

愛滋防治策略與 國際新知



衛生福利部疾病管制署
防疫醫師 黃士澤

什麼是愛滋病毒和愛滋病？



Human Immunodeficiency Virus (HIV)

「人類免疫缺乏病毒」，俗稱「愛滋病毒」，是一種會破壞人類免疫系統的病毒。

Acquired Immunodeficiency Syndrome (AIDS)

人類受到愛滋病毒感染後，若未以藥物有效控制，可能導致身體免疫力降低，而容易發生伺機性感染或腫瘤，此種症狀稱為「後天免疫缺乏症候群」，俗稱「愛滋病」。

愛滋病毒的傳染途徑有哪些？

- 愛滋病毒是透過帶有愛滋病毒的體液(血液、精液、陰道分泌物或母乳)，接觸被感染者的黏膜或破損皮膚而傳染，傳染途徑包括：
 - **性行為傳染**：與愛滋病毒感染者發生無保護性的口腔、肛門、陰道等方式之性交。
 - **血液傳染**：輸進或接觸被愛滋病毒污染的血液、血液製劑；與愛滋病毒感染者共用注射針頭、針筒或稀釋液；接受愛滋病毒感染者之器官移植。
 - **母子垂直感染**：感染愛滋病毒的母親在妊娠期、生產期、或因授乳傳染給嬰兒。



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愛滋感染之風險性

不同HIV傳染途徑的風險	每暴露10,000次可能有幾次會造成感染？
輸血	9,250
共用針具	63
針扎	23
肛交（接受方）	138
肛交（進入方）	11
陰道交（女性）	8
陰道交（男性）	4
口交	很低
咬傷	可以忽略的
吐口水	可以忽略的
揮濺體液（包含精液）	可以忽略的
共用性道具	可以忽略的

Anon, (2017). Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV—United States, 2016.



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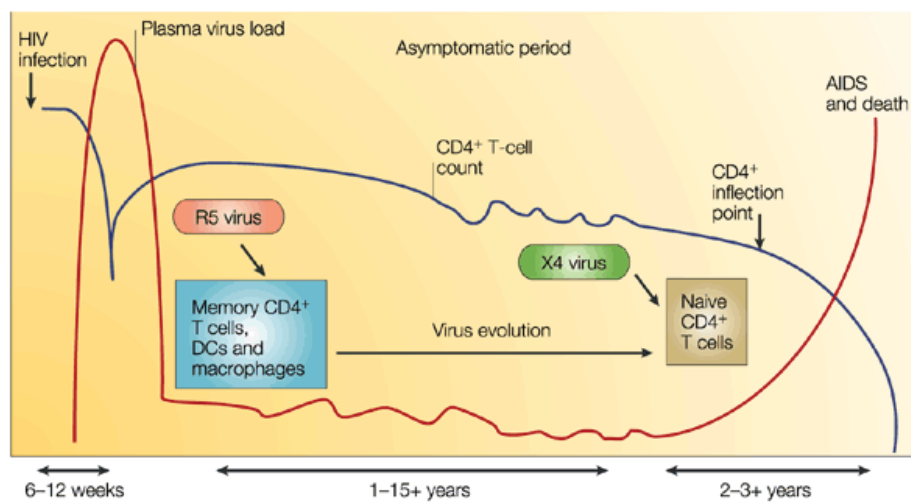
影響風險因子

- 增加感染機率的因子
 - 高病毒量
 - 生殖器官潰瘍
 - 急性HIV感染期
 - HIV末期
- 減少感染機率因子
 - 感染者及早治療
 - 感染者接受治療
 - 預防性投藥
 - 保險套使用

Estimating per-act HIV transmission risk: a systematic review. AIDS. 28(10):1509-1519, June 19, 2014.

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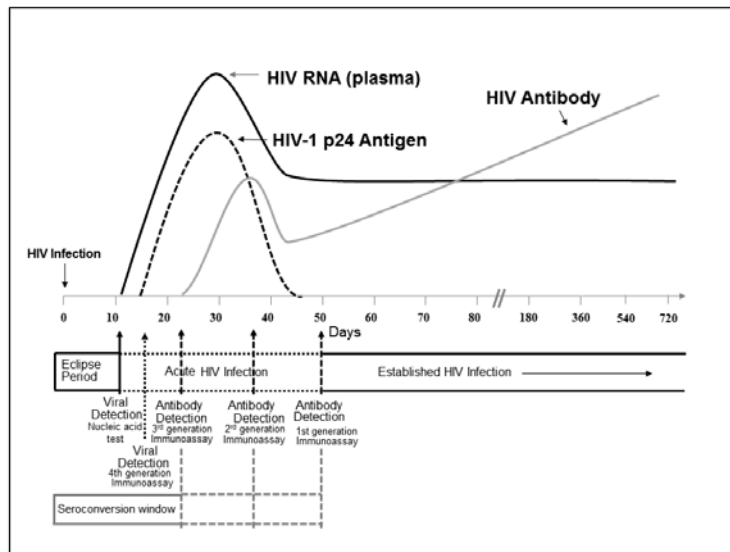
愛滋病毒感染病程



Nature Reviews | Immunology

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檢驗空窗期的差別



Laboratory testing for the diagnosis of HIV infection : updated recommendations. CDC. 2014

Summary of the global HIV epidemic

36.9 million
people living with HIV
[31.1 million – 43.9 million]

2017



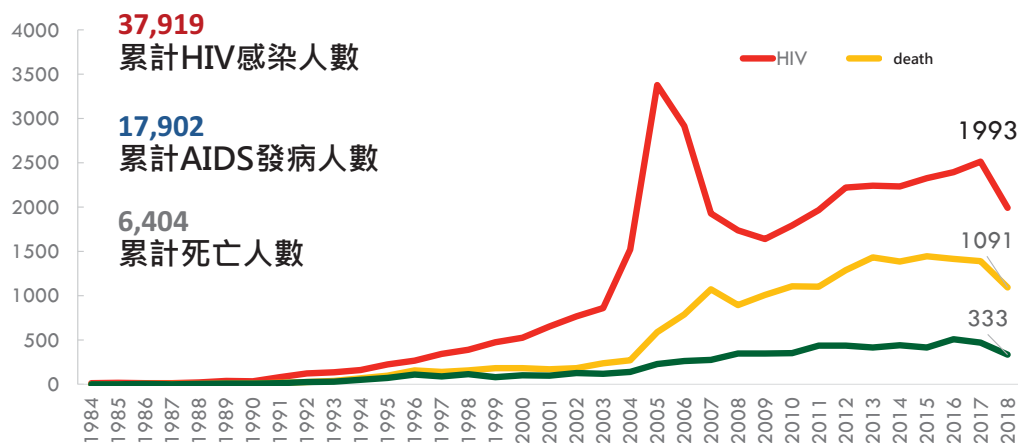
1.8 million
people newly infected
[1.4 million – 2.4 million]



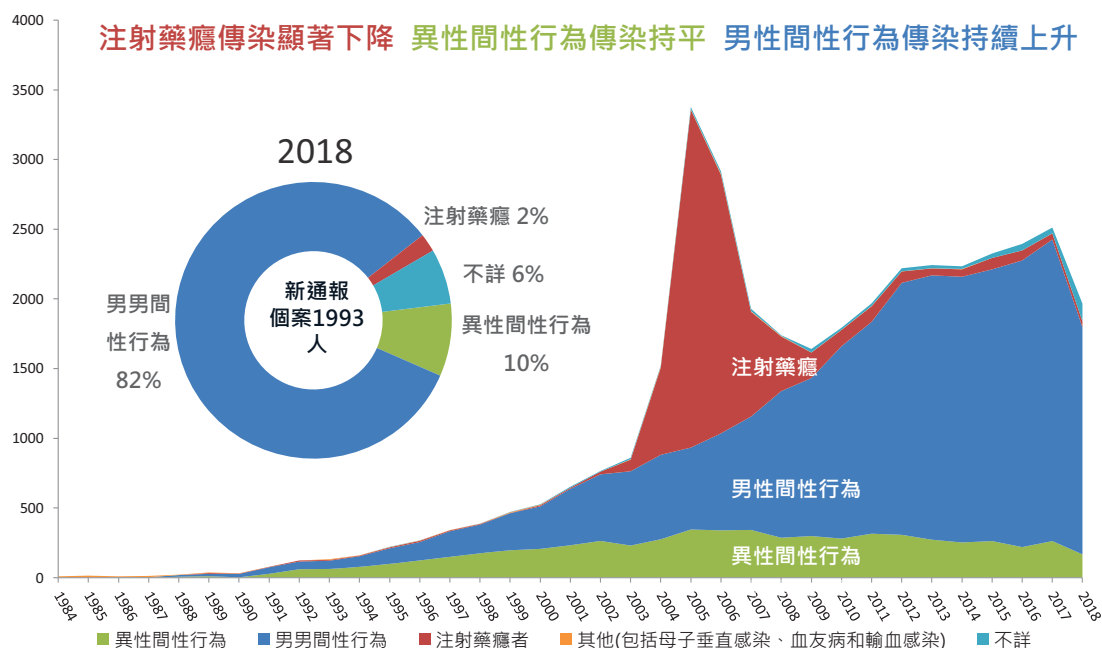
0.9 million
HIV-related deaths
[0.7 millions – 1.3 million]

Source: UNAIDS/WHO estimates

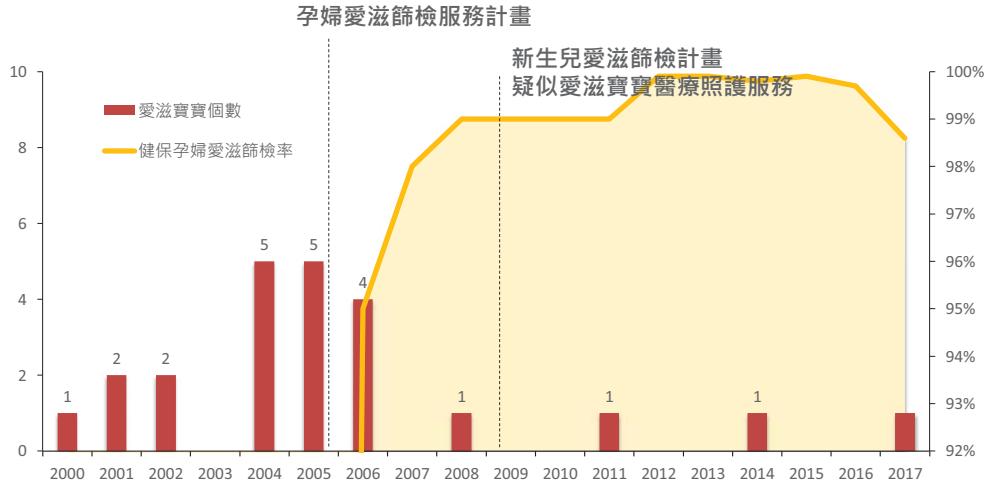
我國HIV/AIDS通報、死亡人數



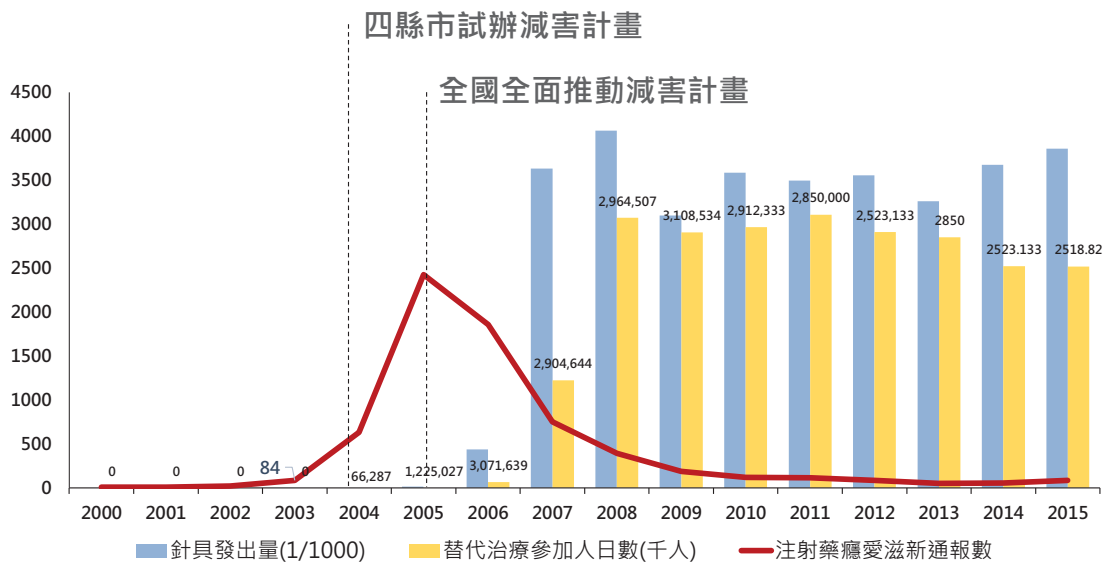
不安全性行為已成主要傳染途徑



母子垂直感染防範成效

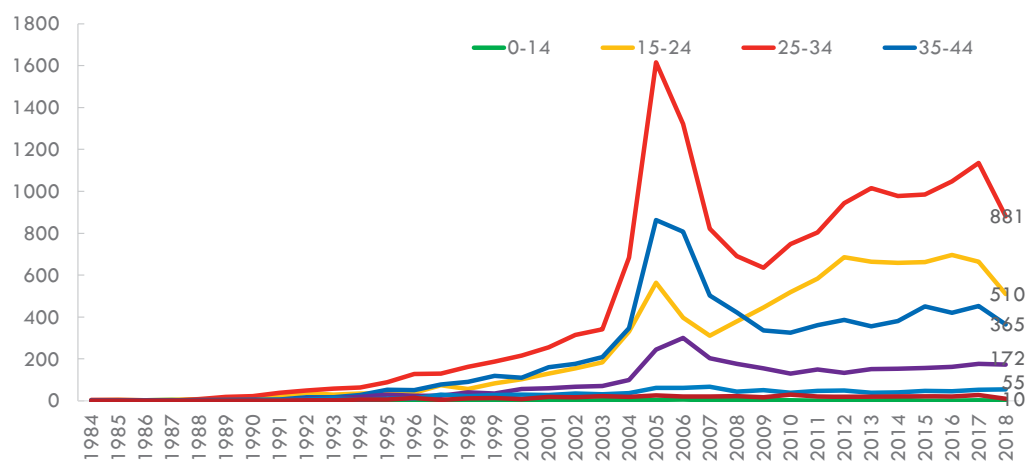


減害計畫降低藥癮疫情



目前我國於22縣市，共設847處衛教諮詢服務站，416台針具自動服務機

歷年HIV通報人數-依年齡別



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HIV預防的ABCD

- A: Abstain 節制
- B: Be faithful 忠實
- C: Condom 保險套
- D: Drug 藥物的給予 (PrEP, PEP, Treatment)

