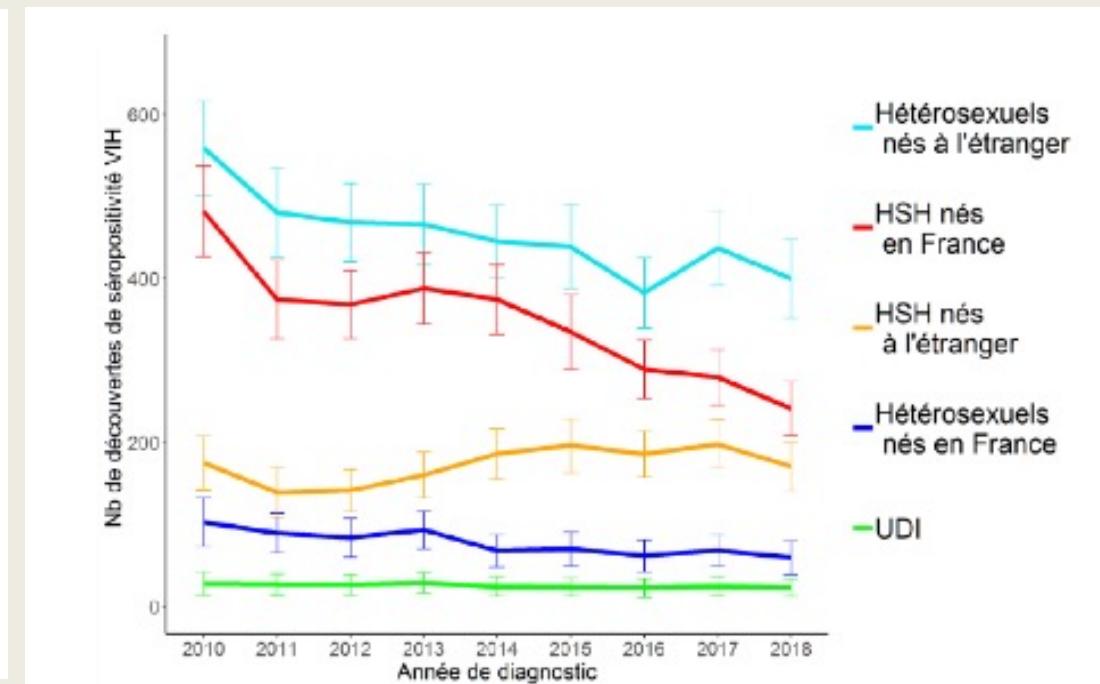
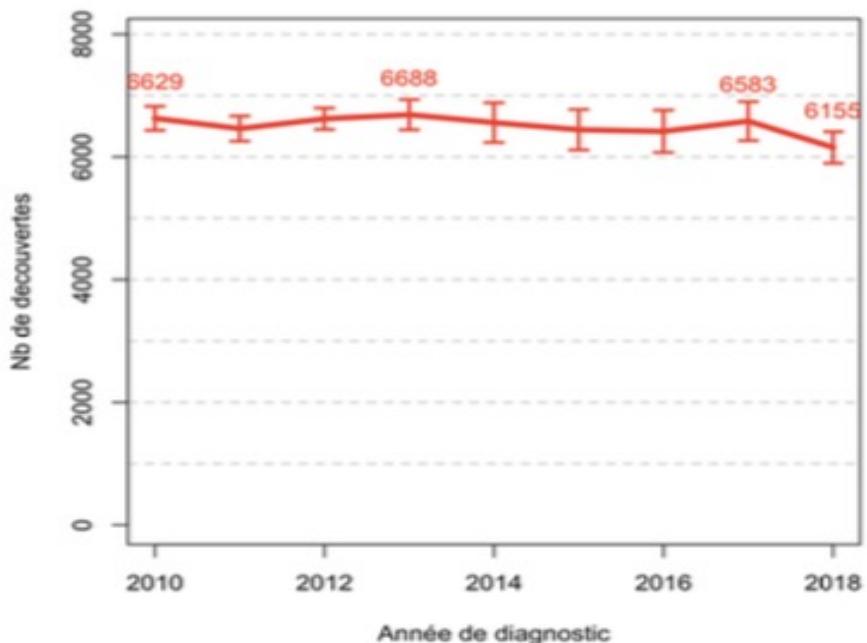


VIH et Hépatite C : éradication un jour ?

Pr Firouzé BANI-SADR

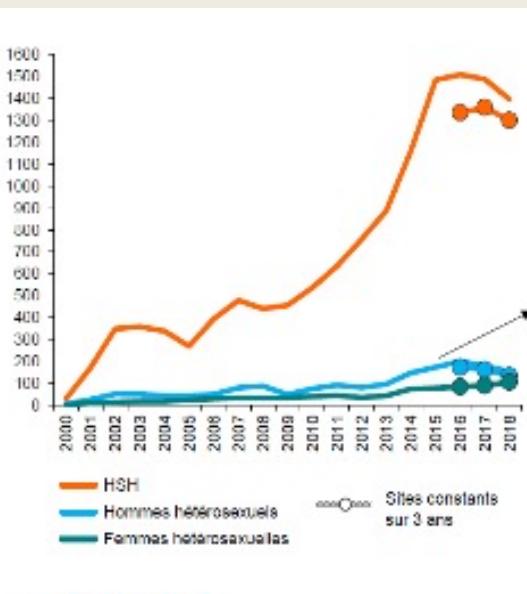
Service des Maladies Infectieuses et Tropicales
CHU REIMS

Découvertes de séropositivité VIH, France 2010-2018

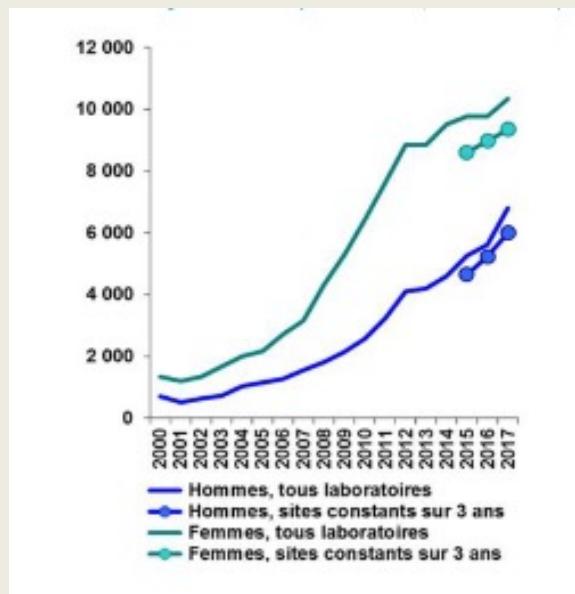


HSH : hommes ayant des rapports sexuels avec des hommes

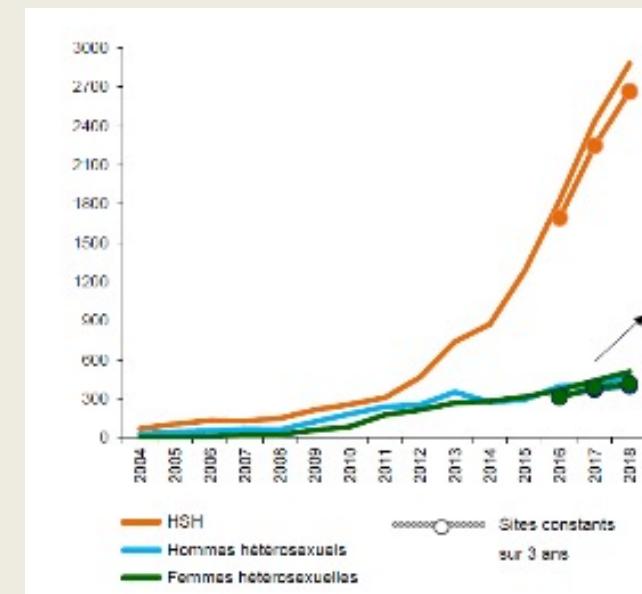
Flambée des infections sexuellement transmissibles



Syphilis



Chlamydia

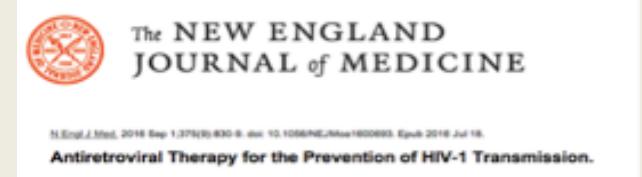


Gonocoque

Prévention pour l'infection à VIH

- Le pilier comportemental : éducation, information et préservatifs
- Le pilier biomédical :
 - Prévention de la transmission mère-enfant
 - Le traitement post exposition
 - Le traitement préventif (Treatment as Prevention = TasP)
 - La prophylaxie pré-exposition (PrEP)

N Engl J Med 2016; JAMA 2016



Treatment as Prevention = TasP

- **HPTN 052 (2015) :**
 - 1763 couples « sérodiscordants » hétérosexuels suivis en Afrique pendant 18 mois : aucune transmission si le partenaire infecté est traité et est indétectable depuis au moins 6 mois
- **Partner (2019) :**
 - Etude prospective, européenne
 - Couples hétéroS et homoS sérodiscordants avec le partenaire séropositif indétectable depuis au moins 6 mois : 135 000 rapports non protégés : aucune contamination



La prévention aujourd'hui

1. Le traitement comme prévention : TasP / I = I – Fin 2013 en France

- Axe stratégique prioritaire
- Améliorer le dépistage et la mise sous traitement et le maintien dans le soin
- Dépister les populations cibles
- Répéter ce dépistage chez HSH* et personnes à haut risque d'acquisition

2. La prévention pré exposition au VIH : PrEP

- Modèle animal : preuve du concept à la fin des années 2000
- Validée par de grands essais chez hétérosexuels en Afrique et chez HSH* aux US et Europe
- Implémentée et remboursée à 100 % en France depuis le 01 Janvier 2016
- Initiation à l'hôpital ou en Cegidd, renouvellement possible par MG

*Hommes ayant des rapports sexuels avec des hommes

WHO- Goals and Targets

2030

**End of AIDS epidemic
as Public Health threat**

**2016
95-95-95**

2020

- Reduce new HIV infections by 75% (Baseline 2010)
- Achieve treatment targets of 90-90-90
- Eliminate Mother to Child Transmission of HIV
- Eliminate HIV-related stigma and discrimination

**2013
90-90-
90**

90-90-90 By 2020

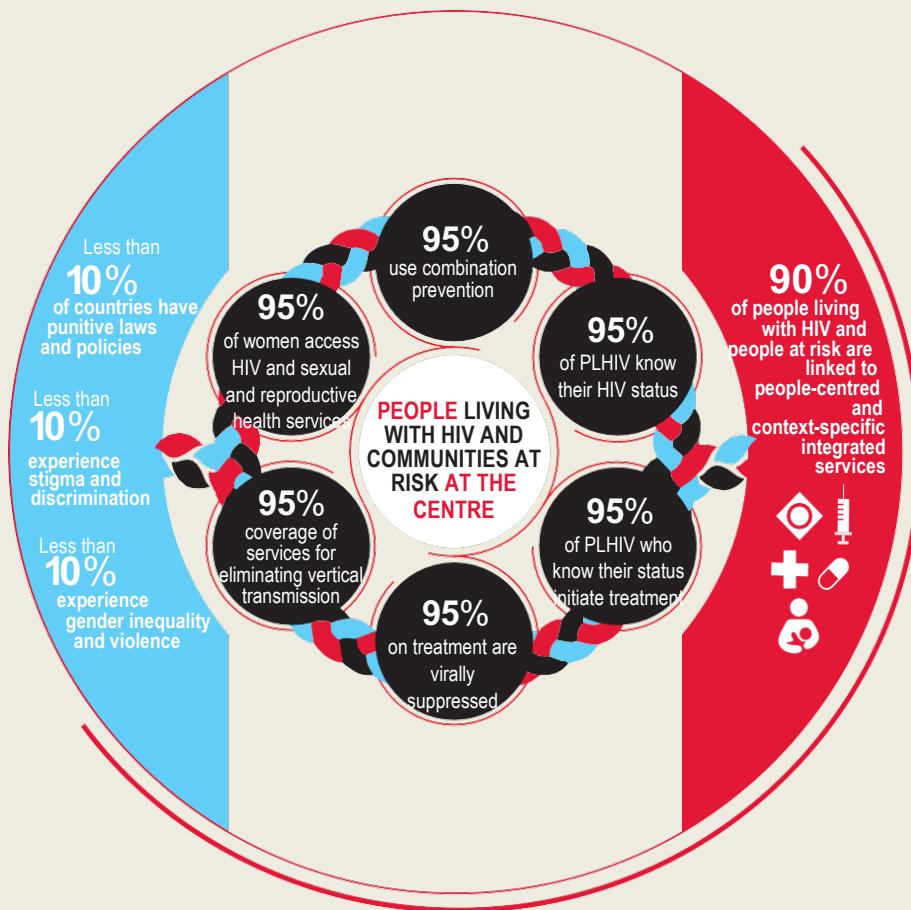
90% of all people living with HIV will know their HIV status

90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy

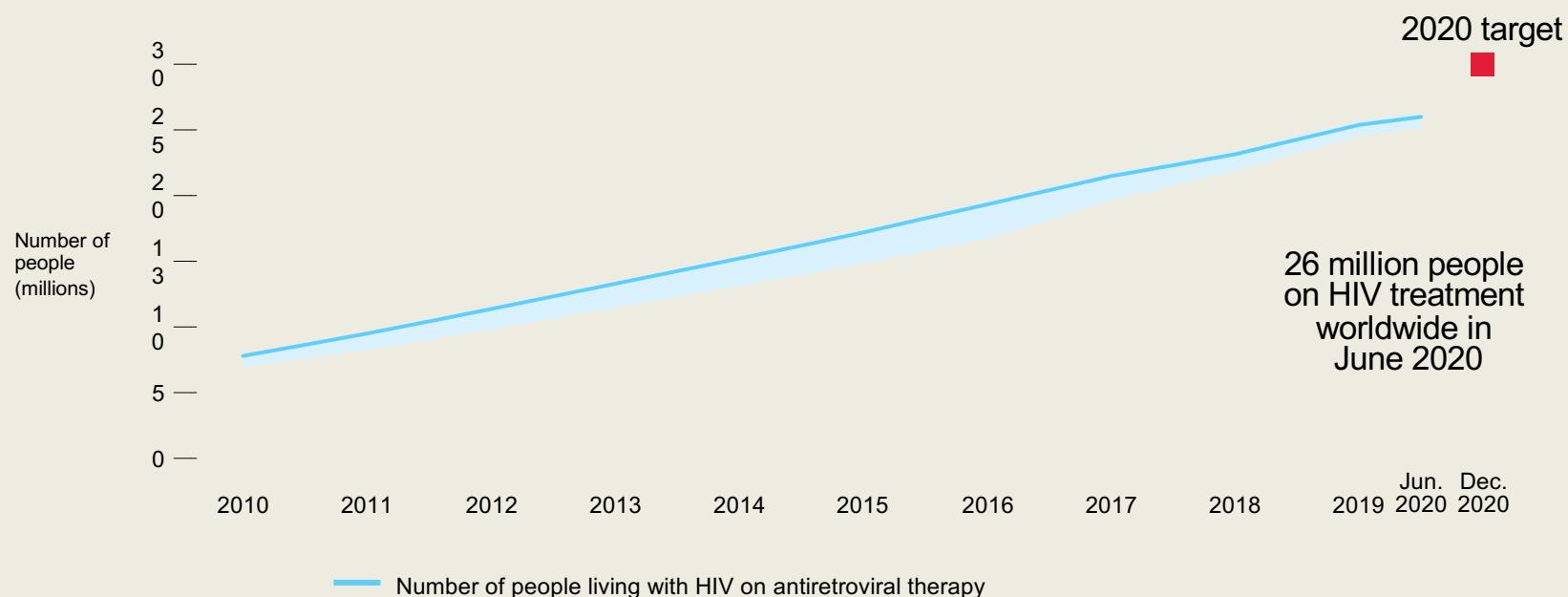
90% of all people receiving antiretroviral therapy will have viral suppression

