PRISE EN CHARGE MÉDICALE DES PERSONNES VIVANT AVEC LE VIH

RECOMMANDATIONS DU GROUPE D'EXPERTS
Sous la direction du Pr Philippe Morlat
et sous l'égide du CNS et de l'ANRS

Prevention and screening

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Summary

Introduction

The 2013 version of the expert report included a chapter focusing on screening (1) and another on prevention (2). In 2015, a new chapter was added to the report, examining in detail the progress made in pre-exposure prophylaxis (PrEP) and making specific recommendations in this area (3). The current version of the expert report intends to bring together in a single chapter all the issues relating to prevention and screening and formulates global recommendations combining behavioral and biomedical approaches.

The dynamics of the epidemic have changed in France and so have its challenges. The chapter " Epidemiology "Of this report presents in detail the epidemiological indicators and their trends. Without repeating all this data, the situation can be summarized as follows:

- The number of new contaminations has remained stable from one year to the next for several years (around 6,000 infections per year) and the epidemic, described as concentrated, is no longer declining. We no longer describe a French epidemic but epidemics of different
- level and evolution between the territories: the metropolitan regions of Ile-de-France, Provence Alpes Côte d'Azur (PACA) and Auvergne Rhône Alpes, as well as the French Territories of America (TFA) are clearly more affected than other regions.

- The most affected population groups are more than ever men who have sex with men (MSM) and populations of both sexes from sub-Saharan Africa and ASWs. Risky behaviors and practices persist but are found at varying levels across all age groups, and young adults are not spared. Testing for HIV infection is well established in medical and community practice. Its use now increases little in frequency and its performance (number of new positive tests out of the total number of tests carried out) changes little. The corollary is
- that diagnoses at an advanced stage (CD4 <200 / mm 3 or AIDS stage) or at a late stage (CD4 <350 / mm 3 or AIDS stage) remain too numerous. The number of undiagnosed people is not decreasing and therefore has a ripple effect on the dynamics of the epidemic. However, the screening offer has diversified both in terms of tools and structures.

- The use of the tenofovir disoproxil fumarate / emtricitabine combination is too recent (January 2016, if we take into account the provision by RTU prior to the MA in PrEP) so that the expected preventive effect of PrEP on the target populations could be observed.

In this chapter, we propose to define prevention as the set of measures for which the right level of scientific evidence justifies their application to achieve a maximum effect of reducing HIV transmission at the population level (4). This prevention is qualified as diversified because it associates structural measures with biomedical and behavioral interventions, knowing that none of them taken in isolation can lead to the expected effect and therefore does not constitute a panacea. The group of experts and its “prevention and screening” commission have decided to replace the name “combined prevention”, often used until now, by “ **diversified prevention** »Considering that at the individual level, prevention tools and strategies were not always combined but that their diversification at the population level was necessary to impact the dynamics of infections. This diversified prevention must target the use of resources on a large proportion of the most exposed populations by offering, with its multiple measures of proven effectiveness, a real opportunity to increase the overall level of prevention and reduce the pandemic to very low levels in a country like France.

The cornerstone of any prevention policy remains screening and knowledge of HIV status. Here we will update the recommendations on HIV screening and then develop the issue of screening for viral hepatitis and other sexually transmitted infections (STIs). The condom remains today a key preventive measure in the diversified prevention, recommendation confirmed by the most recent knowledge. Despite an effectiveness observed in certain epidemiological contexts, medicalized male circumcision has no place as a public health measure in France. The preventive effects of universal and early antiretroviral therapy are increasingly well documented and the so-called “Treatment as Prevention” (TasP) approach now has its place in this chapter. Similarly, PrEP is now a high priority in the diversified prevention strategy, especially for MSM. The prevention of STIs by vaccination is the subject of specific and updated recommendations here. Post-exposure treatment (TPE) is the subject of a separate chapter and remains an important tool at the individual level (*Cf.* chapter "Management of sexual and blood exposure accidents (BSE) in adults and

the child "). After having recalled the need for a global risk reduction policy for drug users, we will address to end this synthesis of diversified prevention the emerging issue of drug use in a sexual context.

Methodology of work

Two initiatives led by the High Council for Public Health (HCSP) in 2015-2016 on referral from the Directorate General of Health (DGS) provided the group of experts with an assessment of the public policies that have been implemented over the last few years. years and a first set of recommendations, including a number on prevention and screening:

- The evaluation report of the 2010-2014 national HIV / AIDS and STI plan, which includes seven proposals on prevention policy and six on screening (5)
- The opinion on sexual and reproductive health, the fourth axis of which is dedicated to the prevention and screening of STIs (6)

Five framework documents, the last four of which have been published since the start of 2017, formed the basis of the proposals made here:

- The decree of 1 er July 2015 relating to the free information, screening and diagnostic centers (CeGIDD) for HIV infections, viral hepatitis and STIs, the appendix of which sets out the specifications for these new forms of organization put in place since 1 er January 2016 (7). The opinion of the CNS followed by recommendations on the prevention and management of STIs in adolescents and young adults (8).
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- The national sexual health strategy (9).
- The report on the reassessment of the screening strategy for HIV infection in France prepared by the Haute Autorité de Santé (HAS) (10).
- The ministerial decree relating to the establishment of the coordination of the fight against sexually transmitted infections and the human immunodeficiency virus (COREVIH) in 2017 (11).

The recommendations were drawn up collegially by 13 multidisciplinary experts based on a critical analysis of the best available knowledge and the experience of the members.

The progress of the committee's work was presented three times for discussion and amendment to the plenary group of experts, whose methodology for drawing up recommendations is set out in the appendix, and the final version was validated after discussion between the chairman of the committee. group and that of the commission.

Five members of the “prevention and screening” commission participated as experts in the drafting of the HAS reassessment report and two others were part of the reading group (10). It did not therefore appear appropriate to conduct a new independent expert appraisal on screening within the framework of this report. The expert group thus approves the conclusions formulated in the HAS report and endorses the recommendations formulated therein, specifying certain elements here.

A survey of a dozen centers prescribing PrEP within the framework of the RTU was carried out by semi-open questionnaire, the answers being obtained in writing or by telephone interviews.

Screening

HIV infection

Context

Screening for HIV infection is the subject of a **Politics** public supported by HAS recommendations, the last version of which dated from 2008-2009. The recently completed reassessment (10) was made necessary, as recommended by the HCSP in the evaluation of the last National Plan (5): the epidemic continues on French territory and this, unevenly; coordination between the different forms of screening, in particular towards the most exposed or minority and marginalized populations, is insufficient despite the deployment of community screening; finally, the policy of screening the general adult population was little followed and had little effect.

The **organization** current screening for HIV infection in France is based mainly on the healthcare offer: health professionals working in health establishments and in town medicine, public and private medical biology analysis laboratories. The associative structures authorized by the Regional Health Agencies (ARS) can since November 2010 carry out rapid diagnostic orientation tests (TROD). The reform of structures specializing in screening materialized in the decree of 1 er July 2015 creating the CeGIDD (7), with single financing of health insurance and management by the ARS. We therefore now have a frame of reference advocating a territorial organization of the information, screening and diagnosis system for HIV, viral hepatitis and other STIs. The objective is to increase the accessibility and the quality of the offer, in particular for the most vulnerable, the most exposed and the most remote people. We define in this chapter these **key populations** as follows: Men who have sex with men (MSM), heterosexual women and men born in sub-Saharan Africa and in the French territories of America (TFA) and injecting drug users (IDU). This simplified offer is supposed to guarantee a better treatment path starting from screening. Finally, a single legal and financial organization should facilitate the management of these organizations. The CeGIDD reform aims to unify screening for HIV and other STIs and to create, beyond simple screening, a genuine network of sexual health centers. It should also be noted that the CeGIDDs are strongly encouraged to develop their activities outside the walls. One year after the start of the first CeGIDDs, it is still too early to assess the impact of this reform, in particular on the volume of screening activities, their targeting and changes in the quality of the services provided. The expert group recalls, however, that the current functioning of CeGIDDs began in the majority of cases with means substantially equivalent to those of the structures previously in place, although the missions have been extended and that it is rightly recommended that that off-site activities be developed. CeGIDDs must therefore establish priorities to produce the best possible range of services in relation to the new screening objectives appearing in the reference texts (7, 9). The expert group recalls, however, that the current functioning of CeGIDDs began in the majority of cases with means substantially equivalent to those of the structures previously in place, although the missions have been extended and that it is rightly recommended that that off-site activities be developed. CeGIDDs must therefore establish priorities to produce the best possible range of services in relation to the new screening objectives appearing in the reference texts (7, 9). The expert group recalls, however, that the current functioning of CeGIDDs began in the majority of cases with means substantially equivalent to those of the structures previously in place, although the missions have been extended and that it is rightly recommended that that off-site activities be developed. CeGIDDs must therefore establish priorities to produce the best possible range of services in relation to the new screening objectives appearing in the reference texts (7, 9).

Three **modalities** screening tests for the diagnosis of HIV infection are available in France: Elisa and confirmation serological tests which are carried out in the laboratory, TRODs which can be carried out by a third person who is not necessarily a health professional and self-screening tests (ADVIH) on sale in pharmacies and available free of charge in authorized structures. The performance of these tests, summarized in Box 1, is considered globally equivalent for a screening activity, except in the event of recent exposure (<3 months). Self-collection tests for STIs are kits that allow the individual to take the sample himself and send it to a laboratory for a delayed result; they are not currently available in France but are being tested (12).

The **biological diagnosis** HIV infection still relies on a two-step strategy: a screening test followed by a confirmatory test. Screening is now carried out with a single reagent commonly called the combined Elisa test of 4 th generation simultaneously detecting anti-HIV-1 and 2 antibodies and the p24 antigen of HIV-1. Any positive screening must be confirmed by a Western blot or Immunoblot test on the same sample. The affirmation of HIV infection requires having the correct results of two separate samples to rule out an identity error (Box 1). The search for plasma HIV RNA is recommended in several confirmation scenarios (10).

We set out below the most important recommendations of the HAS report (10) by providing additional information and insights that we found useful.

Box 1

Different types of HIV infection screening test available in France - Conditions of use - Source: HAS (10)

Elisa from 4th generation

The test currently carried out in the laboratory is an Elisa test of 4e generation. It is a mixed Elisa test that simultaneously detects anti-HIV-1 and anti-HIV-2 antibodies, and combined, as it also detects the p24 antigen of HIV-1, allowing screening for recent infections. A negative test result indicates no HIV infection, except for suspected HIV exposure less than 6 weeks old.

In case of Elisa test of 4e positive generation a Western-Blot test is carried out on the same sample to confirm the result: it detects different antibodies directed against HIV, thus making it possible to know whether the virus is really present in the body. The confirmatory analysis should thus make it possible to answer the question of the presence or not of an HIV infection and at the same time to differentiate between HIV-1 and HIV-2 infections. If the result of the WB or the IB is negative or indeterminate, in order not to ignore a primary infection at the pre-seroconversion stage, it is necessary to carry out a test to demonstrate the components of the virus (detection plasma viral RNA or detection of p24 Ag with a detection threshold at least equivalent to that of the combined Elisa test used in the screening analysis,

The affirmation of HIV infection always requires the availability of consistent results from two separate samples. If the screening test is positive, the confirmatory test should be performed on the initial sample. If the confirmatory analysis is positive, a second sample must be taken in order to eliminate an identity error. On this second sample, it is recommended to perform a new screening analysis (with the screening reagent previously used or another); it is not necessary to perform a new confirmatory analysis. Only a positive result on the second sample will validate the result and confirm the diagnosis of HIV infection.

