Background

- Telomeres are nucleoproteins with TRF1/2 and TRF3/4 repeats on chromosomes
- Shorten with cell division until critical length of senescence and dysfunction
- Telomere length (TL) maintained by telomerase → ribonucleoprotein enzyme complex with reverse transcriptase (TERT)

Methods (cont.)

- Cases: non-accidental death or confirmed diagnosis of cancer, cardiovascular, liver, renal, neurocognitive, or pulmonary disease, osteoporosis/bone fractures, or diabetes mellitus; and banked PBMC samples pre-ART and prior to event closest with age to death Controls: 2 to 1 matched for sex, age, NRTI duration, and timing of PBMC samples without events listed above
- TL: qPCR with relative TL measured by quantifying a telomere repeat copy (T) versus single copy reference gene (S) ratio

Results

- Analysed 351 ALLRT participants (117 cases and 234 controls) 117 Cases on ART for median of 4.3 years (Table 1): 14 (35%) diabetes, 33 (28%) renal disease, 18 (15%) cancer, 14 (12%) CVD, 7 (6%) death, and 4 (4%) bone fractures
- Pre-ART: C4D (cells/µl): 204 (79, 993), 254 (89, 397), 0.70
- CDR (cells/µl): 58 (50), 90 (38), 0.05
- CDR/CD8 (cells/µl): 857 (115), 752 (511, 1128), 0.38
- HIV RNA (log10): 4.9 (4, 5, 5), 4.7 (4, 5, 5), 0.01
- TL (T/S ratio): 0.42 (0.27, 0.53), 0.40 (0.21, 0.53), 0.19
- TA (log10): 1.98 (1.48, 2.37), 1.34 (1.60, 2.40), 0.67
- Delta***

Table 1. Participant characteristics and comparisons between cases and controls

| TL (T/S ratio) | 0.19 < p < 0.29
|<|>0.26, +0.37 | 0.01 -0.26, +0.28 | 0.44

Future Directions:

- Longer term follow-up (>10 years on ART) in older populations (>60 years) with more use of NRTIs and time vs. NRTI regimen
- Telomeres in PBMCs: TAF > ddC > FTC > TDF

Conclusions

- Prior to ART, telomeres were significantly shorter among participants with higher HIV RNA and lower telomerase activity
- After median of 4 years on ART, telomeres declined (non-significant) and were significantly shorter among women, non-white race and those on ART with TDF
- TA did not change over time on ART
- We found no associations between TL, TA or changes in these biomarkers on ART, and age-related diseases
- The only independent factor associated with age-related disease in this study was smoking

Table 2. Multivariable case-control logistic regression

<table>
<thead>
<tr>
<th>Event</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-ART TL (T/S ratio)</td>
<td>&lt;0.19</td>
<td>1.0, 0.50, 2.0</td>
</tr>
<tr>
<td>Pre-ART C4D (&gt;200 cells/µl)</td>
<td>0.19 -0.33</td>
<td>0.97, 0.45, 1.3</td>
</tr>
<tr>
<td>Pre-ART HIV RNA log10 copies/cell/µl</td>
<td>0.34 -0.65</td>
<td>0.93, 0.47, 1.83</td>
</tr>
<tr>
<td>Controls: 2 to 1 matched for sex, age, and pre-ART VL</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Case (n=117) | Control (n=234) | p-value* |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV RNA (log10)</td>
<td>4.9 (4, 5, 5)</td>
<td>4.7 (4, 5, 5)</td>
</tr>
<tr>
<td>TL (T/S ratio)</td>
<td>0.42 (0.27, 0.53)</td>
<td>0.40 (0.21, 0.53)</td>
</tr>
<tr>
<td>TA (log10)</td>
<td>1.98 (1.48, 2.37)</td>
<td>1.34 (1.60, 2.40)</td>
</tr>
<tr>
<td>Delta***</td>
<td>0.0006 (-0.22, +0.37)</td>
<td>-0.01 (-0.26, +0.28)</td>
</tr>
</tbody>
</table>

*ref to median of 4 years on ART