95-95-95 By 2030

WHO- Top-line targets for 2025

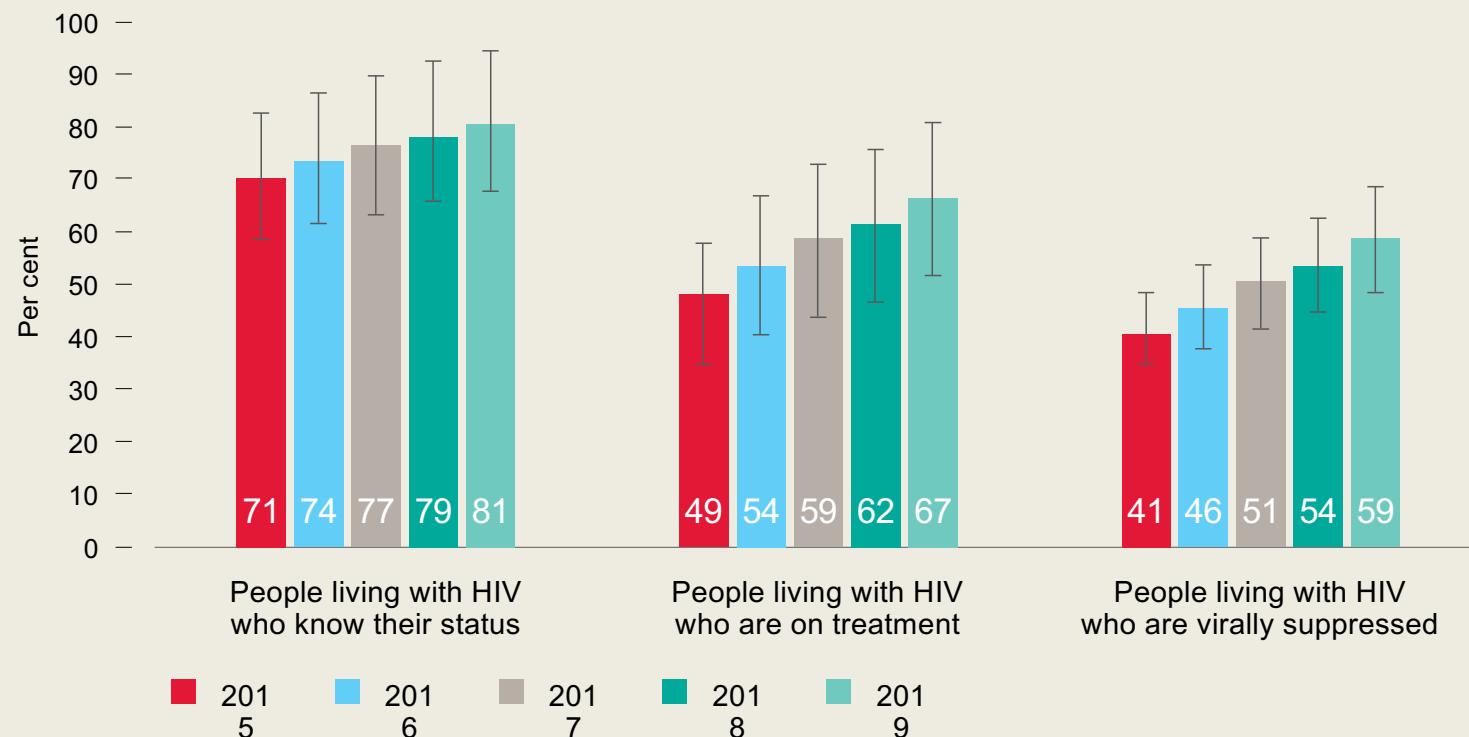


Number of people living with HIV accessing antiretroviral therapy, global, 2010–June 2020 and end–2020 target



Source: UNAIDS 2020 estimates; UNAIDS Global AIDS Monitoring, 2020 (<https://aidsinfo.unaids.org/>); UNAIDS/WHO/UNICEF HIV services tracking tool, November 2020.

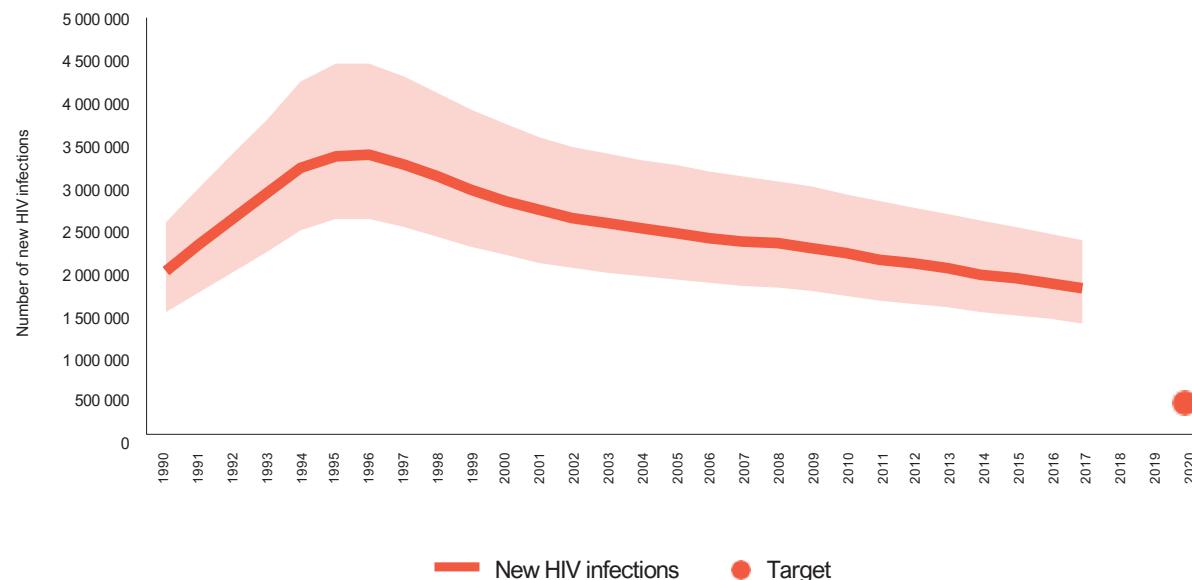
HIV testing and treatment cascade, global, 2015–2019



Source: UNAIDS special analysis, 2020 (see annex on methods).

Insufficient progress on prevention

Number of new HIV infections, global, 1990–2017 and 2020 target

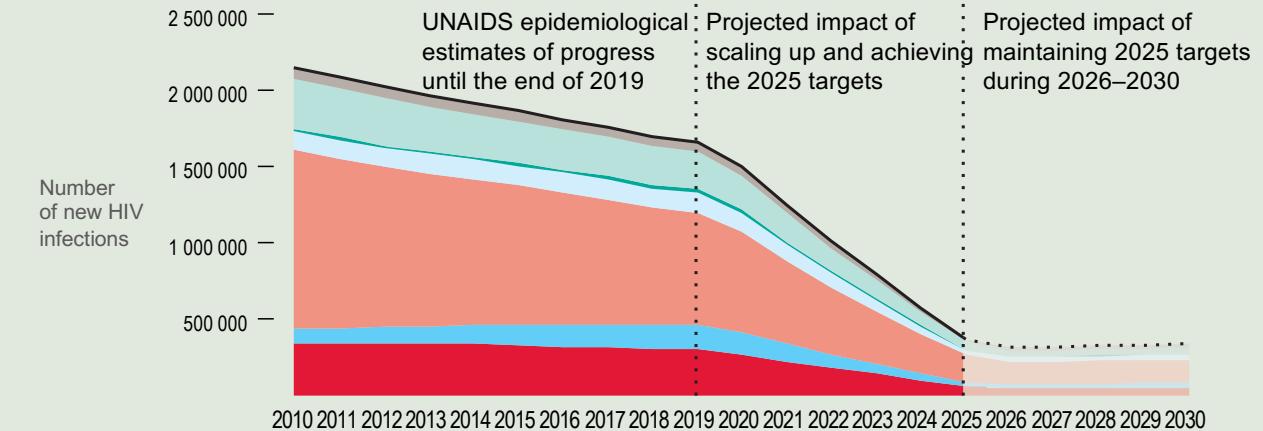


Source: UNAIDS 2018 estimates.

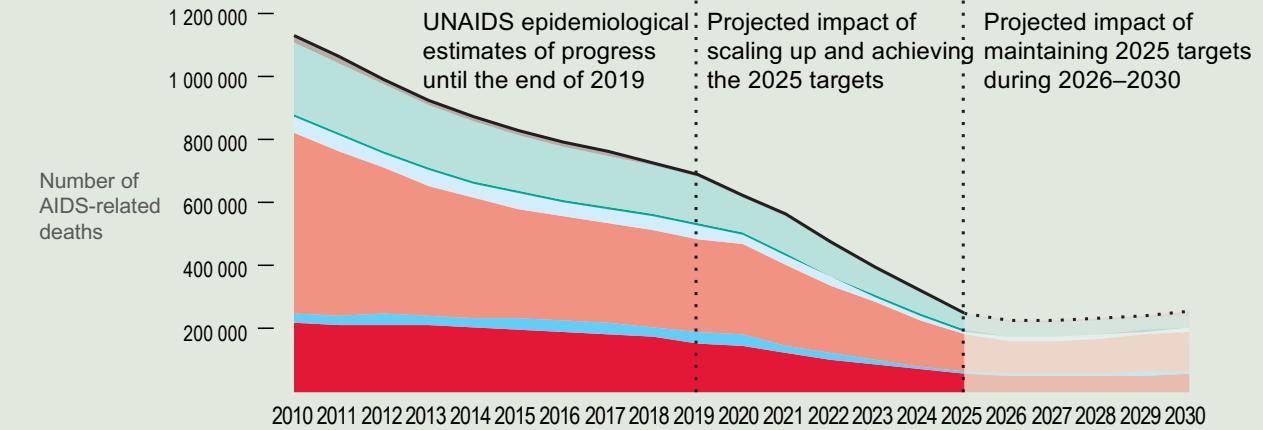
Projected impact of reaching the 2025 targets

- Asia and the Pacific
- Eastern Europe and central Asia
- Eastern and southern Africa
- Latin America and the Caribbean
- Middle East and North Africa
- Western and central Africa
- Western and central Europe and North America
- Total

HIV infections



AIDS-related deaths



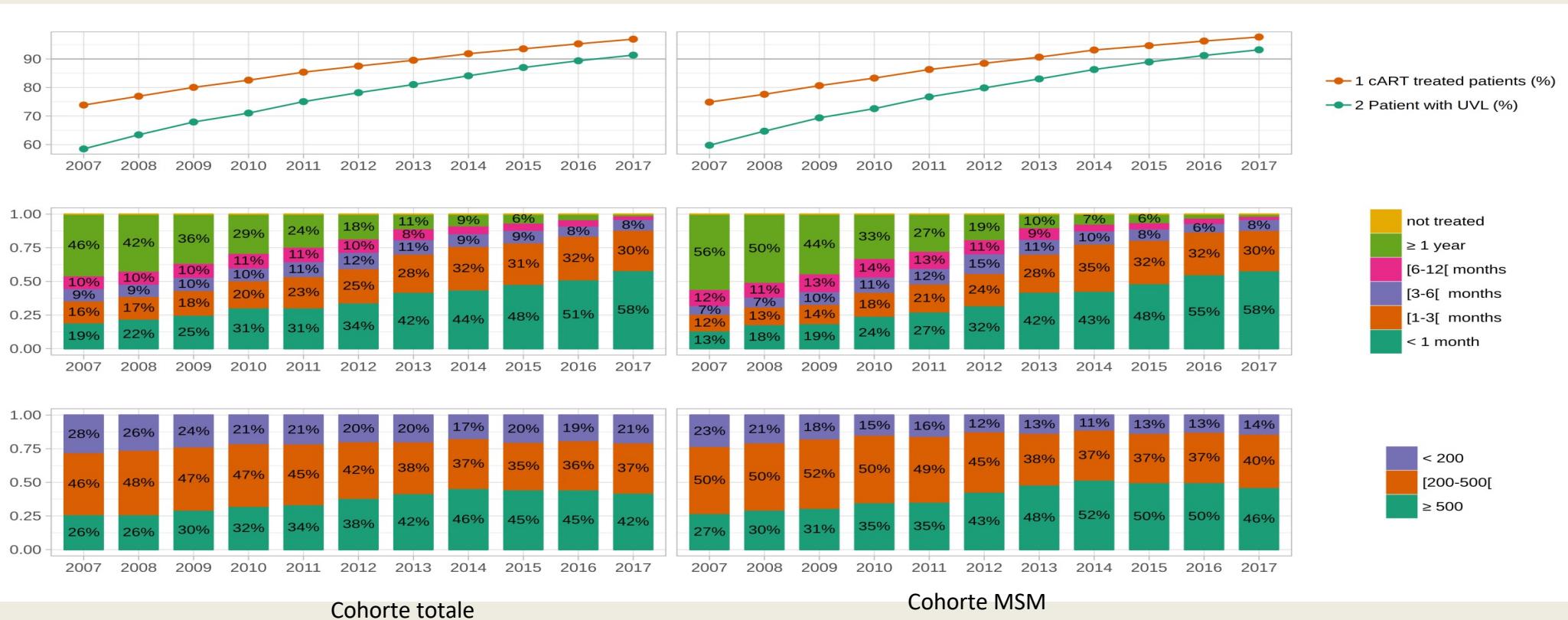
Source: Special analysis by Avenir Health using 2025 targets and UNAIDS epidemiological estimates, 2020 (<https://aidsinfo.unaids.org/>) (see annex on methods).