Diagnostic-Oriented Rapid Screening Test (TROD)

The TROD is defined as a unit test, with subjective visual reading, simple to perform and designed to give a result within a short time (generally less than 30 minutes). This test is performed on whole blood, serum, plasma in accordance with the manufacturer's instructions, using a reagent detecting HIV-1 and HIV-2 infection with a CE mark. There are now tests combining the search for antigen and antibodies. In the event of a positive TROD, the person concerned is systematically referred, or even accompanied if necessary, to a doctor, a health establishment or a health service with a view to carrying out a medical biology laboratory, public or private, laboratory diagnosis of HIV 1 and 2 infection. In the event of negative TROD, the person tested is informed of the limits inherent in the interpretation of the test result and of the possibility of carrying out the aforementioned biological diagnosis, in particular in the event of a recent risk of HIV transmission. A negative result cannot be interpreted in the event of risk taking less than 3 months.

Self-test for HIV infection (ADVIH)

ADVIHs are rapid tests, performed on whole blood, which use the same technology as TRODs. They are intended for use in a domestic environment by lay users. Sampling and interpretation are carried out directly by the interested party. The positive result of an ADVIH must be confirmed by a conventional Elisa type test of 4e generation. A negative result cannot be interpreted in the event of risk taking less than 3 months.

Where, when and how to screen

- The French epidemic is concentrated, that is to say that it disproportionately affects certain population groups and hardly affects the general population apart from key populations: MSM, heterosexual women and men born in sub-Saharan Africa and in TFA and IDU. These key populations are particularly found in Ile-de-France, PACA, Auvergne Rhône Alpes and in TFAs, in particular in Guyana. The two dimensions, population and region must therefore now be taken into account.

- The frequency of proposing screening of key populations must be increased in a sustainable manner:

  - **Screening at least once a year** among MSM, and closer **every three months** among those **at high risk of exposure and in the most affected regions;**
  - Screening **every year for IDUs and for people from high prevalence countries;**

  - In practice, **any screening opportunity** should be encouraged with these groups regardless of the screening technique used and if possible by combining HIV, HBV and HCV (*Cf.* Box 1).

- **The proposal for screening in the general population at least once in a lifetime between 15 and 70 years must be maintained.** This incentive to screen is particularly important to implement as soon as an opportunity arises among men and in the following regions: TFA, Ile-de-France, PACA and Auvergne Rhône Alpes. This strategy remains ambitious but necessary and can only be carried out with increased resources. Women often have the opportunity of such screening during pregnancy but this proposal must be systematized, as well as during consultations for a pregnancy, contraception or voluntary termination of pregnancy project (*Cf.* chapter "Desire to have a child and pregnancy"). In all these cases, when possible, screening should also be offered to the partner. In addition to the usual indications (clinical or biological signs suggestive of immunosuppression or primary infection), many individual situations, including the diagnosis of STIs, tuberculosis, medical treatment of people who have suffered rape and incarceration should also encourage screening.

- **The three screening methods (by a health professional, an association or at the initiative of the individual himself) are considered to be complementary and must all be encouraged.** Screening is therefore always part of a diversified preventive offer as defined at the beginning of this chapter.

  - As regards the associative structures, enough experiments have been carried out and evaluated (13, 14) so that they can now be considered as essential actors and to be favored to reach the key populations. Their added value lies in their ability to reach out to key populations, outside the walls. Their ability to have a downstream network for confirmation of the diagnosis and early management must always be guaranteed. Co-testing for HIV, HBV and HCV is especially important in these settings. The use of TRODs and self-tests should be widely promoted here because they have a good yield, and the quality of these services should be able to be verified. The experimental evaluation of self-samples should also be encouraged in this context.

  - The CeGIDD have extended missions compared to structures previously specialized in screening. Advanced consultations and prevention and off-site screening activities in search of key populations and the comprehensive approach to sexual health that is advocated must be fully developed. The group of experts insists, however, on the need to mobilize additional resources adapted to the contexts (human resources, opening hours, etc.) without which these actions cannot be carried out correctly: to offer the populations most distant from the system. care screening for HIV, hepatitis B and C as well as STIs under appropriate technical conditions and by associating a real range of services in terms of contraception and vaccination (see following sections).

  - Liberal physicians are key players in encouraging their patients to be screened: general practitioners as well as specialists in dermato-venereology, gynecology, hepatology, proctology and oncology. This approach should apply to the general adult population when it has never been screened, with an emphasis on men and especially in the most affected regions (see above), but also on consultants from key populations.

- The addition to a prescription of any other biological examination of Elisa screening tests to jointly test for HIV, HBV and HCV is recommended.
- Liberal physicians should also encourage this screening in the face of suggestive clinical or biological elements in order to reduce the frequency of late diagnoses. The exhaustive list of indicator diseases that should lead to the prescription of screening, as proposed in Appendix 10 of the HAS report (10), is presented in Box 2.

- TRODs have their place in the practice of private doctors, especially in the most affected regions and if the patient population is at least partly made up of key populations. Their use on a sufficiently large scale can only be considered if these tests are made available free of charge in practices and if the medical act which consists in offering them and performing them in good conditions is rated.

- To enhance this responsibility in terms of screening, liberal doctors should on the one hand benefit from an important communication and training action, in particular from COREVIH, in order to support them in the construction of a health consultation. sexual or in the integration of this dimension in consultations for other grounds of recourse. Information and communication with the general public are also necessary to generate demand from private practitioners. Finally, this type of activity should become a marked act or a possibility of remuneration for public health objectives (ROSP).

o Hospital stays are all opportunities to offer screening to the general population in the absence of a test performed previously, as well as to key populations. This proposal must be systematic and carried out in an incentive-based manner, including without specific prior consent (simple information and reporting of results whether positive or negative / so-called " *opt-out* "). The health care access hotlines (PASS) are particularly useful mechanisms for implementing this strategy with the most vulnerable groups who stay in hospital.

o Hospital emergencies are an obvious gateway to screening but the experiments already carried out and which aimed at the generalization of the screening offer now lead to recommend screening targeted at key populations or on the basis of clinical information and / or laboratory tests suggestive of a primary or more advanced form of HIV infection.

o University medicine must be an opportunity for screening young people, particularly in relation to associations and with the use of Elisa or TROD tests made available. This screening strategy must be part of a more comprehensive sexual health approach, including screening for other STIs, HBV and HPV vaccinations and contraception. It must be particularly put in place in the most affected regions.

o Occupational medicine has so far been little involved in screening policy. Occupational physicians can perform screening by being particularly attentive to information and respecting the confidentiality of their consultants. The expert group strongly supports the involvement of occupational physicians for at least two reasons: men use occupational health more than any other component of the health system; integrating HIV testing into the preventive occupational health consultation is an opportunity to put an end to the exceptionalism of HIV infection in France.

o Medical biology analysis laboratories must continue to offer any client the possibility of performing an Elisa test on site and without a medical prescription. Reimbursement would require regulatory change or the formulation of a public health policy. The identification of a downstream medical referral and support system is recommended.

o Community pharmacists should promote the dispensing of self-tests which should be available in all pharmacies. For the moment, this dispensation goes through the pharmacist; it should be freely accessible in pharmacies. Community pharmacists must also be able to perform TRODs. In both cases, the regulations must be changed. The identification of a downstream medical referral and support system is recommended.

o Finally, the offer of joint HIV-HBV-HCV testing in places of deprivation of liberty must not only be systematically offered at entry but also during and at the end of imprisonment.

- Screening at the initiative of the individual is one of the cornerstones of the screening strategy in France. Institutional campaigns must clearly and repeatedly encourage screening at least once in the life of the general population and after possible exposure to HIV (see above). Information campaigns comprising messages specific to key populations (frequency and regularity of screening) must also be carried out regularly and use the means of communication adapted to each of them. The three methods available in France (Elisa test, TROD and self-test) must be accessible to everyone under the best possible conditions. Free,

- Partner notification brings together all actions aimed at: informing the sexual partners of people newly diagnosed with HIV, any other STI or viral hepatitis and partners who share injection equipment; to advise these partners and to offer them services and first of all screening and then appropriate care. This notification can be done using different methods. The United States, Canada, Sweden and the United Kingdom have long practiced this notification. France has neither the legislative framework nor the specialized professionals nor the mechanism facilitating this type of intervention whereas it exists for other communicable diseases such as tuberculosis.

- Health mediation is a new form of service provided for by the 2016 law on the modernization of the health system targeting access to rights, prevention and care for people far from health systems and which must take into account their specificities. . Key populations from endemic countries are one of the priority audiences for peer health mediation. Their use must be promoted at the various stages of support of the screening process in order to limit any form of stigma. The professional guidelines for health mediators were published by the HAS on October 26, 2017.

Box 2

Evocative signs, symptoms and pathologies for which
a screening test must be systematically requested

Source: HAS (10)

- Signs compatible with a primary infection:

Clinical signs consistent with persistent acute viral syndrome (fever, arthralgia, pharyngitis, myalgia, asthenia) more or less associated with polyadenopathy, cutaneous-mucous manifestations (maculo-papular rash, oral and / or genital ulcers) and / or neurological (headache, mononeuritis etc.) and / or digestive disorders (diarrhea, weight loss etc.).

Or biological abnormalities: haematological (thrombocytopenia, neutropenia, hyperlymphocytosis in the context of a mononucleosis syndrome or precocious lymphopenia) more or less associated with hepatic cytolysis.

- Discovery of opportunistic pathologies as described in stage C of the CDC classification or in the context of other indicator diseases (Source: European HIDES study,

pathologies associated with a prevalence of undiagnosed HIV infection> 0.1%). As a reminder, the eight pathologies indicative of HIDES are:

- Sexually transmitted infections (STIs);
- Malignant lymphomas of any type *;
- Anal or cervical dysplasia / cancer *;
- Shingles;
- Infection with hepatitis B or C virus, acute or chronic, regardless of the date of diagnosis;
- Mononucleosic syndrome;
- Unexplained leukocytopenia or thrombocytopenia of more than 4 weeks;
- Seborrheic dermatitis / exanthema.

** Pathologies which may correspond according to their type or extension to opportunistic infections classifying AIDS - stage C classification CDC*

Viral hepatitis and other sexually transmitted infections

The chapter " Epidemiology Reports an increased incidence of viral hepatitis and bacterial STIs. Recommendations concerning screening for viral hepatitis and STIs other than HIV are scattered and are only rarely formulated in a population-based approach.

For hepatitis A, which has become epidemic among MSM in several French regions since the end of 2016, as in other European countries, vaccination is the reference preventive strategy (*Cf.* section on immunization in this chapter)

For hepatitis B and C, we recall here the recommendations of the report led by Professor Dhumeaux that the group of experts approves. The update published in 2016 is in favor of broadening the screening strategy (15). The three main recommendations are therefore:

- The pursuit of a targeted screening strategy for viral B and C infections in people with one or more risk factors for contamination (except for hepatitis B in the event of knowledge of a positive anti-HBs serological status synonymous with protection), to know :
    - The promotion of all screening actions for MSM, in particular those who are eligible for PrEP, those who declare several partners, those who report the use of so-called recreational drugs, traumatic practices, insertion or fist as well as MSM already known to be infected with HIV. In addition, the risk of new contamination in MSM co-infected with HIV and HCV and cured of their hepatitis C is now well known and requires the continuation of screening (search for HCV RNA) beyond the end of hepatitis C treatment period every six months.
    - The promotion of screening and counseling actions at the initiative of the caregiver in prevention and care settings frequented by IDUs, including outside the city, so that this screening is carried out every 12 months and more frequently in the event of use of PrEP.
    - Continuation of the systematic offer of screening on the occasion of the medical examination on entering prison, and its renewal during incarceration, including with the help of TRODs;
    - The development of a one-stop-shop strategy (screenings carried out in a unit of time and place) which is financially accessible for migrants and foreigners born in highly endemic countries;
- The extension of screening strategies for viral hepatitis in the general population at least once in life to all adults of both sexes who have never been screened;
- The association in all cases of the research of the three viruses VHB, VHC and HIV (except for hepatitis B in the event of knowledge of a positive anti-HBs serological status synonymous with protection).

