Ospedale San Paolo
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Regione Lombardia
ASST Santi Paolo e Carlo

UNIVERSITÀ DEGLI STUDI DI MILANO

L'importanza della prevenzione: proposta vaccinale e PreP

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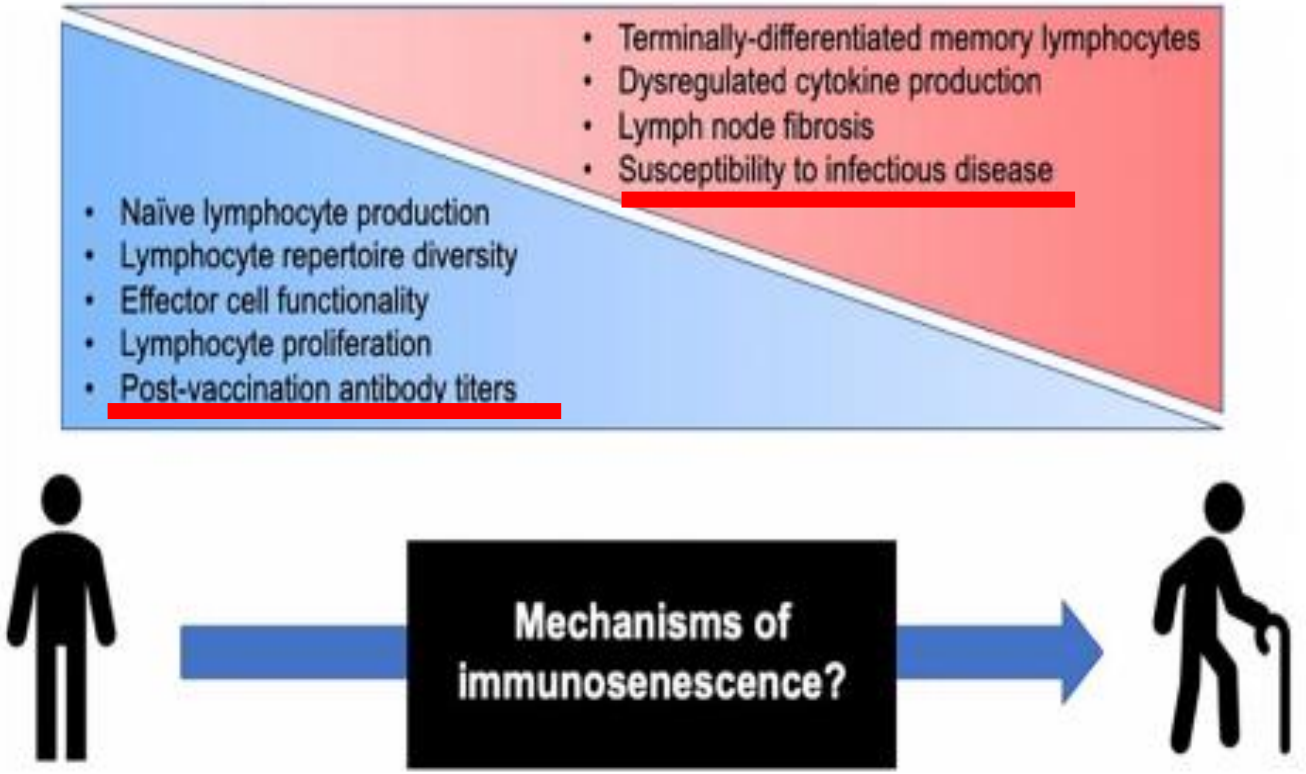
Disclosure of potential conflicts of interest, last 3years

- Advisor for AbbVie, BMS, Gilead, Janssen-Cilag, MSD and ViiV
- Speakers' honoraria from AbbVie, BMS, Gilead, Janssen-Cilag, MSD and ViiV
- Support for travel meetings from AbbVie, BMS, Gilead, and ViiV
- Grant for research from AbbVie, Gilead, Janssen-Cilag, MSD and ViiV

Importanza della prevenzione in PLWH

- ✓ **Vaccinazioni in HIV**
- ✓ PrEP

Invecchiamento e immunità



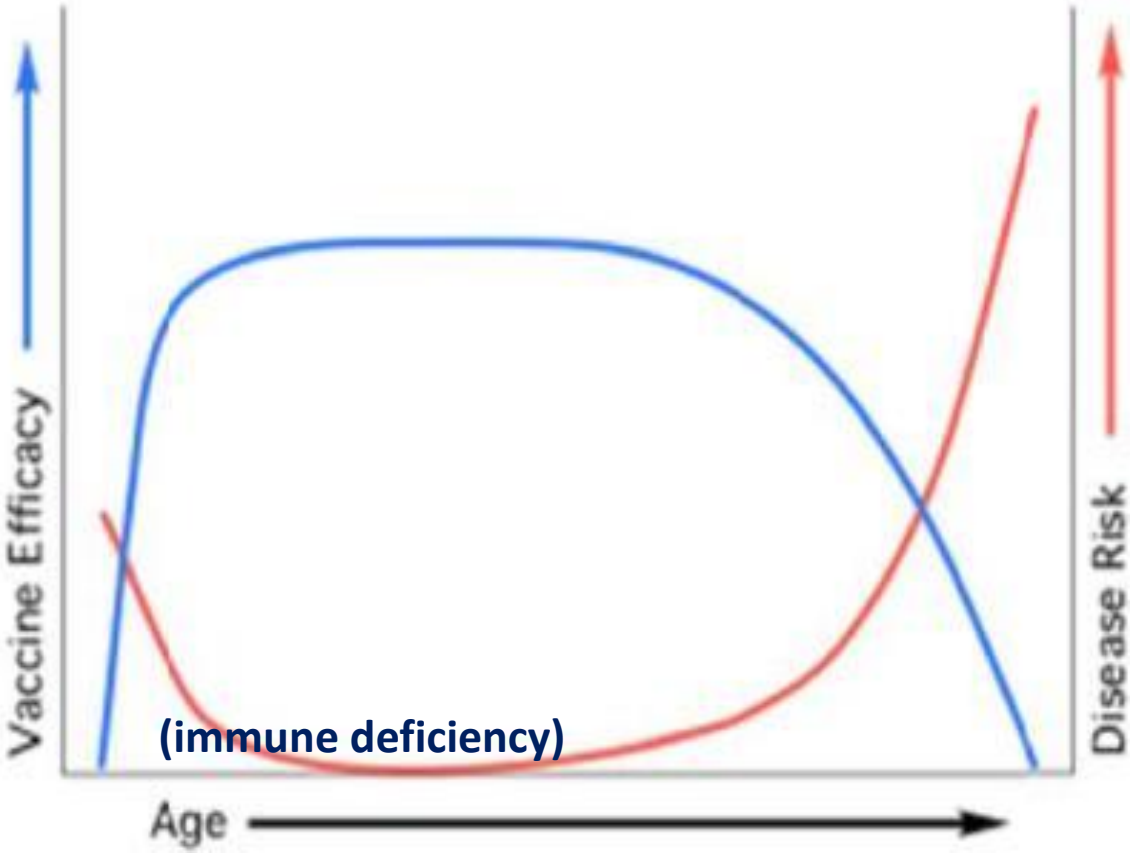
Crooke SN, Immun Ageing. 2019; 16: 25.

DELLE VACCINAZIONI NEGLI IMMUNODEPRESSI E NEGLI ANZIANI

EFFICACIA

BACKGROUND (1)

Increasing risks



Decreasing vaccines efficacy

Amanna IJ, Open Longev Sci. 2012 Jun 29; 6(2012): 64–72.