Traitements comme prévention- impact sur les primo-infection VIH et infections récentes

- Etude longitudinale cohorte Dat'AIDS 2007-2017 (61 822 patients dont 20 263 nouveaux sur la décennie)
 - 20 263 new patients *44% MSM*
 - 2 027 (10%) primary HIV infections
 - *71% MSM 74% born in France*
 - 7 314 (36%) recent HIV infections
 - *56% MSM 60% born in France*

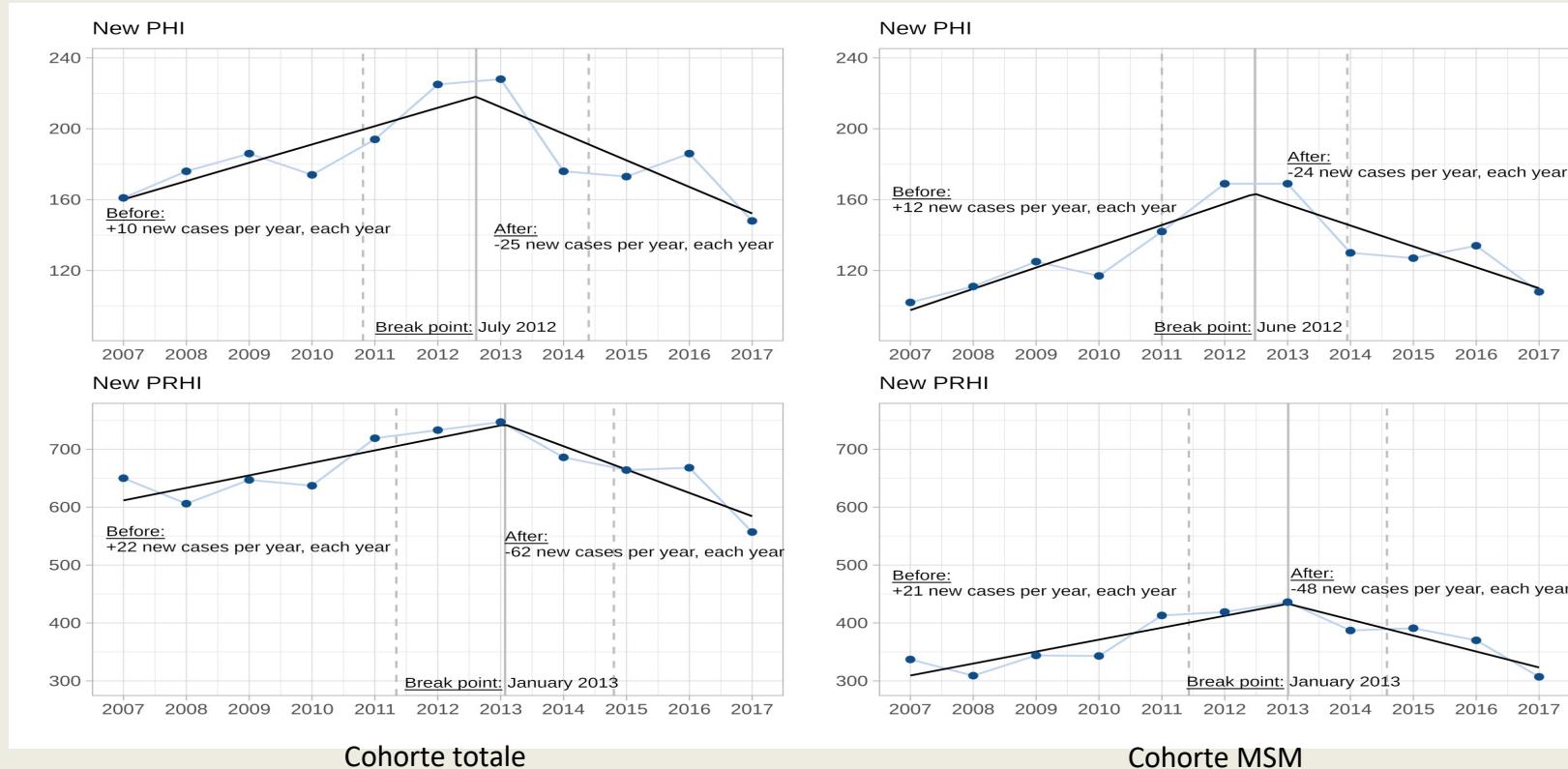
Le traitement comme prévention:

Plus de 90 % de cas traités depuis 2013 et plus de 90 % de contrôle viral depuis 2016



1 Bani Sadr et coll, Clin Infect Dis, 2020 Jul :293-300,

Plus de 90 % de cas traités et plus de 90 % de contrôle viral Réduction massive des nouveaux cas de Primo-infection et des Infections récentes



Baisse des cas de primo-infections VIH et des infections récentes entre 2013 et 2017

Primary HIV infections

- 35.1% in full cohort
- 36.1% in MSM cohort

Recent HIV infections

- 25.4% in full cohort
- 29.6% in MSM cohort

Impact of PrEP ?

Only 2,614 persons in 2016 and 6,039 in 2017 were receiving PrEP in France

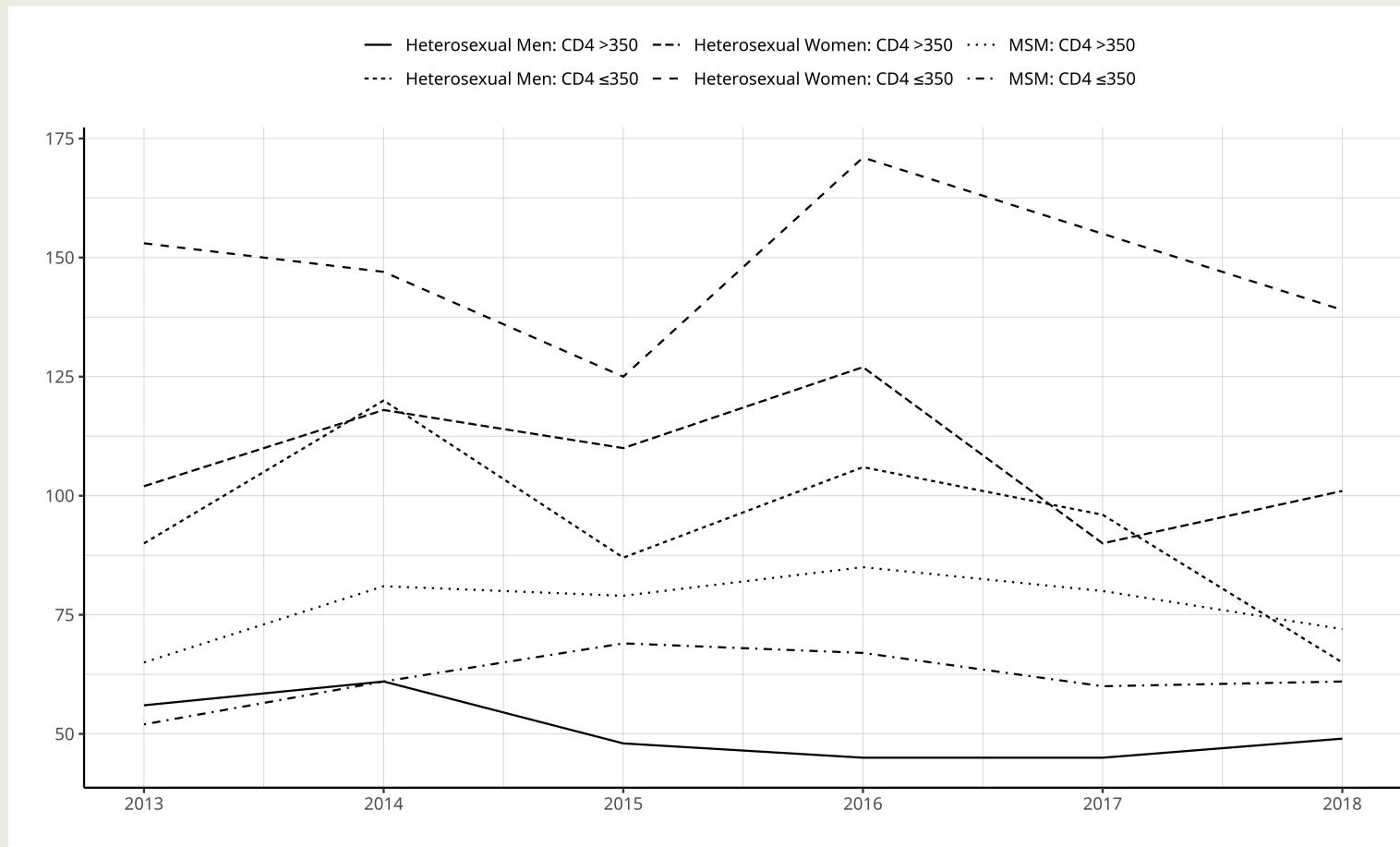
Dramatic decline in new HIV diagnoses in persons born in France in a large nationwide HIV cohort

- Between 2013 and 2018, a total of 68,376 people living with HIV were followed in the Dat'AIDS cohort;
- 9,543 subjects were newly diagnosed with HIV
 - 4253 born in France (90% male; 70.5% MSM),
 - 4,737 born abroad (39.1% heterosexual women; 23.0% heterosexual men, 21.9% MSM).
- The annual number of new HIV diagnosis decreased from 1,856 in 2013 to 1,149 in 2018 (-38.1%);
 - Decrease was more pronounced among subjects born in France, from 858 to 484 (-43.6%) than in those born abroad (-23.8%, from 821 to 626).

Dramatic decline in new HIV diagnoses in persons born in France in a large nationwide HIV cohort

- Among subjects born in France, the decrease over the period
- -46.7% among MSM,
- - 43.5% among heterosexual women
- - 33.3% among heterosexual men
- 10,405 persons received PrEP between 01/01/2016 and 30/06/2018 in France; 97.7% of them were men
- Over the past 6 years (2013-2018) new HIV diagnoses in France decreased by over 40% among MSM and heterosexual women born in France

Nx diagnostics chez les personnes nées à l'étranger



France - Nouveaux patients pris en charge entre 2017 et 2019

Cohortes Corevih

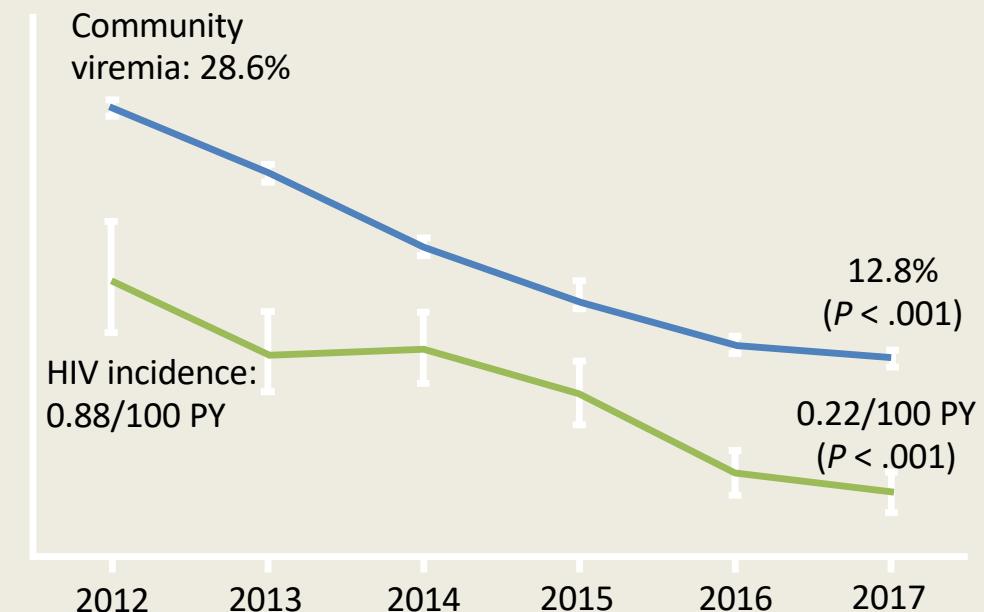
- N= 10 396
- Age médian: 37,09 ; ≥ 60 ans : 7,30 %
- Sexe M : 66,56 %
- **Sexe et Pays de naissance**
 - Homme France 39,77 % - Femme 6,46 %
 - Homme Afrique subsaharienne 13,91 % Femme 20,75 %
 - Homme Autres pays 12,88 % Femme 6,22 %
- **Groupe de transmission**
 - HSH 31,47 %
 - UDI 1,75 %
 - Hétérosexuel 57,34 %

TAIPAN: Prospective, Longitudinal Cohort Study in Australia

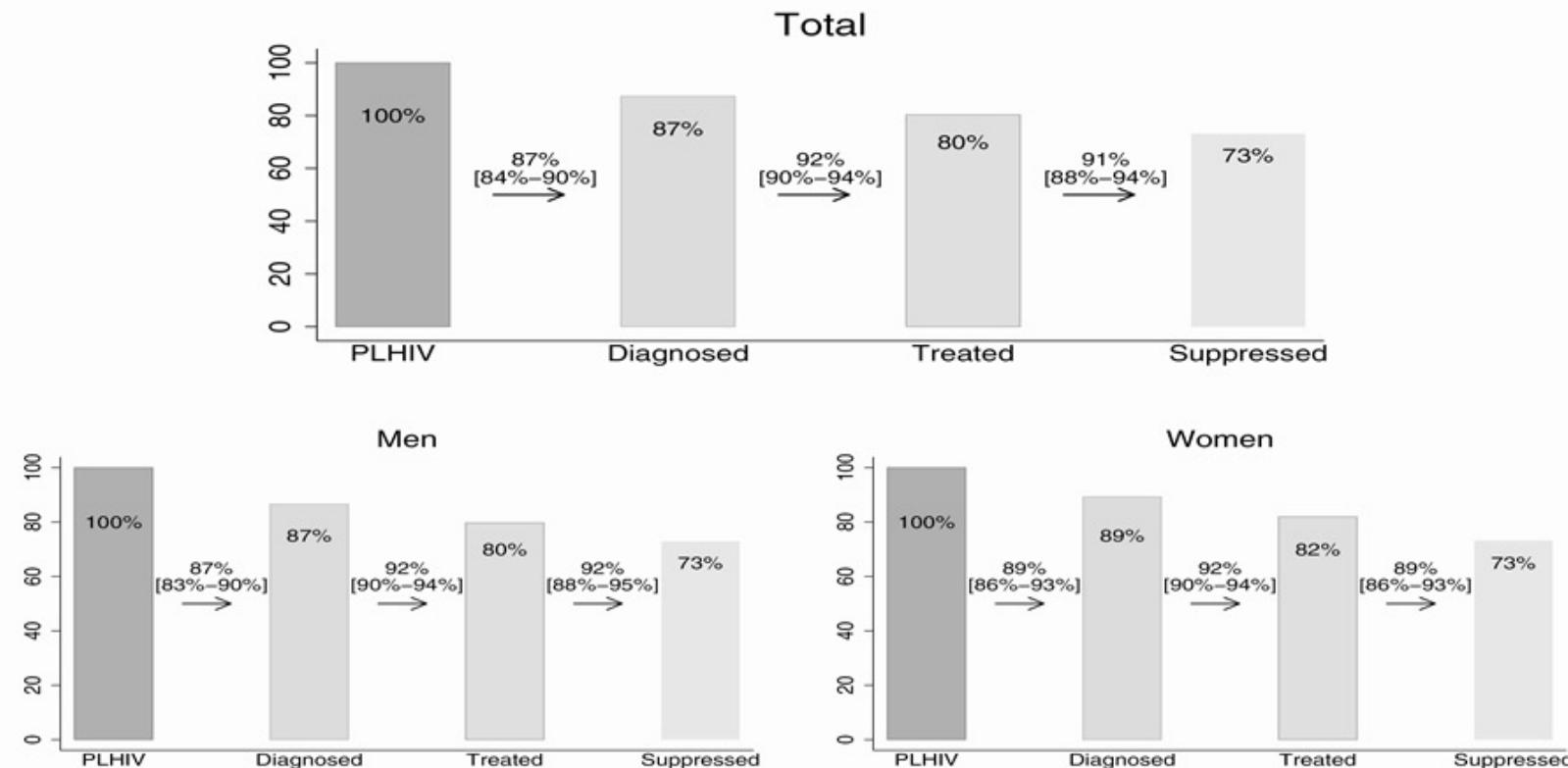
- Prospective, longitudinal cohort study from 2012-2017 in New South Wales and Victoria^[1]
 - Represent ~ 57% of Australia's population; study captures ~ 80% of gay and bisexual male population
 - Data extracted from deidentified EMRs of patients visiting publicly funded sexual health clinics (n = 34), general practices (n = 25), hospitals (n = 3), and peer-based HIV testing sites (n = 5)^[1,2]
- Study population: N = 115,982 men aged ≥ 16 yrs reporting same-sex partner(s) or orientation, or undergoing specific procedures (eg, anal swab for STI testing)^[1,2]
 - HIV negative: n = 101,143; HIV positive at some point: n = 14,839^[1]
- Primary study aim: determine temporal relationship between community viremia and HIV incidence at population level^[2]