For Chlamydia *trachomatis,* systematic screening by PCR remains recommended to this day for women under 25 and men under 30 seen in anonymous and free screening consultations (today the CeGIDD) and planning and family education (CPEF). In February 2016, the Société Française de Dermatologie took up this recommendation, specifying that this screening should be repeated every year in the event of unprotected sex with a new partner (16). The 2003 recommendations (17) are currently being reassessed by the HAS.

For syphilis, the HAS in its 2007 recommendations (18) recommended adapting the rate of repetition of screening according to risky situations (from single screening in the event of occasional risk-taking to regular screening, at least once a year , in the event of recurring risk-taking) for the following populations and situations:

- MSM (for any practice including fellatio);
- sex workers having unprotected intercourse (for any practice including fellatio);

- people of both sexes having unprotected sex (for any practice including fellatio) with sex workers;

- at the time of diagnosis or in the event of a history of gonorrhea, lymphogranulomatosis venereal and HIV infection;

- people of both sexes having unprotected intercourse (for any practice including fellatio) with several partners per year;

- migrants from endemic countries (Africa, Asia, Eastern Europe, South America);
- during imprisonment;
- after rape;

- as part of a pregnancy follow-up.

We have no arguments for proposing changes to these recommendations although they are not recent. The group of experts recalls that the TROD syphilis have not yet been validated but that their development would be useful in the offer of combined TRODs.

For gonococcal infection, the HAS, in its 2010 orientation report (19), proposed two complementary approaches on which there is no new evidence:

- Targeted screening in subgroups of the population with risk factors:
  - o People screened for or diagnosed with another STI;
  - o People with a history of STIs, including gonococcal infection;
  - o MSM;
  - o People living with HIV;
  - o Men and women with risky sexual behavior.
- Targeted screening for all people seeking care in CeGIDDs, CPEFs, orthogenesis and sexual health centers.

- To promote this screening, the group of experts recommends a change in nomenclature allowing the coverage of PCRs by health insurance.

For integrated STI screening

We have reported and summarized in the two sections which precede the recommendations on screening for HIV and then for other STIs. We have therefore presented a set of vertical recommendations developed by pathogen over fifteen years. The expert group agrees on the need on the one hand to update the oldest screening recommendations and on the other hand on the importance of having recommendations by population (young people, migrants, MSM in particular but also people living with HIV) specifying the infections to look for, the techniques to be used and the frequency of screening. It is this approach that the French Society of Dermatology implemented in its report of February 2016 (16). We take up the main proposals, supplemented and brought into line with, in particular, the recent reassessment of the HAS on HIV screening (10). The box below (Box 2) therefore proposes an approach by population. These recommendations are similar to those issued in the United States (20), England (21) and Australia (22), in particular for MSM. For the latter, Australians very specifically advocate screening for STIs up to four times a year for MSM who have at least one of the following characteristics: unprotected anal intercourse, more than 10 partners in six months, sexual intercourse in group, taking recreational drugs during sex. These recommendations are similar to those issued in the United States (20), England (21) and Australia (22), in particular for MSM. For the latter, Australians very specifically advocate screening for STIs up to four times a year for MSM who have at least one of the following characteristics: unprotected anal intercourse, more than 10 partners in six months, sexual intercourse in group, taking recreational drugs during sex. These recommendations are similar to those issued in the United States (20), England (21) and Australia (22), in particular for MSM. For the latter, Australians very specifically advocate screening for STIs up to four times a year for MSM who have at least one of the following characteristics: unprotected anal intercourse, more than 10 partners in six months, sexual intercourse in group, taking recreational drugs during sex.

A complementary approach to screening for bacterial STIs would be antibacterial prophylaxis. A randomized trial was conducted during the open phase of the ANRS Ipergay trial (23). The intervention evaluated was doxycycline on demand as post-exposure prophylaxis (200 mg single dose) versus placebo. The primary endpoint was the occurrence of a new episode of gonorrhea, infection with *Chlamydia* or syphilis. After a median follow-up of 8.7 months, the cumulative probability of occurrence of at least one event defining the primary outcome was 22 per 100 person years in the treatment group (N = 116) and 42 per 100 person years in the placebo group (N = 116), i.e. a reduction of 47% (95% confidence interval:

- 15% - -67%) in an intention-to-treat analysis. However, no effect was noted on the incidence of gonorrhea. Conversely, the reduction in incidence reached 70% by intention to treat for infection with *Chlamydia* and syphilis. The side effects were moderate and rare. No behavioral modification of the participants was noted during the trial. Antibiotic resistance data are not yet available and the long-term effects are not known. Although we have a good level of evidence after this first randomized trial, the development of a research program on the subject is necessary before formulating public health recommendations. The expert group advocates the construction of such a research program without delay. This program should also focus on tools for the rapid diagnosis of STIs (point of care).

Box 3

Proposal for a screening strategy for sexually transmitted infections
transmissible diseases (STIs) by population *

Adapted from the recommendations of the French Society of Dermatology (16) and HAS (17, 18, 19)

General population *

- Joint HIV-HBV-HCV testing at least once during life HIV testing at each change of life orientation (including
- multi-partnership) HIV testing when seeking care in the absence of previous screening
-
- HBV screening (HBsAg, anti-HBsAb, anti-HBcab) in the absence of a history of vaccination (prescribe a test for delta virus infection in the event of HBsAg positive)
- HCV screening (anti-HCV Ab) if it has never been performed
- Nucleic Acid Amplification Test (NAAT) for *Chlamydia trachomatis* by vaginal self-sampling in women aged 15 to 25 and in the 1 er urine stream in men from 15 to 30 years old, renewed every year in case of unprotected sex with a new partner; the use of mixed PCR also allows detection of gonococcal infection in this population
- Cervical smear: after two normal smears one year apart, prescribe a smear every three years between 25 and 65 years of age and in the absence of signs or symptoms

Migrants

- In addition to the recommendations for the general population, renew the proposal for coordinated screening at least once a year in the event of risk taking

Sex workers

- In addition to the recommendations for the general population, renew the screening for HIV infection, syphilis and hepatitis B every year (in the absence of vaccination), or even more frequently in the event of risk taking

High risk men who have sex with men and transgender people **

- HIV and HCV serologies at least every three months (HCV RNA if positive serology) Syphilis screening at least once a
- year
- Search for gonococci and *Chlamydia trachomatis* by urine, anal and pharyngeal sampling (due to the high frequency of asymptomatic carriage) every three months (capped support for multi-site screening for these STIs is now a barrier to screening) HBV serologies and VHA followed by vaccination in case of negative serologies.
-

UDI

- HIV and HCV serologies every year (HCV RNA if serology positive)
- HBV serology followed by vaccination in case of negative serology

People living with HIV

- Based on risky behaviors and practices

* Vaccination recommendations are detailed in another section of the chapter
** *Cf.* Box 4, page 25

Condom

The male condom has played a major role in the fight against the HIV epidemic; it remains today an essential tool in the context of diversified prevention, in particular because
that he is the only one to protect against other STIs. **It is therefore necessary to continue to promote it, to facilitate its offer and to allow learning from the start of sexuality.**

The theoretical effectiveness of the male condom is high (98%) but its actual effectiveness varies according to the STI, according to sexual practices and according to whether it is anal or vaginal intercourse. In heterosexual intercourse, the reduction in the risk of HIV infection through consistent condom use is estimated to be 80% [24]. In male homosexual intercourse, the reduction in the risk of HIV infection is estimated, based on a meta-analysis of five cohorts, at 64% [25]. These lower efficiency levels can be explained by the persistence of a certain proportion of incidents by breakage or by slip on a daily basis. In the survey “Context of Sexuality in France” by

2006, 20% of condom users reported breaking or slipping accidents in the past 12 months. This accident rate increased with the number of partners in the year and the number of reports. The lowest rate was reported by male homosexuals (12%) then by heterosexuals (20%); it was much higher among bisexuals (38%). In the 2004 Gay Press survey, 11% of respondents declared condom slips and 13% ruptures. These incidents are not rare according to the available data even if they could be minimized in a context where the condom was the only means of protection available. These factual elements therefore plead for **continue to inform users at a**

good use with particular attention to installation and lubrication. This is all
more important than when used correctly, the condom also protects against other STIs, such as chlamydia, gonorrhea, syphilis or papillomavirus infections [26]. As a contraceptive, the condom is less effective than medical methods. In the COCON survey carried out in France in 2000 with a sample of the general population,

3.3% of women who used it as a method of contraception had a failure in the first year and 12.3% within five years (versus 2.4% and 6.8% for the pill, 1.1 % and 6.8% for the IUD) [27].

This broad protection, its ease of use, its low cost, its good acceptability since the first campaigns against AIDS, make the condom an essential means of prevention for all populations even if strong inequalities are observed as evidenced by the usage indicators reported in detail in the chapter " Epidemiology ". Beyond the declared use data, its appropriation over time is corroborated by the trend in sales of condoms which continued to increase significantly in the 2000s, in particular in supermarkets and pharmacies which remain the most important. two main places of purchase. More than 74 million condoms were sold in 2000 in France and 106 million in 2016 (source: Public Health France), to which must be added online sales, the volume of which remains difficult to assess in the absence of public data. In 2009, the share of online sales was estimated at 5% of the market (or about 5 million condoms) but it is possible that it has increased since. Finally,

The condom is not systematically used beyond the first intercourse during a relationship for reasons of sexual comfort, because it is under the control of one of the partners (of the man in the relations heterosexual) and its image too often associated with multiple or casual relationships. All these elements do not make it possible to achieve sufficient coverage to achieve the objectives of extinguishing the epidemic by 2030 even if the population effect is significant. In England, Phillips estimated, by modeling, that if condom use had stopped in 2000, the incidence of HIV infection would have increased fivefold (+ 424%) between 2001 and 2006 compared to to what has been observed [28]. In this modeling, the “repeated test and immediate treatment” strategy,

As PrEP is reserved for the prevention of HIV alone and, according to current recommendations for individuals and populations most exposed to it (see section PrEP), **the condom is the only one**
a means of prevention of HIV and other STIs that is available to all, men and women, in relationships between men and in heterosexual relationships. It is
therefore essential that each person can obtain it, know how to propose it and use it, and especially

sees its use accepted by its partners. The promotion of condoms therefore remains absolutely topical with the need for renewed content in view of the extent of the protection it provides, its complementarity with other methods of preventing HIV transmission, and respect for the autonomy of each in the choice of prevention and an offer that more adequately meets diversified needs.

In the condom promotion strategy, increased attention should be paid to user demands for better quality and greater sexual comfort. The complaint of discomfort is fueled by the uniformity of the free offer, particularly in places of gay conviviality, despite the very good quality of the condoms routinely distributed in standard and large sizes. If the offer supported by the public authorities or the purchasing centers can be improved, it will remain limited due not only to budgetary restrictions but also to the purchasing rules of public establishments. Adjustment to needs can therefore only be based on individual choices and purchases. The existence of new products offering a good diversity of sizes, materials, textures and thicknesses should favor these adjustments. The promotion of condoms must present the range of products available, their cost and the value of individual choice, and be accompanied by negotiations with manufacturers and distributors to improve physical distribution and online purchase.

The promotion of condoms is particularly necessary in the MSM population at high risk of HIV and other STIs. This population should also benefit from a real offer in terms of STI screening, as developed previously (Box 2). In France, with only 5,352 people on PrEP as of July 31, 2017, 97.5% of whom are men, maintaining condom acceptance and accessibility remain decisive. In the heterosexual population, the adoption of the condom was done mainly by the young people who for many years associated the condom with protection against AIDS. They use it in a very large way during the first relationships but in 2010 pointed to a questioning of the effectiveness of the latter [29].

