The HIV positive patient in 2016

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Disclosures...

• Part of optimisation collaborations – grants to improve testing, new drug regimens, linkage to care

• Pharma (including drug donations for studies) and managed care
The “when to start” debate is over

• Personal benefit vs transmission
HIV-1 levels & HIV-1 infectiousness

• High plasma HIV-1 RNA concentrations are associated with increased HIV-1 transmission risk.

• Plasma and genital HIV-1 levels are correlated (coefficient ~0.5-0.6)
  – But, genital HIV-1 more variable than plasma and tight correlation not found in all individuals.

Quinn et al NEJM 2000

Thanks Connie Cellum
Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model

ART coverage significantly decreased individual risk, KwaZulu Natal, South Africa (2004-11)

- Africa Centre longitudinal surveillance cohort with community and individual data
  - Between 2004 and 2011, 1395 HIV seroconversions and over 53,042 person-years of observation (crude HIV incidence rate of 2.63 (95% C.I. 2.50 to 2.77) per 100 person-years

Every % point increase in ART coverage among all HIV+ adults in a community, was associated with a 1.7% decline in the hazard of HIV acquisition ($p <0.001$)
~4 YEAR LAG BETWEEN SCALE UP OF ART AND DECLINE IN MTB INCIDENCE

Figure 1: Incidence of microbiologically-confirmed pulmonary tuberculosis (per 100,000 population) and antiretroviral treatment coverage rates in HIV-infected individuals nationally in South Africa nationally and provincially from 2004 to 2012

The solid black line represents the estimated trend in PTB incidence per 100,000 population over the study period and the dotted black line the corresponding 95% confidence interval. The overlaid dotted grey line is the ART coverage per 1000 HIV positive individuals based on data from the ASSA 2008 model.

Is sex safe? HPTN 052

And confirmed in Partners study for 96.3% reduction in transmission
Thorn in T&T side: Individual benefit

- Conflicting observational studies
- 052 not convincing re individual data

Interpretation: The benefits of immediate initiation of ART, such as prolonged survival and AIDS-free survival and increased virological suppression, were small in this high-income setting with relatively low CD4 count at HIV diagnosis. The estimated beneficial effect on AIDS is less than in recently reported randomised trials. Increasing rates of HIV testing might be as important as a policy of early initiation of ART.
START and Temprano fixed this

Table 1: Severe morbidity in TEMPRANO study at 30 months

<table>
<thead>
<tr>
<th></th>
<th>% events</th>
<th>n</th>
<th>Rate / 100 PY</th>
<th>adj HR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO ART</td>
<td>11.4%</td>
<td>111</td>
<td>4.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early ART</td>
<td>6.6%</td>
<td>64</td>
<td>2.8</td>
<td>0.56</td>
<td>0.0002</td>
</tr>
<tr>
<td>No IPT</td>
<td>10.7%</td>
<td>104</td>
<td>4.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPT</td>
<td>7.2%</td>
<td>71</td>
<td>3.0</td>
<td>0.65</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Table 1. Primary endpoint and its components in open DSMB report (15 May 2015)

<table>
<thead>
<tr>
<th></th>
<th>Early ART (arm A)</th>
<th>Deferred ART (arm B)</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>rate/100 PY</td>
<td>N</td>
</tr>
<tr>
<td>AIDS, serious non-AIDS, or death (primary)</td>
<td>41</td>
<td>0.60</td>
<td>86</td>
</tr>
<tr>
<td>AIDS or AIDS death</td>
<td>14</td>
<td>0.20</td>
<td>46</td>
</tr>
<tr>
<td>Serious non-AIDS or non-AIDS death</td>
<td>28</td>
<td>0.41</td>
<td>41</td>
</tr>
</tbody>
</table>

* PY = patient years, ** NS = non significant

Thanks: Simon Collins
The medication works like a bomb
Treatment for life

Expect a normal life expectancy:
May et al. AIDS 2014

- UK CHIC: 21,388 people started ART 2000-2010

If 35 year old man started ART:

<table>
<thead>
<tr>
<th></th>
<th>life expectancy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
</tr>
<tr>
<td>CD4 &lt;200</td>
<td></td>
</tr>
<tr>
<td>200-349</td>
<td></td>
</tr>
<tr>
<td>&gt;350</td>
<td></td>
</tr>
<tr>
<td>General population</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: If diagnosed, in care and on effective ART: life expectancy is normal.

Great information to give to people newly diagnosed and encourage good adherence.

Thanks: Julie Fox, Guys
WHO regimens pre-2015

Tenofovir + XTC + Efavirenz

AZT + Lamivudine + PI (lopinavir or atazanavir)

XTC, other nukes

Darunavir + Raltegravir + Etravirine
And its getting better... For South Africa

• The integrase era
TDF + XTC + EFV

Cost driver

Side effect (and size) driver, resistance weak link
1st line....