TAIPAN: Clinical HIV-1 RNA Levels and Rate of Undiagnosed HIV Among Australian GBM

- GBM with HIV-1 RNA ≥ 200 copies/mL decreased from 17% in 2012 to 4% in 2018 ($P < .001$)
- Estimated rate of undiagnosed HIV in GBM decreased from 10.5% in 2012 to 9.12% in 2017 ($P = .05$)
- Statistically significant correlations between community viremia and HIV incidence in period before PrEP introduced (2012-2015; $r = 0.90$; $P < .001$) and for entire study period ($r = .94$; $P < .001$)



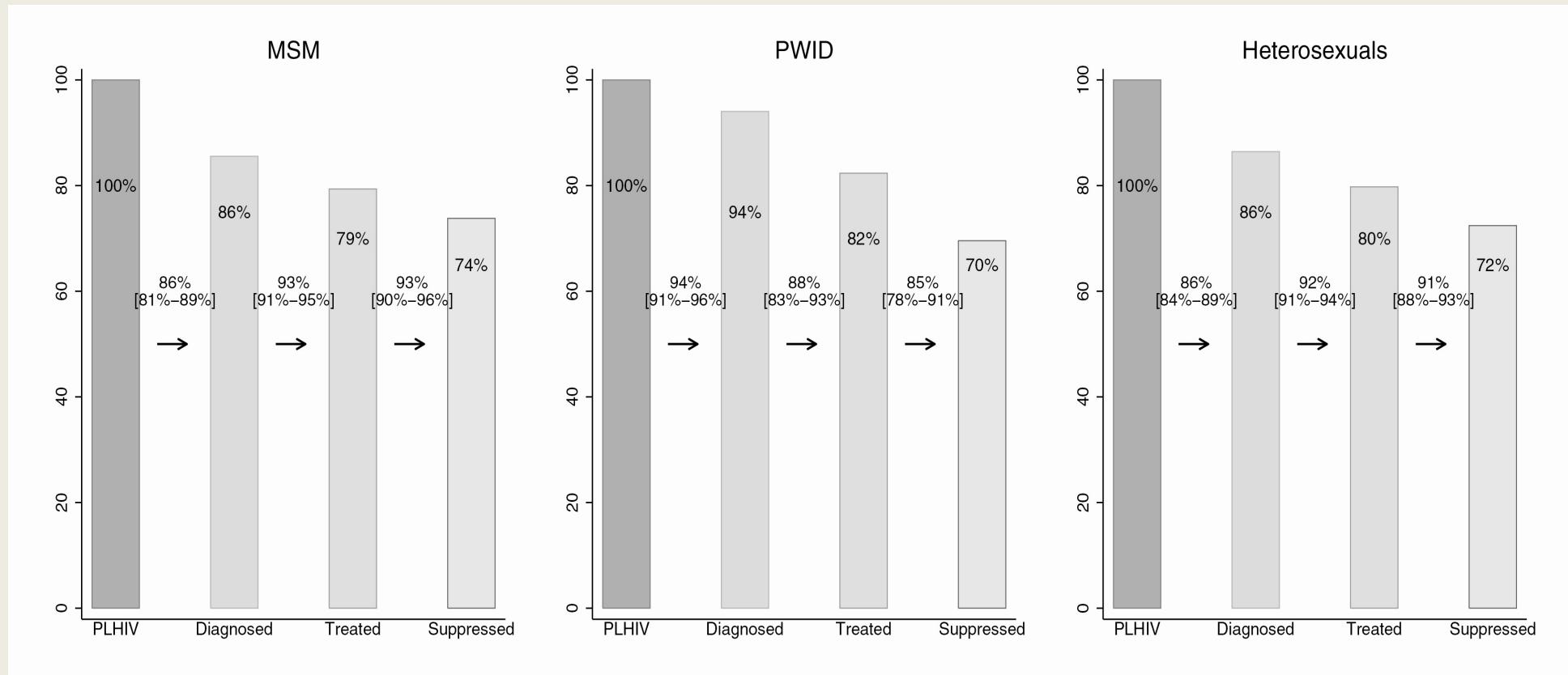
Continuum of HIV care for 2016, overall and by sex in 11 European countries



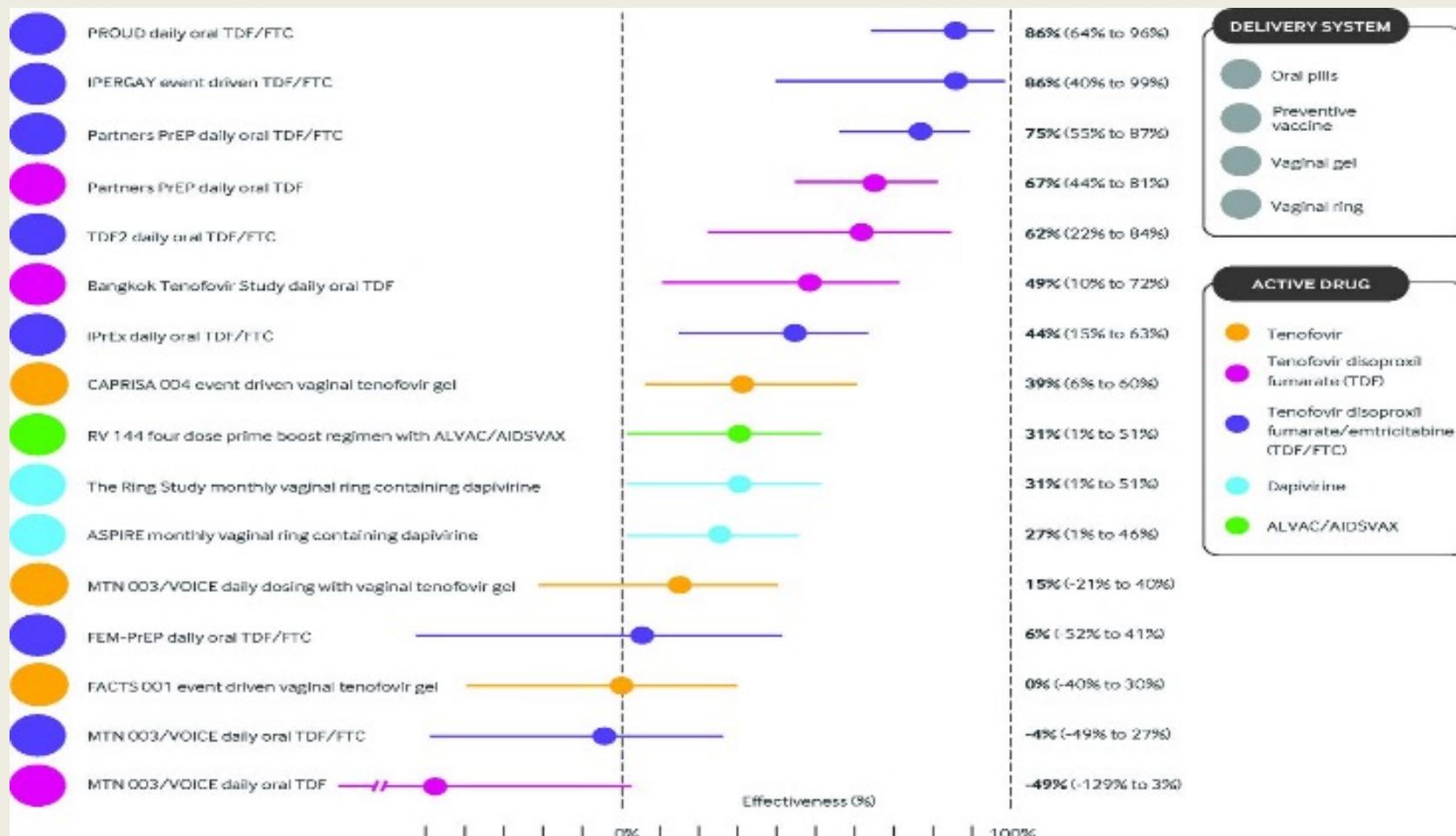
Austria, Denmark, the Netherlands, the United Kingdom,
Croatia, Germany, Greece, Italy, Spain, Sweden and France

Clin Infect Dis, Volume 71, Issue 11, 1 December 2020,
Pages 2905–2916

Continuum of HIV care for 2016, by key population in 11 European countries



La prévention pré exposition : les principaux essais de PrEP



Recent advances in pré exposure prophylaxis for HIV ; BMJ 2018

PrEP Persistence and New HIV Infections

- 12,810 person-yrs of PrEP use (mean: 1.9 yrs/person)
- Of 2525 not persistent on PrEP, 932 (37%) restarted
- No new HIV infections diagnosed in 12,810 person-yrs among patients adherent to PrEP

Timepoint	PrEP Persistent, %
1 yr	73
2 yrs	64
3 yrs	60
4 yrs	57
5 yrs	56

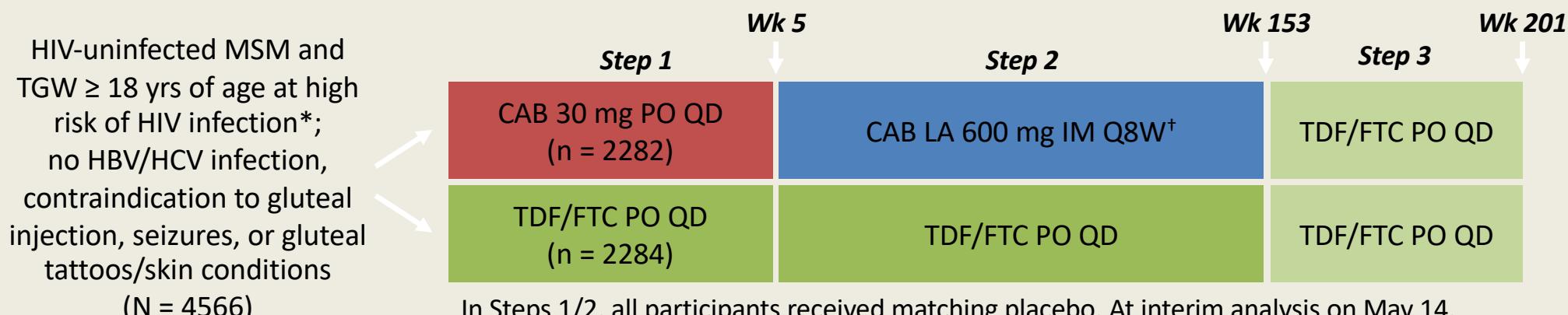
Volk. AIDS 2020. Abstr OAC0807.

*All 6 reported suboptimal adherence

Continuum step	New HIV Infections, % (n/N)
At linkage	0.32 (42/12,963)
Linked but didn't receive prescription	1.4 (37/2653)
Received prescription	0.75 (12/1739)
After discontinuing PrEP	1.5 (38/2525)
While persistent*	0.14 (6/4,238)

HPTN 083: Efficacy and Safety of LA Injectable CAB vs Daily Oral TDF/FTC for PrEP in MSM and TGW

- International, randomized, double-blind phase IIb/III study



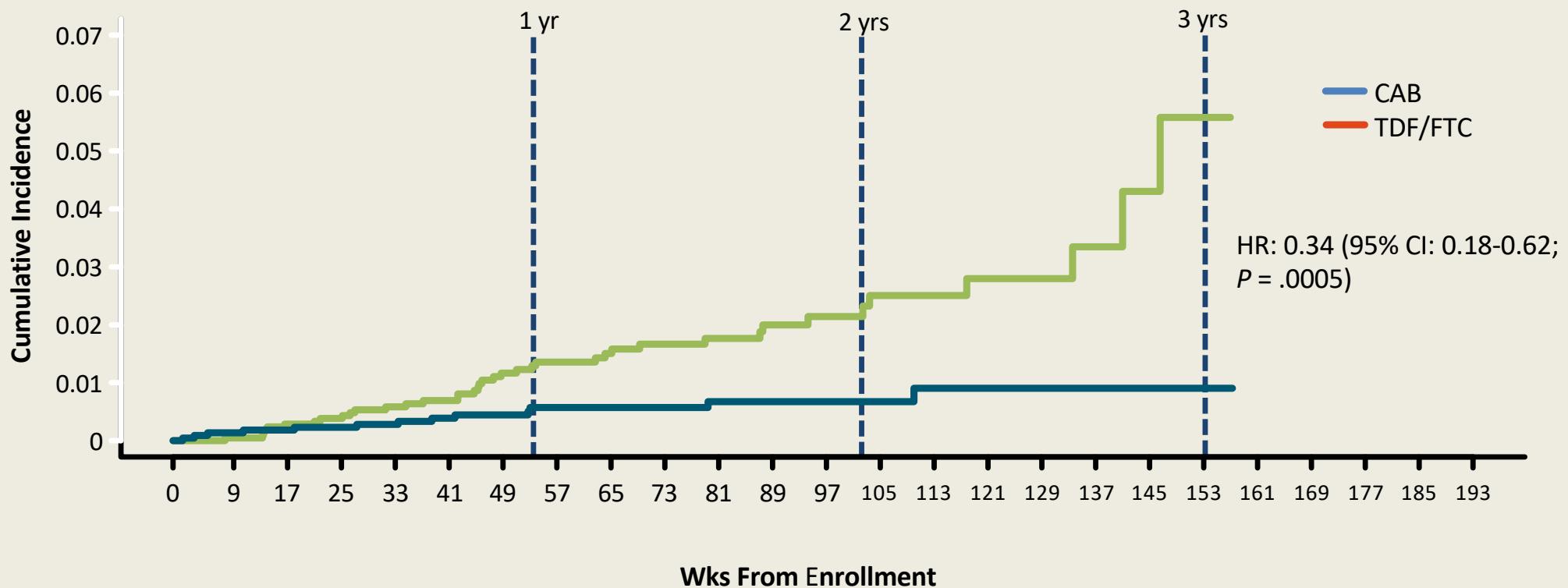
In Steps 1/2, all participants received matching placebo. At interim analysis on May 14, 2020 with 25% of endpoints accrued, DSMB recommended termination of blinded study due to crossing of pre-specified O'Brien-Fleming stopping bound.

*Any non-condom receptive anal intercourse, > 5 partners, stimulant drug use, incident rectal or urethral STI (or incident syphilis) in past 6 mos; or SexPro Score ≤ 16 (US only).

