HIV Drug Resistance Surveillance in Sub-Saharan Africa

Kim Sigaloff, MD PhD
 Amsterdam Institute for Global Health and Development

INTEREST 2015
May 8th 2015, Harare, Zimbabwe
By 2020:

- 90% diagnosed
- 90% on treatment
- 90% virally suppressed

→ how are we doing in terms of virological suppression?

June 2014: 13.6 million people receiving antiretroviral therapy (worldwide)
Systematic review & meta-analysis:
Virological suppression on first-line ART, by region

On-treatment

% virological suppression (summary estimate)

<table>
<thead>
<tr>
<th>Months on first-line antiretroviral treatment</th>
<th>All studies</th>
<th>Sub-Sahara Africa only</th>
<th>Asia only</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>85</td>
<td>84</td>
<td>90</td>
</tr>
<tr>
<td>12</td>
<td>86</td>
<td>84</td>
<td>90</td>
</tr>
<tr>
<td>24</td>
<td>84</td>
<td>84</td>
<td>89</td>
</tr>
<tr>
<td>36</td>
<td>88</td>
<td>87</td>
<td>92</td>
</tr>
<tr>
<td>48</td>
<td>89</td>
<td>89</td>
<td>89</td>
</tr>
<tr>
<td>60</td>
<td>86</td>
<td>87</td>
<td>84</td>
</tr>
</tbody>
</table>

Based on 164 studies from LMICs

Boender et al. Submitted
Systematic review & meta-analysis:
Virological suppression on first-line ART, by region

**Intention-to-treat**

<table>
<thead>
<tr>
<th>Months</th>
<th>ITT</th>
<th>Sub-Saharan Africa only</th>
<th>Asia only</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>75</td>
<td>74</td>
<td>77</td>
</tr>
<tr>
<td>12</td>
<td>67</td>
<td>64</td>
<td>76</td>
</tr>
<tr>
<td>24</td>
<td>65</td>
<td>62</td>
<td>74</td>
</tr>
<tr>
<td>36</td>
<td>68</td>
<td>62</td>
<td>75</td>
</tr>
<tr>
<td>48</td>
<td>62</td>
<td>63</td>
<td>61</td>
</tr>
</tbody>
</table>
Question:

What is the estimated rate of pretreatment drug resistance (i.e. before start of first-line ART) in Southern Africa?
Global trends in antiretroviral resistance in treatment-naive individuals with HIV after rollout of antiretroviral treatment in resource-limited settings: a global collaborative study and meta-regression analysis

Gupta et al. Lancet 2012
Prevalence of pretreatment resistance in Southern Africa

Overall increase: 14%/yr (0-29; p=0.05)
NNRTI: 23%/yr (7-42; p=0.0049)

Prevalence of resistance at ART roll-out: 1.4%
10 years later: 3-4%??

Every circle is a study and the size of the circle is proportional to the precision of the estimate from the individual study

Gupta et al. Lancet 2012
Prevalence of pretreatment resistance in East Africa

Overall increase: 29%/yr (15-45; p=0.0001)
NNRTI: 36%/yr (21-52; p<0.0001)

Prevalence of resistance at ART roll-out: 1%
10 years later: 4-5%??

Gupta et al. Lancet 2012
Question:

What % of people – infected with drug resistant HIV – will achieve virological suppression after 2 years?
PDR doubles risk of VF and acquired drug resistance

**Virological failure** (HIV RNA >400 cps/ml)

- **No PDR**
  - Odds ratio: 1
  - Virological failure: 66%

- **PDR**
  - Odds ratio: 2.80 (p = 0.004)
  - Virological failure: 42%

Unadjusted analysis vs. Adjusted analysis*

PDR doubles risk of VF and acquired drug resistance.

*S for sex, age & adherence

Sonia Boender, Bernice Hoenderboom et al. In preparation
Effect of drug resistance on switch to second-line

PDR = Pretreatment drug resistance. Tarone-Ware test, $p < 0.0001$

**adjusted HR 3.80**

$p = 0.005$

Number on first-line ART (switches):

<table>
<thead>
<tr>
<th></th>
<th>No PDR</th>
<th>PDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>2337</td>
<td>131</td>
</tr>
<tr>
<td>Days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-90</td>
<td>90</td>
<td>20</td>
</tr>
<tr>
<td>90-365</td>
<td>102</td>
<td>90</td>
</tr>
<tr>
<td>365-730</td>
<td>1286</td>
<td>186</td>
</tr>
<tr>
<td>730-1096</td>
<td>327</td>
<td>127</td>
</tr>
</tbody>
</table>

*Sonia Boender, Bernice Hoenderboom et al. In preparation*
Increasing 2\textsuperscript{nd}-line reduces PDR
Summary & implications

Pretreatment drug resistance is rising with more exposure to ART
→ Drug resistance is *not* an argument against early initiation
→ national estimates are lacking

Drug resistance increases risk of virological failure and switching
→ Modelling indicates that timely switch decreases PDR
→ Increased access to second-line drugs needed

On-treatment virological suppression rates are favorable
→ But programs are threatened by attrition
→ Long-term data is scarce
Acknowledgments

Special thanks to all study participants, study doctors, laboratory staff, study coordinators and data team

The PASER network
Maureen Wellington, Margaret Siwale, Mariette Botes, Cissy Kityo, Sulaimon Akanmu, Kishor Mandaliya, Nicaise Ndembi, Kim Steegen

AI GHD Amsterdam & Kampala
Tobias Rinke de Wit, Raph Hamers, Sonia Boender, Pascale Ondoa, Bernice Hoenderboom, Julien Schrijver, Marloes Nijboer, Cathy Nalubwama, Miriam Nakitto, Martin Omello