# Increase of HIV-1 non-B subtype infections in men who have sex with men in Germany

Kücherer C[1], Bartmeyer B[1], Meixenberger K[1], Scheufele R[1], Kollan C[1], Bieniek B[2], Dupke S[3], Jessen H[4], Schürmann D[5] and Hamouda O[1] and the German HIV-1 Seroconverter Study Group

1 Robert Koch-Institute, Berlin; 2 Medical Practice, Gubener Str. 37, 10234 Berlin; 3 Medical Practice, Driesener Str. 11, 10439 Berlin; 4 Medical Practice, Motzstr. 19, 10777 Berlin; 5 Tagesklinik Station 58, Campus Virchow Klinikum, Berlin

## Background

Genetically divergent subtypes and recombinant forms (CRF) are causing the global HIV-1 epidemic. Nine subtypes (A - D, F - H, J, K) and 45 CRF are actually classified within the HIV type 1 clade, but only some of them are epidemically relevant.

In Germany as in other European countries subtype B is dominating the epidemic; however, non-B subtypes occur at varying prevalence. It is still a matter of debate if there are subtype-specific transmission efficiencies driving the divergent global spread of HIV-1 subtypes. Progression of disease might also be affected by the HIV subtype.

The analysis of trends is commonly hampered by the fact that the date of diagnosis does not reflect the date of infection, because infection might have occurred years to weeks before diagnosis.

## Aims

The aim of the study was to analyse the dynamics of spread of HIV-1 subtypes in patients with a known date of infection (German HIV-1 seroconverter study).

## Methods

The subtype of HIV-1 *pol*-sequences (protease and reverse transcriptase) from 1603/1639 drug-naïve patients who were infected between 1996 and 2009 and who had a documented date of HIV-1 seroconversion was determined by phylogenetic analysis. The date of seroconversion was used as best approximation for the date of infection. Characteristics of the study population and *pol*-sequencing are described in Meixenberger K et al (Poster number PW53).

Subtype was analysed using the REGA-tool. Subtypes not assigned by the REGA tool were analysed by additional phylogenetic analysis (Neighbor joining and Maximum Likelihood (PHYLIP package version 6.5, Felsenstein J) using an extended set of reference sequences. In the sequence alignments (CLUSTAL W) part of the pol-sequence encoding the 99 amino acids of the viral protease and 296 amino acids of the reverse transcriptase. Bootstrap analysis was performed with 1000 pseudo data sets. The $\chi 2$ test or the Fisher exact test was used, as appropriate, to compare categorical variables. Logistic regression was used to calculate time trends.

## Results

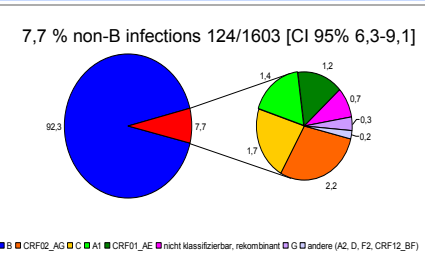


**Figure 1. Prevalence of non-B subtypes in the seroconverter cohort (1996-2009)**

**Table 1. Origin of non-B infections**

| Origin | N 124 | % | Country of risk | % |
|---|---|---|---|---|
| Germany* | 81 | 65,3 | 74 | 59,7 |
| EU | 5 | 4,0 | 3 | 2,4 |
| Northafrica | 2 | 1,6 | 0 | 0,0 |
| Subsaharan Afr. | 26 | 21,0 | 22 | 17,7 |
| Latinamerica | 4 | 3,2 | 0 | 0,0 |
| Russia | 3 | 2,4 | 2 | 1,6 |
| Thail/Vietn/Phil | 2 | 1,6 | 11 | 8,9 |
| unknown | 1 | 0,8 | 12 | 9,7 |

* 41% (50/124) of German were infected in Germany and 25% (31/124) of Germans were infected in another country

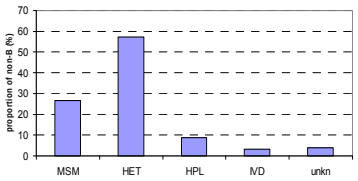


**Figure 2. Proportion of non-B Infections in transmission groups**

- Non-B infections in all transmission groups
- 57% of the non-B infections acquired by heterosexual contacts

