
<td>2.62, 3.82</td>
<td>2.96</td>
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<tr>
<td>50 and over</td>
<td>1,509,749</td>
<td>1,615,140</td>
<td>88.5</td>
<td>87.1, 89.9</td>
<td>8,510</td>
<td>1,132,643</td>
<td>4.91</td>
<td>4.03, 5.97</td>
<td>5.38</td>
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</tbody>
</table>

### Sex

<table>
<thead>
<tr>
<th>Sex</th>
<th>n</th>
<th>N</th>
<th>VLS%</th>
<th>95% CI</th>
<th>n</th>
<th>N</th>
<th>Mortality per 1000 persons</th>
<th>VLS-adjusted Mortality</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>2,298,670</td>
<td>2,554,640</td>
<td>85.7</td>
<td>84.4, 87.0</td>
<td>13,877</td>
<td>2,244,331</td>
<td>5.08</td>
<td>4.19, 6.17</td>
<td>4.90</td>
</tr>
<tr>
<td>Female</td>
<td>5,070,967</td>
<td>5,549,200</td>
<td>87.9</td>
<td>86.7, 89.1</td>
<td>15,490</td>
<td>4,746,130</td>
<td>3.05</td>
<td>2.52, 3.69</td>
<td>3.25</td>
</tr>
</tbody>
</table>
Sex Differences in Mortality in Select PEPFAR countries — 2020 q2

**Graphs showing mortality figures for select PEPFAR countries: Botswana, Cote d’Ivoire, Mozambique, Zambia, Nigeria, South Africa.**

**Legend:**
- **Female** in blue
- **Male** in orange

**Countries and Mortality Data:***
- **Botswana:**
  - TX_CURR: 0
  - TX_ML: 0
  - TX_PVLS: 0
- **Cote d’Ivoire:**
  - TX_CURR: 0
  - TX_ML: 0
  - TX_PVLS: 0
- **Mozambique:**
  - TX_CURR: 0
  - TX_ML: 0
  - TX_PVLS: 0
- **Zambia:**
  - TX_CURR: 0
  - TX_ML: 0
  - TX_PVLS: 0
- **Nigeria:**
  - TX_CURR: 0
  - TX_ML: 0
  - TX_PVLS: 0
- **South Africa:**
  - TX_CURR: 0
  - TX_ML: 0
  - TX_PVLS: 0

**Important Note:**
- The data provided is preliminary and subject to validation. The accuracy of these figures is ongoing and may change as more information becomes available.
Men are less likely to engage in care, present to care late and have greater rates of virologic failure, loss-to-follow-up, higher rates of AIDS-defining illnesses: Predisposition to earlier mortality, HIV-related mortality

Women are more likely to be diagnosed and retained in care

Cohn, Moorhouse, Ake, Godfrey 2020
Increased inflammation and immune activation

- Genes on X chromosome produce IFN alfa
- Micro RNAs with immune activity
- Estrogens
- Antibody response
- Soluble CD14, CD 163
- D-dimers, neopterin

Better viral control
Better control of bacterial illnesses
Cardiac risk
Obesity

Cohn, Moorhouse, Ake, Godfrey 2020
Interventions to reduce mortality

Rapid initiation of ART in the absence of contraindications
Cotrimoxazole
TB action
Cryptococcal action
TB Still Plays a Major Role in HIV Mortality
In the context of COVID-19, PEPFAR is firmly focused on:

1. Ensuring continuity of care for people living with HIV
2. Leveraging PEPFAR-supported health systems and infrastructure
3. Reducing exposure of staff and HIV clients to health care settings that may be overburdened and/or sources for potential exposure to COVID-19
4. Providing flexibility for PEPFAR programs in how to optimally serve our HIV clients in areas affected by COVID-19
Should evaluation of newly diagnosed clients for advanced disease continue during the COVID-19 pandemic?

Yes. Extant activities for the evaluation and management of advanced disease in clients newly diagnosed during the COVID-19 pandemic should continue.

Other interventions in our guidance:

- Streamlined access for individuals with advanced disease
- Multimonth dispensing: policy changes allowing individuals with advanced disease to access MMD
- Separation of drug delivery from clinical care.
- Enhanced infection protection and control
- https://www.state.gov/pepfar/coronavirus/
Acknowledgments

Danielle Fernandez
Ikwo Oboho and the Advanced Disease unit at CDC Atlanta
Hammad Ali
PEPFAR Interagency Short Term Task Team on Advanced Disease