CDC recommendations for PrEP

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Dear Readers,

In our last HIVreport, we reported on the iPrEx study, a study to investigate the possibility to prevent an HIV infection by proactively taking antiretroviral drugs (pre-exposition prophylaxis = PREP).

The American Centers for Disease Control have now published first recommendations for the implementation of PrEP – exclusively for application in men who have sex with men (MSM).

This step is astonishing, since PREP has not yet established itself as a method of prevention and the efficacy of PREP demonstrated in the iPrEx study clearly fell behind the expectations.

Therefore, these recommendations focus on harm reduction and do not constitute a conventional CDC “guideline” for the application of a new method. The recommendations are to prevent the incorrect application of PrEP – if applied at all. Because both in the USA and in Germany, drugs outside their actual purpose of use (marketing authorisation) are available on private prescription only.

This HIVreport is to present the US-American recommendations.

If you have any further questions on the iPrEx study or the significance of PREP in prevention, please refer to the HIVreport of December 2010.

Best regards,
Armin Schafberger, Steffen Taubert

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Preliminary CDC Recommendations for PREP

In late January 2011, the American Centers for Disease Control and Prevention (CDC) published preliminary recommendations for the application of antiretroviral drugs to prevent HIV infections (pre-exposition prophylaxis, PrEP). The CDC is thus the first state authority to provide a frame for medication-based HIV-PREP.

By announcing the preliminary recommendations for PrEP in the “Morbidity and Mortality Weekly Report” (MMWR), the authority responded to the results of the iPrEx study. This study, published in November 2010, demonstrated that regular, proactive administration of the HIV pharmaceutical Truvada® can reduce the probability of an HIV transmission by 44%.

In the last issue of the HIVreport (05/2010), we presented the study and elaborated on the weaknesses and limitations of the study results. In the aggregate, we considered an average protective effect of 44% to be too low for a prevention method. Although the protective effect increased in the study group taking Truvada® on a regular daily basis, PrEP, with a protective effect of 72.8% in this “highly compliant group” is still clearly behind already established methods of prevention such as the use of condoms.

Particularly practical questions were left open by the study. For example, it did not clearly define how long before and after a risk exposure PrEP needs to be applied to take effect. During the study, the men were urged to take PREP daily over a long period of time of many months. Furthermore, the question of developing resistance was not sufficiently reflected. In addition, the cost factors should also be taken into account for a public health strategy using medication-based PrEP. In the last HIVreport, we discussed the question of how many persons would have to be treated with PrEP to prevent an infection (“number needed to treat”). Please find a comprehensive presentation of the iPrEx study here.

Some of these critical questions also seemed to bother the authors of the current CDC recommendations. In the MMWR, the authority expressed its “concerns that various unsafe and potentially less effective PREP strategies may be applied without the provision of clear directions at an early stage (by the CDC, Author’s note)”.

The CDC summarises its concerns in the “Morbidity and Mortality Weekly Report” as follows:

- PrEP could be applied with other HIV drugs than those proved safe for HIV-negative persons.
- PrEP could be applied differently, e.g. by taking a tablet before or after sex, although there is no sufficient evidence of this strategy yet.
- Omission of an HIV test before applying PrEP.
- PrEP could be applied without consulting a physician, neglecting other methods of prevention (namely condoms).

Until official PrEP guidelines are published, the CDC recommends considering the following when prescribing drugs for pre-exposition prophylaxis:

PrEP only for MSM

PrEP is only considered for people who are exposed to permanent high risk of an HIV infection. Due to the study type, the recommendations only apply to MSM. It is unclear why the recommendations should not also apply to heterosexual persons exposed to high risk.

The CDC points out that the prevention of an HIV infection takes place outside the market authorisation of Truvada® (off-label). Furthermore, it is not yet known how safe it is for HIV-negative persons to take Truvada over a very long period of time.

The CDC Recommendations in Detail

Measures to be taken before PrEP

Exclusion of an acute HIV infection:

- Documentation of a negative HIV antibody test directly before starting PrEP (this excludes anonymous testing, Author’s note)
- In case of symptoms indicating an acute HIV infection, further tests (e.g. PCR) should be conducted in order to exclude an acute HIV infection with certainty (otherwise risk of developing resistance).