AIDS-Defining Illnesses

- Candidiasis of esophagus, trachea or lungs
- Cervical Cancer (invaisive)
- Coccidiomycosis
- Cryptococcosis
- Cryptosporidiosis
- Isosporiosis
- Cytomegalovirus disease
- HSV (> 1 month duration)
- Disseminated histoplasmosis
- HIV encephalopathy
- Kaposi's sarcoma
- Lymphoma (CNS or Burkitt's)
- Mycobacterium avium complex
- Mycobacterium tuberculosis (pulmonary)
- Pneumocystis pneumonia
- Recurrent bacterial pneumonia
- Progressive multifocal leukoencephalopthy
- Recurrent Salmonella septicemia
- Toxoplasmosis of the brain
- HIV wasting syndrome

Letter to the Editor

Pneumococcal vaccination in people living with HIV

John Thornhill, Anand Sivaramakrishnan, Chloe Orkin

Show more

https://doi.org/10.1016/j.vaccine.2014.07.086

Abstract

Streptococcus pneumoniae is the leading bacterial opportunistic infection (OI) in HIV positive individuals. Anti-retroviral treatment (ART) reduces their risk of invasive Pneumococcal Disease (IPD), however, it remains 20- to 40-fold greater than that of the general population. In HIV-infected adults, pneumococcal vaccination (PCV) induces more durable and functional antibody responses in individuals on ART at the time of vaccination than in ART-naive adults, independently of the baseline CD4+ cell count. National guidelines in the UK recommend vaccination in HIV-infected adults with CD4 count >200 cells/mL and advise that it be considered for those with CD4 count <200 cells/mL[3].

We report data on IPD from a London HIV cohort of 3500 north-east London patients from 2009 to 2012. IPD was defined as a positive pneumococcal culture from blood, CSF, joint aspirate or pericardial fluid. HIV positive cases were identified by cross-referencing hospital identifiers with a positive HIV Ab/Ag test result or HIV viral load test result on the virology database. There were a total 189 cases of Invasive Pneumococcal Disease identified over the three years. 4.8% (n = 9) were known to be HIV positive at the time of their Invasive Pneumococcal infection. The serotypes of *S. pneumoniae* in the HIV positive cases included 3, 7F, 10F, 19A (n = 2), 19F and 31. The estimated incidence of IPD in our HIV cohort was 85.7 per 100,000, (based on an overall HIV cohort size of 3500) which is significantly higher when compared to the general population in London (local epidemiological data reported the incidence rate for IPD at 7.5 per 100,000 in London).

Given the higher burden of Invasive Pneumococcal Disease in this cohort, low levels of vaccination, and the predominance of vaccine sensitive strains in our cases, vaccination and strategies to improve vaccine uptake is a priority in this at risk group.

Simmons et al. BMC Medicine (2015) 13:297
DOI 10.1186/s12916-015-0538-6

BMC Medicine

RESEARCH ARTICLE Open Access

Risk of invasive meningococcal disease in children and adults with HIV in England: a population-based cohort study

Ruth D. Simmons[1*], Peter Kirwan[2], Kazim Beebeejaun[1], Andrew Riordan[3], Ray Borrow[4], Mary E. Ramsay[1], Valerie Delpech[2], Samuel Lattimore[1] and Shamez Ladhani[1]

Abstract

Background: Recent studies have identified HIV infection as a potential risk factor for invasive meningococcal disease (IMD), suggesting that HIV-infected individuals could benefit from meningococcal vaccination to reduce their risk of this rare, but severe and potentially fatal infection. In the United Kingdom, as in most industrialised countries, HIV is not considered a risk factor for IMD.

Methods: IMD incidence and relative risk by age group and meningococcal capsular group in HIV-positive compared with HIV-uninfected individuals was estimated through data linkage of national datasets in England between 2011 and 2013.

Results: IMD incidence among persons diagnosed with HIV was 6.6 per 100,000 compared to 1.5 per 100,000 among HIV-negative individuals, with a relative risk of 4.5 (95 % CI, 2.7–7.5). All but one case occurred in adults aged 16–64 years, who had a 22.7-fold (95 % CI, 12.4–41.6; P <0.001) increased risk compared with the HIV-negative adults. IMD risk by capsular group varied with age. HIV-positive children and adolescents had a higher risk of meningococcal group B disease, while adults were at increased risk of groups C, W and Y disease. Most HIV-positive individuals had been born in Africa, had acquired HIV through heterosexual contact, and were known to be HIV-positive and receiving antiretroviral treatment at IMD diagnosis. The most common clinical presentation was septicemia and, although intensive care admission was common, none died of IMD.

Conclusions: HIV-positive children and adults are at significantly increased risk of IMD, providing an evidence base for policy makers to consider HIV as a risk factor for meningococcal vaccination.

Keywords: HIV, Invasive meningococcal disease, Serogroup, Vaccination, Relative risk

Increased Risk for Meningococcal Disease Among Men Who Have Sex With Men in the United States, 2012–2015

Temitope A Folaranmi, Cecilia B Kretz, Hajime Kamiya, Jessica R MacNeil, Melissa J Whaley, Amy Blain, Mike Antwi, Marie Dorsinville, Massimo Pacilli, Shamika Smith ... Show more

Clinical Infectious Diseases, Volume 65, Issue 5, 1 September 2017, Pages 756–763, https://doi.org/10.1093/cid/cix438

Abstract

Background

Several clusters of serogroup C meningococcal disease among men who have sex with men (MSM) have been reported in the United States in recent years. The epidemiology and risk of meningococcal disease among MSM is not well described.

Methods

All meningococcal disease cases among men aged 18–64 years reported to the National Notifiable Disease Surveillance System between January 2012 and June 2015 were reviewed. Characteristics of meningococcal disease cases among MSM and men not known to be MSM (non-MSM) were described. Annualized incidence rates among MSM and non-MSM were compared through calculation of the relative risk and 95% confidence intervals. Isolates from meningococcal disease cases among MSM were characterized using standard microbiological methods and whole-genome sequencing.

Results

Seventy-four cases of meningococcal disease were reported among MSM and 453 among non-MSM. Annualized incidence of meningococcal disease among MSM was 0.56 cases per 100000 population, compared to 0.14 among non-MSM, for a relative risk of 4.0 (95% confidence interval [CI], 3.1–5.1). Among the 64 MSM with known status, 38 (59%) were infected with human immunodeficiency virus (HIV). HIV-infected MSM had 10.1 times (95% CI, 6.1–16.6) the risk of HIV-uninfected MSM. All isolates from cluster-associated cases were serogroup C sequence type 11.

Conclusions

MSM are at increased risk for meningococcal disease, although the incidence of disease remains low. HIV infection may be an important factor for this increased risk. Routine vaccination of HIV-infected persons with a quadrivalent meningococcal conjugate vaccine in accordance with Advisory Committee on Immunization Practices recommendations should be encouraged.

Clinical characteristics of acute hepatitis A outbreak in Taiwan, 2015–2016: observations from a tertiary medical center

Nan-Yu Chen, Zhuo-Hao Liu, Shian-Sen Shie, Tsung-Hsing Chen and Ting-Shu Wu

BMC Infectious Diseases BMC series – open, inclusive and trusted 2017 17:441 | https://doi.org/10.1186/s12879-017-2555-

Received: 8 December 2016 | Accepted: 16 June 2017 | Published: 20 June 2017

Abstract

Background

Acute hepatitis A is a fecal-oral transmitted disease related to inadequate sanitary conditions. In addition to its traditional classification, several outbreaks in the men who have sex with men (MSM) population have resulted in acute hepatitis A being recognized as a sexually transmitted disease. However, few studies have clarified the clinical manifestations in these outbreaks involving the MSM population.