HIV prevention is diversifying, **it is necessary to ensure, among young people, knowledge of the condom, its preventive qualities, as well as their ability to use it.**

Sex workers do not ask for a questioning of regular condom use with the onset of PrEP. This is what the associations which deploy support and prevention strategies for these particularly exposed populations in France are reporting. Sex workers continue to need a strong collective standard on condoms and a comprehensive approach to sexual and reproductive health that matches their living conditions and access to care. But the use of condoms by sex workers is today weakened by structural factors such as the regulation of foreigners and its application, the penalization of clients, the diversification of forms of prostitution as well as the growing intolerance of local residents with regard to prostitution in the public sphere. This context, which also results in the increasing precariousness of the practice of prostitution, undermines the standard of condom use which makes it possible to resist the demand of clients for unprotected sex for a higher price. The promotion and distribution of condoms suitable for sex work therefore remain essential, particularly through associative activity.

Available on the European market since 1991, the female or “internal” condom remains little used. The offer, the price and its distribution are not favorable to its distribution. Imported and marketed by a single company, it is sold on the market at a price of 7 euros per box of three; in practice, it is still not readily available and hardly visible in pharmacies and shops. The internal condom is mainly distributed free of charge by Public Health France, via associations and family planning centers. This distribution has tended to decline in recent years; less than 500,000 internal condoms were distributed in 2017. Knowledge and use of internal condoms can be determined by surveys conducted among the general population. The data is however quite old, these questions have not been systematically included in the latest editions of these surveys. In 2004, 78% of respondents in France and 85% in TFAs knew about the internal condom (30). This knowledge obeyed the same criteria (age, level of education, importance of religion, use of male condoms) as those which govern attitudes towards condoms in general. At this date, the reported use ranged from 2 to 4%. On the other hand, it increased in the West Indies and Guyana between 2004 and 2011 where, according to the latest KABP survey [31], 13% of men and 8% of women declared having already used an internal condom. These percentages were higher in Guyana than in the other two TFAs,

Medicalized male circumcision

Voluntary and medicalized adult male circumcision has proven its effectiveness as part of a diversified prevention strategy in the most affected countries of Southern and Eastern Africa and in populations where it was not. practiced for religious or cultural reasons. This preventive measure has no place in the public health strategies of countries like France.

Antiretroviral therapy

The main goal of antiretroviral therapy is to reduce the amount of virus in the body, measured in practice by the plasma viral load, with a view to maintaining or restoring the immune system. In most patients, antiretroviral therapy lowers the plasma viral load to an undetectable level, that is, the amount of HIV in the blood has reached a level below the threshold of 50 copies / ml of virological tests. Achieving and maintaining an undetectable viral load is essential for reducing the risk of HIV / AIDS-related morbidity and mortality for people living with HIV, but also for preventing transmission of the virus to others. We then speak of treatment as a prevention tool, or “Treatment as Prevention” or TasP.

Effectiveness of antiretroviral therapy in reducing transmission

In heterosexual couples

Seven observational studies (32-38) and one clinical trial (39-41) evaluated the effectiveness of antiretroviral therapy in reducing HIV transmission in heterosexual serodiscordant couples. In these studies, HIV-positive partners received comprehensive care, including support for adherence and treatment of STIs, as well as regular monitoring, every three to six months, of plasma viral load. . In four observational studies (32-35), HIV incidence rates in couples where the HIV-positive partner was on antiretroviral therapy were compared to HIV incidence rates in couples where the HIV-positive partner was not receiving antiretroviral therapy. no such treatment. These studies have shown that antiretroviral therapy can reduce the incidence rate of HIV from 81% to 92%. These results were confirmed by the HPTN 052 clinical trial, conducted in 1,763 couples, followed on a median of 5.5 years, which showed that antiretroviral therapy reduced the incidence rate of HIV by 93% (CI: 78 -

98) (39-41). In observational studies and in the HPTN 052 trial, a total of 261 transmissions definitively linked to the HIV-positive partner were reported during follow-up: 248 transmissions occurred when the HIV-positive partner did not receive antiretroviral therapy over a follow-up period. of 10,519 person-years and 13 when the HIV-positive partner was on treatment over a follow-up time of 8,605 person-years (Table 1). Eight of these 13 transmissions occurred when the HIV-positive partner had been on antiretroviral therapy for less than six months, and therefore potentially before the plasma viral load became undetectable. Four other transmissions occurred after six months of antiretroviral treatment, in a situation of treatment failure. The last case of transmission, observed in the study conducted by Apondi (36), occurred during the first 12 months of treatment. The data from the latter study cannot determine whether transmission occurred before or after the partner's viral load became undetectable, or whether transmission occurred before or after the first six months of antiretroviral therapy.

In male couples

Two observational studies evaluated the effectiveness of antiretroviral therapy in male couples (Table 1); in these studies there was no control group, ie couples where the HIV-positive partner was not treated. In the Partner study (38), conducted in 340 male couples, no transmission occurred when the HIV-positive partner was on antiretroviral therapy and had an undetectable viral load. In the Opposites Attract study (42, 43), conducted in 152 male couples, no transmission occurred while the HIV-positive partner was on treatment. These two studies are still ongoing. There was therefore no transmission of HIV observed in these two studies. In all the scientific literature we can find in 2002 a case of possible transmission of HIV,

was on antiretroviral therapy with an undetectable viral load (44). The description of this case is, however, retrospective. This was neither a population-based observational study nor a trial.

Periods of risk for HIV transmission when initiating antiretroviral therapy

From this set of studies, three periods of decreasing levels of HIV transmission to the partner can be identified when the HIV-positive partner initiates antiretroviral therapy (Table 1): (i) six months after initiation of treatment and before that the plasma viral load has become undetectable; (ii) beyond six months after initiation of treatment and as long as the plasma viral load has not become undetectable; (iii) after treatment failure.

Table 1: Observational studies and clinical trial evaluating the impact of antiretroviral therapy (ART) on the risk of HIV transmission in serodiscordant heterosexual couples (A) and men (B).

1 er author, year publication (reference)	Number of couples	HIV positive partner not on ART		HIV positive partner on TARV		HIV positive partner on ART for> 6 months and / or with an undetectable viral load	
		Time to followed (people-years)	Number of transmissions (people-years)	Time to followed (people-years)	Number of sexual transmissions not	Number of	Number valued acts protected by a condom**
(AT)							
Melo, 2008 (32)	93	106	6	90	0	0	8,329
Del Romero, 2010 (33)	648	863	5	417	0	0	10 286
Donnell, 2010 (35)	3 381	4,558	102	273	1	0	1,324
Reynolds, 2011 (34)	250	459	42	54	0	0	805
Apondi, 2011 (36)	62	- -	- -	184	1 *	1 *	4 266
Mujugira, 2016 (33)	1,573	2,644	55	168	3	0	2,551
Rodger, 2016 (37)	548	- -	- -	799	0	0	35,940
Cohen, 2016 (39-41)	1,763	1,889	38	6 620	8	0	84,679
Total	**8 338**	**10,519**	**248**	**8,605**	**13**	**1 ***	**148 180**
(B)							
Rodger, 2016 (38)	340	- -	- -	439	0	0	22,273
Grulich, 2015 (42, 43)	152	- -	- -	150	0	0	5,905
Total	**492**	- -	- -	**589**	**0**	**0**	**28 178**

- -: No couple where the HIV-positive partner was on ART

* This case of transmission occurred within 12 months of starting ART, it is not possible from the study data to determine whether transmission occurred before or after the partner's viral load became undetectable, or whether the transmission occurred within the first six months of ART or later

* * For heterosexual couples, estimated numbers include sexual acts where the condom was not used or the condom did not work

Risk of transmission of HIV through sex not protected by a condom on antiretroviral treatment for more than six months and with a controlled viral load

Data from studies can be compiled to estimate and quantify the risk of HIV transmission through unprotected sex when the HIV-positive partner is on antiretroviral therapy (45). In heterosexual couples, when the HIV-positive partner had been on treatment for more than six months and had a controlled viral load, at most one case of HIV transmission was documented during 148,180 sex acts not protected by a condom (Table 1). These

data allow us to estimate that **the risk of HIV transmission during sex without condom protection with an HIV-positive partner on antiretroviral therapy for more than six months ranges from zero to a maximum of one transmission per 38,500**

unprotected sex acts by a condom (Supervie V, Brebant R. Personal communication).

In male couples, when the HIV-positive partner was on antiretroviral therapy and had a controlled viral load, no transmission occurred after 28,178 sexual acts
not protected by a condom (Table 1). **These data allow us to estimate that the risk of transmission of HIV during a sexual act not protected by a condom with an HIV-positive partner on ART for more than six months is between zero and a maximum of one transmission for 7600 sexual acts. unprotected** by a condom (Supervie

V, Brebant R. Personal communication).

Communicate on the effectiveness of antiretroviral therapy as a highly effective HIV prevention tool

The data summarized here clearly show that when the HIV-positive partner has been on antiretroviral treatment for more than six months, has an undetectable viral load and benefits from regular and comprehensive clinical monitoring (support for compliance, detection and treatment of STIs), the risk of HIV transmission under treatment is negligible for heterosexual couples as well as for male couples. As with any other health risk, it is not possible to conclude that this

risk is zero (46). **This information on a risk that has become negligible must be widely disseminated, not only to people living with HIV but also to the general public.** The
clinicians have a key role in disseminating this information to patients and their partners. Communication around these data has indeed become essential to make a significant contribution to the quality of life of people living with HIV (quality of sexual life, adherence to treatment, discussion around HIV, fear of transmitting HIV) but also to facilitate procreation and finally to reduce the stigmatization of people living with HIV.

The impact of antiretroviral therapy on the epidemic

Several studies using mathematical models (47, 48) have shown that the large-scale and early use of antiretroviral therapy could have a considerable impact on the transmission of HIV in the population, if people infected with HIV have access to treatment. within one year of becoming infected with HIV. In France (*Cf.* chapter "Epidemiology"), the median time from HIV infection to HIV diagnosis is 3.2 years. Once screening has been carried out, the median time between diagnosis and entry into care is less than one month and the median time between entry into care and starting antiretroviral treatment is around one month. **It is therefore the time between infection**

and diagnosis of HIV which delays the initiation of antiretroviral treatment and does not reduce the number of new infections in France, especially among MSM, key population
where HIV transmission remains high. The first randomized trial to introduce the “repeated test and immediate treatment” strategy in South Africa, a highly endemic country, failed to measure a decrease in incidence at the population level (49) . This is partly explained by the difficulties in bringing screened people into care and also by the high mobility of populations in the region studied. These results do not call into question the principle of the TasP approach.

Pre-exposure prophylaxis

Place of PrEP in diversified prevention

PrEP involves the use of antiretroviral drugs to prevent the acquisition of HIV in uninfected people. Several clinical trials of oral PrEP have shown efficacy between 44% and 86% in reducing the incidence of HIV in key high incidence populations (Table 2) (50). Based on these data from randomized trials, PrEP is set to become in most countries a pillar of the preventive arsenal in key populations in complementarity with other existing tools and strategies.

Thus, after the success of the ANRS IPERGAY trial conducted in France (51), the health authorities quickly decided to make PrEP available through a Temporary Recommendation for Use (RTU) for the tenofovir disporoxil fumarate (DF) / emtricitabine for this indication from January 2016 to February 2017. From March 2017, the Marketing Authorization (AMM) of this association for the prevention of HIV through a daily intake for MSM made it the reference framework for prescribing PrEP in France with full reimbursement of the drug.