TAF + XTC + Dolutegravir

Safer, cheaper

Safer, cheaper, resistance barrier
And they do well in the real (US) world!

Thanks Joe
Weak rand means South Africa pays more for ARVs in latest tender

NSP REVIEW COMMENT:

The National Strategic Plan for HIV/AIDS STIs and TB has set as a target that 80% of people living with HIV must be on antiretrovirals by 2016. This equates to about 4.8 million people. In his lat

Price tag of HIV response to more than double by 2033

By Laura Lopez Gonzalez on June 12, 2015 in HIV – Antiretrovirals (ARVs), HIV/AIDS

With 3.1 million people on antiretrovirals (ARV), South Africa has the world’s largest ARV programme, but sustaining it – and the HIV response – will more than double in the next two decades, according to new research.
SA cost....

In press, SAMJ
Rich countries too

Projected UK ARV costs, if branded drugs used (8% growth/year)

N on ARVs: 78,000  84,000  91,000  98,000  106,000

Annual ARV costs (UK £ millions)

2015  £411m
2016  £444m
2017  £480m
2018  £518m

£559m

Does not include:
PreP
HCV treatment

Thanks: Andrew Hill
We need things to go faster
Do we have a resistance problem?
Global epidemiology of drug resistance after failure of WHO recommended first-line regimens for adult HIV-1 infection: a multicentre retrospective cohort study

The TenoRes Study Group*

Summary
Background Antiretroviral therapy (ART) is crucial for controlling HIV-1 infection through wide-scale treatment as needed programs (TANs) in resource-limited settings. However, drug resistance is a key challenge that impacts the effectiveness of ART. This study investigates the global impact of drug resistance and identifies strategies for improving treatment outcomes.
“Researchers at University College London said the study could mean that, after a year of treatment, up to 15% of people in sub-Saharan Africa and 10% in South Africa were resistant to the drug.”
Resistance IS a problem....

• But not yet at a public health level
HIV prevention remains a disaster
Several things happened...

- 90-90-90 success stories (Botswana, Havlir, Sweden)
- But failure to link to care in some RCTs - Swaziland, KZN
- And no impact on new incidence (KZN)
Incidence still remains stubbornly high...
**CAPRISA: HIV prevalence in school boys and girls in a rural South African district (grades 9 and 10)**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>HIV Prevalence (Oct/Nov 2010) % (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
</tr>
<tr>
<td>≤14</td>
<td>1.0</td>
</tr>
<tr>
<td>15-16</td>
<td>1.4</td>
</tr>
<tr>
<td>17-18</td>
<td>1.2</td>
</tr>
<tr>
<td>19-20</td>
<td>1.1</td>
</tr>
</tbody>
</table>

RHIVA collaboration with MiET Africa and DoE with funding from the Royal Netherlands Embassy
And does not correlate well with ART...

Source: Leigh Johnson, Spotlight, 2016
Troubling....

• Julio Montagner in Vancouver: MSM vs intravenous drug users

Some ideas why: missing men?

• We are probably very close to the 3rd 90
• Second 90: probably there for women; not men – and that’s a huge problem

90% of all living with HIV will know their HIV status
90% of all living with HIV will receive sustained antiretroviral therapy
90% of all receiving antiretroviral therapy will have durable viral suppression
Some ideas why: missing populations?

• Sex workers and gay men? But smallish population
Or is it something else?

The cycle of infection in South Africa

Young women between 16 and 23 acquire HIV from older men.

Mean: 18

Men between 23 and 35 have a high incidence of HIV.

Mean: 27

Women in their mid-20s infect and are infected by similarly aged men.

Mean: 26
Prevention still suffers from intuitive thinking
Non-communicable diseases and HIV

• The new tsunami (or maybe not)
Changing Life-Expectancy

Infectious diseases eradicated

Chronic diseases

AGE AT DEATH
An aside...

• You have to die of something!
• Beware of ‘tsunami of xxx disease’ people...
Dementia not the epidemic it was feared to be, say academics

Figures suggesting condition could become an epidemic are out of date, with numbers of patients stabilising across western Europe, say experts

Sarah Boseley Health editor
The Number Of People With Dementia Is Exploding, New Report Says

BY SAM P.K. COLLINS  AUG 26, 2015 10:53AM
Mortality and causes of death in South Africa, 2013: Findings from death notification

Table 4.3: Number and percentage distribution of deaths by main groups of causes of death, 2013*