Methods

Beginning in June 2015, there was an outbreak of acute hepatitis A involving the MSM population in Northern Taiwan. We conducted a 15-year retrospective study by recruiting 207 patients with the diagnosis of acute hepatitis A that included the pre-outbreak (January 2001 to May 2015) and outbreak (June 2015 to August 2016) periods in a tertiary medical center in Northern Taiwan. Using risk factors, comorbidities, presenting symptoms, laboratory test results and imaging data, we aimed to evaluate the clinical significance of acute hepatitis A in the MSM population, where human immunodeficiency virus (HIV) coinfection is common.

Results

There was a higher prevalence of reported MSM ($p < 0.001$), HIV ($p < 0.001$) and recent syphilis ($p < 0.05$) coinfection with acute hepatitis A during the outbreak period. The outbreak population had more prominent systemic symptoms, was more icteric with a higher total bilirubin level ($p < 0.05$) and had a 7-times higher tendency ($p < 0.05$) to have a hepatitis A relapse.

Conclusions

The clinical course of acute hepatitis A during an outbreak involving the MSM and HIV-positive population is more symptomatic and protracted than in the general population.

HIV, HPV and associated disease

- Impaired immune response increases susceptibility to
  - acquisition of HPV infection
  - reactivation of latent HPV infection
- Impaired clearance of oncogenic viral infections

- Chronic inflammation promotes carcinogenesis by
  - generation of genotoxic reactive oxygen and nitrogen species
  - procarcinogenic cytokines and growth factors
- HIV +ve individuals are more likely to have
  - prevalent and persistent HPV infection
  - to progress in pre-cancerous lesions or cancer

Phanuphak et al., J Acquir Immune Defic Syndr, 2014
Vessely et al., Annu Rev Immunol, 2011
Schottenfield et al., CA Cancer J Clin ,2006
Dubrow et al., Curr Opin Oncol ,2012

Linee guida Simit per HIV

- Norme generali di prevenzione oncologica (AI).
  I più importanti strumenti di Prevenzione Oncologica sono:
  - L'inizio precoce della terapia antiretrovirale*
  - Le modificazioni dello stile di vita (interruzione del fumo ed astinenza da alcolici)
  - La terapia delle infezioni da HBV/HCV
  - **La vaccinazione anti-HPV****

*I pazienti coinfetti con HPV e con nadir di T CD4+ < 200 cellule/µL e/o viremia HIV persistentemente elevata (>100.000 cp/mL), rimangono ad alto rischio di neoplasie anogenitali invasive da HPV, anche dopo il recupero viro-immunologico;

raccomandata nella fascia di età 9-26 anni, **consigliata senza limite di età, con vaccino quadrivalente in soggetti con viremia HIV soppressa e conta dei CD4 > 350/µL.

Linee Guida Italiane sull'utilizzo dei farmaci antiretrovirali e sulla gestione diagnostico-clinica delle persone con infezione da HIV-1

22 Novembre 2016

Delibera FVG 365 (3/3/2017)

- Il vaccino deve essere offerto per la prevenzione dei tumori HPV correlati a:
  - soggetti affetti da HIV
  - MSM
  - soggetti affetti da patologie che richiedono immunomodulatori ed immunosopressori che possono aumentare il rischio di infezione da HPV (MICI, sclerosi multipla, ecc)

- Gratuità per entrambi i sessi dal 12 anno di vita esteso fino al compimento dei 25 anni

Copertura vaccinale nella popolazione HIV

Valour F et al. Vaccine 2014, 32:4558				
	Status non noto	Infez. naturale	Non immuni vaccinati	Non immuni non vaccinati
HBV	21 /2467	1189	**778 (61.9%)**	479
HAV	762/2467	1116	**279 (47,9%)***	310

** 54.5 % MSM*

	Vaccinati	Non vaccinati
Pneumococco^	**1594 (64.6%)**	873
Influenza^	**762 (30,9%)^**	1705

^sign. più vaccinati i pz con comorbosità

→ scarsa sensibilizzazione?, insufficiente conoscenza delle raccomandazioni? preoccupazione circa efficacia/sicurezza dei vaccini? costi? organizzazione dei servizi?)

Tabella: Vaccinazioni nelle persone infettate dal virus HIV

Delle schede informative specifiche sono disponibili per molte delle vaccinazioni citate.

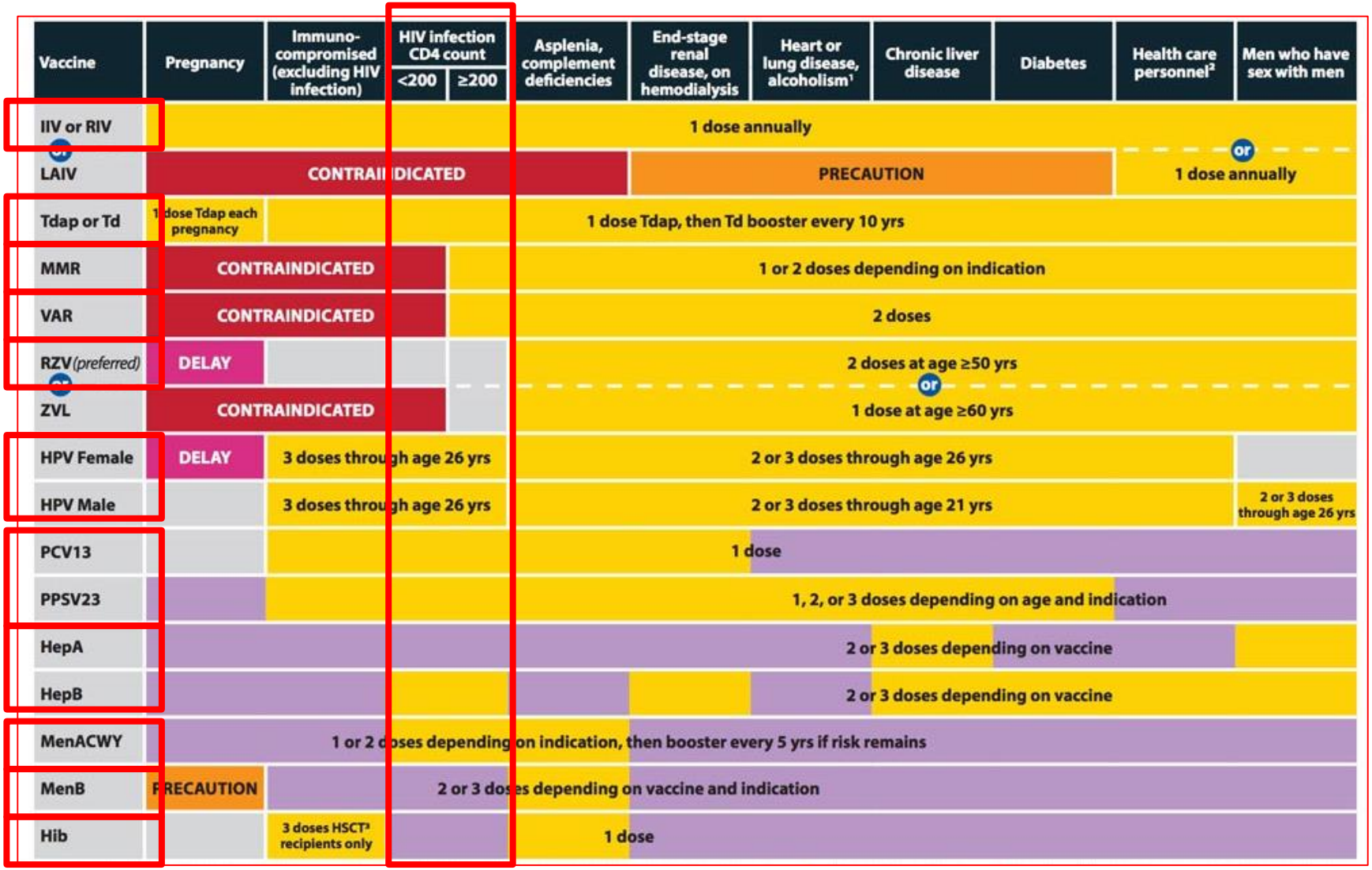
Vaccinazioni raccomandate di base per i bambini e gli adolescenti	Per tutti i pazienti	Difterite*, tetano*, pertosse*, poliomielite*, Haemophilus influenzae b*, epatite B, pneumococchi*, meningite da meningococchi*, influenza* (annuale)
	Per i pazienti con **un tasso sufficiente** di linfociti T CD4***	Morbillo*, orecchioni*, rosolia* e varicella*
Vaccinazioni raccomandate di base negli adulti	Per tutti i pazienti (richiami e ricupero)	Difterite*, tetano*, pertosse*, poliomielite*, Haemophilus influenzae b*, epatite B, pneumococchi*, meningite da meningococchi*, influenza* (annuale)
	Per i pazienti con **un tasso sufficiente** di linfociti T CD4***	Morbillo*, orecchioni*, rosolia* e varicella* (per le persone che non hanno avuto la varicella nella loro infanzia)
Vaccinazioni raccomandate in particolari situazioni a rischio	Per tutti i pazienti	Epatite A**, meningoencefalite da zecche* (FSME), meningite da meningococchi*, rabbia**, febbre tifoide (vaccino inattivato)**, encefalite giapponese**
	Per i pazienti con **un tasso sufficiente** di linfociti T CD4***	Febbre gialla**
Vaccini composti da microbi vivi che non devono essere somministrati		Tubercolosi, vaccino orale contro la febbre tifoide