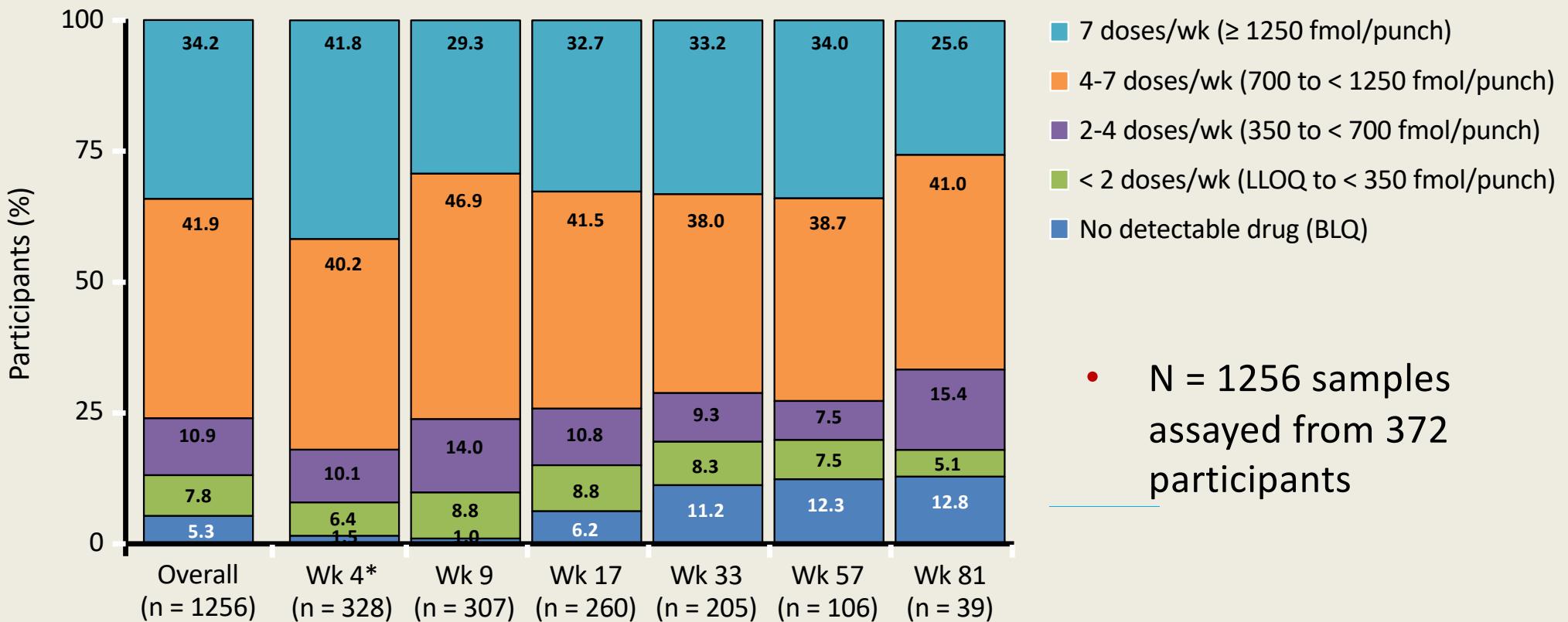
[†]First 2 doses given 4 wks apart then every 8 wks thereafter.

- Primary endpoints: incident HIV infections in Steps 1/2, grade ≥ 2 AEs

HPTN 083: HIV Incidence (ITT) With LA Injectable CAB vs Daily Oral TDF/FTC PrEP



HPTN 083: Adherence by DBS TTV-DP in Random Subset



* Because steady state was not yet achieved at this time point, category values were adjusted for days receiving therapy.

Landovitz. AIDS 2020. Abstr OAXLB0101. Reproduced with permission.

Objectif simple : dépister !

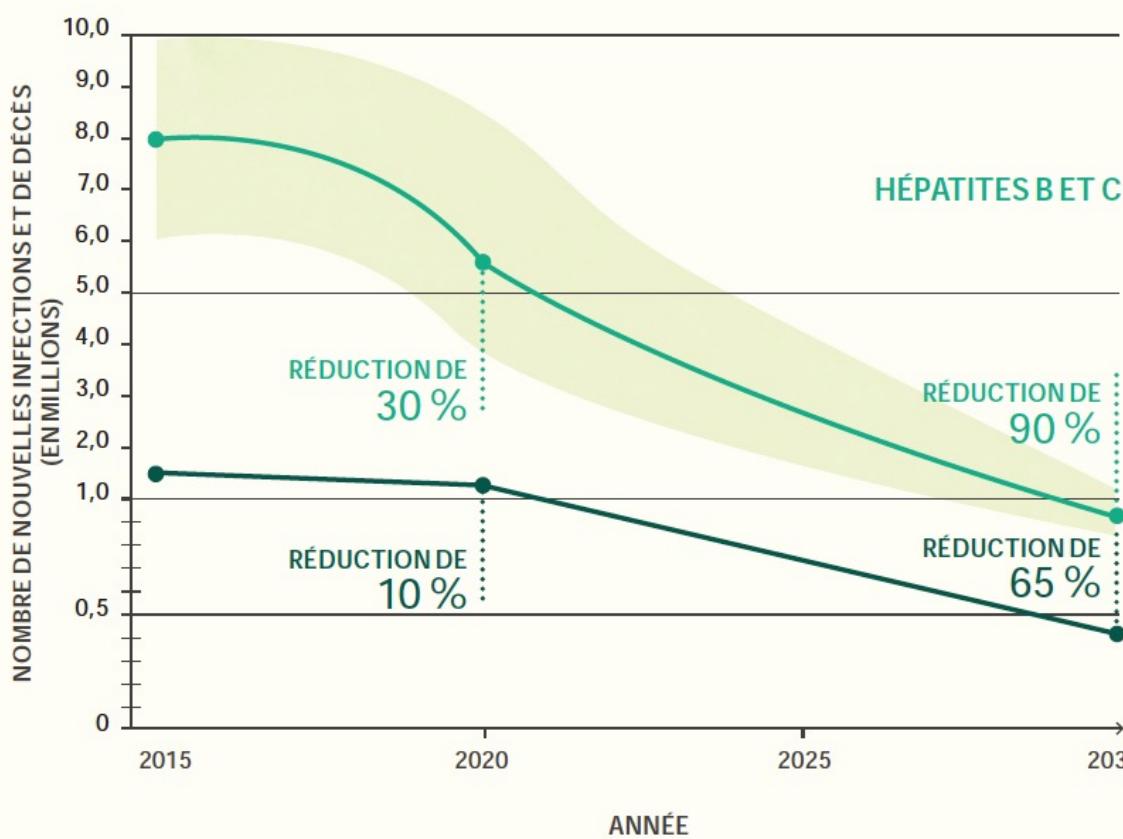
- **Suivre les recommandations de la HAS :**
 - Dépister au moins une fois en population générale
 - Quatre fois par an si HSH (homme ayant des rapports sexuels avec des hommes)
 - Une fois par an si utilisateur de drogue injectables ou personnes originaires de zones de forte prévalence
- **Ne pas manquer les occasions :**
 - Grossesse, test à renouveler au troisième trimestre et penser à dépister les pères
 - Diagnostic d'une IST
 - Délivrance contraception
 - Divorce, changement de situation amoureuse
 - Retours de voyage « au pays »
 - Situation clinique : lymphopénie, thrombopénie, zona , pneumonie, diarrhée chronique
- **Orienter ou informer sur la PrEP**

Messages clés

- Nouveaux outils de prévention biomédicale
 - Le traitement préventif (TasP)
 - La prophylaxie pré-exposition (PrEP)
- Le médecin généraliste doit être au centre de ces nouvelles stratégies
 - Politique de prévention et de sensibilisation
 - HIV et recherche des autres IST
- Innover et lutter contre la stigmatisation
 - Ne pas hésiter à en parler avec les patients

Objectif : élimination de l'infection par le VHC

Envisageable



Méthodes diagnostiques simples

Traitements efficaces

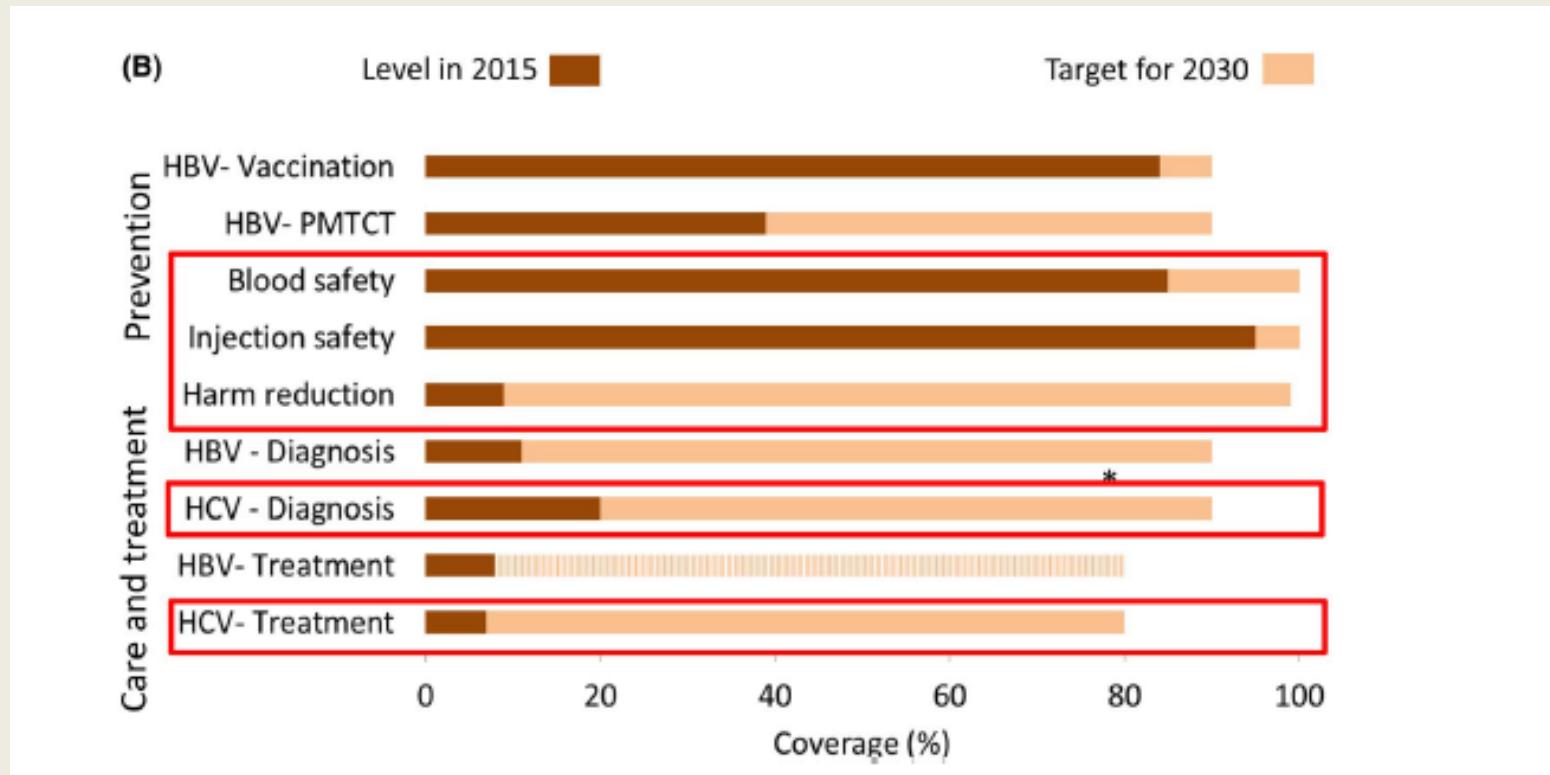
A condition d'intensifier
les politiques de dépistage
et d'ouverture au traitement

Source : Global Burden of Disease

Global Call for HCV Elimination

- WHO vision^[1]: “*Eliminate viral hepatitis as a major global public health threat by 2030*”
- 2030 Targets
 - 90% Diagnosed
 - 80% Treated
 - 65% Reduced mortality
- WHO. *Global Health Sector Strategy on Viral Hepatitis, 2016-2021.*, 2016-2021

Objectives of the WHO for the hepatitis plan elimination by 2030



Epidemiology of HCV

Global Hepatitis Report 2017

- More than 1 750 000 new infections in 2015 (defect in hemovigilance and harm reduction in PWID)
- 1 % of the population HCV-infected ([71 millions](#))
- 2.3 millions HIV/HCV co-infected



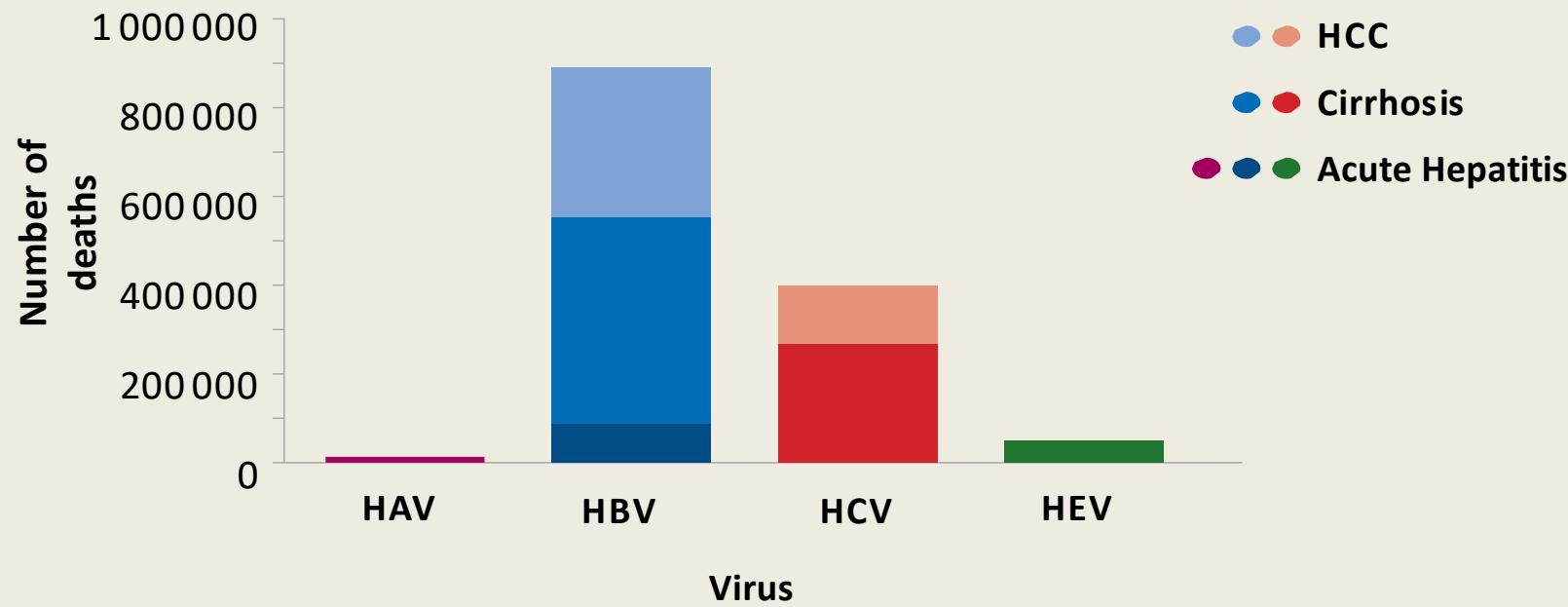
WHO region	Map key	Incidence of HCV infection			
		Incidence rate (per 100 000)	Total number (000)		
		Best estimate	Uncertainty interval	Best estimate	Uncertainty interval
Africa	●	31.0	22.5–54.4	309	222–544
America	●	6.4	5.9–7.0	63	59–69
Middle East	●	62.5	55.6–65.2	409	363–426
Europe	●	61.8	50.3–66.0	565	460–603
South East Asia	●	14.8	12.5–26.9	287	243–524
Ouest Pacific	●	6.0	5.6–6.6	111	104–124
Total		23.7	21.3–28.7	1 751	1 572–2 120