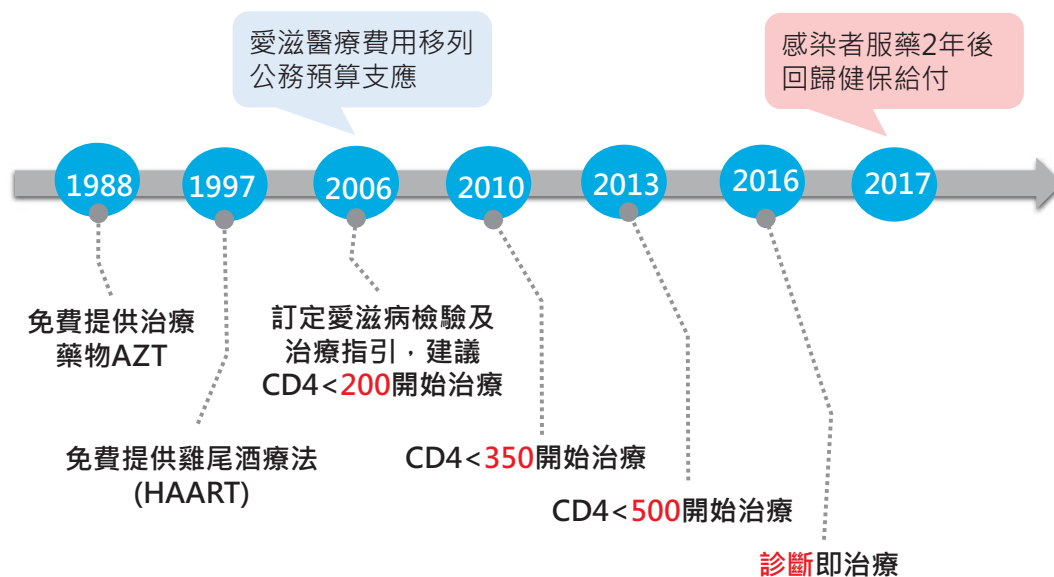
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愛滋病毒感染要怎麼治療？

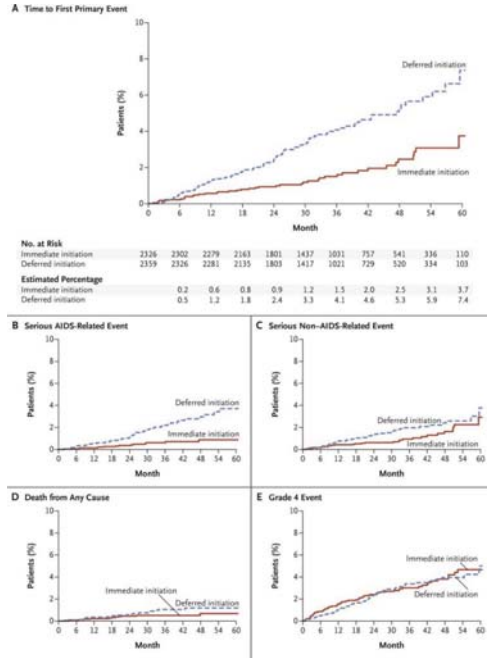
- 「高效能抗愛滋病毒治療」，俗稱「雞尾酒療法」，是組合至少三種抗愛滋病毒藥物，可以有效控制感染者體內的病毒量，大幅降低發生相關伺機性感染、腫瘤的風險，並減少愛滋病毒傳播。
- 高效能抗愛滋病毒治療已將過去普遍致死的愛滋病毒感染，變成長期、可處理的慢性病。不過目前仍然沒有辦法治癒愛滋病毒感染，感染者必須耐心持續服藥才能控制病情。

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愛滋治療藥物政策



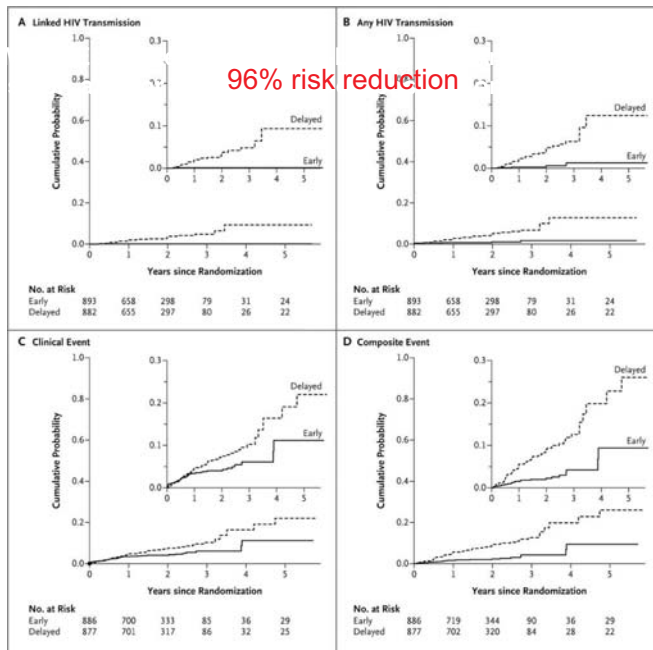
治療可降低發病與死亡等不良事件



57% reduction

The INSIGHT START Study Group. N Engl J Med 2015;373:795-807.

治療可降低病毒傳播



Cohen MS et al. N Engl J Med 2011;365:493-505.

終結愛滋 全球三零



新感染數少於50萬

愛滋死亡少於50萬

消除愛滋相關歧視

2016現況

180萬

100萬

2020目標



感染者知道自己
已感染之比率

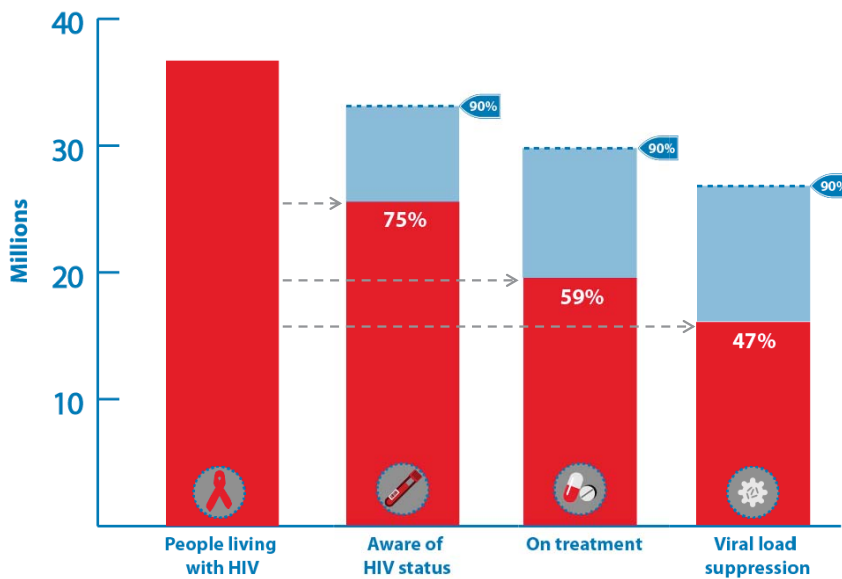


已知感染的人
數中，有服藥
之比率



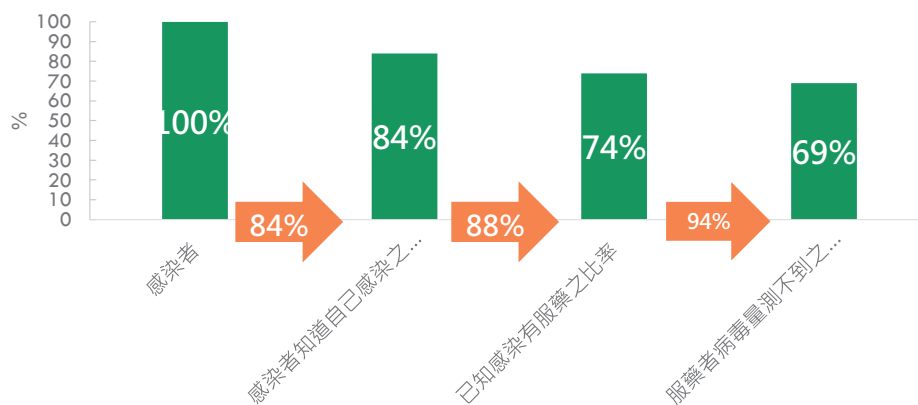
有服藥的感染
者中，病毒量
測不到之比率

HIV testing and care continuum (2017)

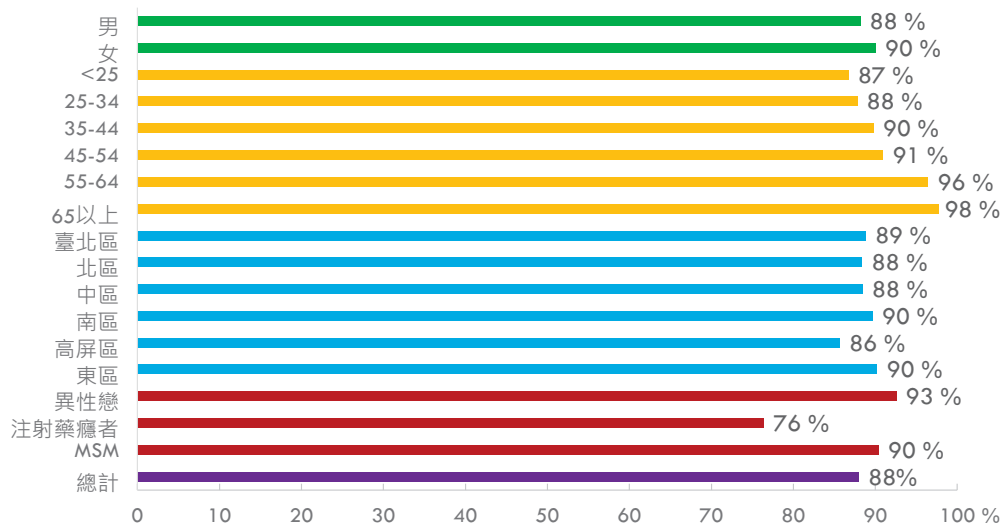


Source: UNAIDS/WHO estimates

台灣90-90-90現況 2018



2018年累積存活個案服藥比率



過去病毒量相關研究

- PARTNER1 study assessed rate of HIV transmission within serodifferent heterosexual and MSM couples during periods of CL sex while HIV-positive partner had HIV-1 RNA < 200 copies/mL
 - No linked within-couple transmissions observed
- Opposites Attract study assessed rate of HIV transmission within serodifferent MSM couples during periods of CL sex while HIV-positive partner had HIV-1 RNA < 200 copies/mL
 - No linked within-couple transmissions observed

Rodger AJ, Cambiano V, Bruun T, et al. JAMA. 2016;316:171-181.
Bavinton BR, Pinto AN, Phanuphak N, et al. Lancet HIV. 2018;[Epub ahead of print].

PARTNER2: HIV Transmission

- No linked transmissions documented in ~ 77,000 condomless sex acts when HIV-positive MSM partner suppressed to HIV-1 RNA < 200 copies/mL

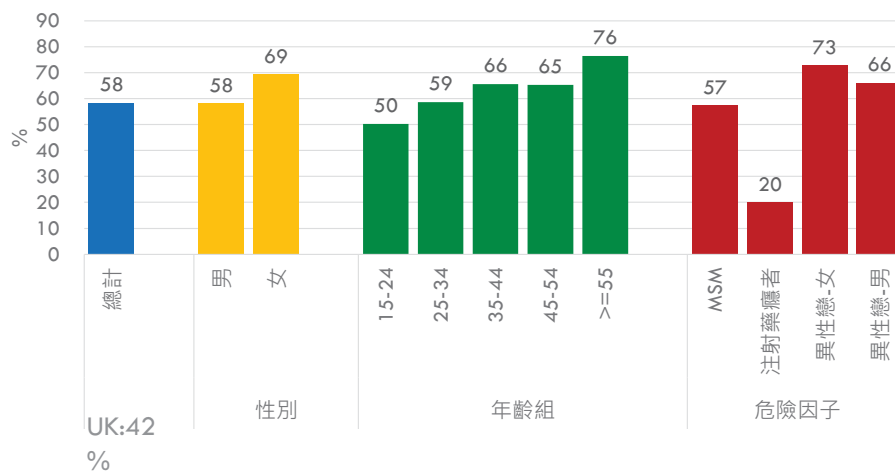
Sexual Behavior Reported by HIV-Negative Partner	Linked Transmissions, n	Upper 95% CI*	Condomless Sex Acts, n	CYFU
Any sex	0	0.23 [†]	76991	1596
Anal sex	0	0.24	70743	1546
Insertive anal sex	0	0.27	52572	1345
Receptive anal sex without ejaculation	0	0.43	23153	867
Receptive anal sex with ejaculation	0	0.57	20770	652
Any sex with an STI	0	2.74	6301	135

*For rate of within-couple HIV transmission per 100 CYFU. [†]Compared with 0.84 for MSM and 0.46 for heterosexuals in PARTNER1.

Rodger A, et al. AIDS 2018. Abstract WEAX0104LB.