*Queste vaccinazioni sono considerate come molto importanti dalle autorità sanitarie, per cui il loro finanziamento è a carico dell'assicurazione malattia di base.

**Il rischio di contrarre queste infezioni in Svizzera è molto limitato o inesistente, motivo per cui il finanziamento di queste vaccinazioni essenzialmente destinate ai viaggiatori è a loro carico.

***Certe vaccinazioni possono essere raccomandate ai pazienti che hanno un tasso sufficiente di linfociti T CD4.

Recommended Adult Immunization Schedule by medical condition



Recommended

Recommended if additional risk factors

Recommended based on shared clinical decision making

Principi generali che devono essere applicati all'utilizzo dei vaccini nella popolazione immunodepressa e HIV

- Massimizzare i benefici delle vaccinazioni riducendo al minimo possibili eventi avversi: evitare vaccini vivi a meno che
  - L'immunomodepressione sia lieve e vi siano dati di sicurezza del vaccino in questo contesto
  - Il rischio di infezione naturale sia maggiore di quello di possibili eventi avversi della vaccinazione
- La suscettibilità alle infezioni e la capacità di rispondere a un vaccino variano a seconda del grado di risposta immunitaria: immunizzare quindi nel momento in cui è possibile prevedere la massima risposta immunitaria
  - se possibile, prima di qualsiasi immunosoppressione programmata
  - ritardare se l'immunodeficienza è transitoria (se ciò può essere fatto in sicurezza perché l'esposizione è improbabile)
- L'entità e la durata della risposta vaccinale sono spesso ridotte
  - Monitorare, se possibile, la risposta anticorpale e somministrare una dose di richiamo se il titolo è inadeguato
- Considerare di estendere la vaccinazione nell'ambiende del paziente
  - Conviventi
  - Operatori sanitari che hanno il cura il paziente
- Considerare l'immunizzazione passiva (Ig specifiche o non specifiche) per la protezione pre- e post- esposizione