Checking whether PREP is indicated:

- The PrEP should only be applied in patients exposed to high risk of an HIV infection.
• Checking the renal function (creatinine clearance ≥ 60 ml/min) because of the possible side effects of Truvada®

Further recommendations:
• Screening for hepatitis B infection. If no immunity exists, vaccination is needed. If a hepatitis B infection exists, it should be treated irrespective of PREP.
• Screening for and treatment of other STIs

Rules for the application of PrEP
• Dosage schedule: one Truvada® tablet (300 mg Tenofovir plus 200 mg Emtricitabin) per day
• Prescription interval: Physicians should always prescribe Truvada only for a maximum period of 90 days. After this, an HIV test should be conducted. Only when this test is negative, may the PrEP be continued.
• Duration of treatment: The CDC states no maximum period
• Note: In case of an acute hepatitis B infection, Truvada® can be applied to treat hepatitis B, in addition to using it for HIV-PrEP.
• Consultation: Physicians should advice the users of PrEP on the necessity of regular intake (referred to as adherence or compliance) as well as on other risk reduction measures (condoms).

Checking the success of PrEP

Every 2-3 months:
• Conducting an HIV test to clarify whether the PrEP user is still HIV-negative. The test result should be documented!
• Evaluate and support PrEP medication adherence at each follow-up visit, more often if inconsistent adherence is identified.
• Sexual anamnesis (definition of risks), risk-reduction counseling and provision of condoms. Regarding this recommendation, it should be considered that American health care providers often work at public health care establishments, where prevention is more firmly established than at the private practices of German registered physicians.

Every 6 months:
• STI tests in patients without symptoms, or earlier if symptoms exist

Annually:
• Checking serum creatinine and blood-urea-nitrogen (renal function) 3 months after starting PrEP, later on annually.

Measures to be taken when terminating PrEP

The termination of PrEP can have various reasons: side effects, an HIV-positive test result (which may occur in spite of PrEP) or just the unwillingness to take a drug on a long-term basis exclusively for the purpose of prevention.

When terminating PrEP, the following measures should be taken:
• HIV test
• If the HIV test is positive: Conducting a resistance test¹ and ensuring medical care
• If the HIV test is negative: Referral of the patient to a “risk-reduction counseling” (the CDC does not specify what it means by that)
• If Truvada was taken on a daily basis to treat a hepatitis B infection simultaneously to PrEP, it should be determined how the treatment can be continued.

¹ The (irregular) intake of Truvada® with an existing HIV infection may have caused resistance to TDF or FTC; however, an HIV infection with an HIV variant that is already resistant to antiretroviral drugs is also possible.
All these recommendations are considered to be preliminary. Official guidelines for PrEP are still in process in the USA. They are expected to be published in the next few months.

In Germany, PrEP can be privately prescribed by physicians within the scope of off-label use. Please find more information about the legal implications and the costs in the HIVREPORT 12/2010.

Assessment and Criticism
“Exciting new method, but not yet suitable for everyday use”

It is a positive fact that the possibility of medication-based prevention is now also confirmed by official bodies. The message is: *The transmission of HIV can be generally prevented by taking antiretroviral drugs.*

The CDC recommendations, however, also leave some questions open. Why should PrEP only be offered to MSM with frequently changing partners? Should the rules not also apply to heterosexual persons exposed to high risk? However, not all MSM are actually exposed to high risk, which is why the assignment of this prevention method to a group seems to be doubtful.

But the CDC also recommends that PrEP should be preceded by a consultation to clarify whether the “prospective PrEP patient” is actually exposed to high risk. Certainly not all physicians will find this easy. Trainings of Deutsche AIDS-Hilfe with physicians demonstrate that many physicians reach their limits already during everyday work routine when it comes to sexual consultation and the practical handling of transmission risks.