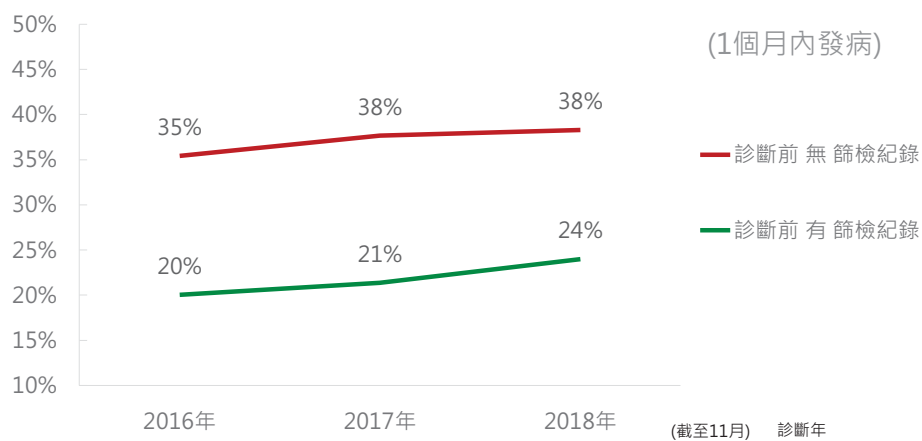
Slide credit: clinicaloptions.com

2018年新診斷個案延遲診斷



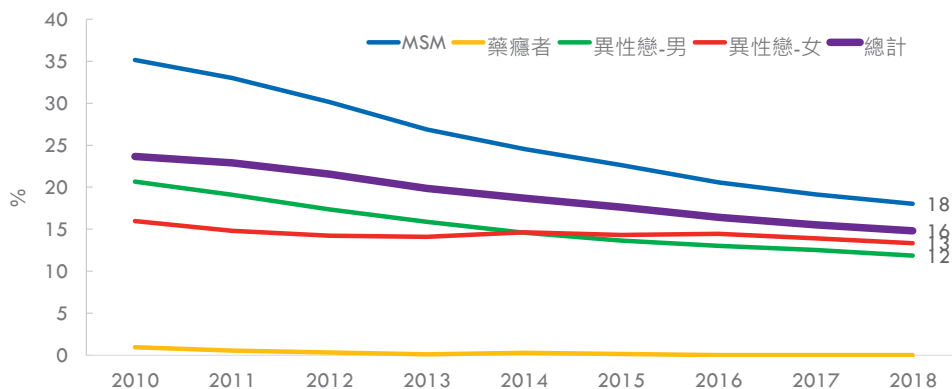
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通報個案篩檢與延遲診斷分析

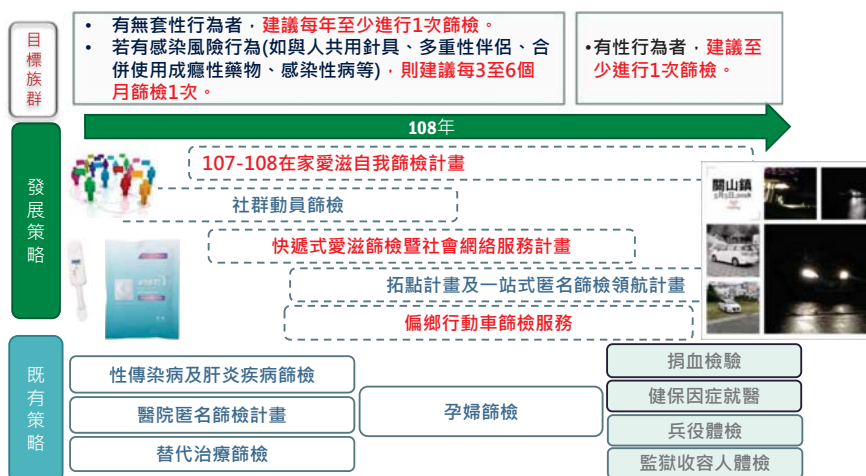


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歷年未診斷率估計



多元諮詢篩檢服務



106年自我篩檢成果

- 截至106年12月11日為止，總共發放16953支
 - 店利商店：6863支
 - 實體點：5317支
 - 販賣機：4773支
- 其中有6749人次登錄結果 (登錄率39.8%)
 - 檢驗陽性有85人 (陽性率1.26%)
 - 無效結果為53人 (無效率 0.79%)
- 過去是否篩檢：1219 (33.3%)沒有接受過篩檢

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一站式愛滋匿名快速篩檢領航計畫

縮短篩檢→確診→就醫服藥的時間

優先使用快速檢驗試劑

由本署統一採購愛滋抗原/抗體複合型快篩試劑以及抗體免疫層析快速確認檢驗試劑配送至醫院，提供民眾快速檢驗服務。

確診流程加速

引導快篩陽性民眾當日接受快速確認檢驗，並由醫事機構專任助理親自或電話連繫個案師協助將個案轉介至門診。



補助PrEP諮詢費用

匿篩民眾經衛教後願意至服用PrEP的個案，提供PrEP諮詢費(無論公費或自費)。

常客梅毒篩檢及獎勵

常客免費提供梅毒篩檢，並依據篩檢次數達目標且HIV未陽轉者提供獎勵。

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須具備觀念

- 抗病毒藥物無法取代，避免與HIV病毒有所接觸的相關行為 (e.g., sexual abstinence, sex only in a mutually monogamous relationship with an HIV-uninfected partner, consistent and correct condom use, abstinence from injection drug use).
- 在發生單一事件的性行為接觸、靜脈藥物注射、或其他非職業性暴露後，給與預防性藥物的效果，比起避免與HIV接觸的預防效果會比較差

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暴露前預防性投藥

- HIV Pre-exposure prophylaxis (PrEP) ，愛滋病毒暴露前預防性投藥，是一個新的預防策略
- 固定成份的複方藥物叫做Truvada，由HIV檢驗陰性的人每天服用
- 體內若有足夠的抗病毒藥物濃度，可以抑制HIV的複製
- PrEP可以降低在性行為中接觸HIV的人感染的機率

Plosker, G. L. (2013). Emtricitabine/tenofovir disoproxil fumarate: a review of its use in HIV-1 pre-exposure prophylaxis. *Drugs*, 73(3), 279-291.

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PrEP效果相關臨床試驗

Trial	Population and Setting	Study Design	HIV Incidence, %			Relative Reduction (vs Placebo) in HIV Incidence, Intent-to-Treat Analysis, % (95% CI)		Population Adherence Estimate, % ^c
			TDF	TDF/Emtricitabine ^b	Placebo	TDF	TDF/Emtricitabine ^b	
VOICE, ¹⁹ 2015	3019 Women (South Africa, Uganda, and Zimbabwe)	1:1:1 Randomization to daily oral TDF, TDF/emtricitabine, or placebo	6.0	4.3	4.2	-49 (-129 to 3)	-4 (-49 to 27)	29
FEM-PrEP, ²⁰ 2012	2129 Women (Kenya, South Africa, and Tanzania)	1:1 Randomization to daily oral TDF/emtricitabine or placebo	NA	4.7	4.8	NA	6 (-52 to 41)	37
iPrEx, ¹¹ 2010	2499 MSM and transgender women (United States, Peru, Ecuador, Brazil, Thailand, and South Africa)	1:1 Randomization to daily oral TDF/emtricitabine or placebo	NA	2.1	3.7	NA	44 (15 to 63)	50
Bangkok Tenofvir Study, ¹⁷ 2013	2413 Injection drug users (Thailand)	1:1 Randomization to oral TDF or placebo	0.5	NA	0.9	49 (10 to 72)	NA	67
TDF2 Study, ¹⁶ 2012	1219 Heterosexual men and women (Botswana)	1:1 Randomization to daily oral TDF/emtricitabine or placebo	NA	1.2	3.1	NA	62 (22 to 83)	79
Partners PrEP Study, ¹² 2012	4747 Heterosexuals (2877 men and 1857 women) in HIV-serodiscordant couples (Kenya and Uganda)	1:1:1 Randomization to daily oral TDF, TDF/emtricitabine, or placebo	0.7	0.5	2.0	67 (44 to 81)	75 (55 to 87)	81
IPERGAY, ¹⁸ 2015	400 MSM (France and Canada)	1:1 Randomization to TDF/emtricitabine or placebo, used "on demand" (4 pericoital tablets used over 3 d)	NA	1.0	6.8	NA	86 (39 to 99)	86
PROUD, ¹³ 2016	545 MSM in 13 sexual health clinics (England)	1:1 Randomization to immediate vs 12-mo deferred daily oral TDF/emtricitabine	NA	Immediate: 1.3 Deferred: 9.0	NA	NA	86 (58 to 96) ^d	100

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藥物動力學的優勢

- 藥物在生殖道體液中的濃度，比起血液中的濃度高2.5倍以上
- 直腸組織中的藥物濃度，比起陰道或子宮頸組織中的濃度，甚至大於100倍
- Anal sex is the major sex behavior among MSM, PrEP could become the important HIV prevention methods

Patterson. (2011). Penetration of tenofovir and emtricitabine in mucosal tissues: implications for prevention of HIV-1 transmission. *Sci Transl Med*, 3(112), 112re114.

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2015年WHO最新建議

Recommendation

NEW

Oral PrEP containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches (*strong recommendation, high-quality evidence*).

提供**愛滋高風險族群(substantial risk)**，口服含有TDF成分之**暴露前預防性投藥策略(PrEP)**，此應該是完整愛滋預防策略的一部分(強烈建議，研究證據高)



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台灣PrEP指引

- 每日口服tenofovir (TDF) 300 mg合併emtricitabine (FTC) 200 mg的固定劑量複方製劑，作為
 - 高感染風險男男間性行為者與高感染風險跨性別女性
 - 異性戀血清相異伴侶中陰性方
 - 注射藥物者
 - 高風險異性戀男性與女性者
- 依需要時使用TDF/FTC的固定劑量複方製劑
 - 高感染風險男男間性行為者與高感染風險跨性別女性
- 在一般預防措施之外，預防感染HIV的方式。

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投藥實務

- 確定使用者沒有 HIV 感染，由於 PrEP 僅使用 TDF/FTC 兩種核苷酸反轉錄酶抑制劑（NRTI）藥物，若已經感染了 HIV，可能會導致抗藥性的產生
- 尚須詢問是否有急性 HIV 相關症狀，如發燒、頭痛、全身痠痛、喉嚨痛、起疹子、淋巴結腫大等。
- 目前 PrEP 的研究對象僅止於成年人，因此必須年滿 18 歲方符合使用 PrEP 的條件。
- 因此 6 個月內若無性行為、也無具有風險的注射藥物行為，尚不具備足夠高的 HIV 感染風險

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投藥實務

- 不建議依需求使用的對象
 - B 型肝炎病毒帶原者
 - 無法記住或是容易混淆依需求時使用 PrEP 的服用方式（包括可能忘記在性行為中或是最後一次性行為後兩次的服藥時間）
 - 無法事先計劃發生性行為的時程
 - 一個禮拜超過兩天非連續發生的性行為

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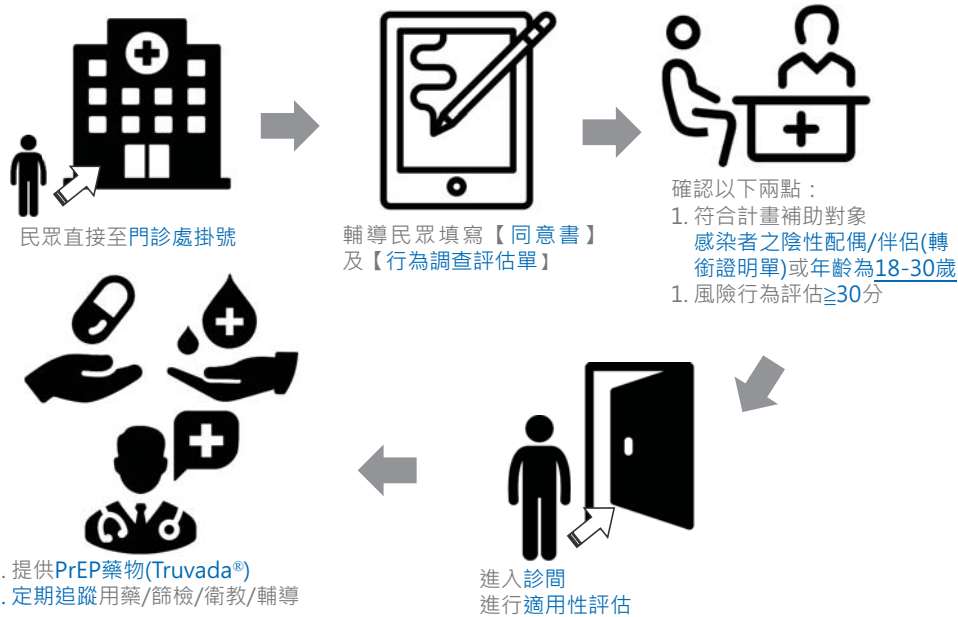
PrEP補助計劃

- 愛滋感染者之年滿18歲的配偶或伴侶（尤以女性為優先），高風險行為指標達30分（含）以上者。須由衛生局認定並轉銜至執行機構
- 年滿18歲至30歲（含未滿31歲）的年輕族群，高風險行為指標達30分（含）以上者
- **Truvada**：開立藥物處方箋時，執行機構每次須開立1個月30顆藥物，每名補助對象至多補助360顆藥物。若依醫囑依需求(on demand)使用藥物者，則無須每個月回診
- **HIV testing fee**：適用性評估、及服藥後第3、6、9、12個月愛滋病毒檢驗，採論件計酬