Importanza della prevenzione in PLWH

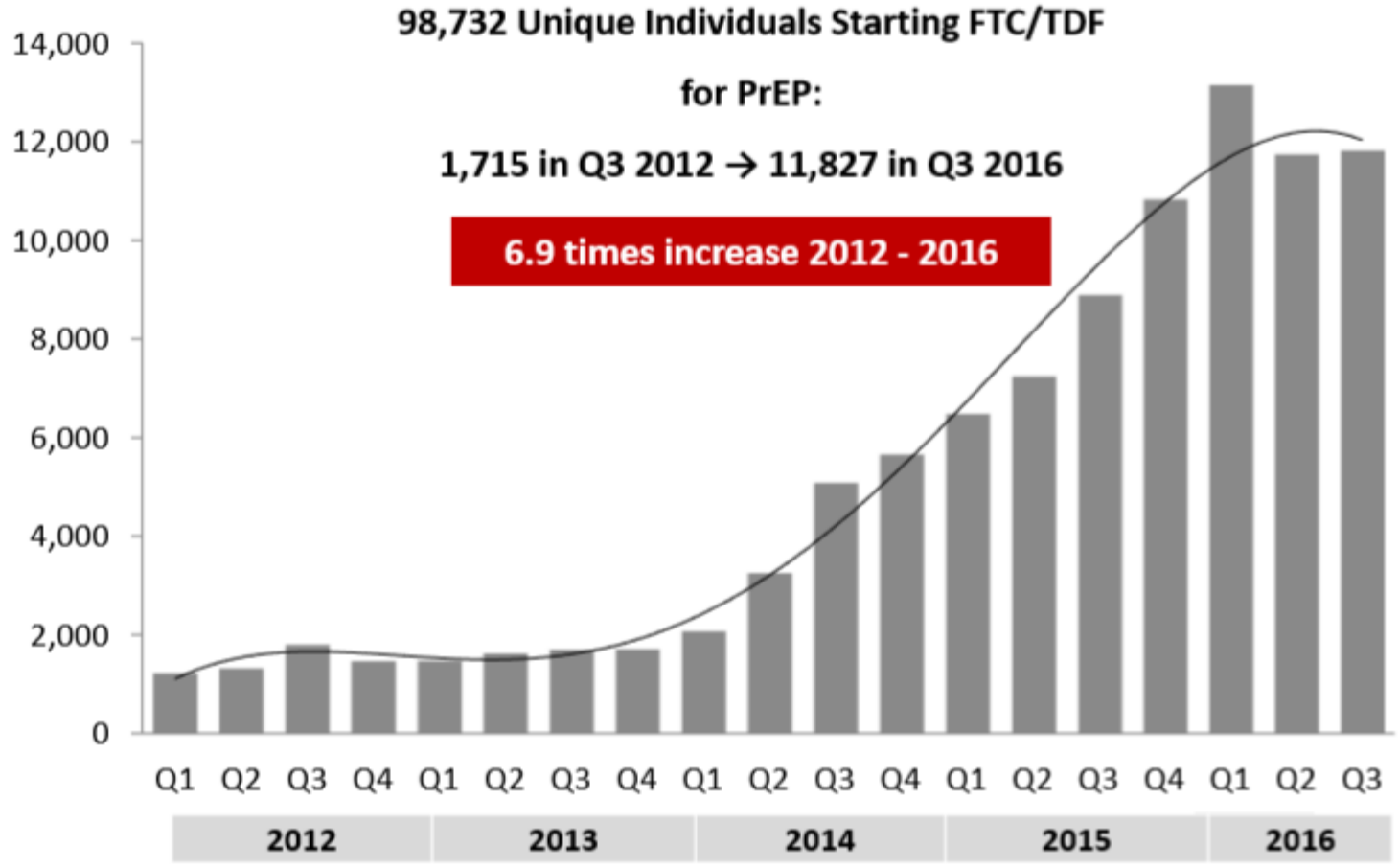
- ✓ Vaccinazioni in HIV
- ✓ **PrEP**

Tabella 1 – Principali trial sulla PrEP con TDF/emtricitabina o TDF orale

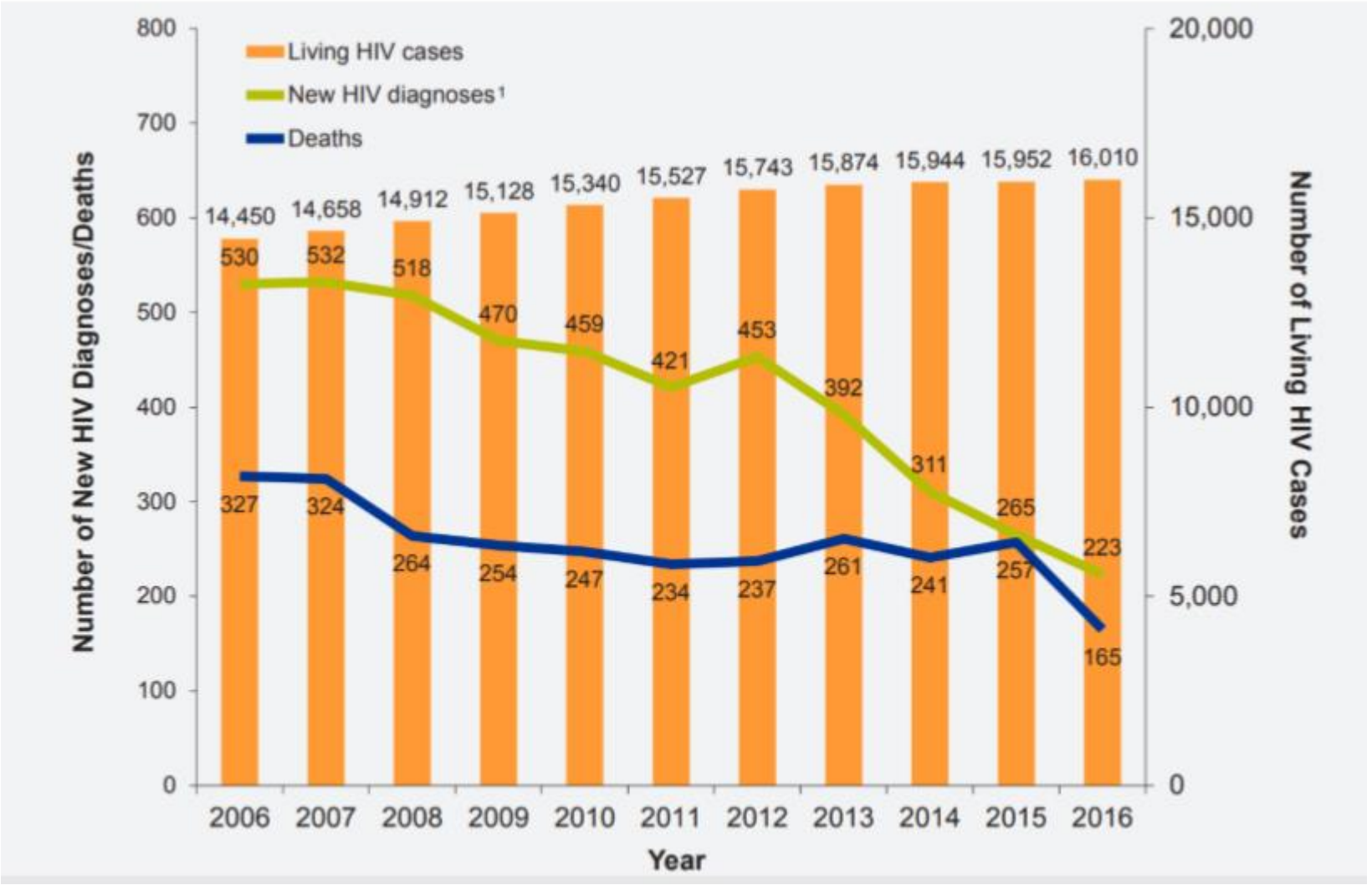
Clinical trial	Participanti	Numero	Farmaco	mITT[a] efficacia come % di riduzione della acquisizione dell'infezione[b]		Aderenza[c]	Efficacia corretta per tasso di aderenza basata sulla rilevazione di TDF nel sangue[d]	
				%	(95% CI)	%	%	(95% CI)
iPrEx	MSM, TGW	2.499	FTC/TDF	44	(15-63)	51	92	(40-99)
Partners PrEP	coppie eterosessuali HIV sierodiscordanti	4.747	TDF	67*	(44-81)	81	86	(67-98)
			FTC/TDF	75*	(55-87)		90	(58-9)
TDF2	uomini e donne eterosessuali attivi	1.219	FTC/TDF	62**	(21-83)	84	78	(41-94)
Bangkok Tenofovir Study	PWID	2.413	TDF	49	(10-72)	84	84	(73-99)
PROUD	MSM	544	FTC/TDF	86	(64-96)	88	----	----
ANRS-IPERGAY	MSM	400	on-demand FTC/TDF[e]	86	(40-98)	86 (TDF) 82 (FTC)	circa 100%	----
Fem-PrEP	donne eterosessuali attive	2.120	FTC/TDF	6	(-52 41)	26	< 40%	----
VOICE	donne eterosessuali attive	5.029	FTC/TDF	-4	(-49 27)	29	<30%	----

[a] criterio intention-to-treat modificato (mITT);

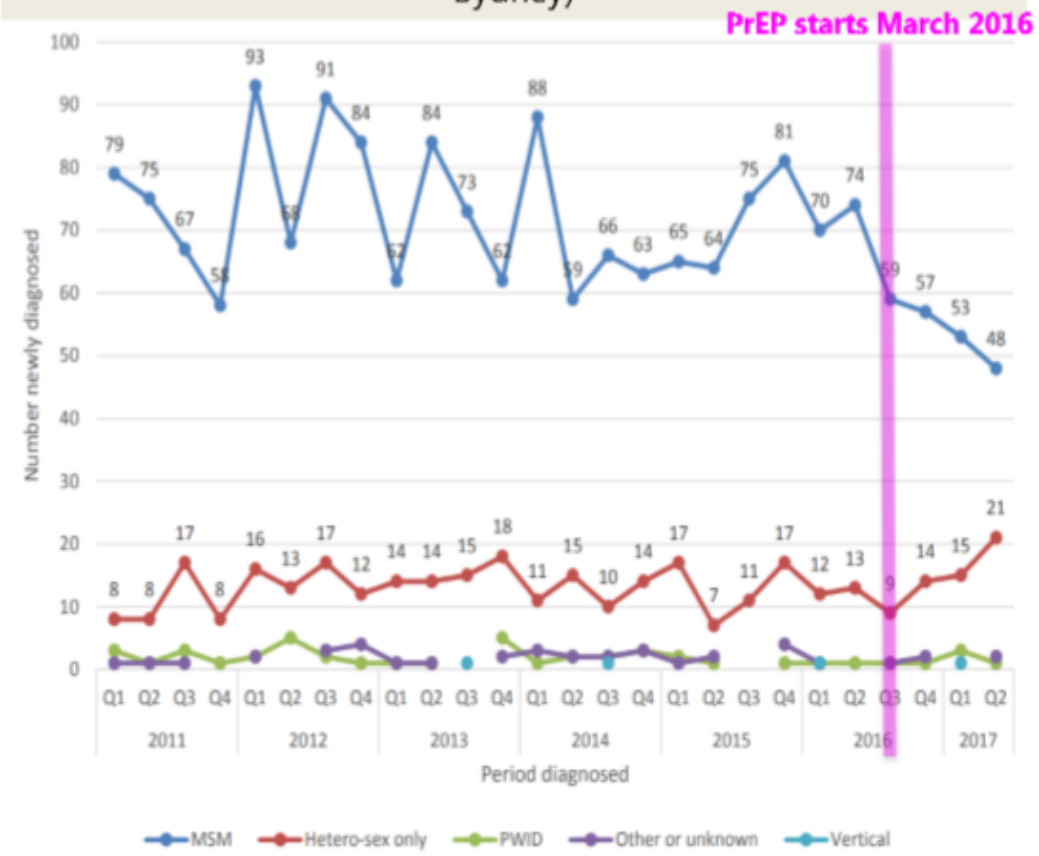
Unique Individuals Starting FTC/TDF for PrEP in US, 2012 to 2016 (by quarter)