Epidemiology of HCV

Global Hepatitis Report 2017

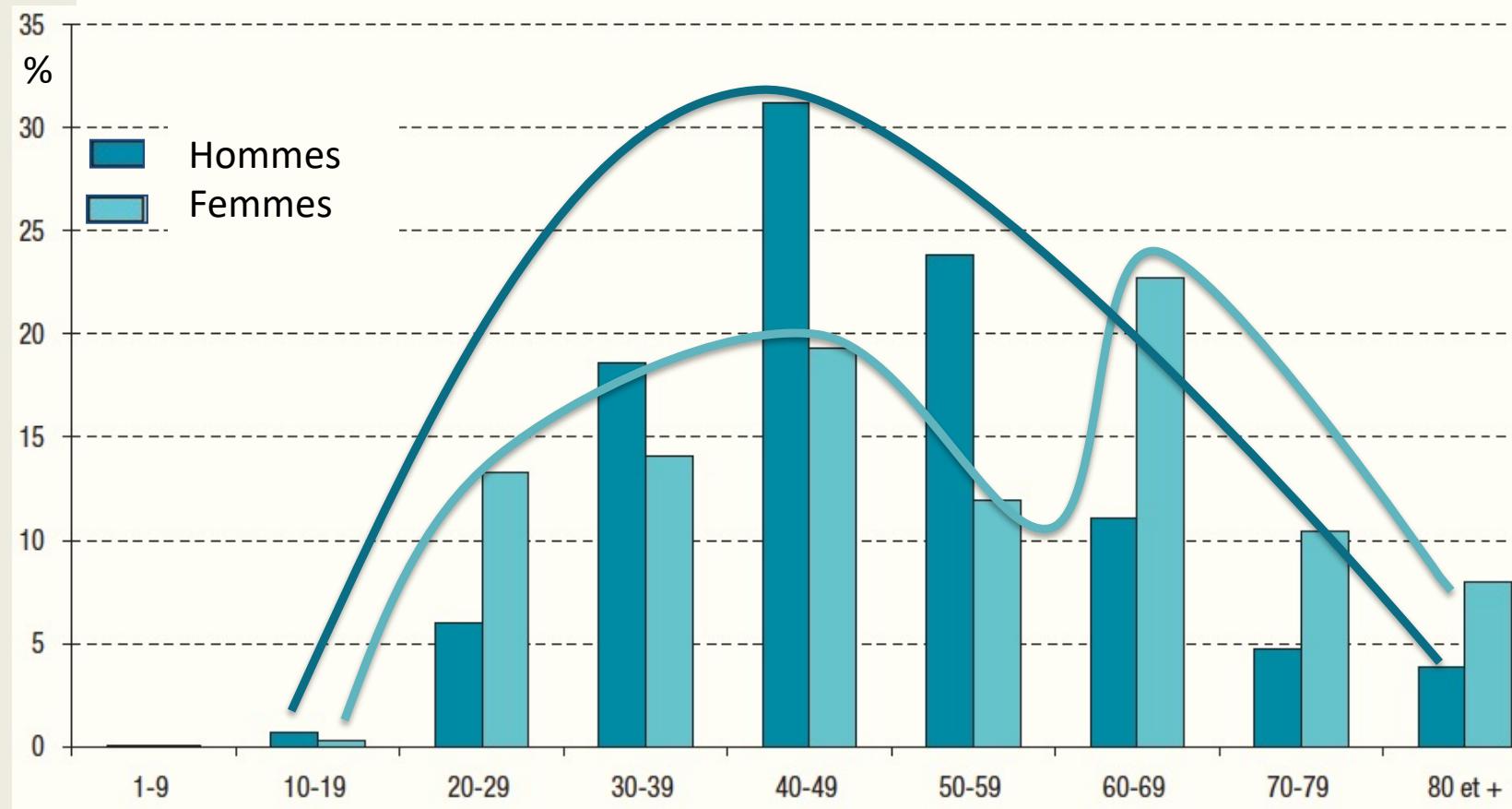
Mortality related to Viral Hepatitis in 2015

- 720 000 deaths related to cirrhosis
- 470 000 deaths related to hepatocellular carcinoma
- 22 % increase since 2000



Prévalence de l'hépatite C en France

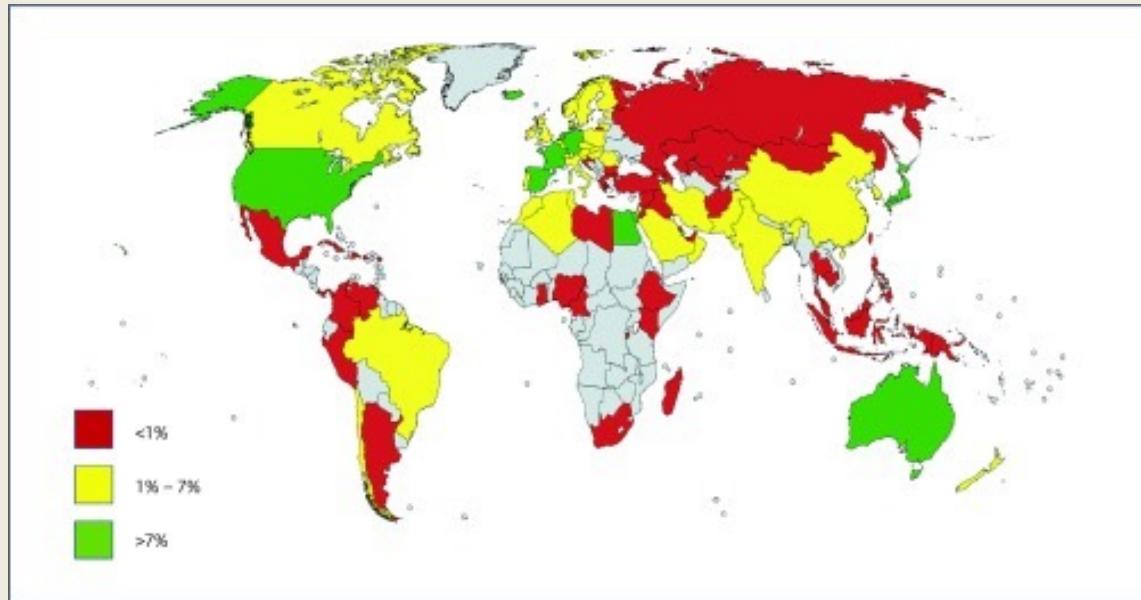
Répartition par âge et sexe des sérologies VHC confirmées +
(enquête LaboHep 2013)



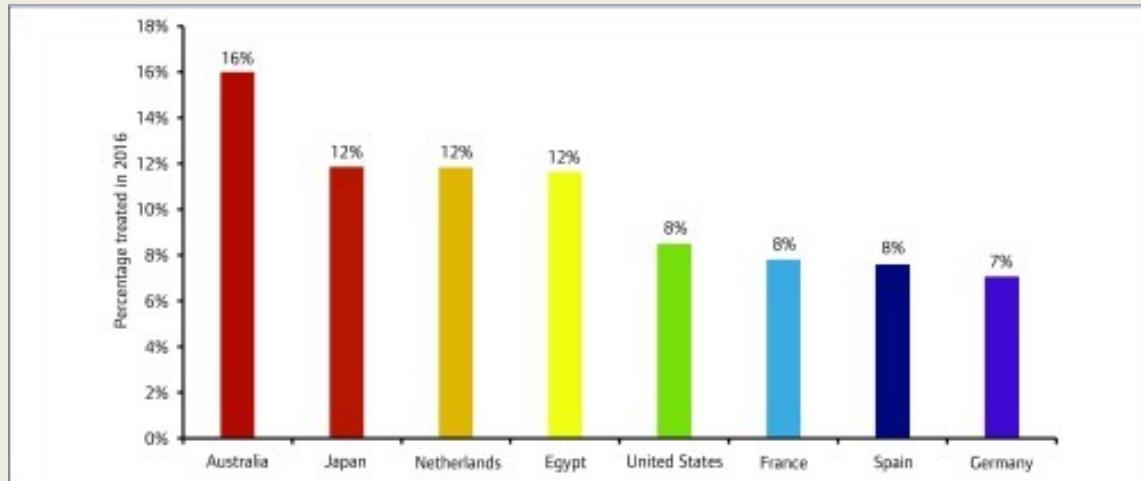
Estimation du nombre de malades par groupe à risque

Sous-groupe	Effectif	Prévalence Ac anti-VHC	Prévalence ARN-VHC	Médiane Ac anti-VHC	IC 95% Ac anti-VHC	Médiane ARN VHC
UD IV	148 000	63.8	29.6	94 450	87 732-100 900	43 860
UD non IV	132 000	4.9	2.2	6 325	3 573-10 155	2 935
Transfusés <1992	2 831 391	3.41	2.1	93 219	44 652-167 123	59 859
Immigrés	4 938 439*	1.83	1.0	90 035	75 151-108 902	51 166
Reste de la population	38 114 942	0.15	0.09	58 718	39 587-83 579	33 210
Population totale	46 164 772	0.75	0.42	344 503	287 373-423 549	192 730

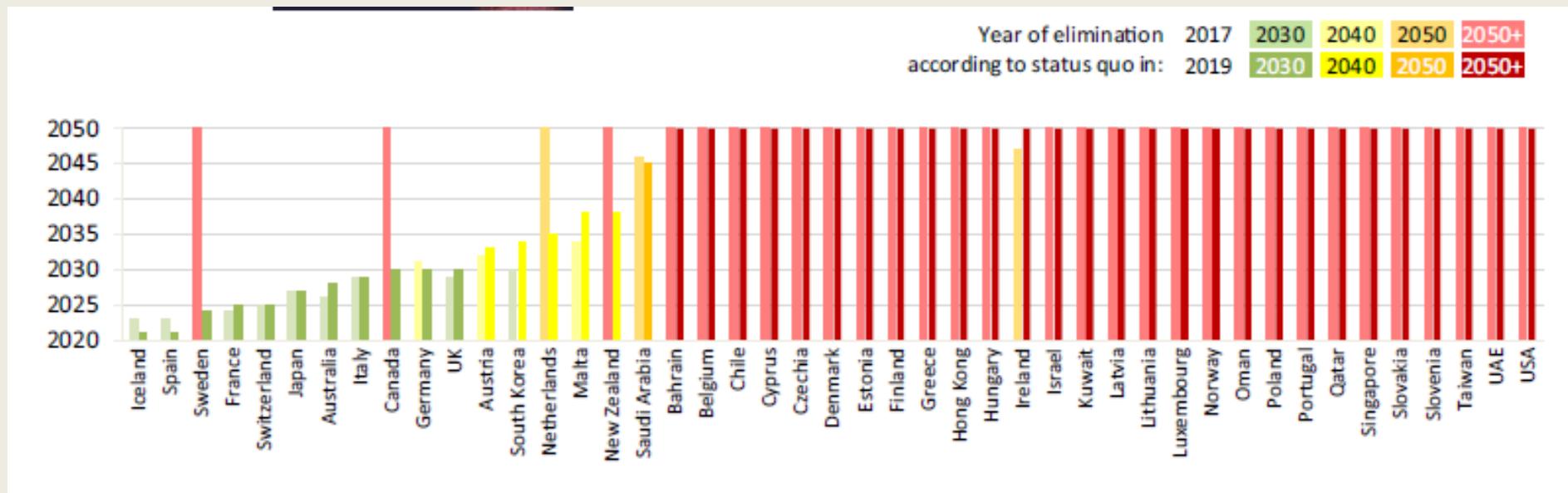
Map showing the percentage treatment rate by country for HCV in 2016



Graph showing the eight countries treating the most people by percentage in 2016



HCV elimination



Sexual HCV Transmission Among MSM With HIV Infection in New York City

- 2005-2010: 74 HIV+ MSM with recently acquired HCV infection and no IDU history
- Phylogenetic analyses identified 5 clusters of closely related HCV variants among 26 of 47 men with GT 1a HCV
 - Suggesting networks of transmission
- Matched case-control study showed high-risk sexual behavior most likely mode of transmission

Factor	Univariate OR (95% CI)	P Value
Receptive anal intercourse, no condom, with ejaculation*	24.87 (3.18-194.55)	.002
Insertive anal intercourse, no condom, no ejaculation	8.13 (1.76-37.55)	.007
Insertive anal intercourse, no condom, with ejaculation	2.62 (1.00-6.87)	.05
Receptive fisting	10.08 (2.03-50.02)	.005
Insertive fisting	7.90 (1.96-31.84)	.004
Use of sex toys	4.38 (1.35-14.26)	.01
Group sex	19.28 (2.51-148.23)	.005
Previous syphilis	8.80 (1.88-41.05)	.006
Adjusted OR in multivariate analysis: 23.00 (95% CI: 2.17-243.84; P = .009).		
Previous gonorrhea	5.02 (1.40-18.05)	.01
Sex while high on drugs	11.37 (2.51-51.52)	.002

*Adjusted OR in multivariate analysis: 23.00 (95% CI: 2.17-243.84; P = .009).