The first 18-month post-trial follow-up data from the IPERGAY cohort confirm the excellent efficacy of on-demand PrEP in MSM, estimated at 97% (52). The national medico-administrative databases of the National Health Insurance Inter-Regime Information System (SNIIRAM) recently made it possible to describe the conditions of use of PrEP from 1 er January 2016 to July 31, 2017, or 5,352 people (97.5% men) who initiated this combination of antiretroviral drugs for preventive purposes (53). The increase in new prescriptions is regular but moderate and the characteristics of people exposed and initiating PrEP changed little between the period of RTU and the first months of MAID. At this stage, less than one in six MSM at high risk of acquiring HIV through sexual intercourse has therefore initiated PrEP in France if the target population is estimated at 32,000.

There are currently no data in humans on the use of the tenofovir alafenamide / emtricitabine combination in PrEP, but studies are ongoing.

Table 2: Main PrEP Trials (50)

Population	Testing	Reduction of the incidence HIV	Antiretroviral Administration mode
MSM / Transgender	- iPrEX - PROUD - IPERGAY	44% 86% 86%	TDF / FTC oral daily TDF / FTC oral daily TDF / FTC oral on demand
Men and women heterosexual	- Partners PrEP - TDF 2	63 - 75% 62%	Daily oral TDF Daily oral TDF / FTC
Women	- CAPRISA - FACTS - FEM-PREP - VOICE	39% 0% 6% - 49% -15%	TDF gel on demand TDF gel on demand TDF / FTC oral daily TDF oral / gel daily
Injection drug users - BTS		49%	Daily oral TDF

MSM: men who have sex with men; FTC: emtricitabine; TDF: tenofovir disoproxyl fumarat

Medico-economic considerations

The results of existing medico-economic studies show the cost-effectiveness of PrEP in the MSM and IDU population at high risk of HIV infection (Table 3). In France, the results of the medico-economic study associated with the IPERGAY trial show that PrEP in MSM at high risk of infection has a cost-effectiveness ratio of € 75,258 per infection avoided (54). For the IDU population, existing studies highlight more contrasting results, with PrEP being cost-effective in only one of the three available studies. The cost-effectiveness ratios obtained in the various studies appear sensitive to the incidence / prevalence of HIV in the target population, the effectiveness of PrEP and the cost of PrEP. In these studies,

The placing on the market of the generic tenofovirDF / emtricitabine since July 2017 has led to a significant reduction in the cost of treatment (from € 346 per month to € 176 / city public price including tax in March 2018) and substantially modifies the results of cost analyzes. -effectiveness of PrEP, in particular in France: the cost-effectiveness of PrEP is clearly reinforced in MSM at high risk of infection since the ratio per infection avoided drops to € 39,970 (54) and the gain compared to the cost of annual management of a case of HIV infection is substantial. Thus, PrEP is likely to become rapidly cost-effective in IDUs and in MSM at lower risk of infection.

Table 3. Medico-economic studies on PrEP

Country	Modality	Efficiency of an annual cost load under Prep	Annual cost of PrEP	Results	Source
MSM					
France	To the request	86%	€ 4,812	€ 3,129	MSM at high risk of infection [1]: € 75,258 / infection avoided	Durand-Zaleski, 2018
Canada Daily		44%	-	CAD $ 10,012	25 to 100% of MSM: CAD $ 500,000 - 800,000 / QALY 25 to 100% of the 10% of MSM most at risk of infection [2]: CAD $ 35,000 - 70,000 / QALY	McFadden, 2016
Netherlands	Daily To the request	80%	Daily : € 7,400 On demand: 3 850 €	-	10% of MSM most at risk infection [3]: Daily PrEP: € 11,000 / QALY PrEP on demand: € 2,000 / QALY	Nichols, 2016
United States	Daily To the request	58%	Daily : $ 8,700 On demand: 5 $ 900	-	50% of MSM: US $ 1,474,000 / QALY MSM at high risk of infection US $ 45,000 / QALY	Ross, 2016
USA Daily		44%	-	$ 9,312	10% of MSM most at risk infection [4]: US $ 27,863-37,181 / QALY	Drabo, 2016
Canada	To the request	44%	12 001 CAD $	CAD $ 9,505	MSM at high risk of infection [5]: CAD $ 46,000 to 59,000 / QALY	Ouellet, 2015
USA Daily		44%	$ 9,762	-	50% of MSM: $ 1,600,000 / infection averted 50% of high risk MSM infection [6]: $ 1,100,000 / infection averted	Kessler, 2014
Australia Daily		40%	$ 10,362	$ 9,597	10 to 30% of MSM: > AUS $ 400,000 / QALY 15 to 30% of MSM with more than 10 partners: AUS $ 110,000 / QALY 25 to 30% of MSM in a relationship serodifferent: AUS $ 8,399 - 11,575 / QALY	Schneider, 2014
USA Daily		44%	$ 10,331	$ 9,312	All MSM: US $ 160,000 / QALY	Chen, 2014
USA Daily		44%	-	$ 9,312	All MSM: 216,480 US $ / QALY 20% of MSM: 172,091 US $ / QALY MSM with more than 5 partners / year: US $ 52,443 / QALY	Juusola, 2012
USA Daily 44 - 73% USA Daily			-	$ 8,030	All MSM: US $ 353,739 - 570,273 / QALY	Koppenhaver, 2011
		50%	$ 9,024	$ 8,688	MSM at high risk of infection: [7] $ 298,000 / QALY	Paltiel, 2009
USA Daily		50%	$ 11,740	$ 10,683	25% of high risk MSM infection [8]: $ 31,970 / QALY	Desai, 2008
UDI					
USA Daily		48.9%	US $ 10,800	$ 10,000	25% of IDUs: $ 253,000 / QALY	Bernard, 2016
USA Daily		44%	US $ 9,762	-	50% of IDUs: $ 9,000,000 / infection averted	Kessler, 2014
Ukraine Daily		49%	US $ 950	US $ 450	25 to 50% of IDUs: $ 1,379-1,410 / QALY	Alistar, 2014

[1] Unprotected sex with at least 2 partners in the last 6 months
[2] 36 partners in the last 12 months
[3] More than 5 new partners / year
[4] 12% of MSM have the most unprotected sex
[5] On average 8 partners in the last 2 months
[6] IDU, multiple and parallel partnerships
[7] 1.6% annual incidence
[8] Unprotected intercourse with an HIV-positive partner, priced sex,> 5 partners, to - 1 IDU partner, STI diagnosis

Prescription indications and contraindications

PrEP is recommended for people at high risk. The MA for the tenofovirDF / emtricitabine combination in PrEP specifies the factors that make it possible to identify high-risk subjects (Box 4).

MSM and transgender people: Beyond these factors, given the prevalence and high incidence in MSM and transgender populations and the generally long time between contamination and diagnosis, the expert group considers that **any uninfected MSM or transgender person by HIV is potentially eligible for PrEP. Serodifferent couples:**

- **When the HIV-positive partner is taking antiretroviral therapy and has had an undetectable viral load for more than six months, treatment is the first line of prevention.**

- **In other situations, prescribing PrEP may be considered.**

- The chapter " Desire to have a child and pregnancy Specifies the use of PrEP in the context of the desire for conception.

Individual situations: The expert group recommends, as in the 2015 update of the report (3), that PrEP can be offered on a case-by-case basis to the following people: intravenous drug users with shared needles, people in prostitution and exposed to sexual relations unprotected, vulnerable person exposed to unprotected sex at high risk of HIV transmission.

Adolescents: Adolescents at high risk of acquiring HIV through sexual intercourse should have access to PrEP, especially in CeGIDDs. This recommendation is consistent with
the extension of indication formulated on December 14, 2017 by the European Medicines Agency (55).

PrEP is contraindicated in the following situations:

- HIV seropositive or unknown HIV serology;
- presence of signs or symptoms of acute HIV infection (*Cf.* Box 5);
- renal disorders characterized by creatinine clearance <60 ml / min or signs of tubulopathy;

- feeding with milk ;
- hypersensitivity to any of the active ingredients or excipients of the product.

Box 4

Factors used to identify subjects at high risk of acquiring HIV-1

*Source: ATU / AMM Prescriber Brochure **

The following criteria can help identify high risk individuals:

• Man who has sex with transgender men or people AND at least one of the following criteria:

- Unprotected anal sex with at least 2 different sexual partners in the last six months;

- Episodes of sexually transmitted infections (STIs) in the last 12 months (syphilis, gonorrhea, infection with *Chlamydia,* primary hepatitis B or hepatitis C infection);

- Several use of post-exposure prophylaxis (PEP) in the last 12 months;

- Use of psychoactive drugs (cocaine, GHB, MDMA, mephedrone) during sexual intercourse (*Cf.* other section of this same chapter).

• **Other people at high risk of acquiring HIV infection in whom PrEP may be considered on a case-by-case basis:**

- Subject in a situation of prostitution subjected to unprotected sex;

- Subject in a vulnerable situation exposing to unprotected sex with people belonging to a group with high HIV prevalence:

• Subject from a region with a high prevalence of HIV

• Subject having multiple sexual partners

• Subject injecting drug users

- Subject having unprotected sex with people having physical factors increasing the risk of transmission of HIV infection in the exposed person: genital or anal ulceration, associated STI, bleeding;

- Another situation considered to be high risk of acquiring HIV through sexual intercourse.

* Source: http://ansm.sante.fr/S-informer/Points-d-information-Points-d-information/Prophylaxie-pre-exposition-au-VIH-l-ANSM-reminds-additional-measures-of- risk-reduction-information-Point (accessed January 1, 2018)

Box 5

Symptoms suggestive of a recent infection

*Source: ATU / AMM Patient Brochure **

- Tired
- fever
- Joint pain or stiffness
- Headache
- Vomiting or diarrhea
- Skin rash
- Night sweats
- Swollen lymph nodes in the neck or groin

* Source: http://ansm.sante.fr/S-informer/Points-d-information-Points-d-information/Prophylaxie-pre-exposition-au-VIH-l-ANSM-reminds-additional-measures-of- risk-reduction-information-Point (consulted on 1er January 2018)

Methods of administration, monitoring and support for PrEP users

Prescription

Initiation and termination

Although different active ingredients and administration methods have been tested or are in the process of being tested, continuous daily intake of one tenofovirDF / emtricitabine tablet

is the only PrEP strategy recommended in the Marketing Authorization. However, the Haute Autorité de Santé authorizes administration on demand according to the outline of the IPERGAY study (56), in line with European recommendations (57). The preventive activity is *a priori* related to the concentration of tenofovirDF / emtricitabine in peripheral blood mononuclear cells, in mucous membranes or both.

The current recommendation in view of the still relatively incomplete data is to wait seven days after the first intake for a risky report. Optimal protective activity is in fact reached after seven days of taking in MSM and transgender people having anal sex and after 21 days in women, periods corresponding to the time periods for reaching the maximum concentration in the exposed mucous membranes.

In MSM, the ANRS IPERGAY trial demonstrated the effectiveness of discontinuous (or on-demand) intake of PrEP in reducing the risk of contracting HIV (51). This regimen included two tenofovirDF / emtricitabine tablets taken between 24 hours and two hours before intercourse, then one tablet 24 hours and another 48 hours after taking before intercourse (or one continuous daily dose if intercourse took place before intercourse. additional take following the act). This discontinuous regimen has shown its effectiveness not only in the masked phase of the study (51) but also in the open-label phase with a follow-up of nearly two years (52). RTU data from nearly 3,000 people who are predominantly MSM indicate that on-demand PrEP is the majority (57%),

The presence of an HBV or HCV infection requires consultation in the SPC prior to the initiation of PrEP. PrEP on demand remains contraindicated in people with HBV infection.

No trial of a discontinuous PrEP regimen has yet been conducted in heterosexual women and men.