New HIV diagnoses, deaths, and prevalence, 2006-2016, San Francisco



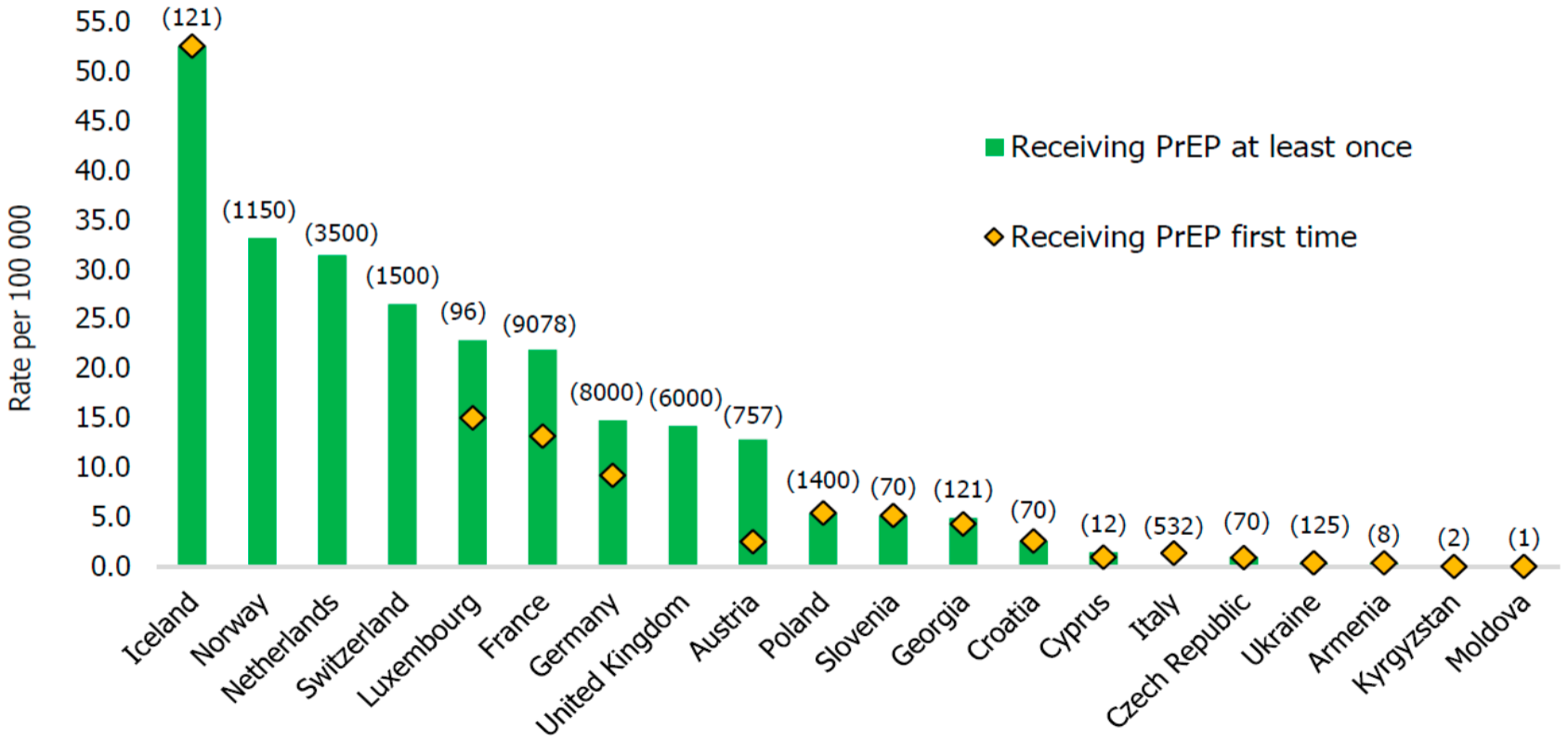
Newly diagnosed HIV cases in New South Wales (including Sydney)



- Educated community and built demand for PrEP among MSM
- PrEP demonstration project at scale
- 25% reduction in the average number of new cases compared to the previous five years.

Source: http://www.health.nsw.gov.au/endinghiv/Documents/q2-2017-nsw-hiv-data-report.pdf

Figure 4. Number of people receiving PrEP in Europe and Central Asia (n=20), reported in 2019[10]



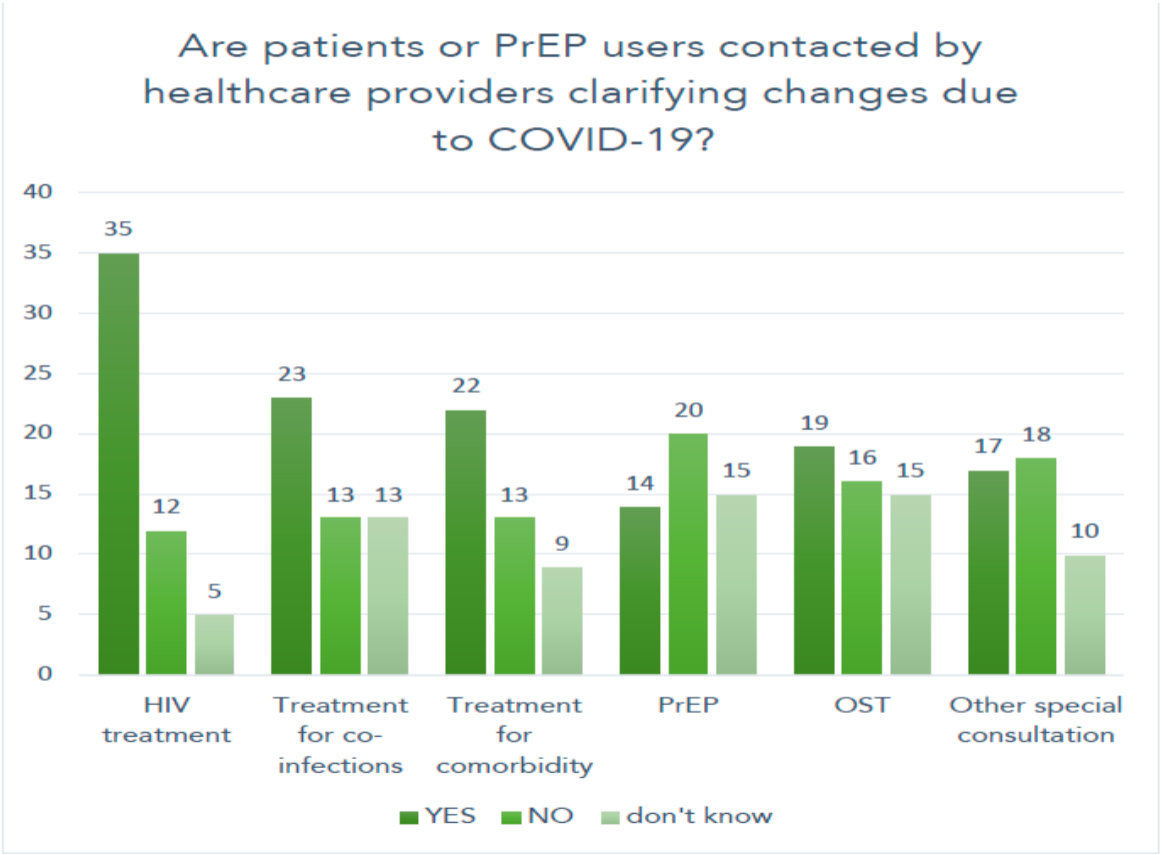


Figure 4. Number of answers regarding contact from healthcare providers about changes due to COVID-19