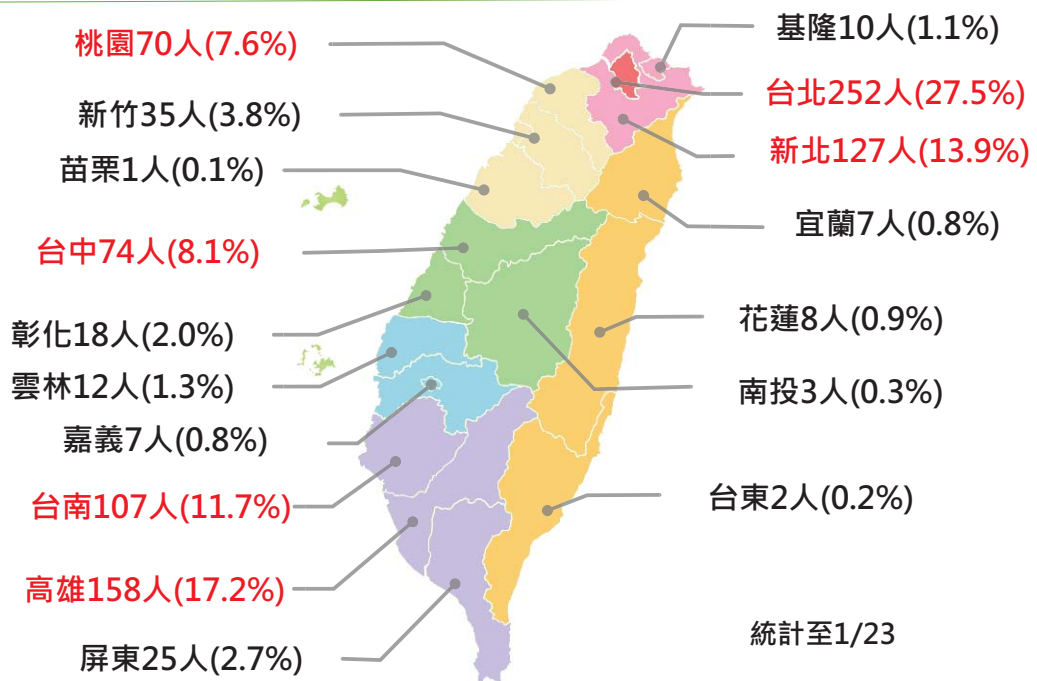
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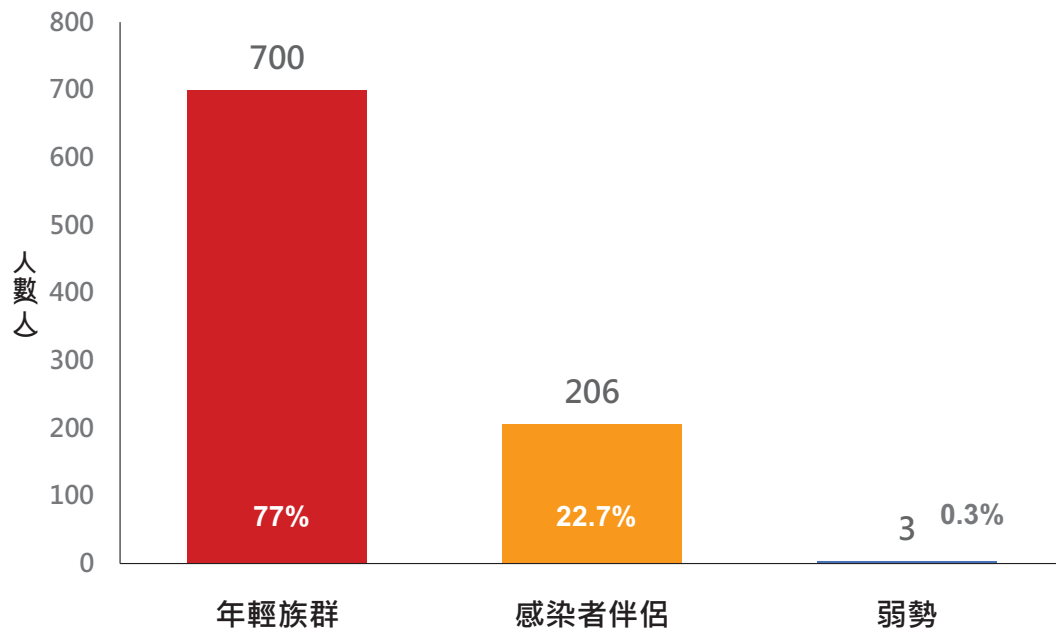
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Recruitment of PrEP users

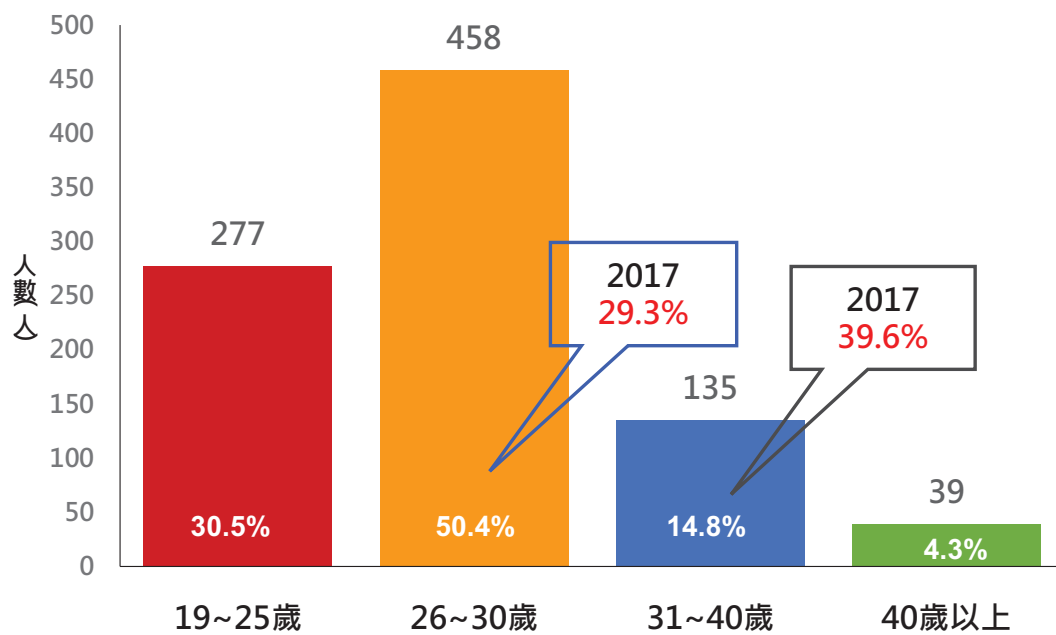


Participants by inclusion criteria



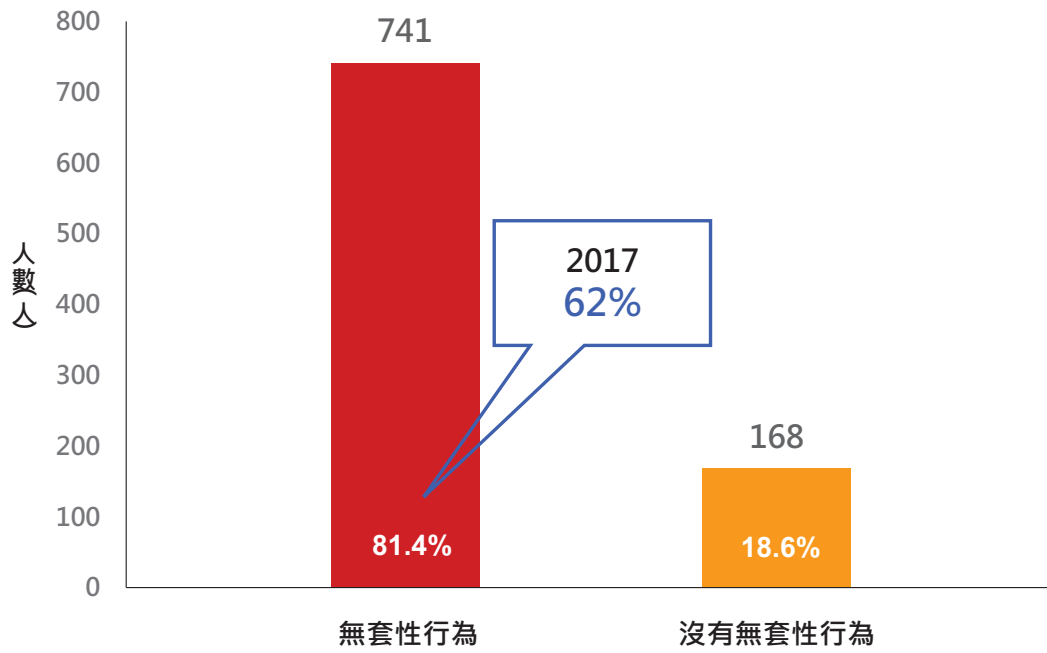
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Participants by age

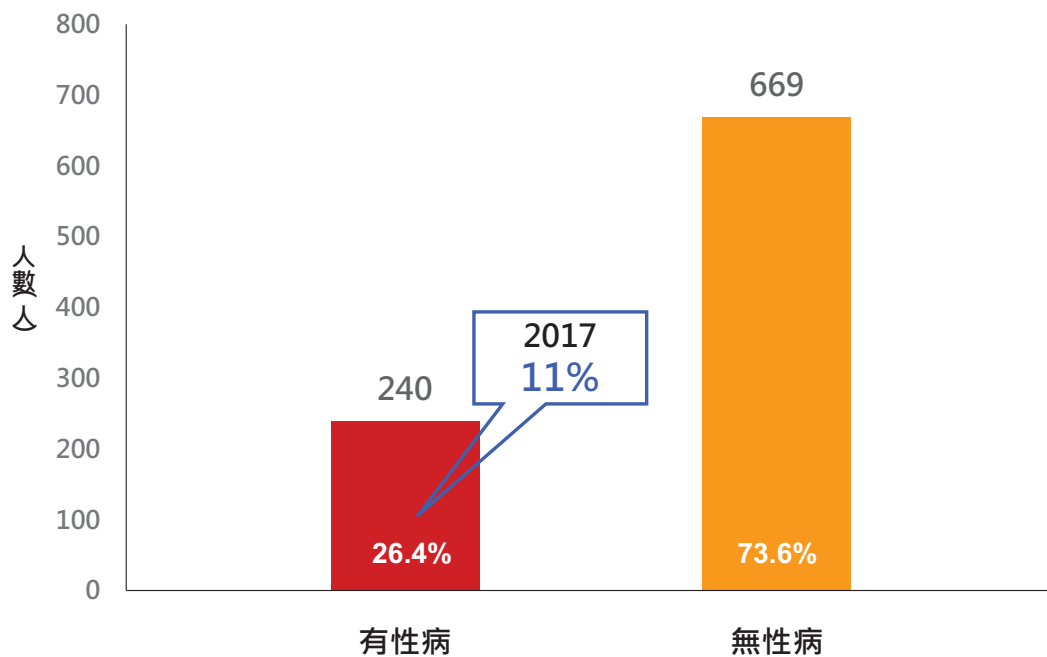


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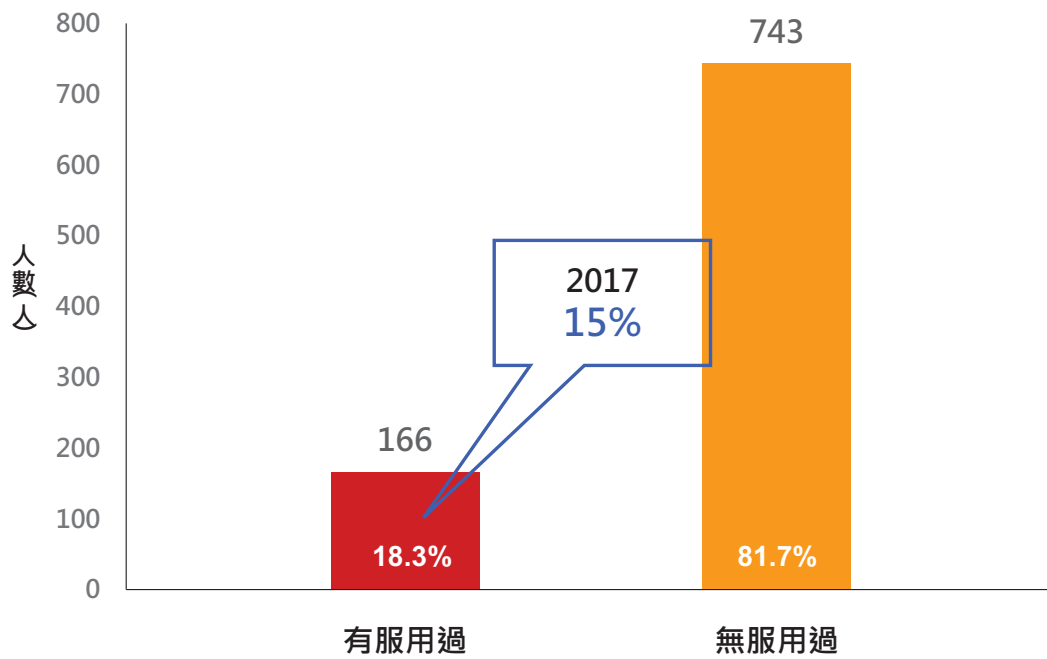
Unprotected sex during last year



STD during last year

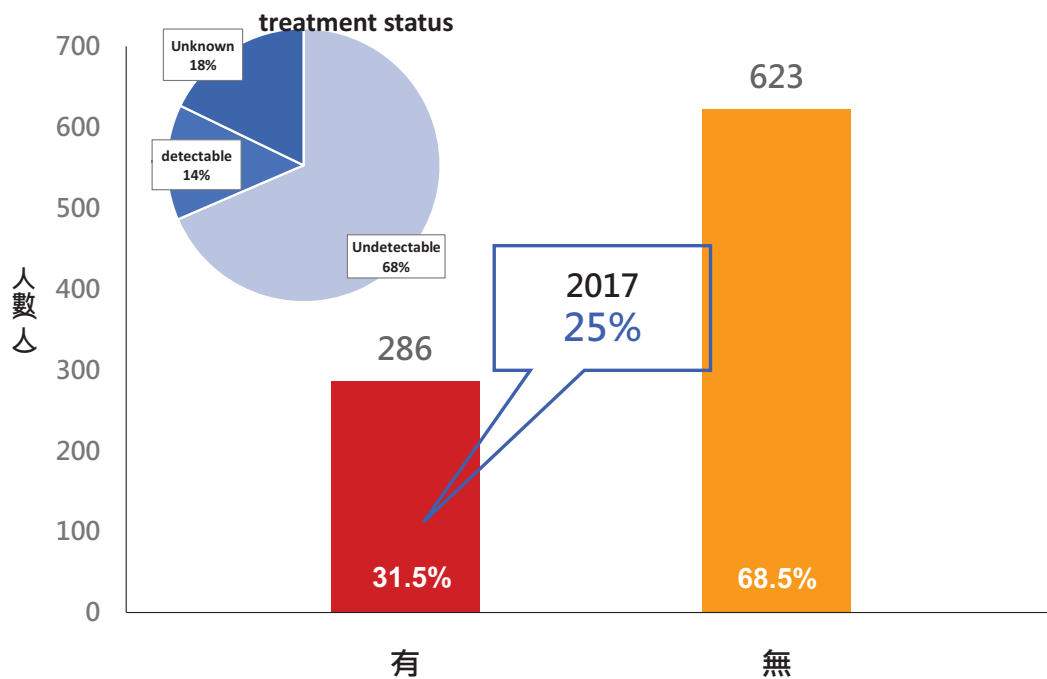


PEP use during last year



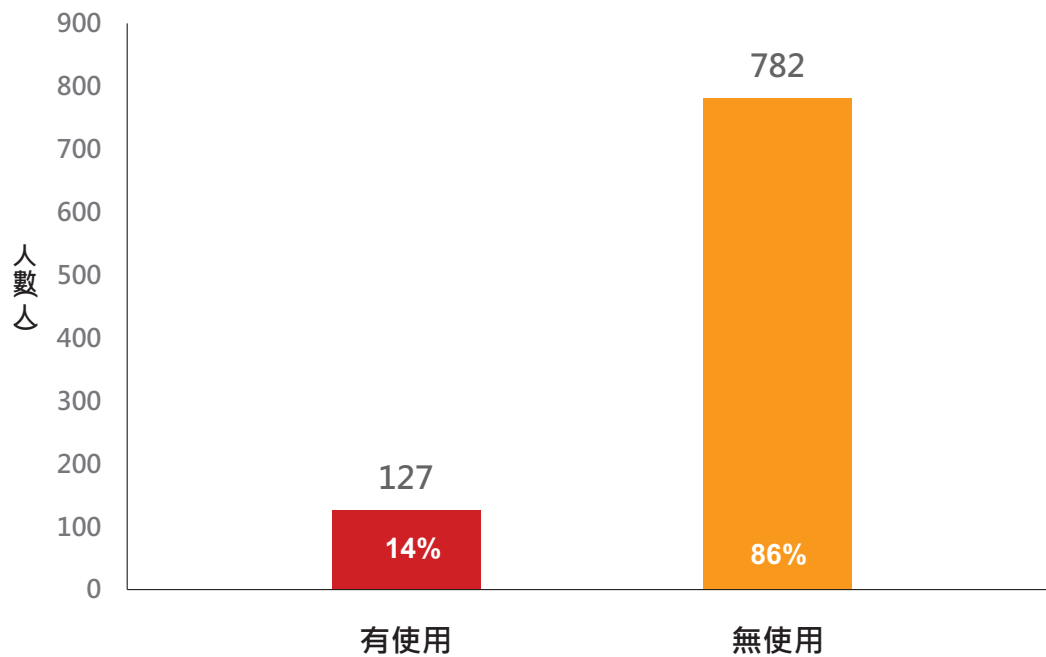
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Having HIV(+) partner