Too **in the current state of knowledge, discontinuous PrEP cannot be recommended to populations at risk other than MSM (adults and adolescents).**

In men and transgender people, the initiation methods are therefore different depending on whether the administration schedule is continuous (one tablet per day for seven days) or discontinuous (two tablets at least two hours before). The deadlines for achieving preventive efficacy are also different between the continuous scheme and the on-demand scheme and therefore difficult to comply with in practice.

Finally, with regard to stopping the continuous regimen, in the absence of new evidence, the group of experts aligns with the American and European recommendations, namely a treatment of 28 days after the last sexual intercourse. as for post-exposure treatment.

Finally, **the expert group recommends continuing research aimed at improving knowledge of intake patterns.**

First consultation

A person requesting PrEP or referred to PrEP should be able to come to the first consultation with a complete biological assessment. This makes it possible to reduce the burden of services initiating PrEP and thereby reducing the time taken to access and initiate PrEP. This makes it easier to take charge of STI treatment straight away and supplement vaccinations if necessary.

The standard laboratory work-up should include tests for HIV, HAV, HBV, HCV and other STIs as well as monitoring of renal function (*Cf.* Table 4).

Table 4

Laboratory tests to be performed before the initiation of PrEP and during follow-up

*Source: ATU / AMM Prescriber Checklist **

Biological examinations	Before initiation of PrEP	Under follow-up, 1 month after initiation, then every 3 months minimum
Creatinine	X	X †
Estimated creatinine clearance	X	X †
HIV serology (Test 4 e generation antigen / antibody)	X	X
HAV serology	X	£
HBV serology	X	£
HCV serology	X	£
STI screening $	X	£
Finding a pregnancy	X	X

* Source: http://ansm.sante.fr/S-informer/Points-d-information-Points-d-information/Prophylaxie-pre-exposition-au-VIH-l-ANSM-reminds-additional-measures-of- risk-reduction-Information-Point (accessed January 1, 2018)

† Follow-up of renal function after 2 to 4 weeks of treatment, at 3 months of treatment and every 3 months thereafter; the frequency of renal function monitoring should be increased in people with risk factors for impaired renal function.

£ Test to be performed once a year or in the event of clinical indication

$ gonococcal infection, chlamydia, syphilis, HPV to look for even in the absence of symptoms (*Cf.* Box 3)

The first consultation should be the occasion for a counseling interview aimed at clarifying the motivations for entering a PrEP system and recalling the risk reduction strategies that have been proven. The questioning and examination look for any clinical signs of a primary infection or an already established and recent infection (Box 5) and make it possible to identify the use of contraindicated drugs or oral contraception.

AT the outcome of this first consultation, the practitioner establishes the prescription of tenofovirDF / emtricitabine for four weeks and decides on the management of STIs and the necessary vaccinations according to the screening laboratory workup.

Second consultation

A second consultation four weeks later should make it possible to draw conclusions on the tolerance of PrEP, to understand the drug regimen used and above all to verify by a second HIV test that the patient was not in primary infection at the time of the prescription. initial. At the end of the second consultation, the practitioner will establish the tenofovirDF / Emtricitabine prescription for the following three months.

In view of the first available data on rare cases of seroconversions under PrEP, including a possible case of acquisition of a wild-type virus in a context of good compliance (58), **the**
group of experts recommends prescribing an HIV PCR if there is any doubt of primary infection, symptomatic or not.

Followed

The taking of antiretroviral drugs by HIV-negative people requires regular monitoring to detect early HIV infection which would then require appropriate treatment (*Cf.* chapter "Treatment of HIV-1 infection in adults: Initiation of a first antiretroviral treatment"). A few documented cases have indeed shown the risk of developing resistance mutations in people continuing dual therapy after acquiring an HIV infection (59, 60). This regular follow-up should also be an opportunity for support in sexual health including counseling interviews, a proposal for psycho-social follow-up, reinforced screening for viral hepatitis and other STIs, clinical surveillance.

and quarterly biological (*Cf.* Table 4), with rapid and appropriate management and the possibility of renewal by the general practitioner for whom it is recommended to provide a liaison letter. This requires a strengthening of networks in ambulatory medicine. If the monitoring is carried out in town medicine, an annual hospital consultation remains recommended to possibly adapt the care.

Thus, because PrEP is a comprehensive preventive approach to sexual health, its deployment must be facilitated and encouraged in hospital services, CeGIDDs and in town medicine; training actions must be developed accordingly.

Close follow-up (ideally every month) should be implemented in adolescents because of more frequent problems of adherence than in adults (61). This follow-up should also take into account the specific vulnerability of adolescents on the psychological level. When the adolescent wishes to maintain confidentiality regarding this care vis-à-vis his parents, he must be accompanied by an adult referent of his choice. In this situation, apart from free care, it is necessary to ensure the administrative confidentiality of the care.

Community support

Community support is currently offered in some care centers. It consists of proposing a follow-up of the PrEP user, complementary to that carried out by the prescribing physician, by a worker from key population communities or nearby. These can be individual interviews or group discussion times when initiating PrEP and throughout follow-up. The guide is trained in diversified prevention and support techniques (counseling, motivational interviews). This monitoring aims to support the user in his health journey and in particular to reinforce compliance with the treatment as well as with the support system indicated in the context of PrEP.

The IPERGAY trial (51) and the opening of joint consultations between medical actors and associations within the framework of the RTU of the tenofovirDF / Emtricitabine combination for its indication in PrEP have shown the feasibility and interest of coupled medical monitoring community support. Partnerships can thus be established with community-based associations. The AIDES Association has written a guide for PrEP support (62).

Operational research must now aim to optimize the large-scale delivery of PrEP and to measure its impact in key populations, as will be done in Ile-de-France by the ANRS Prévenir study (http://prevenir.anrs.fr).

Prevention of sexually transmitted infections through vaccination

Place of vaccination in the prevention of STIs in people not infected with HIV

Several vaccines have shown their effectiveness in preventing STIs and are recommended in the general population or in targeted populations. Unfortunately, there is growing mistrust of vaccination in France, which results in insufficient coverage for several vaccines, a situation likely to have serious infectious consequences. At the request of the Minister responsible for health, in 2016 a steering committee for citizen consultation on vaccination drew up recommendations for action to remedy this public health problem [63]. The expert group supports all the measures recommended in this report, and more particularly the need to restore confidence through efforts to train health and education professionals as well as through public information and awareness. This report rightly underlines that full coverage by the community of the cost of vaccines and facilitating their availability would directly improve the coverage of vaccination against papillomavirus (HPV). These decisions would mark the commitment of the public authorities to this policy [1]. The emergence of prolonged periods of stock-outs or of supply tensions for essential vaccines is also a worrying phenomenon, which undermines the application of prevention policies in France. This report rightly underlines that full coverage by the community of the cost of vaccines and facilitating their availability would directly improve the coverage of vaccination against papillomavirus (HPV). These decisions would mark the commitment of the public authorities to this policy [1]. The emergence of prolonged periods of stock-outs or of supply tensions for essential vaccines is also a worrying phenomenon, which undermines the application of prevention policies in France. This report rightly underlines that full coverage by the community of the cost of vaccines and facilitating their availability would directly improve the coverage of vaccination against papillomavirus (HPV). These decisions would mark the commitment of the public authorities to this policy [1]. The emergence of prolonged periods of stock-outs or of supply tensions for essential vaccines is also a worrying phenomenon, which undermines the application of prevention policies in France.

In recent years, several opinions emanating from the HCSP relate to the prevention of STIs by vaccination:

- HPV vaccination. Vaccination coverage data indicate that it is low and declining among young girls: in 2015, 13.7% of 16-year-old girls had received three doses of the vaccine, this proportion was 27.1% in ten years. earlier. However, increasing the vaccination coverage of young girls remains the priority for the prevention of diseases linked to HPV infection, in addition to the regular screening of lesions of the cervix by cervico-uterine smear, which remains essential. To this end, access to the HPV vaccine should be systematically offered and available in CeGIDDs and vaccination centers to young women but also to MSM up to the age of 26 years.

- HBV vaccination. In the general population, vaccination coverage against HBV (three doses) in two-year-old children is relatively high in France (87.5% for those born in 2013), and increases over time. This coverage is still insufficient among children aged six (51% in 2012-2013) and among those aged 11 (45.9% in 2014-2015). The following categories are concerned by the general recommendations but are exposed to an increased risk of contamination by HBV which should be remembered: people of both sexes who have sex with multiple partners, IDUs, people who have resided or brought to reside in moderately or highly endemic areas, people close to a person infected with HBV (people living under the same roof, sexual partners), detainees [65]. Vaccination coverage for these populations is not always known, but is generally insufficient. Excluding people not knowing if they had been vaccinated against hepatitis B, the declared vaccination coverage was 62% in 2011-2013 among Parisian IDUs [66] and 71% in 2009 among MSM frequenting places of Parisian gay friendliness (this coverage was no different in the 2011 EPGL survey). Data from the 2016 AfroBarometer Health carried out among the Afro-Caribbean population of Ile-de-France indicate that, out of 1,283 adults who answered the questionnaire, 48% declared that they were vaccinated (e) s against hepatitis B, 29% were not vaccinated and 23% did not know. Excluding people not knowing if they had been vaccinated against hepatitis B, declared vaccination coverage was 62% in 2011-2013 among Parisian IDUs [66] and 71% in 2009 among MSM frequenting places of Parisian gay friendliness (this coverage was no different in the 2011 EPGL survey). Data from the 2016 AfroBarometer Health carried out among the Afro-Caribbean population of Ile-de-France indicate that, out of 1,283 adults who answered the questionnaire, 48% declared that they were vaccinated (e) s against hepatitis B, 29% were not vaccinated and 23% did not know. Excluding people not knowing if they had been vaccinated against hepatitis B, the declared vaccination coverage was 62% in 2011-2013 among Parisian IDUs [66] and 71% in 2009 among MSM frequenting places of Parisian gay friendliness (this coverage was no different in the 2011 EPGL survey). Data from the 2016 AfroBarometer Health carried out among the Afro-Caribbean population of Ile-de-France indicate that, out of 1,283 adults who answered the questionnaire, 48% declared that they were vaccinated (e) s against hepatitis B, 29% were not vaccinated and 23% did not know. the declared vaccination coverage was 62% in 2011-2013 among Parisian IDUs [66] and 71% in 2009 among MSM frequenting gay places of Parisian conviviality (this coverage was not different in the EPGL 2011 survey) . Data from the 2016 AfroBarometer Health carried out among the Afro-Caribbean population of Ile-de-France indicate that, out of 1,283 adults who answered the questionnaire, 48% declared that they were vaccinated (e) s against hepatitis B, 29% were not vaccinated and 23% did not know. the declared vaccination coverage was 62% in 2011-2013 among Parisian IDUs [66] and 71% in 2009 among MSM frequ
- VHA vaccination. Exposed and unimmunized MSM should receive preventive vaccination against HAV. The prior practice of a serology proving their absence of immunization is recommended. This recommendation is all the more important in the context of an upsurge in hepatitis A cases among MSM in several European countries as well as in France since the end of 2016. Vaccination of this target population is a priority and this recommendation remains valid even. in times of shortage of this vaccine [67].

