Title: Prevalence and risk factors of syphilis infection among drug addicts

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Author's response to reviews: see over
Author’s reply to reviewers’ comments

Reviewer’s report from Christina Marra

Reviewer’s comment:
1. “The assessment that only individuals with a reactive TPHA and a reactive FTA-ABS IgM require treatment differs from what is recommended in the US and may be confusing to a US audience. Please provide the rationale (and a reference) for this approach. Were nontreponemal serological tests, such as the RPR or VDRL, performed? If not, again please provide the rationale. If they were performed, please provide the data.”

Author’s response:
1. German guidelines for syphilis screening and testing allow for the use of the TPHA test as a screening test and the FTA-ABS-IgM-test as a confirmatory test in reactive TPHA tests. The confirmatory test is essential for the treatment decision. Thus, in our study treatment was recommended in TPHA positive and FTA-ABS-IgM positive cases. We provided a reference for this approach in the text (page 5-6).
Again, German guidelines allow for the use of the nontreponemal serological VDRL test in treated patients as a serological marker for the evaluation of Penicillin treatment. WE provide a reference for this approach (page 6).

Reviewer’s comment:
2. “In the US and in the UK, IV penicillin is not used to treat active syphilis without neurosyphilis. Please provide more information regarding why subjects with active syphilis in this study were treated with IV penicillin.”

Author’s response:
2. Under common medical conditions German and other European guidelines recommend the use of Penicillin G i.v. only in case of neurosyphilis. The same guidelines recommend the use of Penicillin G i.v. in case of unknown state and duration of the syphilis infection and potential simultaneous HIV-infection. In our sample the state and duration of syphilis was unknown and the risk of a potential simultaneous HIV-infection was high among the study population of injecting drug users. Thus, active syphilis cases were treated with Penicillin G i.v. We explain the rational of this approach and provide references on page 5.

Reviewer’s comment:
3. “It would probably be best to avoid the term promiscuity. It is pejorative, and furthermore it is not defined in the context of this study.”

Author’s response:
3. We replaced the term promiscuity by the expression “number of sexual partners”.

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Reviewer’s comment:
4. “In the Discussion, the authors state that they could not demonstrate a protective effect of the participation in substitution programs on the syphilis serostatus. Please provide these data in the results section.

Author’s response:
4. The corresponding figures have been provided in the result section at the end of the first paragraph on page 8 (middle of the page).

Reviewer’s comment:
5. “The range of seroprevalence for the 8 participating hospitals is mentioned in the Discussion. Please provide this information in the Results section.”

Author’s response:
5. We provide the range of the seroprevalence for the 8 participating hospitals in the last paragraph of page 7.

**Reviewer's report from M Ross**

Reviewer’s comment:

1. Reporting gonorrhea at some time is probably not reliable as a significant amount of gonorrhea is asymptomatic, especially in women. In the recommendations, the authors might want to suggest testing for gonorrhea and chlamydia as well as syphilis in people in drug treatment programs.

Author’s response:
1. We have mentioned the recommendation to testing for gonorrhea and Chlamydia as well as syphilis in people in drug treatment programs in the section conclusions on page 12.

Reviewer's comment:
2. Rather than "promiscuity", the authors might want to use the expression "number of sexual partners", since "promiscuity" is a very value-laden term.

Author’s response:
2. We replaced the term promiscuity by the suggested expression “number of sexual partners”.

Reviewer’s comment:
3. Since injecting drug users may inject in ways other than into veins (eg subdermal, intraperitoneal) it might be preferable to use the terms "injecting drug user" and "IDU".

Author’s response:
3. We replaced the term intravenous drug users (IVDU) by the suggested expression “injecting drug users (IDU)".