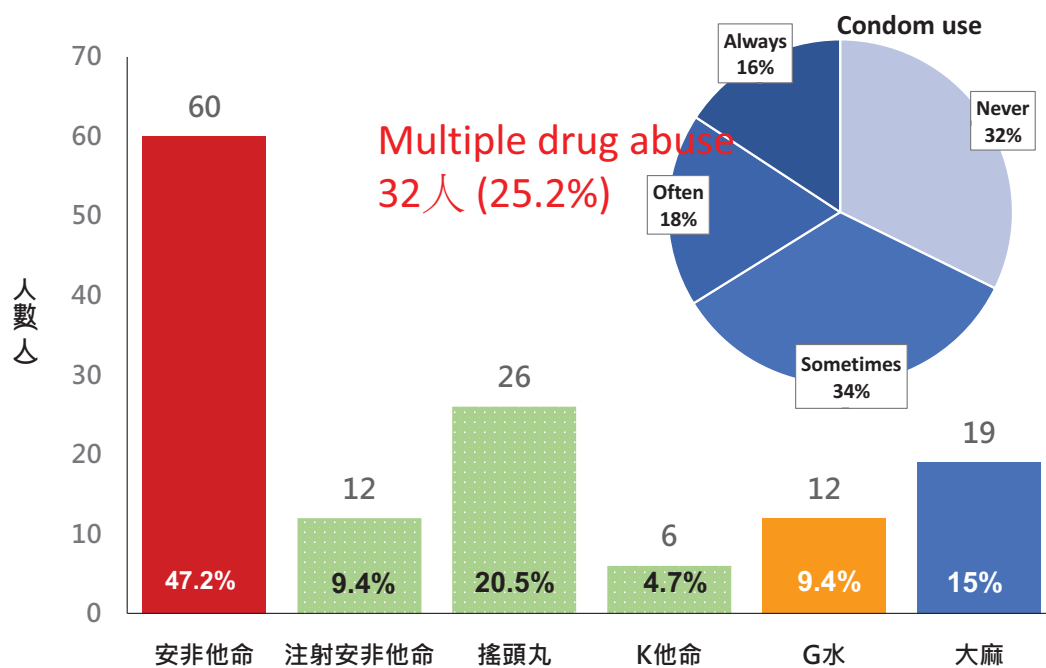


48

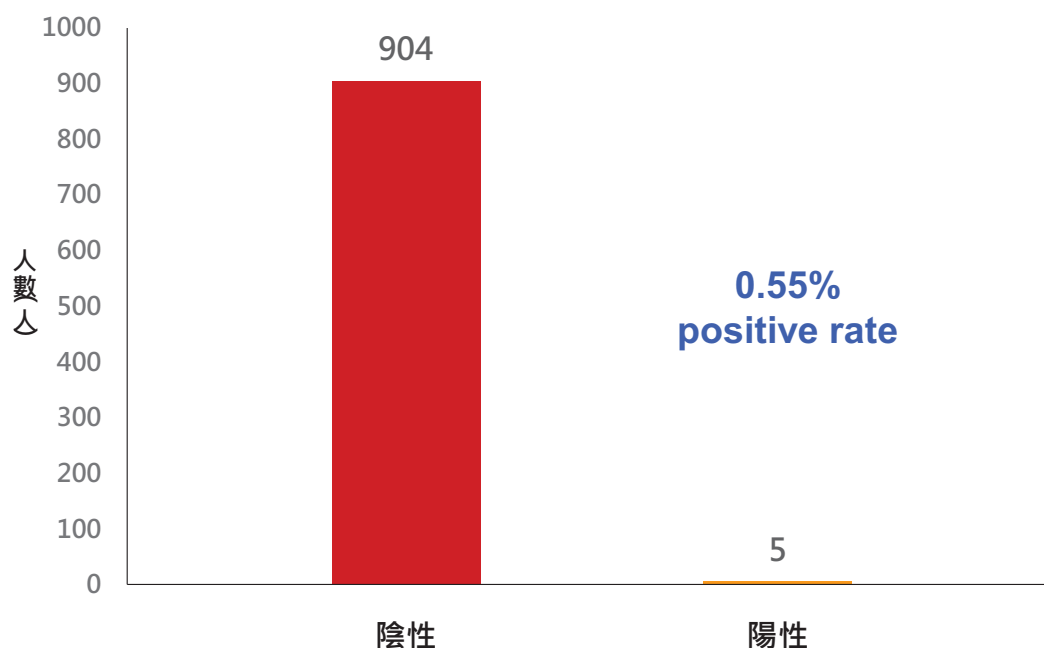
Addictive substances use during last year



Addictive substances categories during last year



Initial HIV screening



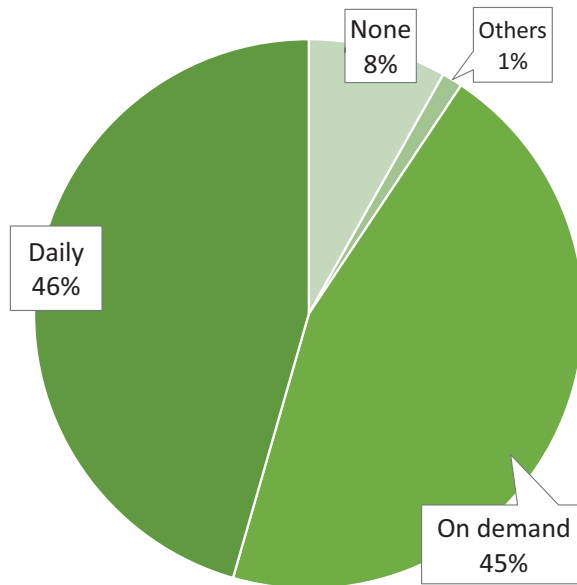
51

HIV(+) at screening process

- 1人(20%)梅毒檢驗陽性
- 過去一年100%都有過無套行為
- 3人(60%)過去一年曾感染過性病
- 過去一年無感染者伴侶
- 1人(20%)使用過PEP
- 2人(40%)有使用成癮物質(皆有安非他命使用且皆為多重藥物使用)
 - 使用安時都不使用保險套，且每次性行為皆會使用安非他命
 - 認識的朋友約有4-7成的人有使用成癮藥物

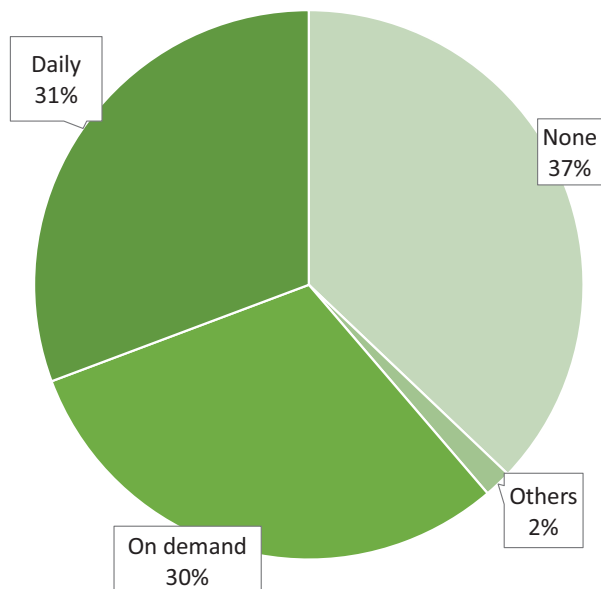
52

Regimen of PrEP use – last month



53

Regimen of PrEP use – total months



54

Sero-conversion cases

- 至目前為止，有三名個案新診斷為HIV感染，皆為年輕族群
- 2名個案領藥但未確實服用，另1名個案 on-demand 使用但服藥順從度不佳。
- 1人(33.3%)梅毒檢驗陽性
- 過去一年100%都有過無套行為
- 2人(67.7%)過去一年曾感染過性病
- 過去一年無感染者伴侶也無使用過PEP
- 0人(0%)有使用成癮物質

55

Side effects

- 目前有副作用回報者有154人 (17.5%)
- 噁心為最占四成，其次超過兩成有腹瀉症狀
- 沒有人因為副作用停藥

56

Difference between youths and sero-discordant partners

- 回診28天前，沒吃藥的比例較高 9% vs 5%
- 回診28天前，每天服用的比例較低 42% vs 56%
- 回診28天前，On-demand的比例較高 48% vs 37%
- 過去一年無套性行為比例高 83.6% vs 74.8%
- 過去一年曾得性病比例高 28.9% vs 17.5%
- 自覺感染風險是較低 38% vs 44%
- 認為PrEP花費是負擔的比例低 52% vs 73%
- 擔心有副作用比例高 30% vs 50%

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Difference between daily and on-demand users

- 自覺有較高的感染風險 44% vs 35%
- 加入時，具有感染者伴侶者 39% vs 25%

58

PrEP補助計劃讓我們學習

- PrEP計劃的確可以涵蓋到具有高風險者，及早在評估時診斷出HIV感染者
- 年輕族群的服藥衛教與風險認知評斷能力，需要加以強化
- 感染者的陰性伴侶，在PrEP的推廣較容易上手，只是對於感染者的健康了解度，仍有改進空間
- On-demand的使用技巧，不一定適用在每個人身上，若先傳遞daily use的方式讓使用者熟悉後，或許可以讓on-demand的推動更有效益
- 成癮藥物使用者的愛滋防治是一大挑戰，尤其在如何維持PrEP的服藥順從性上

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AIDS 22ND INTERNATIONAL AIDS CONFERENCE
2018 AMSTERDAM, NETHERLANDS
23-27 JULY 2018
BREAKING BARRIERS • BUILDING BRIDGES

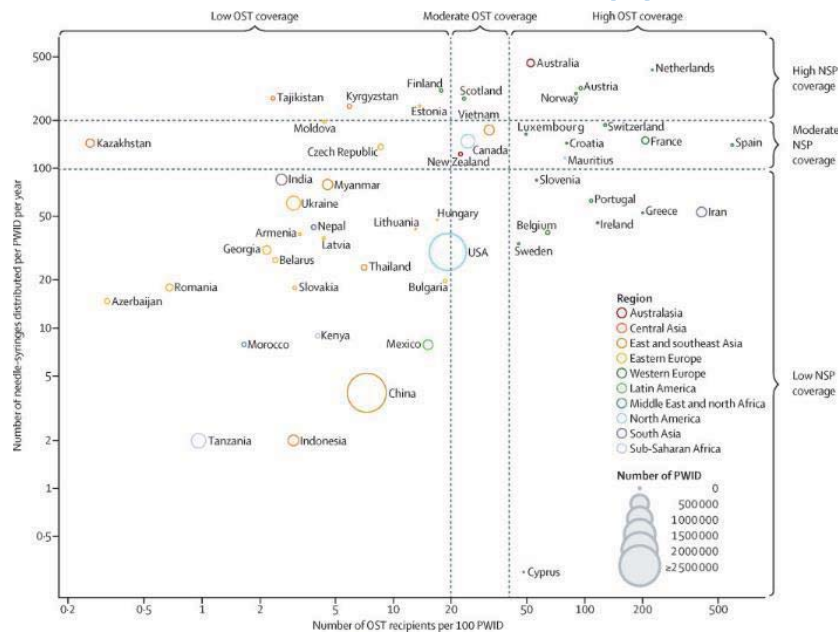
60

愛滋大會的重點觀察

- 預防性投藥正如火如荼的推廣中
- 自我篩檢也是重要的防治策略
- DTG 甚至是其他II 成為治療HIV的主流藥物
- 青少年的聲音與青少年愛滋防制是重要的
- 更多的感染者擔任講者分享經驗
- 愛滋防制教育與尊重多元文化

藥物濫用的問題舉世皆然

Coverage of needle and syringe programs and opioid substitution therapy



The Lancet Global Health 2017 5, e1208-e1220DOI: (10.1016/S2214-109X(17)30373-X)

New psychoactive substances

- 643 new psychoactive substances reported by 101 countries by the end of 2015 (348 in 2013)
- Current estimate for one NSP emergence is one substance per week
- Use mostly concentrated among youth aged 16-24
- Most NSP are sold via internet
- Lower price
- OST and naloxone provision are not effective

創新的篩檢是需要的

65

HIV testing services

- Facility-based
- Community-based
- Assisted partner notification
- HIV self-testing
- Multi-disease testing at point-of-care
- Apps and social networks

66

藥物做為防治策略 治療感染者

67

PARTNER2: HIV Transmission

- No linked transmissions documented in ~ 77,000 condomless sex acts when HIV-positive MSM partner suppressed to HIV-1 RNA < 200 copies/mL

Sexual Behavior Reported by HIV-Negative Partner	Linked Transmissions, n	Upper 95% CI*	Condomless Sex Acts, n	CYFU
Any sex	0	0.23 [†]	76991	1596
Anal sex	0	0.24	70743	1546
Insertive anal sex	0	0.27	52572	1345
Receptive anal sex without ejaculation	0	0.43	23153	867
Receptive anal sex with ejaculation	0	0.57	20770	652
Any sex with an STI	0	2.74	6301	135

*For rate of within-couple HIV transmission per 100 CYFU. [†]Compared with 0.84 for MSM and 0.46 for heterosexuals in PARTNER1.