<table>
<thead>
<tr>
<th>No.</th>
<th>Main groups of underlying causes of death (based on ICD-10)</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Certain infectious and parasitic diseases (A00-B99)*</td>
<td>103 708</td>
<td>22.6</td>
</tr>
<tr>
<td>2</td>
<td>Neoplasms (C00-D48)</td>
<td>38 034</td>
<td>8.3</td>
</tr>
<tr>
<td>3</td>
<td>Diseases of the blood and immune mechanism (D50-D89)</td>
<td>10 357</td>
<td>2.3</td>
</tr>
<tr>
<td>4</td>
<td>Endocrine, nutritional and metabolic diseases (E00-E59)</td>
<td>28 974</td>
<td>6.3</td>
</tr>
<tr>
<td>5</td>
<td>Mental and behavioural disorders (F00-F99)</td>
<td>1 787</td>
<td>0.4</td>
</tr>
<tr>
<td>6</td>
<td>Diseases of the nervous system (G00-G99)</td>
<td>10 998</td>
<td>2.4</td>
</tr>
<tr>
<td>7</td>
<td>Diseases of the eye and adnexa (H00-H59)</td>
<td>18</td>
<td>0.0</td>
</tr>
<tr>
<td>8</td>
<td>Diseases of the ear and mastoid process (H60-H95)</td>
<td>58</td>
<td>0.0</td>
</tr>
<tr>
<td>9</td>
<td>Diseases of the circulatory system (I00-I99)</td>
<td>76 408</td>
<td>16.7</td>
</tr>
</tbody>
</table>
### Table 1

Age-standardised death rates for broad cause categories and broad health-care categories in Agincourt subdistrict, 1992–2005

<table>
<thead>
<tr>
<th>Broad cause categories</th>
<th>Years</th>
<th>Relative change</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All causes</td>
<td>593</td>
<td>604</td>
<td>737</td>
</tr>
<tr>
<td>Infectious and parasitic</td>
<td>74</td>
<td>147</td>
<td>255</td>
</tr>
<tr>
<td>diseases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-communicable diseases</td>
<td>197</td>
<td>158</td>
<td>187</td>
</tr>
<tr>
<td>External causes*</td>
<td>76</td>
<td>63</td>
<td>61</td>
</tr>
<tr>
<td>Ill defined or unknown</td>
<td>198</td>
<td>178</td>
<td>115</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Broad health-care categories</th>
<th>Years</th>
<th>Relative change</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All health care</td>
<td>593</td>
<td>604</td>
<td>737</td>
</tr>
<tr>
<td>Acute care†</td>
<td>162</td>
<td>148</td>
<td>192</td>
</tr>
<tr>
<td>Chronic care‡</td>
<td>209</td>
<td>230</td>
<td>330</td>
</tr>
<tr>
<td>Ill defined/unknown care§</td>
<td>222</td>
<td>225</td>
<td>215</td>
</tr>
</tbody>
</table>

All rates are per 100 000 person years (N=6153). RR=rate ratio. All rates are significant at p<0.05.

*External causes include homicide, suicide, road traffic accidents, accidents.
†Acute care: for disorders that are potentially curable with up to 1 month of illness.
‡Chronic care: for disorders that are incurable or need more than 1 month of illness.
§Difficult to classify as acute or chronic care.
“Homeopathy outperformed medicine till the 70s…”
To put these figures into everyday terms, in a clinic with 1000 patients who had all been living with HIV for at least 15 years, two to three patients could be expected to have a heart attack each year. This rate is in fact fairly low in comparison with some other studies of heart attack risk, and Alexandra Knox said that it was possible that heart attacks had been under-reported.
Medical News & Perspectives

Exploring Statins to Decrease HIV-Related Heart Disease Risk

Mike Mitka, MSJ

Antiretroviral therapy (ART) has been a lifesaver for untold numbers. The number of studies is large, and the number of studies is small and further studies are promising, the number of study participants was small and further studies are needed. Cardiovascular Disease Prevention

With such promising findings, researchers are looking at the potential of statins in HIV-related heart disease. The study comes amidst efforts to find new treatments for this deadly condition.
MUST pause: we DON’T know...

• “Although undoubtedly there are higher rates of comorbidities in the HIV-infected population, there are a number of possible explanations for this as well as the possibility that HIV or HAART causes premature ageing.”
• NOT CLEAR that HIV be people are demented, aggressively ageing, getting more CVS disease/cancer
• We need more data
National Strategic Plan coming end of this year!
So, lifetime treatment means...

- Less and less tolerance for “nuisance” side effects
- Far less focus on the initiation period, sickness
- Interest in contribution of ARVs & HIV to other non-communicable disease risk factors
- Focus on costs – especially of drugs
- Focus on longer-acting injectables, implantables
- Interest in “cure”
- Unacceptable to have “lesser” drugs in lower-income countries – complex!
- Harmonisation between paeds and adults
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