Sleep in rural and urban settings in South Africa: correlates and impact of HIV status
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• South Africa:
  – 40% hypertensives
  – 12% HIV positive, 60% treated.
  – 2nd cause of mortality: diabetes
• Sleep and circadian disorders associated with cardiometabolic risk
• Detection and treatment of sleep disorders: not done in public healthcare

Relationship between sleep disruption and hypertension: epidemiological studies
• USA: Knutson et al, 2009:
  • 578 African Americans and whites, 33–45 years
  • reduced sleep duration / sleep maintenance at baseline: predictor of higher blood pressure levels over 5 years at baseline [OR=1.37 (1.05-1.78)]

• China: Kim et al, 2018
  • 106,385 participants (no hypertension/CVD): repeated measures of sleep duration over 2.4 years.
  • ↓ ≥2 hours of sleep and ↑ ≥2 hours of sleep compared with no change in sleep duration: higher risk of incident hypertension in women [HR 1.46 (1.08-1.98)] and men [HR 1.31 (1.10-1.56)].
  • Women with persistently shorter sleep durations compared with those who maintained 7 hours of sleep: greater risk of developing hypertension during the subsequent follow-up period.

Epidemiological studies
• South Africa: Pretorius et al, 2015
  • 862 women (41 ± 16 years and BMI 29.9 ± 9.2)
    • Longer night time sleep duration ➔ higher diastolic (β = 0.005, p<0.01) and systolic BP (β = 0.003, p<0.05)
  • 449 men (38 ± 14 years and BMI 24.8 ± 8.3).
    • napping for >30 minutes/day: lower SBP and DBP
Sleep, circadian rhythms and non communicable diseases

- physiological underpinnings:
  - Increased sympathetic activity in general sleep disruption \( \rightarrow \) hypertension
  - Specifically sleep apnoea \( \rightarrow \) oxidative stress \( \rightarrow \) endothelial dysfunction \( \rightarrow \) hypertension

Relationship between risk of sleep apnoea and hypertension in urban South Africa

- 204 included in the analysis
- 101 Non hypertensives:
  - Females: 82%
- 103 hypertensives
  - Treated: 46
  - Resistant: 32
  - Untreated: 25

Hypertensives vs. Non hypertensives general characteristics

Hypertensives vs. Non hypertensives sleep/mood characteristics

- No difference in
  - Overall sleep quality PSQI: 6.7 (3.5)
  - Daytime sleepiness ESS: 7.8 (5.2)
  - Depression level BDI: 12.6 (10)
Multivariate analysis

• Does High Risk Sleep apnoea on the Berlin Questionnaire remain a significant predictor of being hypertensive when adjusting for other important covariates? (BMI, age, waist circumference) – logistic regression
  • **YES:**
  • Adjusted Wald OR [95% CI]: 3.3 [1.4 - 7.6]

HIV and sleep?

• Before treatment:
  – More SWS in last part of the night
  – Multiple awakenings
• During treatment:
  – Overall report of ~40-60% of HIV cohorts report sleep disturbances
  – Higher sleep apnoea than expected for equivalent weight/age in non HIV+ population

HIV and sleep: Study in urban clinic

Cross sectional study run in Soweto in 2012 (Redman et al, 2018):
• 139 patients of African ancestry
• ~ 43 years old
• 70% female
• Baseline CD4: 89
• Time since diagnosis ~ 7 years
• Time on treatment ~4 years
• 60% with PSQI>5
• 41% with BDI>17 (clinical depression)
• 55% reported pain at the time of the visit

• Higher PSQI associated with depression, pain and increased CD4 counts, but not with type of ARV treatment (EFV, D4T, TDF, PI tested)

Associated factors

• Treatment with Efavirenz - but not in recent studies
• Peripheral neuropathy/ Pain
• Mitigated association with CD4 counts/ Viral loads.
• Depression
• Lower socioeconomic status
• Fatigue/ daytime sleepiness
Sleep disturbances and CD4 counts

Risk of sleep apnoea, cardiovascular risk and HIV

- Is scoring high risk of sleep apnoea associated with higher blood pressure in South Africa?
- Are treated HIV positive patients at increased risk of developing hypertension compared to matched HIV negative controls?

<table>
<thead>
<tr>
<th>HIV + patients</th>
<th>Controls</th>
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<tbody>
<tr>
<td>N=147</td>
<td>N=200</td>
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- Age, mean (SD)
- Women, %
- Employed, %
- Education, %
  - Grade 6 or less
  - Finished grade 7
  - Finished grade 12
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<th>HIV + patients</th>
<th>Controls</th>
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<tbody>
<tr>
<td>SBP (mm Hg)</td>
<td>132 (23)</td>
<td>134 (26)</td>
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<tr>
<td>DBP (mm Hg)</td>
<td>83 (17)</td>
<td>84 (15)</td>
</tr>
<tr>
<td>Hypertensive (%)</td>
<td>34</td>
<td>39</td>
</tr>
<tr>
<td>BMI (kg.m$^{-2}$)</td>
<td>24 (6)</td>
<td>27 (7)*</td>
</tr>
<tr>
<td>High Risk of Sleep Apnoea (%)</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>CD4 counts /μL</td>
<td>518 (246)</td>
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* p value <0.05 for the comparison between HIV+ patients and controls

**Relationship between systolic blood pressure and BMI in those with low risk of sleep apnoea**

**Relationship between systolic blood pressure and BMI in those with high risk of sleep apnoea**
Summary

• 37% hypertensive
• Higher systolic blood pressure associated with high risk of sleep apnoea
• HIV+ patients: same percentage at high risk of sleep apnoea as controls
• But BMI was significantly lower → HIV+ patients may be at higher risk of developing sleep apnoea than controls
• HIV+ patients: increased risk of developing hypertension compared to matched HIV- controls as their BMI increases

What next?

• Larger longitudinal cohort study: 856 HIV vs 1200 HIV- controls: Ndlovu Cohort study (Vos et al, 2017)
• More measurements of cardiovascular risk and metabolic risk
• Circadian measurements
• Immune measurements

BMI over time in 23 HIV+ patients starting treatment

Risk of sleep apnoea increased with higher BMI
And decreased with increased CD4 counts
(+100 CD4 associated with OR=0.52[0.28-0.98])
Increased BMI and older age associated with higher MAP