European AIDS Treatment Group

4.3. Changes in the amounts of medicines supplied

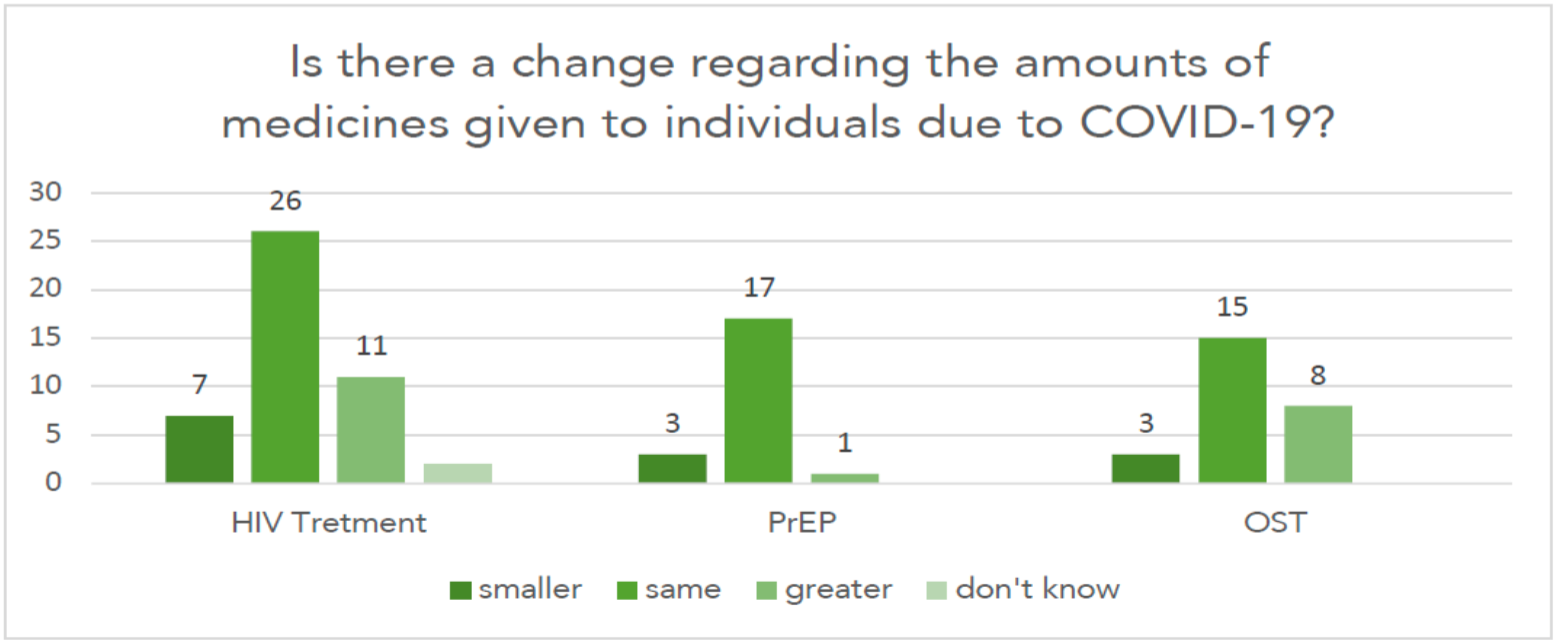


Figure 5. Amounts of medicines given to individuals due to COVID-19

The PrEP programme

Longitudinal open cohort

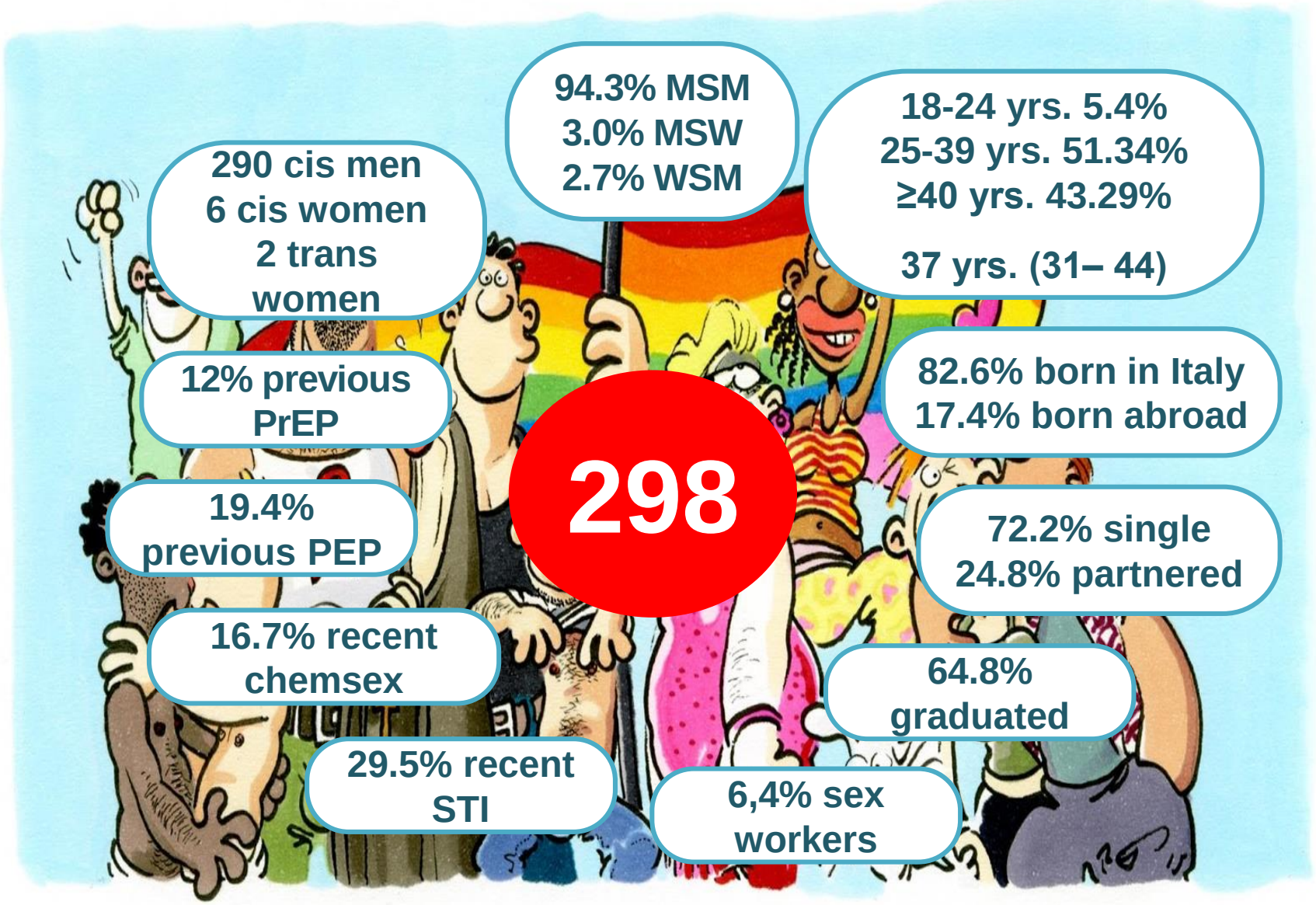
Programme schedule:

- Screening (T_{-1})
- PrEP start (T_0)
- Follow-ups (T_1, T_2, T_3,…)

At each appointment:

- Questionnaire
- Consultation with ID specialist
- STIs testing
- Consultation with psychologist/peer counsellor

Population


94.3% MSM
3.0% MSW
2.7% WSM
18-24 yrs. 5.4%
25-39 yrs. 51.34%
≥40 yrs. 43.29%
37 yrs. (31– 44)
290 cis men
6 cis women
2 trans women
12% previous PrEP
298
82.6% born in Italy
17.4% born abroad
19.4% previous PEP
72.2% single
24.8% partnered
16.7% recent chemsex
64.8% graduated
29.5% recent STI
6,4% sex workers