STI Screening Recommendations for MSM

STI	Screening Recommendation for MSM
Chlamydia	<ul style="list-style-type: none">▪ If sexually active, at least annually at sites of contact (urethra, rectum) regardless of condom use▪ Every 3-6 mos if at increased risk
Gonorrhea	<ul style="list-style-type: none">▪ If sexually active, at least annually at sites of contact (urethra, rectum, pharynx) regardless of condom use▪ Every 3-6 mos if at increased risk
Syphilis	<ul style="list-style-type: none">▪ If sexually active, at least annually▪ Every 3-6 mos if at increased risk
HBV	<ul style="list-style-type: none">▪ Test once for HBsAg and anti-HBc and/or anti-HBs; vaccinate persons anti-HBs negative with confirmation of HBs response 4 wks after last dose
HCV	<ul style="list-style-type: none">▪ MSM born between 1945-1965; other MSM if risk factors are present▪ Annual HCV testing in MSM with HIV infection
Anal cancer	<ul style="list-style-type: none">▪ Annual digital anorectal examination may be useful to detect masses on palpation (HIV, possibly MSM, receptive anal intercourse). Some perform anal cytology to screen for anal cancer among high-risk populations (eg, HIV, MSM, receptive anal intercourse), followed by high-resolution anoscopy if abnormal cytologic results

HCV Treatment as Prevention Among MSM With HCV/HIV Coinfection Is Working in The Netherlands

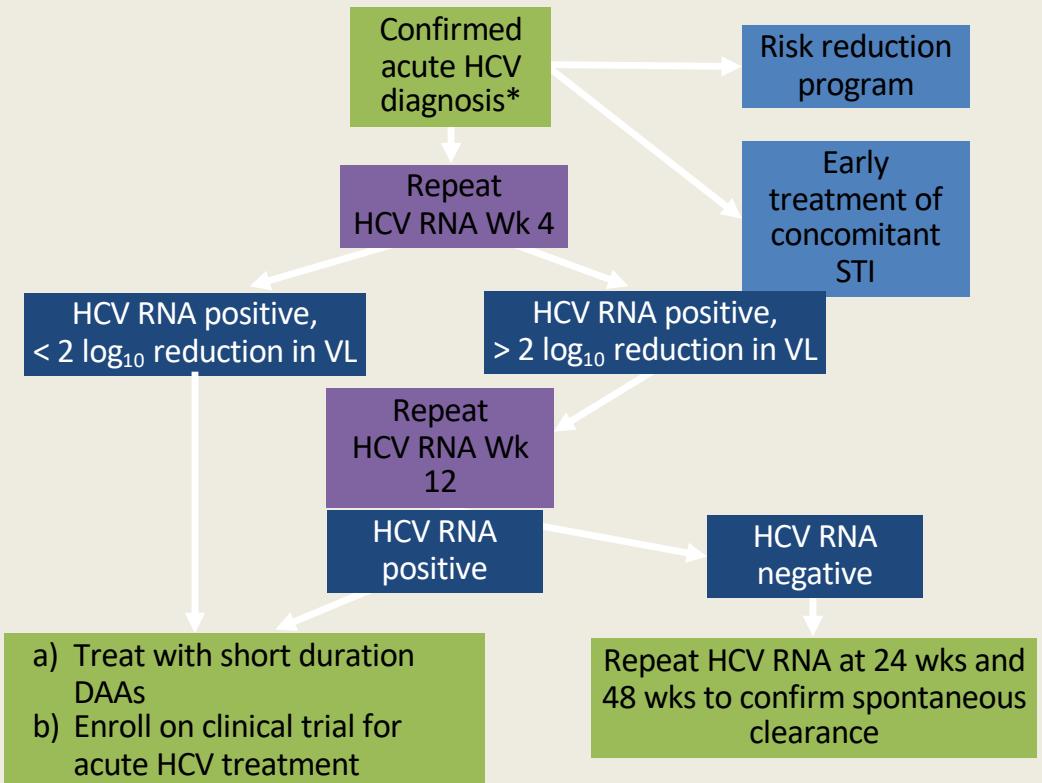
- Universal DAA access began November 2015; by February 2017, **83% (844 of 1022) all HCV/HIV-coinfected MSM had SVR**, 6% awaiting DAA treatment results
- Prevention effect: **50% decrease in acute HCV incidence from 2014-2016**



- During same period, significant increase in positive test rates at sexual health clinics for syphilis (+2.2%) and gonorrhea (+2.8%); thus, acute HCV decrease not likely to reflect decrease in risk behavior

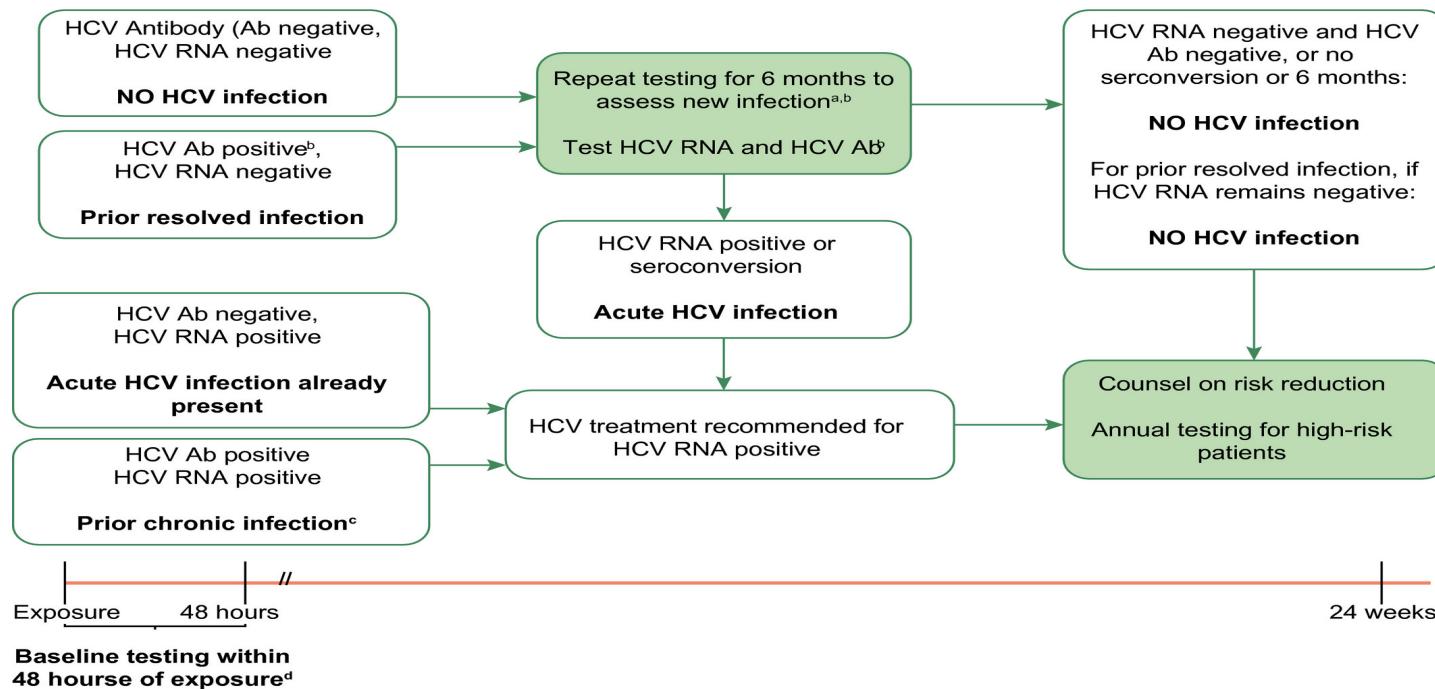
European AIDS Clinical Society (EACS) Recommendations for Acute HCV Management < 2018

- Test HCV RNA again 4 wks after initial diagnosis
 - If level has not decreased by 2 logs, anticipate chronic infection and consider early DAA therapy
 - If level has decreased by > 2 logs, repeat HCV RNA test at Wk 12 and treat if still positive
- ***“Immediate treatment of persons with high risk of transmission should be considered at diagnosis”***

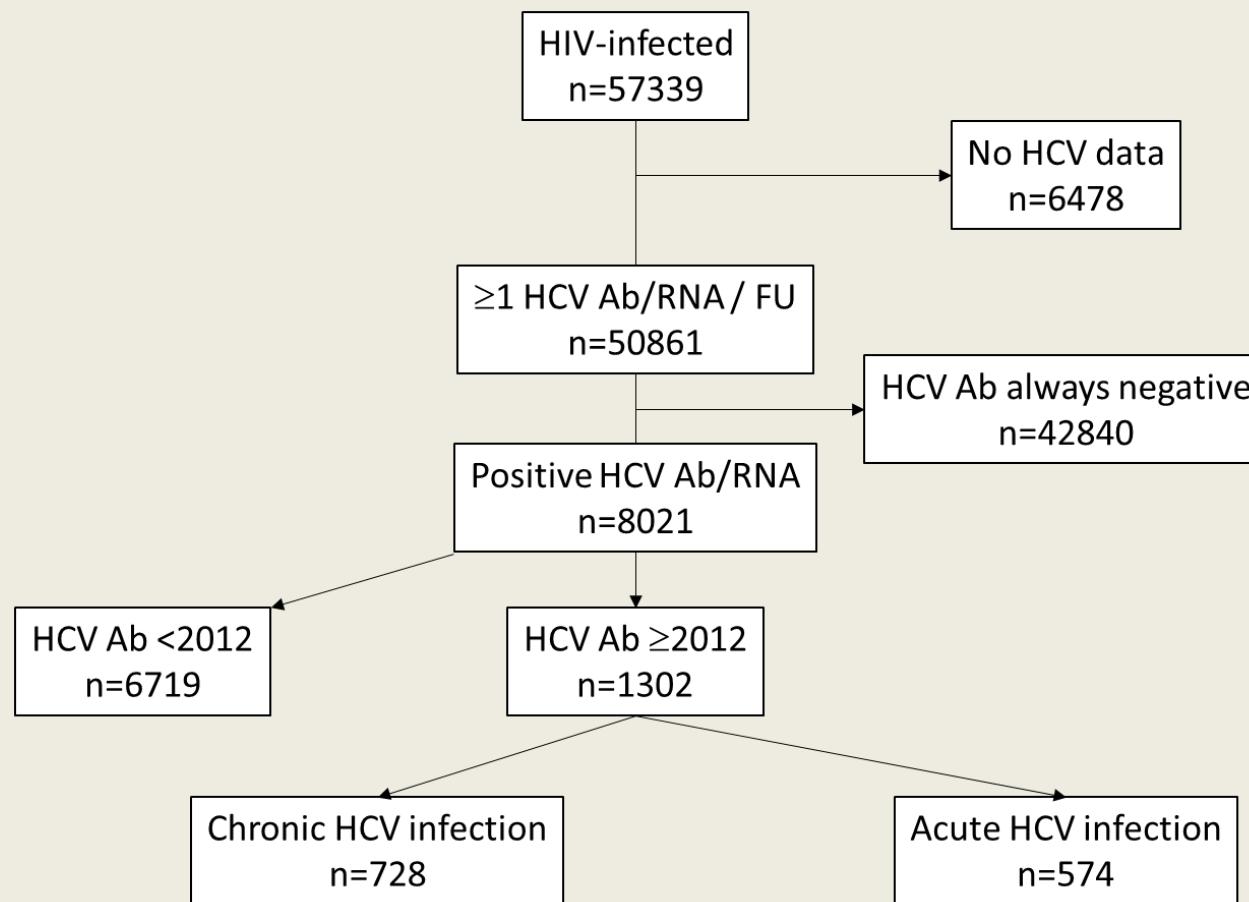


*Where available, initiate DAA treatment immediately in persons at high risk of onward transmission.

Hepatitis C Guidance 2019 Update: American Association for the Study of Liver Diseases–Infectious Diseases Society of America Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection

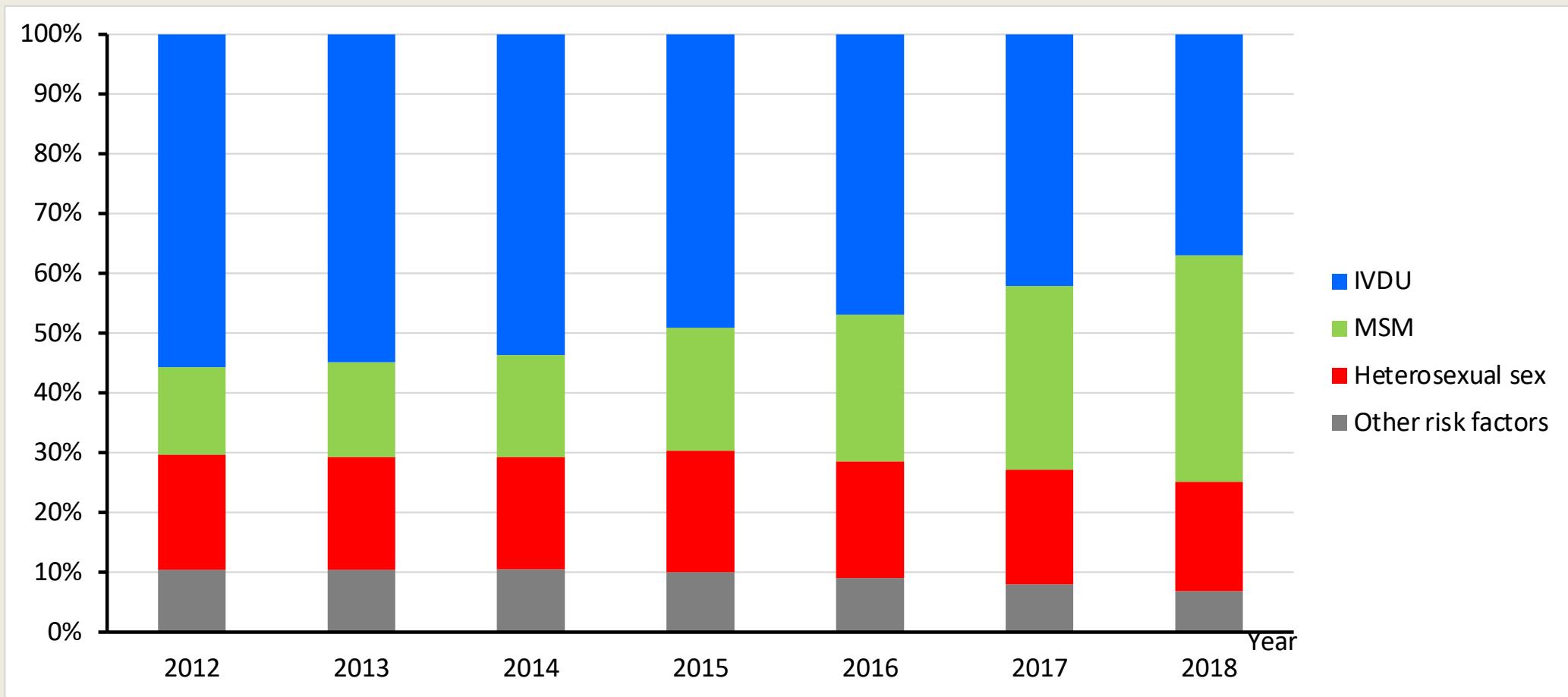


Microelimination or not? The changing epidemiology of HIV-HCV coinfection in France 2012-2018

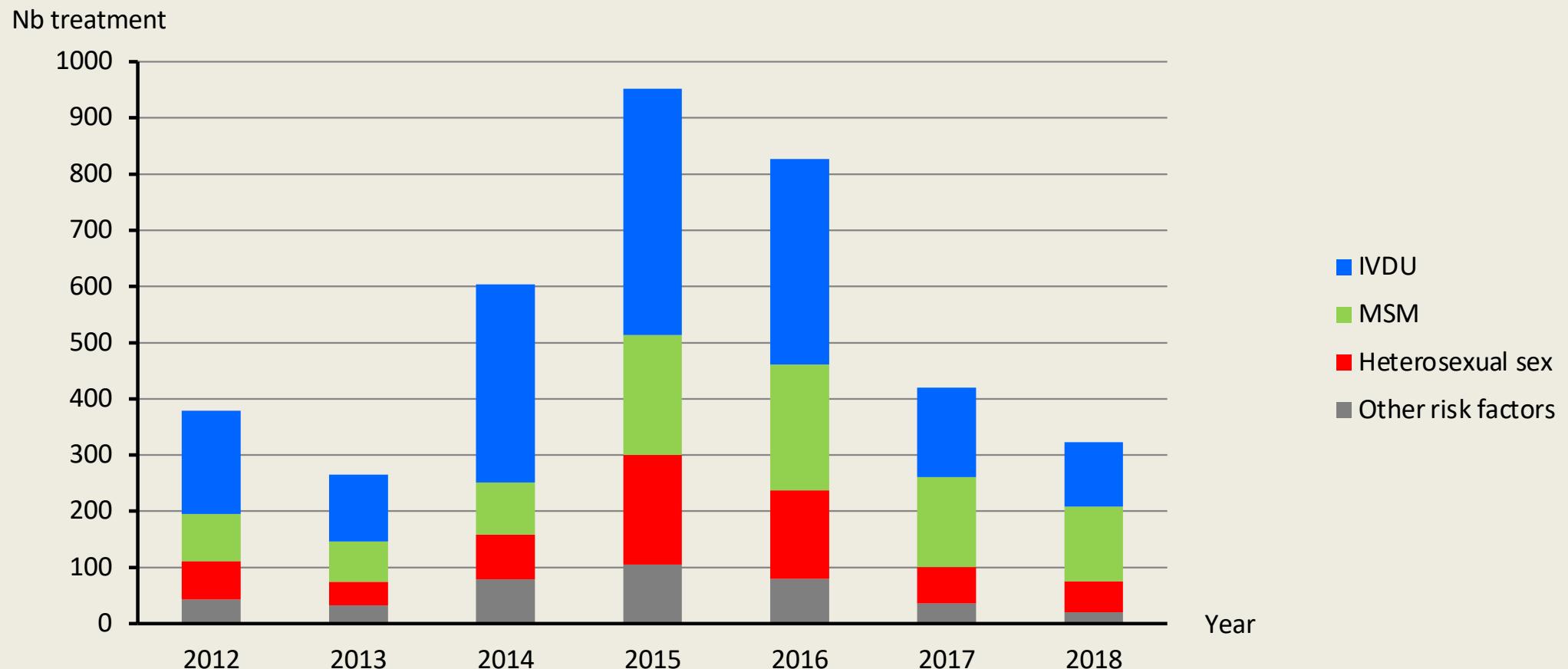


Microelimination or not? The changing epidemiology of HIV-HCV coinfection in France 2012-2018