新增感染者的特質

- 15 HIV-negative men acquired HIV infection11 reported recent CL sex with others
- Phylogenetic analysis found no evidence of link to HIV-positive partner
 - 6 of 15 acquisitions involved non-subtype B virus, whereas all infections in corresponding HIV-positive partners were with subtype B virus
 - No clustering of partners' viral sequences observed

Rodger A, et al. AIDS 2018. Abstract WEAX0104LB.

藥物做為防治策略 預防被傳染

On-demand PrEP

- ANRS IPERGAY: double-blind, randomized, placebo-controlled study of on-demand PrEP with TDF/FTC for prevention of HIV infection in MSM at high risk of HIV infection
- Relative reduction in HIV incidence with on-demand PrEP vs placebo: 86% (95% CI: 40% to 98%; P = .002)
- Relative reduction in HIV incidence during open-label extension phase: 97% (95% CI: 81% to 100%)
- On-demand PrEP endorsed by guidelines from Europe, England, Canada, Australia, and IAS-USA, but limited real-world data on efficacy, safety of on-demand PrEP

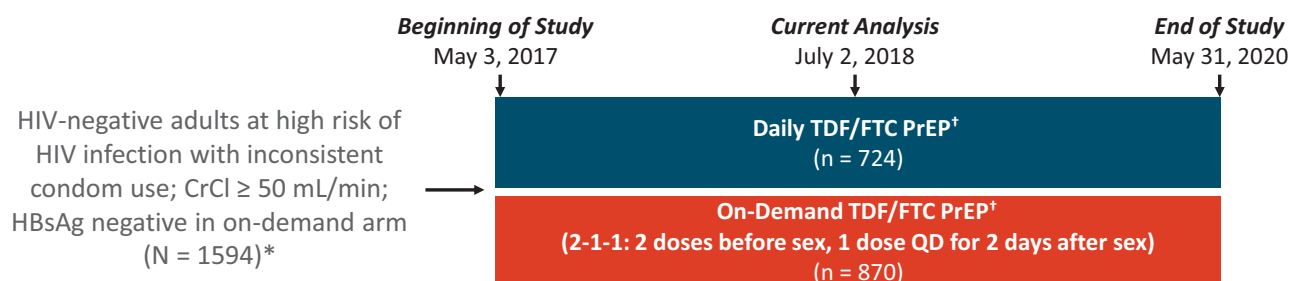
Molina JM, Capitant C, Spire B, et al. N Engl J Med. 2015;373:2237-2246.
Molina JM, Charreau I, Spire B, et al. Lancet HIV. 2017;4:e402-e410.

Follow-up

- Fourth-generation ELISA HIV test and plasma creatinine measured every 3 months
- STI screening at doctor's discretion, where guidelines recommend screening every 3 months in MSM
- Condoms, gels, HIV risk reduction, PrEP adherence counseling provided
- Adherence and sexual behavior assessed at each visit

Daily vs On-Demand TDF/FTC Oral PrEP

- Multicenter, open-label, prospective cohort study in Paris



*Participants enrolled in arm of their choice with ability to switch; target enrollment, N = 3000 (85% MSM).

[†]Plus condoms, gels, risk reduction and adherence counseling, questionnaire on sexual behavior. Follow-up every 3 mos with STI and/or HIV testing, plasma creatinine measurement.

- Predominantly MSM (98.8%), white (85.2%); median age: 36 yrs
- Primary endpoint: \geq 15% reduction in new HIV diagnoses among MSM in Paris vs rate reported by National Surveillance network in 2016
- Secondary endpoints: PrEP adherence, sexual behavior, safety

Molina J-M, et al. AIDS 2018. Abstract WEA0406LB.

Slide credit: clinicaloptions.com



Baseline Characteristics

Characteristics (Median, IQR) or (n, %)	N = 1628
Age (years)	36 (30-44)
Caucasian	1385 (85.2)
MSM	1607 (98.8)
Heterosexual men or women	12 (0.8)
Transgender	8 (0.5)
No regular sex partner	839 (51.7)
History of PrEP use	930 (57.2)
Use of Chemsex*	257 (15.8)
Slam (drug injection during sexual intercourse)	26 (1.6)
On Demand dosing regimen	870 (54.6)
Nb condomless sex acts in prior 4 weeks	2 (0-5)
Nb sexual partners in prior 3 months	10 (6-20)

* at last sexual intercourse : cocaine, GHB, MDMA, mephedrone

PrEP / Condom use at last sexual intercourse

2279 sex acts assessed in 1102 participants \geq M3

(n, %)	Daily n = 1088 acts	On Demand n = 1191 acts	Total n= 2279
Total PrEP use	1068 (98.2)	967 (81.2)	2035 (89.2)
Correct use*	1024 (95.8)	931 (96.2)	1955 (96.1)
Suboptimal	44 (4.1)	36 (3.7)	80 (3.9)
No PrEP	20 (1.8)	224 (18.8)	244 (10.7)
Condoms	206 (18.9)	258 (21.6)	464 (20.4)

* According to the protocol, or at least one pill before (<24h) and one pill after sex (<24h)

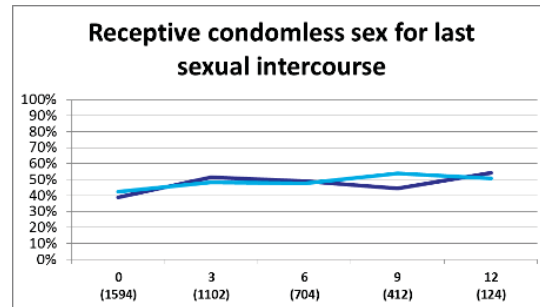
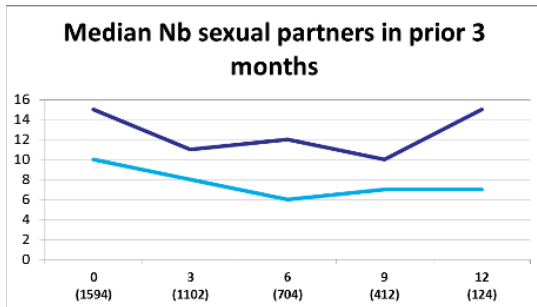
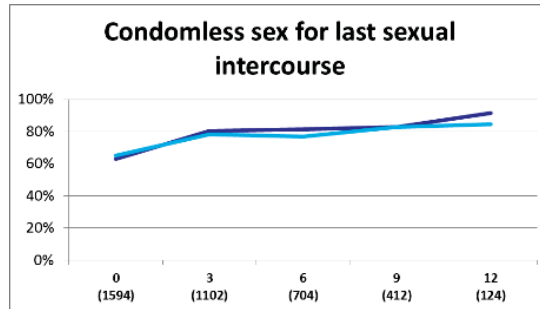
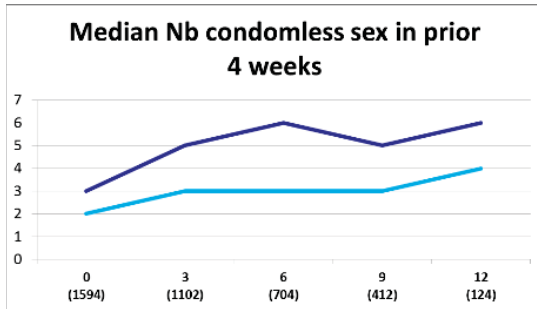
ANRS Prevenir: HIV Incidence

Primary Endpoint	Daily PrEP (443 PYFU)	On-Demand PrEP* (506 PYFU)
HIV incidence/100 PY (95% CI)	0 (0-0.8)	0 (0-0.7)

*On-demand PrEP strategy not FDA approved.

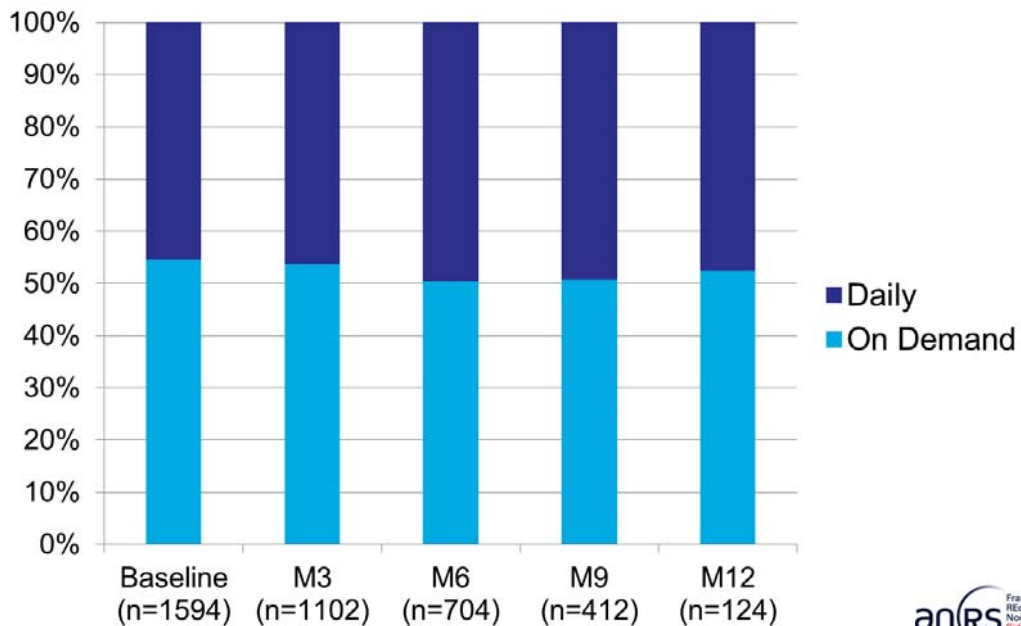
- Mean follow-up: 7 mos
- Overall HIV infections averted, n = 85
 - Assuming incidence of 9.17/100 PY as reported for ANRS IPERGAY study among participants in Paris

Sexual Behavior



■ Daily ■ On Demand

Dosing Regimen over Time



泰國PrEP經驗分享

- KP organization are reaching high-risk individuals in need of PrEP (high rates of drug/stimulants use, group sex)
- 43.9% adherence after 12 months
- Demand creation : social media, crowd-sourcing
- Outreach : use of peer mobilizers, on-line outreach
- HIV testing : making it easier

藥物做為防治策略 預防被傳染 青少年的使用推廣

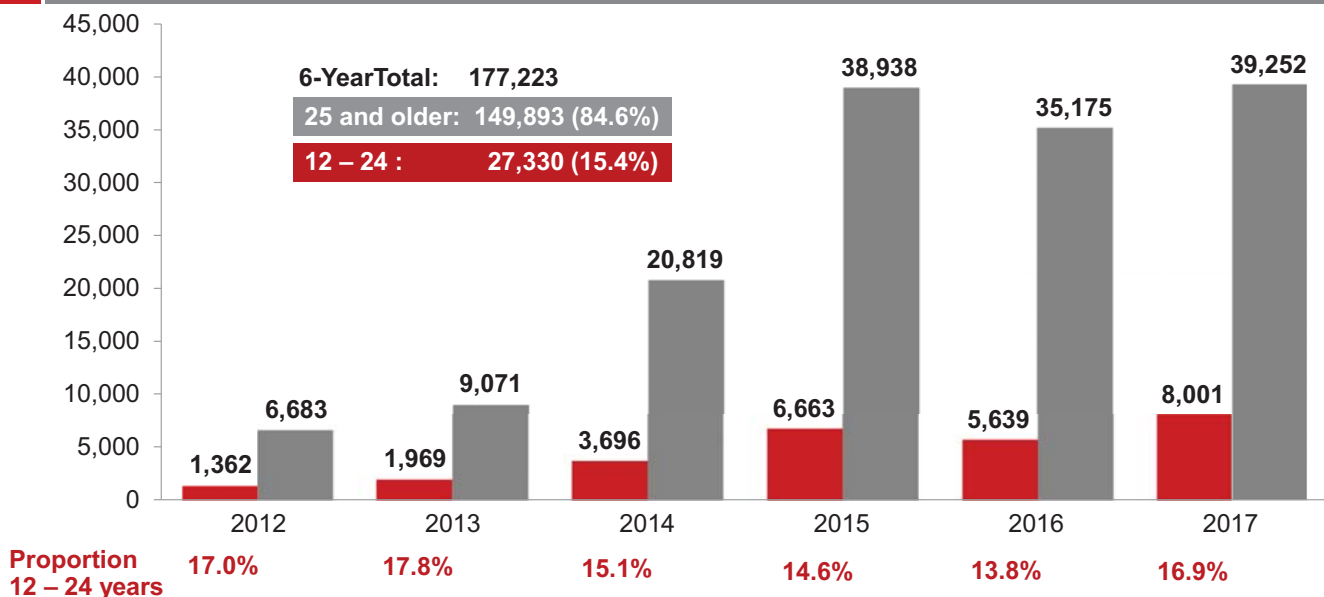
Introduction

- ◆ In 2016, there were 37,782 new HIV diagnoses in the US
 - 8,451 (21%) new HIV infections were in individuals aged 13 – 24 years
 - 6,848 (81%) were in young gay/bisexual men¹
- ◆ ATN 113, a study of HIV PrEP in 79 MSM aged 15 – 17 years in the US, demonstrated good overall safety and acceptability but a high HIV incidence and poor retention in care
- ◆ CHAMPS PlusPills, a study of HIV PrEP adolescents aged 15 – 19 years (99 females, 49 males) in South Africa demonstrated PrEP was well tolerated but that PrEP usage and adherence diminished over time
- ◆ Challenges for PrEP uptake in adolescents in the US include stigma, the need for parental consent in some states, lack of insurance coverage, the potential disclosure of confidential information on the parents' insurance bill and difficulties in adherence with a high rate of discontinuation compared to older adults

David Magnuson, et al. AIDS 2018. Abstract TUAC0305.

