The incidence of serious non-AIDS bacterial infections in the EuroSIDA cohort

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Background

- Risk of pneumonia in the cART era remains 6-8 fold higher among persons with HIV than those without HIV\(^1,2\)

- Similar trends have also been reported for bacterial meningitis and invasive pneumococcal disease\(^3,4\)

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Background

- There is an association between increasing risk of certain non-AIDS defining conditions and decreasing CD4+ count counts\(^5,6\).

- By restoring CD4+ cell counts, cART reduces the risk of some non-AIDS defining diseases.

- It has also been suggested that cART may have a protective effect against certain non-AIDS infections that is independent of CD4+ cell count\(^2\).

Aim

- Estimate incidence rates of serious non-AIDS bacterial infections requiring hospitalization across Europe
- Explore potential risk factors
- Determine the influence of cART on risk of infection at various levels of immune competence defined by CD4+ cell count.
EuroSIDA

EuroSIDA is a large prospective cohort with **16597** patients from 33 European countries, Israel and Argentina.

- From September 2006 onwards data has been routinely collected on serious non-AIDS infections requiring hospitalization.
Methods

- **Inclusion criteria**
  - Patients under follow-up after 1 September 2006
  - CD4+ count available at enrolment

- **Follow up**
  - Patients were followed until their first diagnosis of a non-AIDS bacterial infection or their last visit

- **Statistical methods**
  - Incidence rate calculated per 1000 PYFU
  - Poisson regression used to investigate factors associated with diagnosis
  - Variables that could change over time were included as time-updated covariates
## Baseline characteristics

<table>
<thead>
<tr>
<th>All Patient (N,%)</th>
<th>10851</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (N,%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>7857</td>
<td>72.4</td>
</tr>
<tr>
<td>Ethnic origin (N,%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>9562</td>
<td>88.1</td>
</tr>
<tr>
<td>Age (median, IQR)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>42</td>
<td>35-49</td>
<td></td>
</tr>
<tr>
<td>HIV exposure Group (N,%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homosexual</td>
<td>4210</td>
<td>38.8</td>
</tr>
<tr>
<td>IDU</td>
<td>2346</td>
<td>21.6</td>
</tr>
<tr>
<td>Heterosexual</td>
<td>3461</td>
<td>31.9</td>
</tr>
<tr>
<td>Region of Europe (N,%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>South</td>
<td>2517</td>
<td>23.2</td>
</tr>
<tr>
<td>West Central</td>
<td>2484</td>
<td>22.9</td>
</tr>
<tr>
<td>North</td>
<td>2369</td>
<td>21.8</td>
</tr>
<tr>
<td>East Central</td>
<td>1489</td>
<td>13.7</td>
</tr>
<tr>
<td>East</td>
<td>1546</td>
<td>14.3</td>
</tr>
<tr>
<td>Argentina</td>
<td>446</td>
<td>4.1</td>
</tr>
<tr>
<td>Prior AIDS diagnosis (N,%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3130</td>
<td></td>
<td>28.9</td>
</tr>
<tr>
<td>On cART (N,%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9110</td>
<td></td>
<td>84.0</td>
</tr>
<tr>
<td>CD4 count (median, IQR) cells/mm$^3$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>458</td>
<td>413-641</td>
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</tr>
</tbody>
</table>
Results

- 10,851 HIV patients
- 275 events occurred during 35,839 PYFU
<table>
<thead>
<tr>
<th>CD4 count</th>
<th>≥500</th>
<th>350-499</th>
<th>&lt;350</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacteremia</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
All events (n=275)

CD4 count
- ≥500
- 350-499
- <350

Gender
- Female vs. Male

HIV exposure group
- Homosexual
- IDU
- Heterosexual

Region of Europe
- South
- West Central
- North
- East Central
- East

Prior AIDS
- Yes vs. No

On cART
- Yes vs. No

Age
- per 10 years older

Smoking
- Current vs. never

Diabetic
- Yes vs. No

Also adjusted for race
Pneumonia (n=192)

CD4 count
- ≥500
- 350-499
- <350

Gender
- Female vs. Male

HIV exposure group
- Homosexual
- IDU
- Heterosexual

Region of Europe
- South
- West Central
- North
- East Central
- East

Prior AIDS
- Yes vs. No

On cART
- Yes vs. No

Age
- per 10 years older

Smoking
- Current vs. never

Adjusted incidence rate ratio
(95% confidence interval)
Also adjusted for race and diabetes
Adjusted incidence rate ratio by current CD4 count and use of cART

*Also adjusted for gender, HIV exposure group, region, prior AIDS, age, smoking, diabetes, and race
Limitations

• Data collection
• Not all infections analysed separately
• Unable to control for influenza/pneumococcal vaccination
• Outcome after diagnosis
• Unmeasured confounding
Conclusions

• Non-AIDS bacterial infections remain a significant cause of morbidity

• The risk of bacterial infection was lowest in persons on cART with high CD4+ cell counts

• Timely initiation of cART in treatment naive individuals and adherence to cART is likely to reduce morbidity from non-AIDS infections

• Further investigation of regional differences could contribute to improvement in HIV management across Europe
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