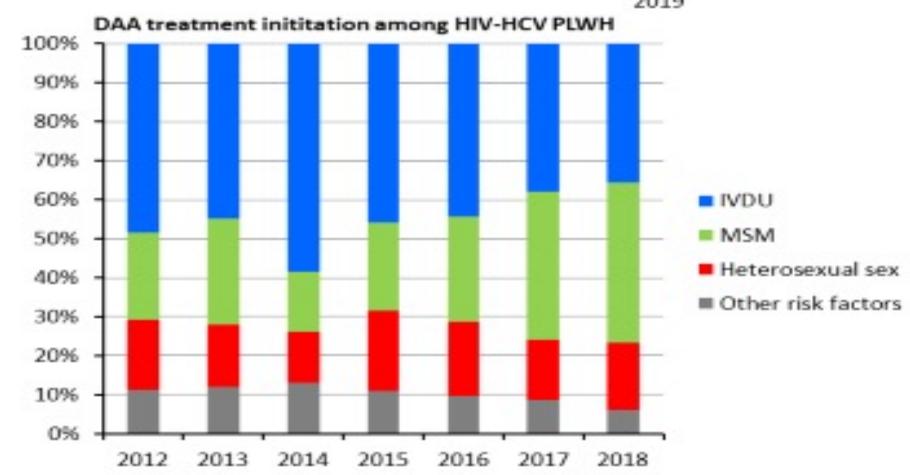
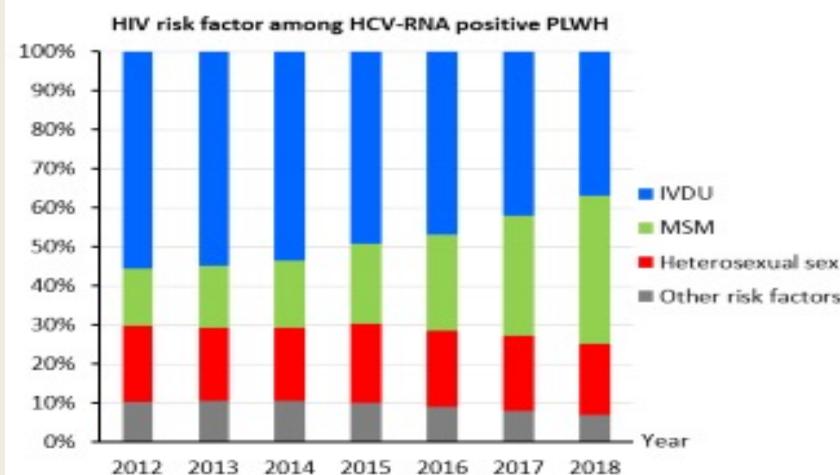
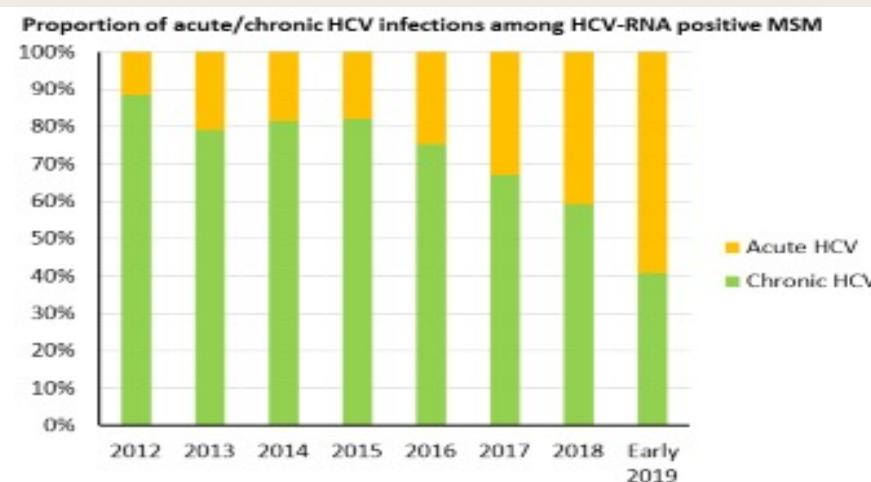
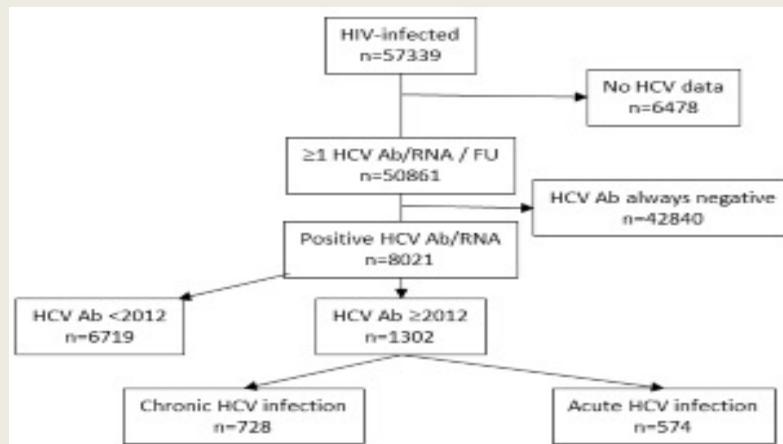
HIV risk factor among HCV-RNA positive PLWH during the 2012-2018 period



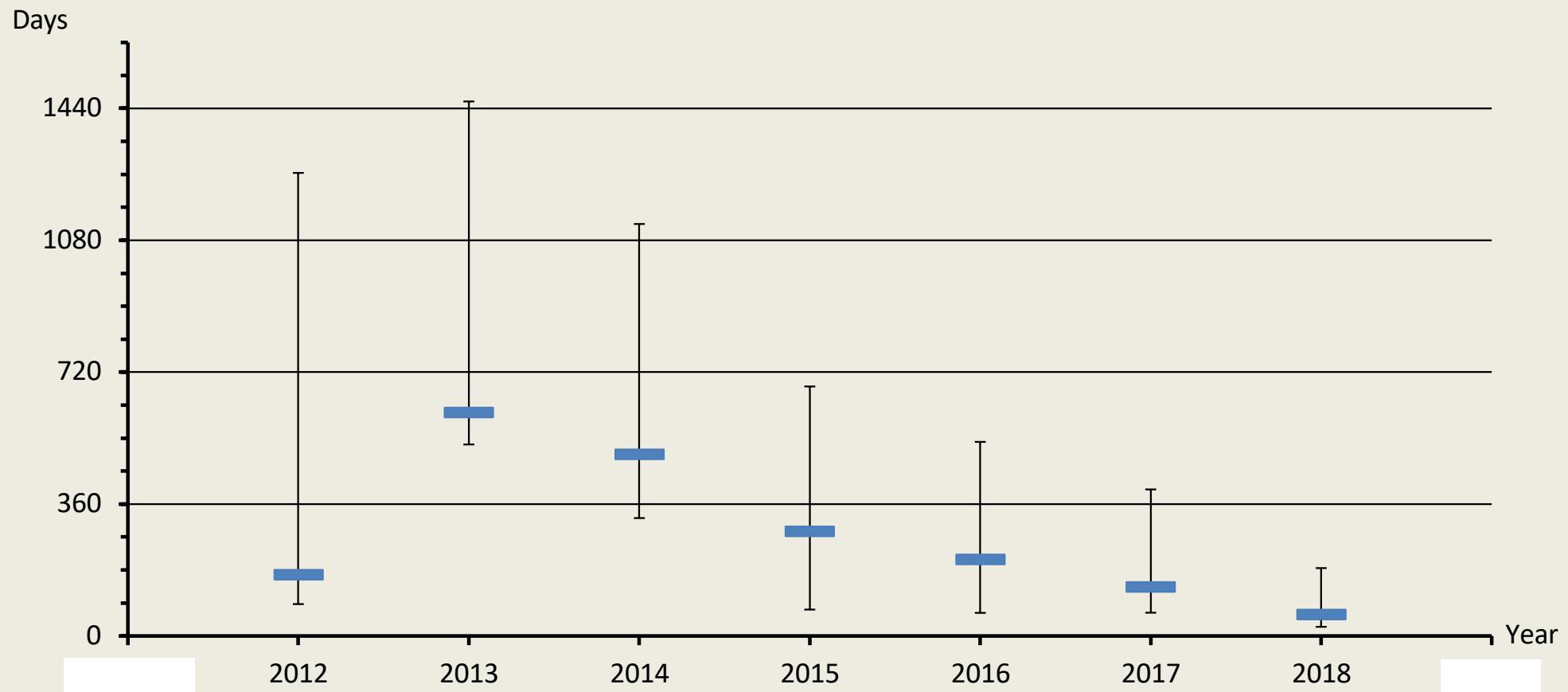
DAA treatment initiation in PLWH per calendar year



Proportion of acute/chronic HCV infections among HCV-RNA positive MSM



Time to treatment of acute HCV infections during the 2012-2018 period



MERCI POUR VOTRE ATTENTION

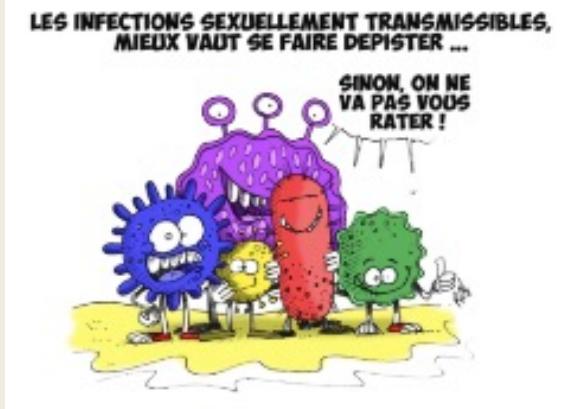
Annexes à imprimer

Documentation:

- [La PREP mode d'emploi. Petit quide pour les \(futurs-es\) utilisateurs-rices de PrEP. AIDES 2018](#)
- [Prise en charge médicale des personnes vivant avec le VIH. Recommandations groupe d'experts - Actualisations avril 2018 - Prévention et dépistage](#)
- [La prophylaxie pré-exposition \(PrEP\) au VIH par Truvada®. Haute Autorité de Santé - Mars 2017](#)
- <http://ansm.sante.fr/S-informer/Points-d-information-Points-d-information/Prophylaxie-pre-exposition-au-VIH-l-ANSM-rappelle-les-mesures-additionnelles-de-reduction-des-risques-Point-d-Information>
- [La prophylaxie pré-exposition au VIH. Accompagner sa dispensation en pharmacie. AIDES, Cespharm. Mars 2018](#)

Traitements des ISTs

- Gonocoque :
 - 50 % fluoroquinolone-R, 60 % doxycycline-R, 10 % azithromycine-R
 - **500 mg de ceftriaxone IM / DU**
 - 240 mg de gentamicine IM / DU (allergie BL)
- Chlamydia sérovars D à K, urétrite non compliquée :
 - **Doxycycline 200mg/j pendant 7 jours**
 - Azithromycine : 1 gramme DU
- Syphilis :
 - **Benzathine pénicilline G : 2.4 MU**
 - Doxycycline 200 mg/j pendant 15 jours



La PrEP en pratique : l'initiation

- Expliquer que la PrEP ne protège que du VIH : ce qui permet la promotion du préservatif
- Expliquer qu'elle n'est efficace que si elle est bien prise ...
- Exposer les deux modalités de prises, que l'on détermine en fonction du nombre de rapports par semaine et leur répartition
- Exposer la surveillance et le suivi, expliquer que la PrEP s'inscrit dans une consultation de santé sexuelle avec vaccinations et surveillance et traitement des autres ISTs
- Exposer les éventuels effets secondaires
- Recueil des pratiques, de l'utilisation de drogues dans un contexte sexuel (Chems)
- Seule contre indication : clairance < 60 ml /mm
- **Connaître la date du dernier rapport insertif ou réceptif non protégé qui est déterminant pour débuter la PrEP**
- **Bilan initial : sérologie VIH (+/- CV), sérologie syphilis, VHB, VHC, VHA (IgG) , PCR chlamydia et gonocoque sur 3 sites . Crétatininémie et clairance estimée , phosphorémie +/- ALAT**

La PrEP en pratique : la prescription

- **Schéma de prise :**
 - Continue : un par jour (protection à J8)
 - A la demande
 - Discontinue : non validée chez les femmes et CI si infection par le VHB
- **Molécules :**
 - Emtricitabine 200 mg / Ténofovir désoproxil 245 mg
- **Coût :**
 - 178 € par mois en prise quotidienne
- **Cibles :**
 - HSH, plusieurs antécédents d'ISTs, multi partenariat, traitement post exposition
 - Migrants
 - Libertins
- **Interactions :**
 - Pas d'interaction en dehors de la co-administration prolongée de médicaments néphrotoxiques (AINS)
- **Toxicité :**
 - Pas de signal à 5 ans de l'implémentation



La PrEP en pratique : le suivi

- Consultation à M1
 - Retours sur observance et bonne compréhension du schéma de prise à la demande
 - Tolérance
 - Bilan biologique : créatininémie et sérologie VIH (Elisa 4)
- Consultation de renouvellement trimestrielle :
 - Observance
 - Poursuite vaccinations : Hépatites A et B , HPV si < 26 ans , méningocoque
 - Orientation vers addictologue ou sexologue si besoin
 - Bilan biologique : Sérologie VIH, Syphilis, Créatinémie, ALAT, PCR chlamydia pharynx, anus et urinaire
 - En cas d'arrêt de PrEP : pas de reprise si fenêtre sérologique
 - Si signe de primo-infection VIH : référent hospitalier

Women in the 2019 hepatitis C cascade of care: findings from the British Columbia Hepatitis Testers cohort study

