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An analysis of the link between antiretroviral therapy and syphilis in men who have sex with men in England 2008-2016

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• Rekart et al. used a mathematical modelling study to investigate the recent rises in Syphilis, Gonorrhoea and Chlamydia among individuals who were on and not on ART (anti-retroviral treatment)

• They hypothesised that the use of ART may affect the immune response to *Treponema Pallidum* and increase susceptibility to syphilis
Aims of the project

• Explore the hypothesis that there is a potential immunological link between the use of ART and syphilis using national level HIV and STI surveillance data:
  • Calculate the rates of syphilis, gonorrhoea, and chlamydia in HIV positive men by ART status, controlling for sexual behaviour
  • Calculate and compare the hazard ratios for each STI

<table>
<thead>
<tr>
<th>% rise in STI diagnoses among HIV positive MSM</th>
<th>Syphilis</th>
<th>Chlamydia</th>
<th>Gonorrhoea</th>
</tr>
</thead>
<tbody>
<tr>
<td>British Columbia 2005-2014</td>
<td>91</td>
<td>40</td>
<td>70</td>
</tr>
<tr>
<td>England 2012-2016</td>
<td>137</td>
<td>43</td>
<td>50</td>
</tr>
</tbody>
</table>
Methods: retrospective cohort study

2008-2016

GUMCAD  HARS

The cohort: 19,429 MSM

113,000 person years

ON ART  Not on ART

Chlamydia  Gonorrhoea  Syphilis

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Methods - Participant follow up periods

Jan 2008 to Dec 2016

Individual 1:
- On ART
- Not on ART
- HIV diagnosis
- Cohort exit date

Individual 2:
- Not on ART
- On ART

Individual 3:
- On ART
Statistical analysis

- The incidence of syphilis, gonorrhoea and chlamydia per 1000 person years at risk was calculated

- Univariable analysis was used to adjust for key variables:
  - CD4 count
  - viral load
  - age
  - Behavioural proxy: diagnoses of more than one bacterial STI during the cohort

- A multivariable random-effects Poisson model was fitted to assess associations with each STI after adjustment for the key variables
Baseline characteristics

88% were on ART at baseline

Yes

No

However, in total 98% of men were recorded as on ART during the study period

 Median age: 42

Majority ethnicity: white

The baseline CD4 was 579 cells/mm³

19,425 men

Viral load count of MSM at first attendance:

- <50
- 50-200
- >200
- Missing VL info

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Results: Rates of STIs per 1,000 person years

An analysis of the link between anti-retroviral therapy and syphilis in men who have sex with men in England 2008-2016
Results: Multivariable results

- Hazard ratio comparing on ART to not on ART

- Adjusting for: CD4 count, viral load, age and the presence of other STI diagnoses

<table>
<thead>
<tr>
<th></th>
<th>Hazard ratio*</th>
<th>lower 95% CI</th>
<th>upper 95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia</td>
<td>1.00</td>
<td>0.90</td>
<td>1.10</td>
<td>0.954</td>
</tr>
<tr>
<td>Gonorrhoea</td>
<td>1.08</td>
<td>0.98</td>
<td>1.19</td>
<td>0.123</td>
</tr>
<tr>
<td>Syphilis</td>
<td>1.31</td>
<td>1.13</td>
<td>1.52</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Hazard ratio adjusted for: CD4 count, Viral load, age & presence of two or more STI diagnoses
Syphilis results. Rates per 1,000 person years

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Absolute rate difference: 4.7
Limitations

• Approximately 37% of eligible individuals were excluded from the study due to incomplete treatment and HIV status data.

• For the purpose of the analysis we applied the most recent ART status within a year prior to each GUM attendance.

• Additionally, a lack of routinely collected data on sexual behaviour necessitated the use of a behavioural proxy and therefore the complexity of the analysis is limited.
Conclusions and summary

• A significant association between the receipt of ART and syphilis was found – immunological mechanism is a possibility but requires further research.

• Limited public health significance - The absolute rate difference between syphilis among those on ART and not on ART was very small.

• STI screening remains important; HIV positive MSM at high risk of syphilis.
Acknowledgments

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Thank you!

Questions?