STIs monitoring

1 HIV infection at T_{-1}
(rapid HIV Ab/Ag test on whole blood)

0 HCV infections
(rapid HCV Ab test on whole blood)

- 7 (2.8%) syphilis infections at $T_{\leq 0}$
- 3 external syphilis diagnoses at $T_{\leq 0}$

- 9 (2.35%) syphilis infections at $T_{>0}$
- 8 external syphilis diagnoses at $T_{>0}$

(rapid Treponemal or Treponemal/non-Treponemal antibodies test on whole blood)

- 20 (9.3%) CT infections at $T_{\leq 0}$ (19 rectal)
- 10 (4.7%) NG infections at $T_{\leq 0}$ (9 rectal)

- 28 (7.1%) CT infections at $T_{>0}$ (24 rectal)
- 24 (6.1%) NG infections at $T_{>0}$ (23 rectal)

<u>Since February 2019</u>

(POC real-time PCR *C. trachomatis*/*N. gonorrhoeae* assay on rectal swab and urine sample)

Changes in sexual behaviours?

How many **occasional partners** did you have in the past 30 days?

	Mean (95% CI)
At T_{-1}	4.5 (3.7 – 5.2)
At latest $T_{>0}$	5.9 (4.9 – 6.9)

	Difference (95% CI)	p-value
T_{-1} vs. latest $T_{>0}$	+1.4 (+2.4 – +0.5)	0.004
T_{-1} vs. T_1	+3.3 (+4.4 – +2.2)	<0.001
T_{-1} vs. latest $T_{>1}$	+0.6 (+1.6 – -0.3)	0.201

(paired t-tests)

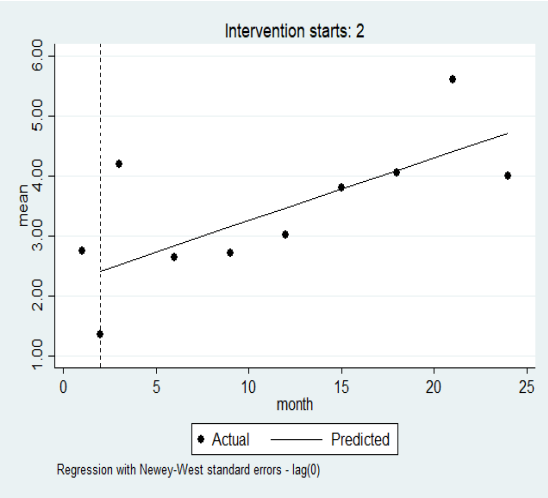
Changes in sexual behaviours?

How many times did you have **condomless anal/vaginal sex** in the past 30 days?

	Mean (95% CI)
At T_{-1}	2.3 (1.7 – 2.9)
At latest $T_{>0}$	4.2 (3.4 – 5.1)

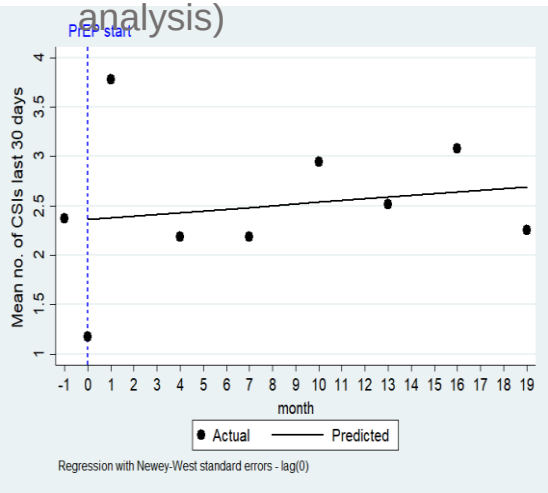
	Difference (95% CI)	p-value
T_{-1} vs. latest $T_{>0}$	+1.9 (+3.0 – +0.8)	<0.001
T_{-1} vs. T_0	-1.4 (-0.5 – -2.4)	0.005
T_{-1} vs. T_1	+2.1 (+3.2 – +1.18)	<0.001
T_{-1} vs. latest $T_{>1}$	+1.1 (+2.5 – -0.3)	0.124

(paired t-tests)



10/10/2020

(interrupted time series analysis)



02/03/2020

COVID-19 and lockdown

Milano CHECKPOINT

Milano Checkpoint closed for **16 weeks**: ≈200 appointments lost

- ID specialist available for PrEP prescription (22 filled)
- Psychologists and peer counsellors available for video-chats
- **Virtual PrEP screening consultations** (66 done)

Since reopening:

- Opening hours increased
- **Virtual PrEP screening → Physical appointment**
  with baseline exams and adequate window period for H test
- POC **HIV RNA** test implemented

84 new PrEP users

Acknowledgments

The Milano Checkpoint Group:

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Monica Massa	Vincenzo Polgati	Roberto Repossi
Federica Rossi	Roberto Rossotti	Elisa Suardi
Daniele Tesoro	Alessandro Tavelli	Pietro Vinti
	Donatello Zagato	

Indicazioni per PrEP dalle Linee-Guida

	WHO 2016[1]	EACS 2017[2]	US CDC 2014[3]	BHIVA–BASHH 2016[4]	SIMIT-MdS 2016[5]
Popolazioni con indicazione alla PrEP groups	MSM, TGW MSM, eterosessuali, PWID	MSM, TGW MSM, eterosessuali	MSM, PWID, eterosessuali	MSM, TGW MSM, eterosessuali	MSM, eterosessuali, sex workers, PWID, partners HIV+, donne in coppie sierodiscordanti al concepimento
Prima della PrEP*					
HIV test	3° generazione	4° generazione	Si	4° generazione	4° generazione
HBV test	Si	Si	Si	–	Si
Test di funzionalità renale	Creatinina sierica	In accordo con le raccomandazioni sull'uso di TDF	Creatinina sierica	–	Creatinina sierica (con e-GFR sec. CG)
Regime					
Quotidiano	–	Si	Si	Si	Si
On-demand	–	Si	–	Si	Si
Follow-up					
Aderenza	Si	Si	Ogni 3 mesi	Entro 1 mese	Si
HIV test	Regolare	Ogni 3 mesi	Ogni 3 mesi	Ogni 3 mesi	Ogni 3 mesi
Test di funzionalità renale	Al 3° mese e poi annualmente	In accordo con le raccomandazioni sull'uso di TDF	Al 3° mese e poi ogni 6 mesi	Ogni 3 mesi	Al 3° mese e poi ogni 6 mesi
Densità minerale ossea	–	In accordo con le raccomandazioni sull'uso di TDF	–	–	
MST screening	–	Regolarmente (incluso HCV)	Ogni 3 mesi	Ogni 3 mesi	Ogni 6 mesi

Confronting Rising STIs in the Era of PrEP and Treatment as Prevention

- PrEP contributed to changes in sexual behaviour in MSM
  - PROUD study: men in the immediate PrEP arm were more likely to have >10 condomless anal sex partners in prior 90 days than men in the deferred PrEP arm (21% vs. 12%, p=0.03)
  - Similar results in other cohort studies and meta-analysis

- Uncertain impact on STI incidence
  - Rising rates of bacterial STI antedate widespread PrEP use
  - PrEP did not cause the current STI epidemic
  - PrEP could exacerbate an already growing problem
  - Early studies did not consistently support the association.
  - PROUD study: no significant increase in STI incidence in both arms

Family Planning and PrEP

- **pregnancy?**
  - we have long time experience with the drug during pregnancy → no obstacles
- **contraception?**
  - no interaction with hormonal birth control reported
- **breast feeding?**
  - drug has been found in milk → ask the doctors!