81

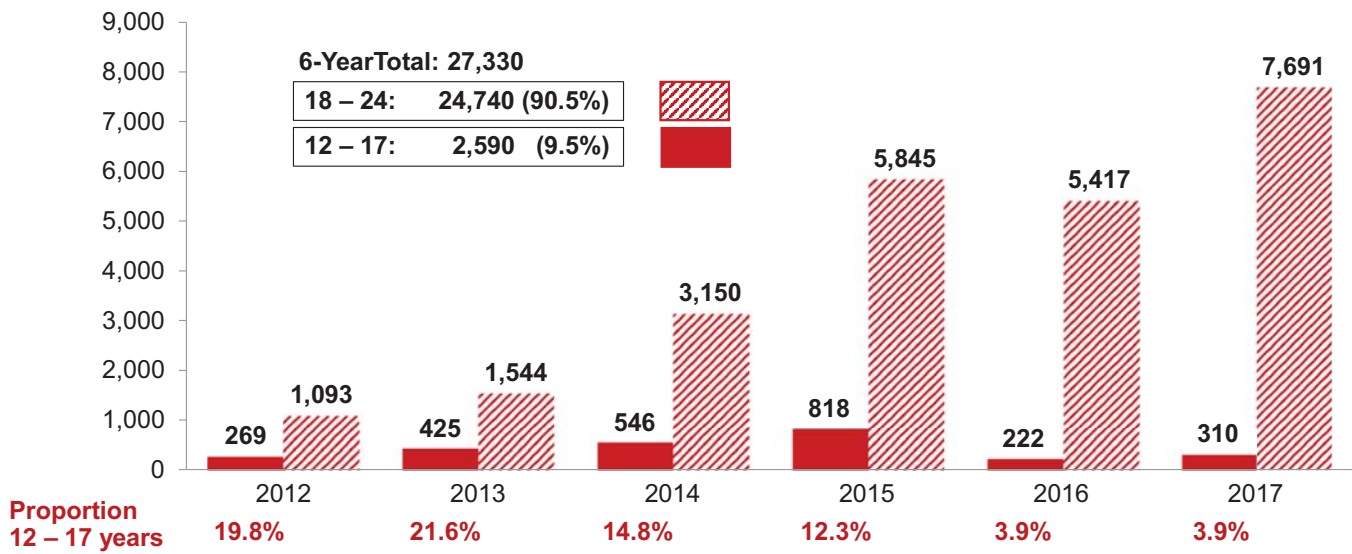
All Individuals Starting FTC/TDF for PrEP in US, 2012 – 2017



David Magnuson, et al. AIDS 2018. Abstract TUAC0305.

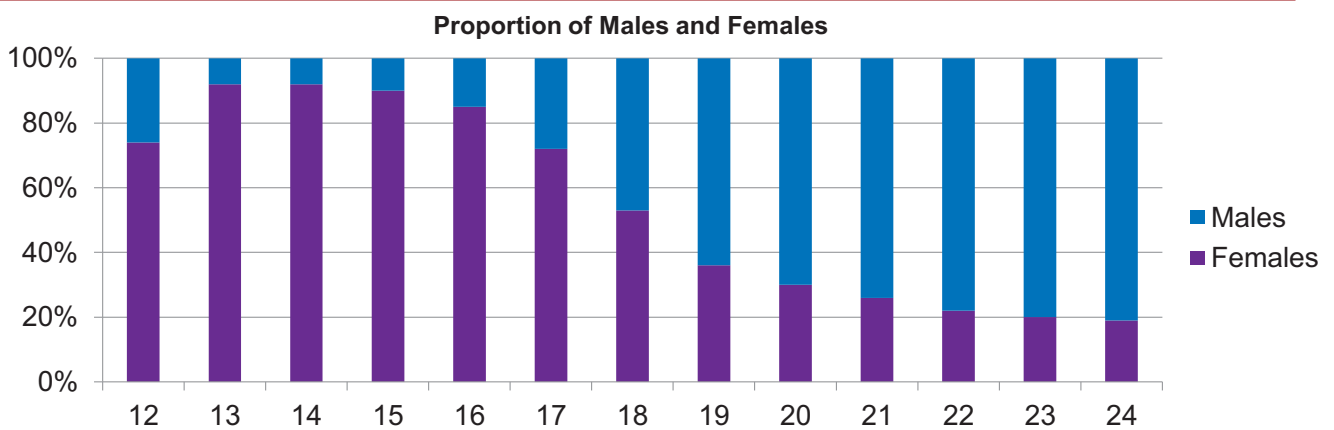
82

Adolescents Starting FTC/TDF for PrEP in US, 2012 – 2017



David Magnuson, et al. AIDS 2018. Abstract TUAC0305.

Comparison of Adolescent Males and Females Starting FTC/TDF for PrEP



Numbers of Males and Females

Age / Sex	12	13	14	15	16	17	18	19	20	21	22	23	24
M	22	16	32	56	93	209	598	1,298	1,776	2,367	3,231	4,296	5,069
F	64	186	352	502	516	542	664	723	771	827	923	1,045	1,152
Total	86	202	384	558	609	751	1,262	2,021	2,547	3,194	4,154	5,341	6,221

David Magnuson, et al. AIDS 2018. Abstract TUAC0305.

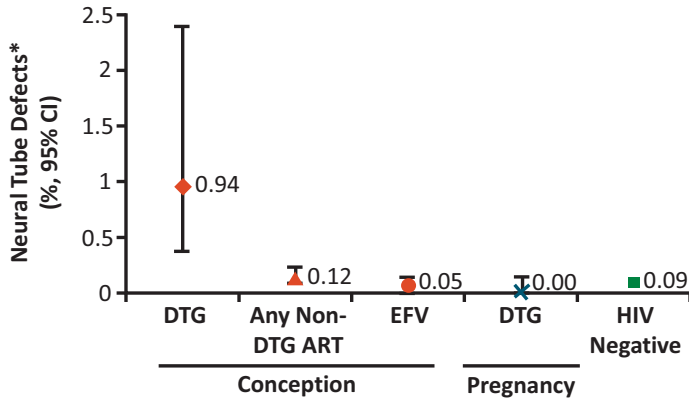
懷孕與抗病毒藥物使用的安全性

Tsepamo study

- Tsepamo study initiated in August 2014 with 2 primary aims
- First aim: Assess risk of adverse birth outcomes associated with HIV infection and ART regimen
- Second aim: Evaluate risk of NTD among infants exposed from conception to EFV
- Study based in 8 of largest maternity wards in Botswana, covering approximately 45% of total births

Neural Tube Defects and DTG Exposure

- Unplanned analysis of ongoing birth outcomes surveillance study among Botswanan women \pm HIV infection^[1,2]



*In 89,064 births as of May 1, 2018.

- At latest analysis on **July 15, 2018**^[2]
 - NTD prevalence with DTG exposure **at conception**: 4/596 (0.67%; 95% CI: 0.26% to 1.7%)
 - NTD prevalence with DTG started **during pregnancy**: 1/3104 (0.03%; 95% CI: 0.01% to 0.18%)
- Next formal analysis to occur after **March 31, 2019**, which will include 72% of national births

1. Zash R, et al. N Engl J Med. 2018;[Epub ahead of print]. 2. Zash R, et al. AIDS 2018. Session TUSY15.

Slide credit: clinicaloptions.com

Recommendations

- In response to May 2018 data from Tsepamo study, a modeling study estimated possible outcomes with recommendation of DTG-based vs EFV-based ART for HIV-infected women of childbearing age and their offspring across 5 years in South Africa
 - DTG-based ART predicted to avert approximately 3-fold more deaths among women than would be added among children
 - DTG use estimated to result in 28,400 fewer deaths among women and 5000 fewer pediatric HIV infections vs EFV use
 - EFV use estimated to result in 10,000 fewer NTD cases and 8400 fewer cumulative pediatric deaths vs DTG use

Dugdale C, Ciaranello AL, Bekker LG, et al. Program and abstracts of the 22nd International AIDS Conference; July 23-27, 2018; Amsterdam, The Netherlands. Session TUSY15.

簡化治療處方的發展

單一藥物處方

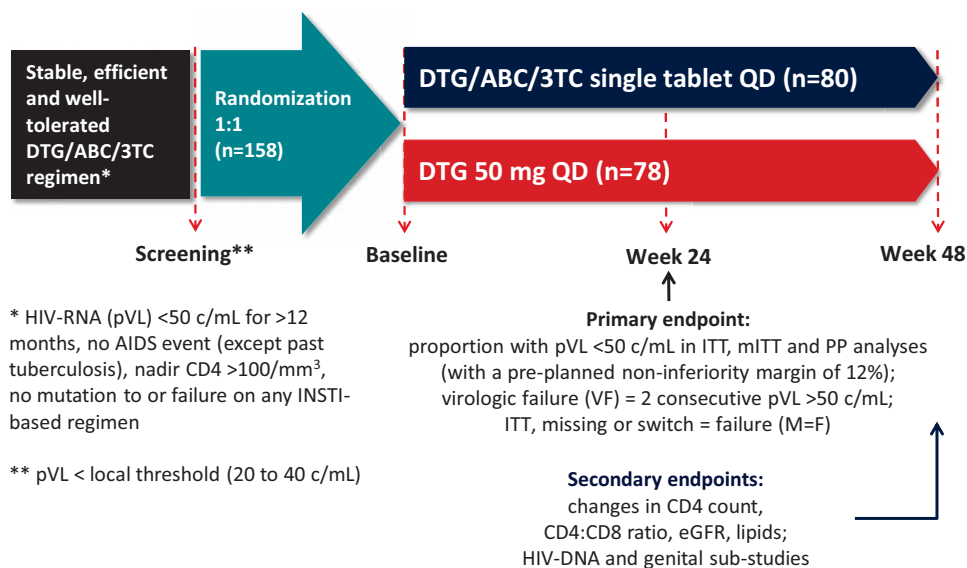
Introduction

- Less-drug regimens may be helpful for ageing PLHIV to endure lifelong antiretroviral therapy
- What we know about less-drug regimens:
 - Some dual therapies have proven to be non-inferior to triple (and now approved worldwide, such as DTG/RPV)
 - Boosted PI monotherapies failed to prove non-inferiority¹
- Dolutegravir (DTG) looked “ideal” for maintenance monotherapy:
 - Potency and high genetic barrier
 - Overall good tolerance
 - Few drug-drug interactions

1- Arribas JR et al. *HIV Med* 2016

Study design

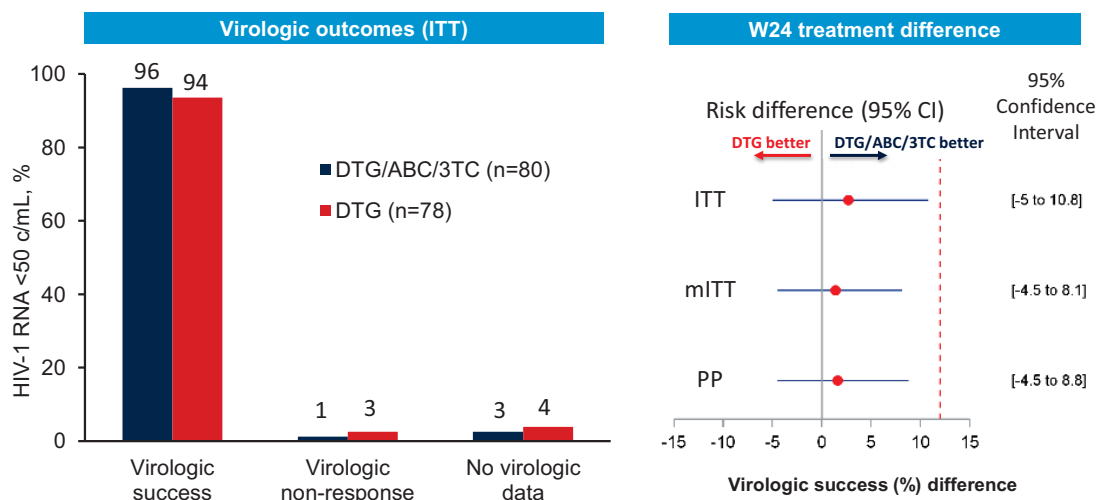
Open-label, randomized, controlled trial in 9 reference centers in France



#AIDS2018 | @AIDS_conference | www.aids2018.org



Primary outcomes at W24

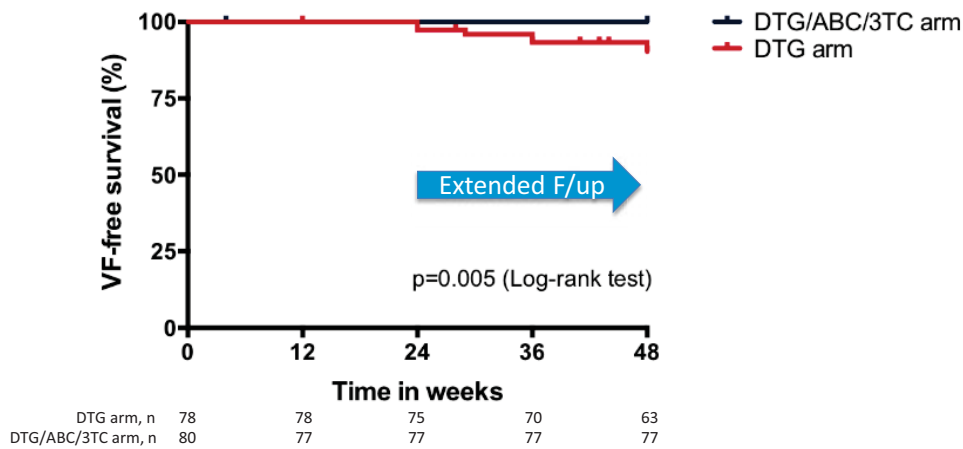


DTG was **non-inferior** to DTG/ABC/3TC at **Week 24**
with respect to snapshot in the ITT, mITT and PP population

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VF incidence after W24



Following a DSMB held on Dec. 21st 2017, the sponsor decided to **stop the monotherapy arm, according to DSMB recommendations**. All patients in the DTG-arm who had not completed the W48-visit (n=8) were re-intensified.