The CDC recommendations are based on the iPrEx study and therefore recommend a daily intake of Truvada® for prevention as long as the transmission risks exist. Since most people have sex over several decades, this would mean a long-term preventive treatment with a highly potent drug. It remains to be seen how many people decide in favour of this treatment. Besides the risk of unknown long-term side effects, it is also uncertain who will bear the costs in the future.

At present, the health insurance funds do not reimburse the costs. The annual costs for treatments with Truvada amount to more than EUR 10,000 in Germany. Are there any people who pay for this out of their own pockets and are additionally willing to “put up” with regular visits to the doctor and HIV tests?

Another sticking point is certainly that the daily intake of a drug over many years requires an extremely high degree of adherence (compliance). Even under the optimum conditions of a study involving regular consultations and supervision, most study participants seemed to be unable to take the substances on a regular basis. Is it possible that people simply stop taking PrEP after a sexless weekend?

Considerations of “intermittent PrEP” appear to be more interesting. Further studies will be needed to investigate the efficacy of PrEP when started shortly before sexual intercourse and stopped some days thereafter. There may also be other drugs that are more effective than Truvada®. Theoretically, substances preventing the entry of viruses into cells (referred to as entry inhibitors) would be a perfect choice for PrEP. However, these substances, e.g. Maraviroc, have only recently been introduced to the market and have not yet even been approved for first-line treatment in Europe.

At present, the state of affairs can be summarised as follows: PrEP strategies show an exciting new way to HIV prevention, but do not yet seem to be suitable for everyday use. In individual cases, however, they may be an approach worth considering, even at this stage.
In case of doubt, I’m all for “harm reduction”

Interview with Dr. Hans Jäger, medical practise specialised on HIV/AIDS, MVZ Karlsplatz, Munich

HIVREPORT: What do you think of pre-exposition prophylaxis?

Jäger: I think it’s the right approach. We had three major studies on this last year. There were the results of the Thai vaccine study and then Caprisa. The Caprisa study examining the efficacy of microbicides for HIV prevention was perhaps a bit overrated at the World Aids Conference in Vienna. It was nevertheless important. Finally, the results of the iPrEx study on PrEP in MSM followed in November.

HIVREPORT: How do you rate the results of iPrEx and the current CDC recommendations?

Jäger: The summary of the CDC is great! iPrEx was able to demonstrate that PrEP can work in men who take a drug compliantly (regularly).

HIVREPORT: Have you already had interesting inquiries from patients at your practice?

Jäger: No, so far, this hasn’t been a big issue here in Munich; perhaps it’s different in Berlin? We shouldn’t forget that there are still some open questions. It’s often the details that are most difficult. Who bears the costs for PrEP? Do the tablets really need to be taken daily over a long period of time to take effect, or can PrEP also be taken shortly before the weekend on which you plan to have sex...

HIVREPORT: Yes, I can imagine that it’s more convenient for many people to take tablets for only a few days instead of taking them over several months or years...

Jäger: Unfortunately, we don’t know yet whether PrEP has the same protective effect when taken this way. Of course, there is also the possibility to let drugs take effect directly in the genital area, for example thin, resolving films.

In this case, we don’t need to take any tablets. All in all, we definitely need further studies. Another question is: What should I do as a doctor if someone comes to me shortly before the weekend, asking for PrEP? First of all, I need to conduct an HIV test, which will take some time. In this case, however, I would say: In case of doubt, I’m on the patients’ side; my goal would always be effective “harm reduction”.

Interviewer: Steffen Taubert

From the Editor’s Desk

New Website for HIVreport

Over the next few months, the HIVreport website will be moving to be integrated into the website of Deutsche AIDS-Hilfe. This will connect the contents of the HIVreport even more closely to the DAH’s other media. The search function on aidshilfe.de will then make it possible to conveniently list all contents of the HIVreport. The “old” web address will remain available for the transition period. Subscribers to the HIVreport will from now on receive their PDF file from “aidshilfe.de”.

References

Grant R.M. et al. (for the iPrEx Study Team): Preexposure Chemoprophylaxis for HIV Prevention in Men who have Sex with Men. NEJM, Nov. 23, 2010 (online first)


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