- Vaccination against invasive meningococcal C infections. This vaccine is recommended in children, with catch-up for all those who have not been vaccinated in childhood, up to

the age of 24. Meningococcal C vaccine coverage in the general population is increasing in all age groups, especially among two-year-olds, where it reached 69.8% in 2015. Among 15-19 year-olds, coverage is lower (23.0%). Between 2012 and 2014, several grouped cases of invasive meningococcal C infections were documented in MSM communities in Europe (including France). In 2014, the HCSP issued a recommendation for vaccination with the meningococcal C conjugate vaccine for MSM and other people aged 25 and over who frequent places of gay socializing or meeting or who wish to attend one or more gay gatherings. . The Prévagay survey, carried out at the end of 2015 among HSH frequenting social centers in five metropolitan cities showed that only 19, 2% of them said they were aware of this recommendation. The proportion of vaccinated MSM was low (14.4%), but higher among those declaring to know the recommendation (40.8% versus 8.1%). Epidemiological data on invasive meningococcal C infections that occurred in 2016 do not suggest the persistence of a higher risk among MSM and the recommendation for targeted vaccination in this population was not renewed in 2017. Note that some strains meningococcal C labeled 'MSM variant' have been observed in the male urogenital tract in MSM in France, with clinical manifestations similar to gonococcal infections [68]. but more important among those declaring to know the recommendation (40.8% versus 8.1%). Epidemiological data on invasive meningococcal C infections that occurred in 2016 do not suggest the persistence of a higher risk among MSM and the recommendation for targeted vaccination in this population was not renewed in 2017. Note that some strains meningococcal C labeled 'MSM variant' have been observed in the male urogenital tract in MSM in France, with clinical manifestations similar to gonococcal infections [68]. but more important among those declaring to know the recommendation (40.8% versus 8.1%). Epidemiological data on invasive meningococcal C infections that occurred in 2016 do not suggest the persistence of a higher risk among MSM and the recommendation for targeted vaccination in this population was not renewed in 2017. Note that some strains meningococcal C labeled 'MSM variant' have been observed in the male urogenital tract in MSM in France, with clinical manifestations similar to gonococcal infections [68].

- Research on vaccines against other STIs should be continued and if possible intensified, in particular against gonococcal infections, chlamydia and syphilis.

In people living with HIV

Vaccination recommendations for people living with HIV are detailed in the chapters " Management of children and adolescents infected with HIV "And" Infections in adults: prophylaxis and curative treatments ". The main differences from the recommendations of the general population are:

- Precautions with respect to live attenuated vaccines: BCG formally contraindicated; yellow fever, chickenpox and measles-mumps-rubella possible depending on CD4 (threshold 200 / mm ^{3} from the age of five)

- The systematic recommendation of 'seasonal flu' and 'pneumococcal' vaccines (according to the schedule proposed to immunocompromised: a dose of 13-valent conjugate vaccine followed by a dose of 23-valent polysaccharide vaccine at least two months later)
- A reinforced schedule for the hepatitis B vaccine: three double-dose injections spaced one month apart and 4 ^{e} double dose six months later, with monitoring of the anti-HBs Ab level after vaccination and then every year (booster injection if <10 mIU / mL)

- The need for two doses of hepatitis A vaccine in people living with HIV, as one dose is often insufficient

- The inability to be satisfied with the two-dose regimen for HPV
- The need for boosters every 10 years in adults at all ages for diphtheria, tetanus and polio vaccines.

Post exposure treatment

Post-exposure treatment is an integral part of the diversified prevention strategy promoted by the group of experts and remains **an important prevention tool at the individual level.** A chapter complete is devoted to it in this report (*Cf.* chapter "Management of sexual and blood exposure accidents (BSE) in adults and children").

Drug users and harm reduction

The risk reduction policy, implemented in France between the end of the 1980s and the mid-1990s, had a positive impact on the transmission of the human immunodeficiency virus (HIV) among people who inject themselves. drugs. In 2002, the feasibility phase of the ANRS-Coquelicot study, conducted in Marseille, showed that none of the 166 drug users surveyed under the age of thirty was HIV-positive (69). Another study, carried out in the north-east of France, also observed at this time the absence of HIV contamination in a group of injecting users followed regularly for a year (70). While drug users constitute a population that is currently little discussed in HIV prevention campaigns,

The data collected within the framework of the French HIV surveillance system, as well as those of the latest edition of the ANRS-Coquelicot study, conducted in 2011-2013 show that among drug users who have injected at least once during their lives, the overall prevalence, all cities and departments combined, is 13% for HIV, Marseille and Seine-Saint-Denis having the highest prevalence, mainly due to the presence of older users (71) . In 2012, the incidence of infection among drug users had not decreased compared to 2003. The incidence of new infections among injection drug users reached 86 per 100,000 person-years in 2012, a much higher rate. than among heterosexuals born in France (5/100

000) or abroad (44/100 000) (72). The share of IDUs in all new diagnoses continued to be stable in 2015, at around 2% of the total or an absolute number of 90 infections. Another worrying data from the HIV surveillance system in France, drug users are often diagnosed at an advanced stage of infection (38% of new diagnoses in

2015). The ANRS-Coquelicot survey provides some explanations: in the last edition of the survey, 26% of drug users declared having shared their syringe at least once during the previous month (they were only 13 % in 2004) (73). In 2011-2013, 30% of drug users expressed their difficulties in obtaining syringes, even in large cities such as Paris. Ile-de-France is one of the regions where users are particularly vulnerable, encounter the most difficulties in obtaining syringes and are therefore more particularly exposed to the risk of HIV transmission. The conditions favoring exposure to many infectious diseases, including HIV, are therefore once again present (74). Epidemiology ". In this context, the strengthening of risk reduction policies, promoting improved access to syringes and the establishment of lower-risk consumption rooms, combined with measures allowing access to care and weaning, as well as that improving the social situation for drug users are essential measures in order to act effectively on reducing exposure to the HIV risk among IDUs.

Drug use in a sexual context

The “Recent Trends and New Drugs” (TREND) system of the French Observatory for Drugs and Drug Addiction (OFDT) confirms in its 2015-2016 report (75) an extension and dissemination of the use of psychoactive products in a sexual framework (Chemsex) since the end of the 2000s and more particularly since 2010 among MSM, although it is difficult to measure its extent. In the PREVAGAY 2015 survey conducted in gay social centers in five French cities (76), 36.4% of MSM living with HIV and 18.2% of seronegative MSM declared that they had consumed at least one psychoactive product before or during sexual intercourse in the 12 months preceding the survey.

The use of New Synthetic Products (NPS), involving a significant "craving" (impulse experienced at a given moment, conveying a desire to consume a psychoactive product and its compulsive research) is particularly developed, NPS being consumed alone or combined with other drugs belonging to the class of stimulants (MDMA, cocaine), depressants (GHB) or hallucinogens. Their access has been made easy in recent years by attractive prices, supply directly on the internet or by user-resellers encountered on virtual dredge applications.

Health professionals observe a significant number of psychosocial and somatic consequences characterized by rapid dependence on products and their use in a context

sexual, physical complications up to overdose and death or venous and cardiovascular damage. The prevalence of HIV and some STIs is high among these users as well as an increased incidence of HCV. Among the practices of Chemsex, “slam”, a term used by users to describe the repeated injection of stimulants, is the subject of testimonies or cases reported by practitioners of aggravated health consequences (77). This practice was reported by 0.9% of seronegative MSM and by 5.2% of seropositive in the PREVAGAY 2015 survey (78).

The national sexual health strategy (9) sets the objective, in its measure 58, to "work to reduce the risks and the damages linked to the practices which consist in consuming psychoactive products within the sexual framework (Chemsex) in that" they help maintain the dynamics of the HIV epidemic and increase HCV infections in the MSM population ”.

We recommend the rapid establishment of a multidisciplinary working group bringing together health professionals, public authorities and risk reduction associations in order to strengthen their coordination on Chemsex and promote the emergence of a response adapted to the needs. health of people practicing it.

Conclusion

None of the preventive approaches presented in this chapter are on their own likely to bring down the epidemic in a lasting and significant way to reduce the incidence of new infections by 2020. But their combination is very synergistic, and probably sufficient if their use is carried out at high levels and by adapting it to different geographical, population and epidemiological contexts. Their deployment will probably not be able to take place in France with the required speed without additional resources. Each method must find its place in the individual choices.

The deployment of such a proactive policy in San Francisco, associating an increase in screening and universal treatment with the provision of a PrEP offer and the fight against stigmatization has made it possible to achieve significant results in terms of reducing new diagnoses. HIV (79). More patchy data collected in London indicates a decline in new HIV diagnoses over the past two years among MSM even though PrEP has yet to be introduced as a public health measure (80).

The Paris sans Sida initiative (https://www.paris.fr/parissanssida) and the ANRS PREVENIR research program associated with it will be privileged contexts for measuring the expected changes in France. The regular and rapid use of epidemiological surveillance data (new diagnoses, screening activities, use of the various prevention methods as described and recommended in this chapter) as well as reinforced surveillance of behavior, particularly in key populations will be the parameters. essential to take into account among the multiple monitoring indicators of the national sexual health strategy (9).

Strong points

- The dynamics of the epidemic have changed in France and so have its challenges: Key
  - populations are defined as men who have sex with men (MSM), heterosexual women and men born in sub-Saharan Africa and in French territories of America (TFA) and injection drug users (IDU).

  - The epidemic affects the territories unevenly. The metropolitan regions of Ile-de-France, Provence Alpes Côte d'Azur (PACA), Auvergne Rhône Alpes and TFAs are clearly more affected than the other regions.

- Prevention is defined here as the set of measures for which the right level of scientific proof justifies their application to achieve a maximum effect of reducing HIV transmission at the population level. This prevention is qualified as diversified prevention because it combines structural measures with biomedical and behavioral interventions, knowing that none of them taken in isolation can lead to the expected effect and therefore does not constitute a panacea. The prevention of HIV, viral hepatitis and STIs is based on a base of tools, strategies and diversified resources whose pillars are screening, the use of condoms and biomedical prevention (vaccinations, TPE, PrEP, TasP) .

- The cornerstone of any prevention policy remains screening and knowledge of HIV status.

- Three types of tests are currently available for HIV screening:
  the Elisa and confirmatory serological tests which are carried out in the laboratory, the rapid diagnostic orientation tests (TROD) which can be carried out by a third party who is not necessarily a health professional and the screening self-tests. Their performance is considered globally equivalent for a screening activity, except in the event of recent exposure (<3 months) where the serological tests prove to be more sensitive. Intensifying and increasing coverage of HIV screening, associated with screening for viral hepatitis and STIs, are key elements in improving the cascade of HIV / AIDS care in France.

- Vertical recommendations have been developed by pathogen over fifteen years for the screening of the main STIs: Chlamydia trachomatis infection, syphilis, gonococcal infection.

- TROD syphilis have not yet been validated, not yet making it possible to enrich the supply of combined TRODs.
- A complementary approach to screening for bacterial STIs could be antibacterial prophylaxis, but the available evidence does not allow public health recommendations to be formulated at this time.

- The male condom has played a major role in the fight against the HIV epidemic; it remains today an indispensable tool in the context of

diversified prevention in particular because it is the only one to protect against other STIs. It is therefore necessary to continue to promote it, to facilitate its offer and to allow learning from the start of sexuality.

- The actual effectiveness of condoms is estimated at 80% in heterosexual intercourse and 64% in homosexual male intercourse. Condom incidents are not uncommon according to the available data.

- Medicalized male circumcision is a preventive measure of proven effectiveness but which has no place in the public health strategies of countries like France.

- Achieving and maintaining an undetectable viral load with antiretroviral therapy is essential in reducing the risk of HIV / AIDS-related morbidity and mortality in people infected with HIV, but also in preventing transmission of the virus to others. . We then speak of prevention by treatment, from the English “Treatment as Prevention” or TasP.

- Three periods of decreasing levels of HIV transmission to the partner can be identified when the HIV-positive partner initiates antiretroviral therapy: (i) six months after initiation of treatment and before the plasma viral load becomes undetectable; (ii) beyond six months after initiation of treatment and as long as the plasma viral load has not become undetectable; (iii) after treatment failure.

- It is the time between infection and diagnosis of HIV that delays the initiation of antiretroviral treatment and does not make it possible to reduce the number of new infections in France, especially among MSM, a key population where HIV transmission remains high.