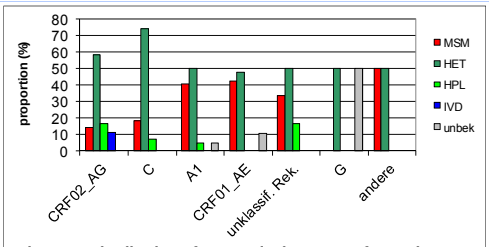


**Figure 4. Distribution of transmission routes for each non-B subtype**

- No hint to preferential transmission routes of subtypes
- All non-B subypes identified also observed in MSM (except from subtype G)

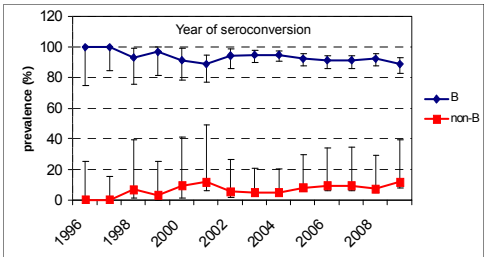


**Figure 5. Prevalence of non-B subtpes over time (1996-2009)**

- $P_{for\ trend}$ =0,0168, significant increase of non-B
- Not due to a particular subtype (data not shown)

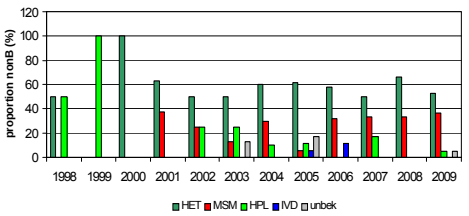


**Figure 6. Proportion of non-B infections per transmissiongroup per year of seroconversion**

- Non-B subtypes observed since 1997
- Highest proportions in heterosexual transmissions
- In MSM since 2001 -> trend of increase?

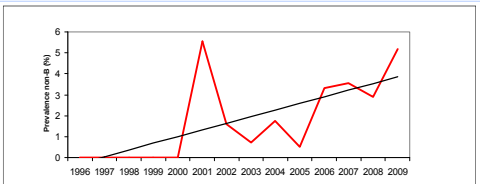


**Figure 7. Prevalence of non-B infections in MSM**

- $p_{for\ trend}$ =0,0129
- Significant increase of non-B in MSM

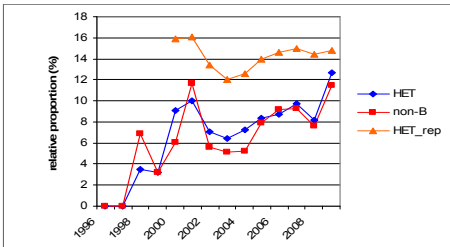


**Figure 8. Prevalence of non-B infections paralles heterosexually transmitted infections**

- parallel to heterosexually acquired infections according to the national records (orange triangles)

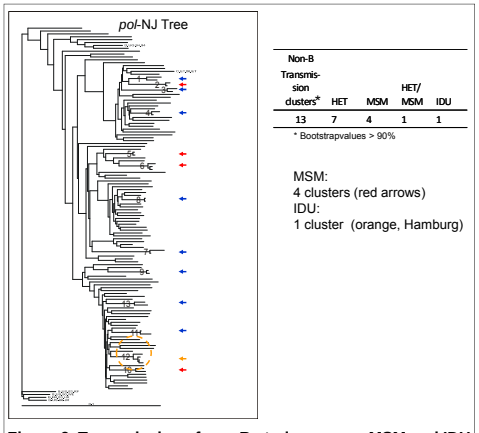


**Figure 9. Transmission of non-B strains among MSM and IDU**

## Conclusion

Although most of the non-B infections were linked to heterosexual and HPL transmission groups in the study cohort, their transmission was not restricted to a particular transmission route as evidenced by the infection of IDU and MSM. Non-B infections are endemically established in Germany as identified unambiguously by transmission between German MSM and also between heterosexual individuals. The increasing trend of HIV non-B infections in MSM should be further monitored. If a selective advantage for a particular non-B subtype as compared to the others indeed exists, this subtype should spread in MSM at the expense of subtypes transmitted less efficiently.

**Acknowledgement:** We thank the patients participating in the seroconverter study of the RKI and all study doctors for their support. We acknowledge the funding of the German Ministry of Health. The study was also performed on behalf of the EuroCoord-CASCADE funded by EU through NoE EuroCoord.

Bundesministerium für Gesundheit

ROBERT KOCH INSTITUT