- Pre-exposure prophylaxis (PrEP) consists of the use of antiretroviral drugs to prevent the acquisition of HIV in uninfected people. Several clinical trials have shown efficacy between 44% and 86% in reducing the incidence of HIV in key populations with high incidence. Based on this data

  Resulting from randomized trials, PrEP aims to become a pillar of the preventive arsenal in key populations in complementarity with other existing tools and strategies.

- Discontinuous PrEP cannot be recommended to populations at risk other than MSM in the current state of knowledge.
- The results of existing medico-economic studies show the cost-effectiveness of PrEP in the MSM and IDU population at high risk of HIV infection. The marketing of the generic tenofovirDF / emtricitabine since July 2017 has significantly reduced the cost of treatment and improved the cost-effectiveness of PrEP in France.

- **In France, there is growing mistrust of vaccination, which results in insufficient coverage for several vaccines, a situation likely to have serious infectious consequences.**

- **The emergence of prolonged periods of stock-outs or of supply tensions for vaccines such as the hepatitis A vaccine is also a worrying phenomenon, which undermines the application of prevention policies in France.**

- **While drug users constitute a population that is not currently talked about in HIV prevention campaigns, recent indicators show that the situation of IDUs vis-à-vis HIV remains worrying and that vigilance needs to be maintained. .**

- **An extension and spread of the use of psychoactive products in a sexual context (Chemsex) has been observed more particularly since 2010 among MSM, although it is difficult to measure the extent. Health professionals observe a significant number of psychosocial and somatic consequences, including for the transmission of HIV and HCV.**

The expert group recommends

A comprehensive approach to sexual health

The combination of the preventive approaches presented in this chapter into a comprehensive sexual health approach is very synergistic, and probably sufficient to bring the epidemic back in a lasting and meaningful way by 2020.

Their use must be done at high levels and in a manner adapted to the different geographical, population and epidemiological contexts.

Their deployment will probably not be able to take place in France with the required speed without additional resources.

In terms of screening

The 2017 HAS report on the reassessment of the HIV infection screening strategy is a reference framework which is supplemented and clarified here:

The frequency of HIV testing of key populations must be increased in a sustainable manner:

- screening at least once a year among MSM, reconciled every three months among those at high risk of exposure and in the most affected regions;

- screening every year for IDUs and for people from high prevalence countries (targeting on behavioral criteria).

In practice, any screening opportunity should be encouraged among these groups regardless of the screening technique used and if possible by combining HIV, HBV and HCV. Strategies must be adapted locally according to regions and populations.

The proposal for HIV testing in the general population at least once in life between the ages of 15 and 70 must be maintained.

The three screening methods (by a health professional, an association or at the initiative of the individual himself) are complementary and should all be encouraged. Screening is therefore always part of a diversified preventive offer.

For infections with hepatitis B and C viruses, the three main recommendations are:

The pursuit of a strategy of targeted screening in people presenting one or more risk factors for contamination (except for hepatitis B in the event of knowledge of a positive anti-HBs serological status synonymous with protection): MSM, IDU, prison environment, migrants and foreigners born in highly endemic countries;

The extension of screening strategies in the general population at least once in life to all adults of both sexes who have never been screened;

The association in all cases of the research of the three viruses VHB, VHC and HIV (except for hepatitis B in the event of knowledge of a positive anti-HBs serological status synonymous with protection).

In terms of STIs, it is necessary to update the oldest screening recommendations as soon as possible and also to present recommendations by population (young people, migrants, MSM in particular) specifying the infections to be sought, the techniques to be preferred and the frequency of screening. The expert group adopted the main recommendations made in 2016 by the Société Française de Dermatologie by proposing for the first time an approach by population (see Box 3).

The free information, screening and diagnostic centers (CeGIDD) must establish priorities to produce the best possible range of services in relation to the new screening objectives appearing in the reference texts.

The complementarity of medical actors (city, CeGIDD and hospital) and associations must be encouraged and facilitated as well as the use of self-tests and the latest generation of screening and diagnostic tools to reduce the time between infections, their diagnosis and their treatment (4th generation TROD, PCR),

The development of a research program on antibacterial prophylaxis of IST is required before the formulation of public health recommendations. This program should also focus on tools for the rapid diagnosis of STIs.

Condom

The high level of protection, its ease of use, its low cost and its good acceptability make condoms an essential means of prevention for all populations. The condom remains the only means of preventing HIV and other STIs (chlamydia, gonorrhea, syphilis, papillomavirus infections) that is available to everyone, men and women, in relationships between men and in heterosexual relationships.

Informing users of proper use must be continued with particular attention to installation and lubrication. In the condom promotion strategy, increased attention should be paid to user demands for better quality and greater sexual comfort.

At a time when information on HIV is less present in the public space and HIV prevention methods are diversifying, it is necessary to ensure, among young people, knowledge of the condom, its preventive qualities, as well as their ability to use it.

The promotion and distribution of condoms suitable for sex work remain essential, in particular through associative activity.

Antiretroviral therapy

When the HIV-positive partner has been on antiretroviral therapy for more than six months, has an undetectable viral load and benefits from regular and comprehensive clinical monitoring (support for adherence, detection and treatment of STIs), the risk of HIV transmission under treatment is negligible between

male heterosexual or homosexual partners. As with any other health risk, it is not possible to conclude that this risk is zero. This information on a risk that has become negligible must be widely disseminated, not only to people living with HIV but also to the general public. Clinicians have a key role in disseminating this information to patients and their partners.

Pre-exposure prophylaxis (PrEP)

Anyone who is MSM or transgender who is not infected with HIV is potentially eligible for PrEP. Users of key populations must benefit from updated and intensified information.

In serodiscordant couples, in which the HIV-positive partner taking antiretroviral therapy has had an undetectable viral load for more than six months, treatment is the first line of prevention. In all other situations, prescribing PrEP may be considered.

Adolescents at high risk of acquiring HIV through sexual intercourse should have access to PrEP, especially in CeGIDDs.

PrEP is contraindicated in the following situations:

- HIV seropositivity or unknown HIV serology;
- presence of signs or symptoms of acute HIV infection;
- renal disorders characterized by creatinine clearance <60 ml / min;
- feeding with milk ;
- hypersensitivity to one of the active ingredients or excipients of the product.

Discontinuous PrEP cannot be recommended to populations at risk other than MSM in the current state of knowledge. Discontinued PrEP remains contraindicated in people infected with HBV.

A person requesting PrEP or referred to PrEP should be able to come to the first consultation with a complete biological assessment. The standard laboratory work-up must include screening for HIV, HAV, HBV, HCV and other STIs as well as a check of renal function. An HIV PCR must be prescribed if there is any doubt of primary infection, symptomatic or not.

The implementation of PrEP must be accompanied by regular medical monitoring (screening, biological monitoring) and, as far as possible, associative to support compliance with the device and information for the user.

Because PrEP must be part of a comprehensive preventive approach to sexual health, its deployment must be facilitated and encouraged in hospital services, CeGIDDs and in town medicine; training actions must be developed accordingly.

Operational research should now aim to optimize the large-scale delivery of PrEP and measure its impact in key populations such as

go the to do in Ile-de-France study ANRS Prevent (http://prevenir.anrs.fr/).

Research aimed at improving knowledge of intake patterns should be continued, especially among women.

Prevention of sexually transmitted infections through vaccination

Confidence in immunization must be restored through efforts to train health and education professionals as well as through public information and awareness.

Full coverage by the community of the cost of vaccines and facilitating their availability would directly improve vaccination coverage for vaccines such as that against papillomavirus (HPV).

Several STIs of public health importance can be prevented by vaccination in people not infected with HIV and the specific recommendations of the High Council of Public Health must be followed: HPV, HAV, HBV, invasive meningococcal C infections.

Research on vaccines against other STIs should be continued and if possible intensified, in particular against gonococcal infections, chlamydia and syphilis.

Drug users and harm reduction

Strengthening risk reduction policies, promoting improved access to syringes and the establishment of lower-risk consumption rooms, combined with measures allowing access to care and weaning, as well as improvement of the social situation for drug users are essential measures in order to act effectively on reducing exposure to the HIV risk among IDUs.

Sexual Drug Use (Chemsex)

A multidisciplinary working group must be quickly set up bringing together health professionals, public authorities and risk reduction associations in order to strengthen their coordination in Chemsex and promote the emergence of a response adapted to the health needs of patients. people practicing it.

Prevention research

Prevention research must be continued and encouraged, in particular for:

- expand the offer of combined screening and in particular TROD and self-sampling;

- shorten the time between infection and treatment for HIV, hepatitis and STIs;

- improve the level of knowledge on biomedical prevention strategies;

- develop new approaches or simplify existing ones (eg: notification to partners, post-exposure prophylaxis of certain bacterial STIs, simplification of PrEP intake schedules, reduction of the risks associated with Chemsex).

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Annex - Methodology for developing recommendations

The group that drafted these recommendations is made up of 23 qualified individuals covering the various fields of expertise identified as necessary for the development of recommendations for the prevention and management of HIV infection in France. These are clinicians (including a general practitioner), virologists, pharmacologists, epidemiologists and public health physicians to whom are added two members of the associative community appointed by the TRT-5. The group's constitution has only undergone two modifications since its constitution in 2013, namely the replacement of an associative member in 2014 and the appointment in 2016 of a specialist in health economics to replace a member called upon to perform functions incompatible with his participation in the work of the group (Prof. François Bourdillon now director of the Public Health France agency). The composition of the initial group followed the engagement letter sent on November 19, 2012 by Mrs. Marisol Touraine, Minister of Social Affairs and Health, to Prof. Jean-François Delfraissy, director of ANRS (France REcherche Nord & sud Sida-hiv Hépatites), and to Prof. Patrick Yeni, President of the National AIDS and Viral Hepatitis Council (CNS).

It is mainly by the analysis of the public declarations of interests (DPI) [in accordance with the decree of July 5, 2012 and the instruction of August 2, 2012] that this was judged initially and then gradually. Works. The updated IPRs were sent annually to the CNS for archiving and uploading of the part likely to be made public.

Within the framework of the multidisciplinary expert group, the development of recommendations is carried out in a collegial manner based on a critical analysis of the best available knowledge and the experience of the members. The expression of the plurality of opinions is fully respected during the various exchanges.

As far as possible, the recommendations issued are accompanied by a gradation associating degree of force and level of proof, and based on the following definitions:

- **Degree of strength of the recommendations**

  A = Data available to support a high level recommendation.

  B = Data available justifying an intermediate level recommendation.

  C = Insufficient data available to justify a recommendation.

- **Level of evidence: type of data used in the recommendations**

  I = At least 1 randomized clinical trial; meta-analyzes of randomized trials.

  II = Non-randomized clinical trials; cohorts or case-control studies; meta-analyzes of cohort or case-control studies.

  III = Expert analyzes based on other available data.

There is a management of the links of interest within the group including mainly the respect of the absence of participation in promotional events of drugs and the capping of personal remuneration possibly awarded by pharmaceutical companies. During the work of the expert group, the chairman was led to ask two members of the group (once) and a third member (twice) not to participate in certain discussions, after having identified a possible conflict of interest. interests with regard to the topic to be dealt with. Since 2016, the president of the group has been subject to receiving no personal compensation from the industry and not being invited to any congress by a pharmaceutical company.

Preparatory work for the meetings of the plenary group is undertaken within thematic committees including additional experts in the group of experts but not participating in the final drafting of the recommendations. However, the commission on “Antiretroviral treatment of

adults ”(in charge of the topic where the issue of links of interest with the drug industry is most sensitive) has since 2016 only been made up of members of the plenary group of experts. The IPRs of committee participants who are not members of the expert group are requested for transparency and accessible on the CNS website.

Qualified personalities may be heard from time to time by the committees or the group of experts. Their DPI is not collected.

Update : **April 2018 -** Editorial manager: **Philippe Morlat** for the expert group

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