Factors associated with VF

Patients who experienced VF (as compared with those who did not) were more likely to have:

- A low nadir CD4 (p=0.004)
- A low CD4 count at screening (p=0.027)
- A « PCR signal » at pVL screening (p=0.026)

In a multivariate analysis two variables remained independent predictors of VF:

- Low CD4 count at screening (per 100 cells decrease):
OR=1.7 (95%CI: 1.1 to 2.8)
- Presence of a « PCR signal » at screening (vs. no):
OR=8.2 (95%CI: 1.4 to 68.6)

Conclusions

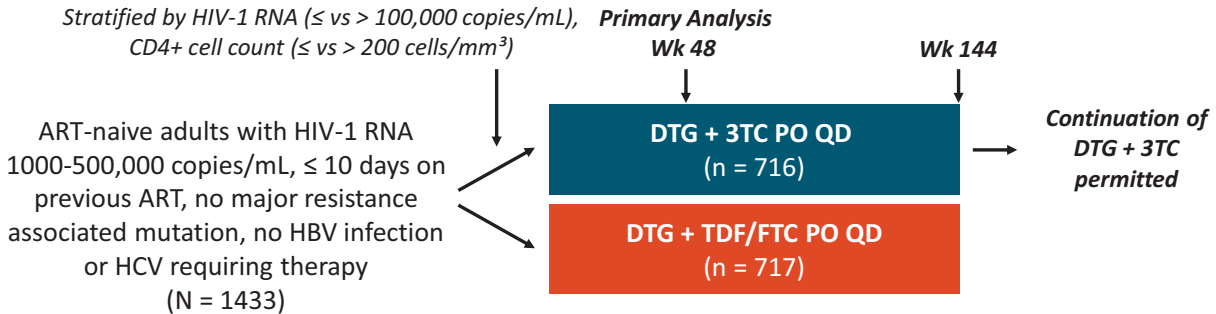
- DTG monotherapy was non-inferior to triple therapy at W24, but not beyond...
 - With a substantial risk of emerging mutations in case of VF
- Our results, together with previous reports, clearly confirm that DTG monotherapy as a maintenance strategy is not safe overtime and should therefore not be used in PLHIV
- A specific study to evaluate the interest of such a strategy in patients with high CD4 count and optimal virologic control (no signal) may be warranted

簡化治療處方的發展

雙藥物處方

GEMINI-1 and -2: DTG + 3TC vs DTG + TDF/FTC in Treatment-Naive Patients

- Parallel, international, randomized, double-blind phase III noninferiority studies



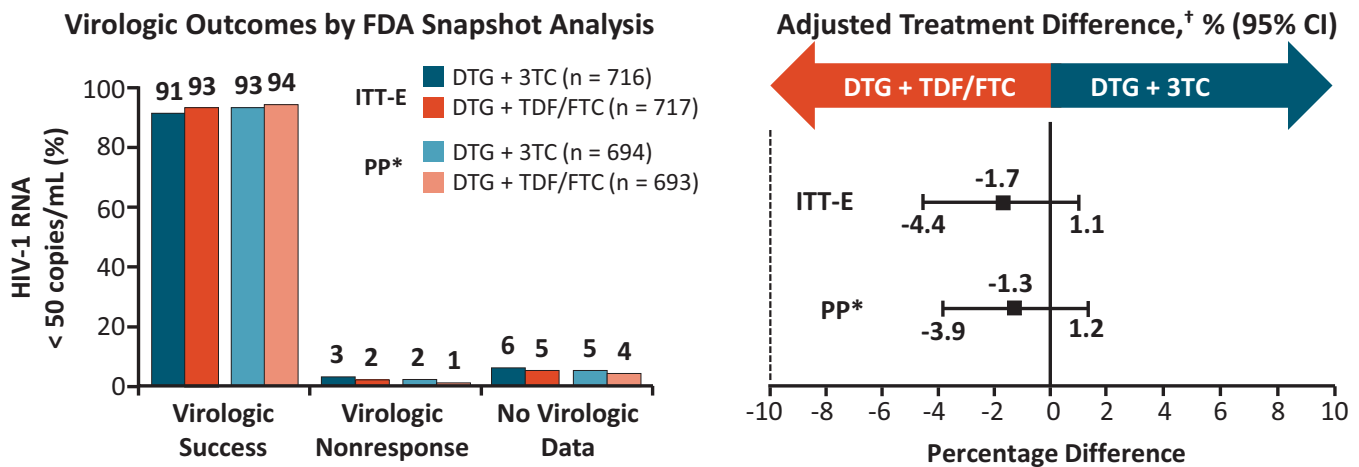
Screening within 28 days of study start; studies double-blinded until Wk 96, open-label until Wk 144.

- Primary endpoint: HIV-1 RNA $<$ 50 copies/mL at Week 48 by FDA Snapshot analysis
 - Noninferiority margin: -10%

Cahn P, et al. AIDS 2018. Abstract TUAB0106LB. ClinicalTrials.gov. NCT02831673. ClinicalTrials.gov. NCT02831764.

Slide credit: clinicaloptions.com

GEMINI-1 and -2: Virologic Response at Wk 48



*ITT-E population excluding significant protocol violations.

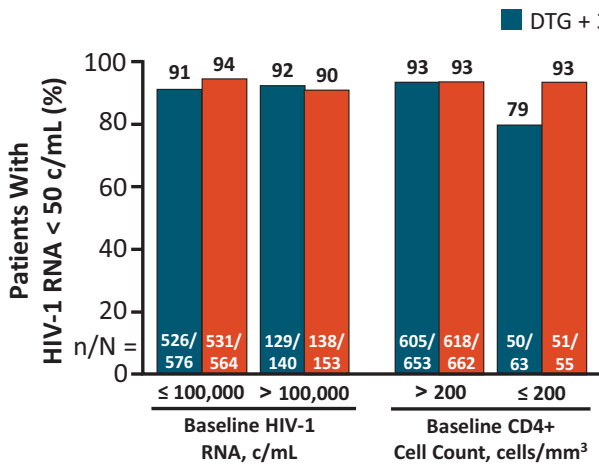
[†]Adjusted for HIV-1 RNA (\leq vs $>$ 100,000 copies/mL), CD4+ cell count (\leq vs $>$ 200 cells/mm³), and study (GEMINI-1 vs GEMINI-2).

Cahn P, et al. AIDS 2018. Abstract TUAB0106LB.

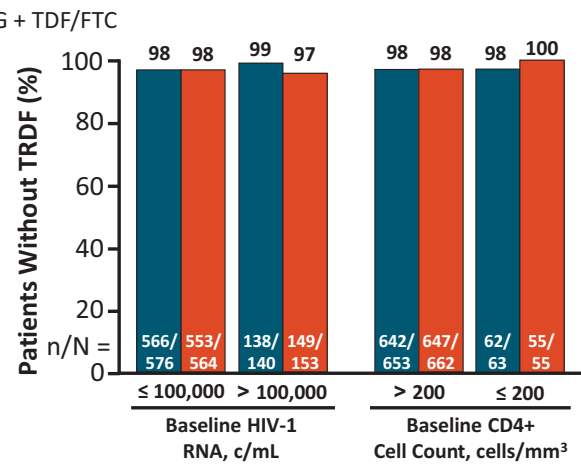
Slide credit: clinicaloptions.com

GEMINI-1 and -2: Virologic Response at Wk 48 by Baseline HIV-1 RNA and CD4+ Cell Count

Virologic Outcomes by FDA Snapshot Analysis



Virologic Outcomes by TRDF Analysis



- TRDF includes confirmed virologic withdrawal, withdrawal for lack of efficacy or treatment-related AEs, and participants meeting protocol-defined stopping criteria

Cahn P, et al. AIDS 2018. Abstract TUAB0106LB.

Slide credit: clinicaloptions.com

GEMINI-1 and -2: Renal and Bone Parameters at Wk 48

Endpoint*	DTG + 3TC (n = 716)	DTG + TDF/FTC (n = 717)
Adjusted mean change from BL in plasma/serum markers [†]		
▪ GFR from cystatin C (CKD-EPI), mL/min/1.73 m ²	6.3	4.1
▪ Creatinine, μmol/L	10.4	13.5
▪ GFR from creatinine (CKD-EPI), mL/min/1.73 m ²	-12.1	-15.5
Change from BL in urine markers [‡]		
▪ Protein/creatinine, g/mol	-13.1	2.9
▪ Retinol-binding protein/creatinine, μg/mmol	-7.4	11.4
▪ β ₂ -microglobulin/creatinine, mg/mmol	-7.7	31.2
Adjusted mean change from BL in bone markers, [§] μg/L		
▪ Serum bone-specific alkaline phosphatase	1.22	4.07
▪ Serum osteocalcin	0.60	6.17
▪ Serum procollagen 1 N-terminal propeptide	0.40	13.10
▪ Serum type 1 collagen C-telopeptide	0.14	0.33

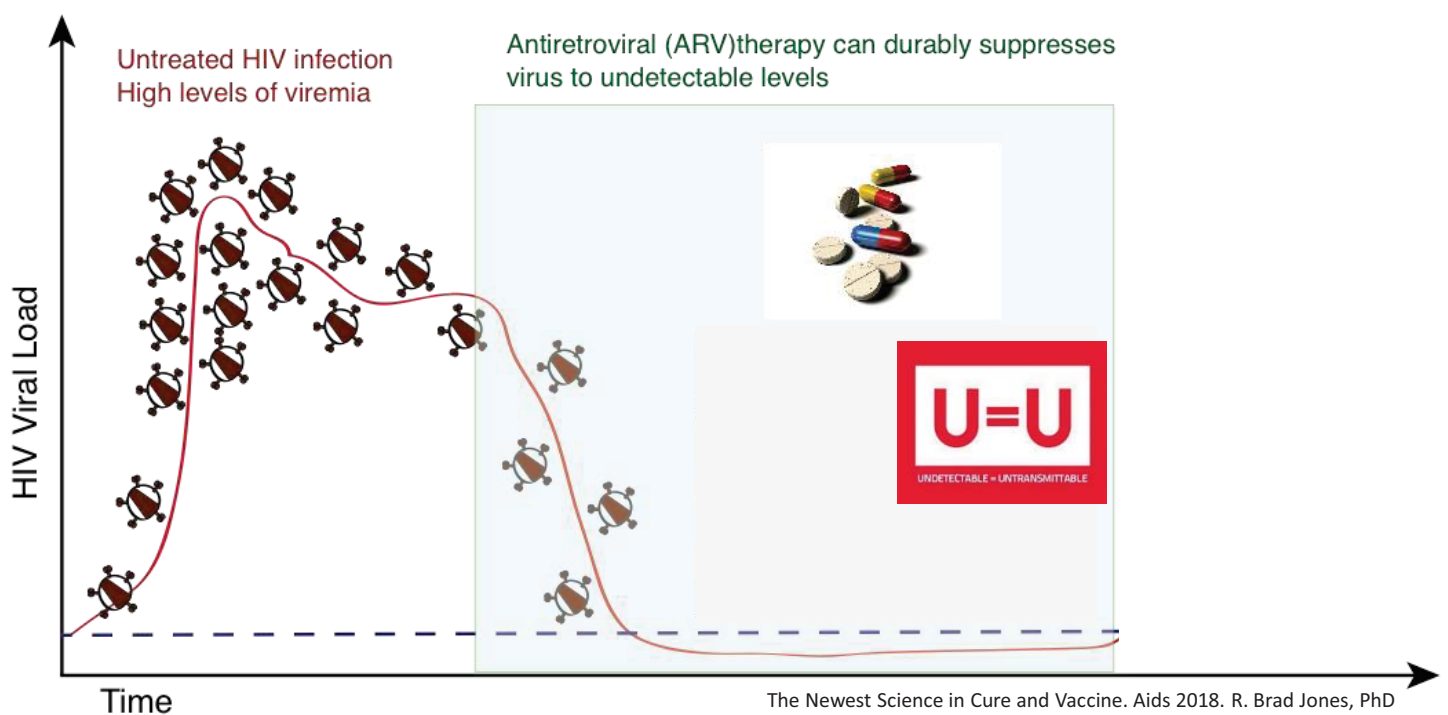
*P < .001 for all comparisons. [†]Adjusted for study, treatment, BL HIV-1 RNA, BL CD4+ cell count, age, sex, race, T2DM, HTN, and BL biomarker value. [‡]Estimated from geometric mean ratio for BL and Wk 48. [§]Adjusted for study, treatment, BL HIV-1 RNA, BL CD4+ cell count, age, sex, race, BMI, smoking status, current vitamin D use, and BL biomarker value.

Cahn P, et al. AIDS 2018. Abstract TUAB0106LB.

Slide credit: clinicaloptions.com

治癒HIV感染是目標

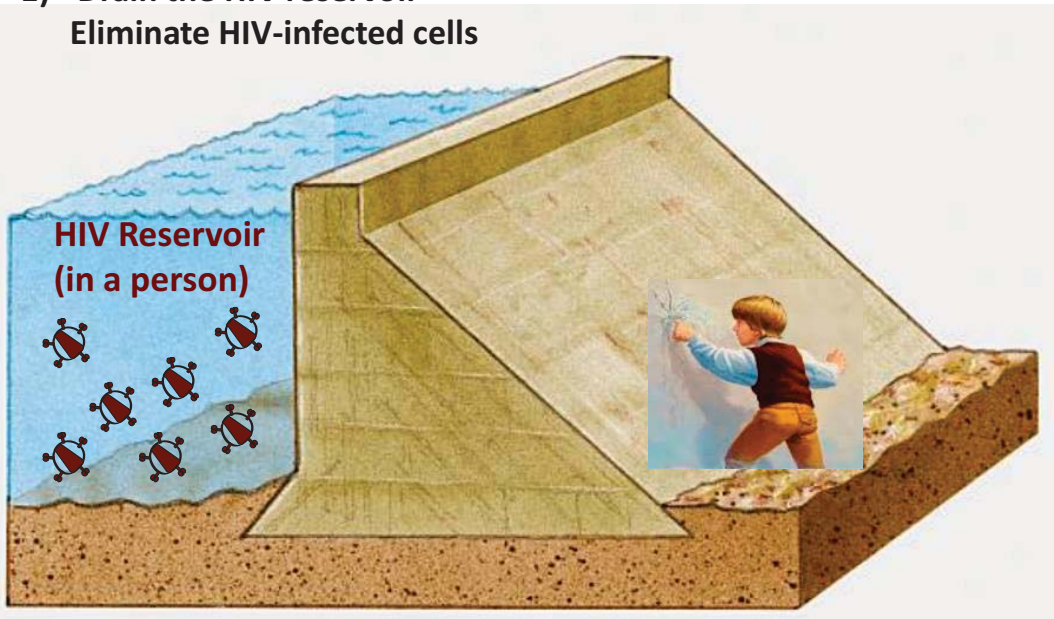
Towards a Potential Cure for HIV



How Can We Prevent HIV From Rebounding Off of Therapy?



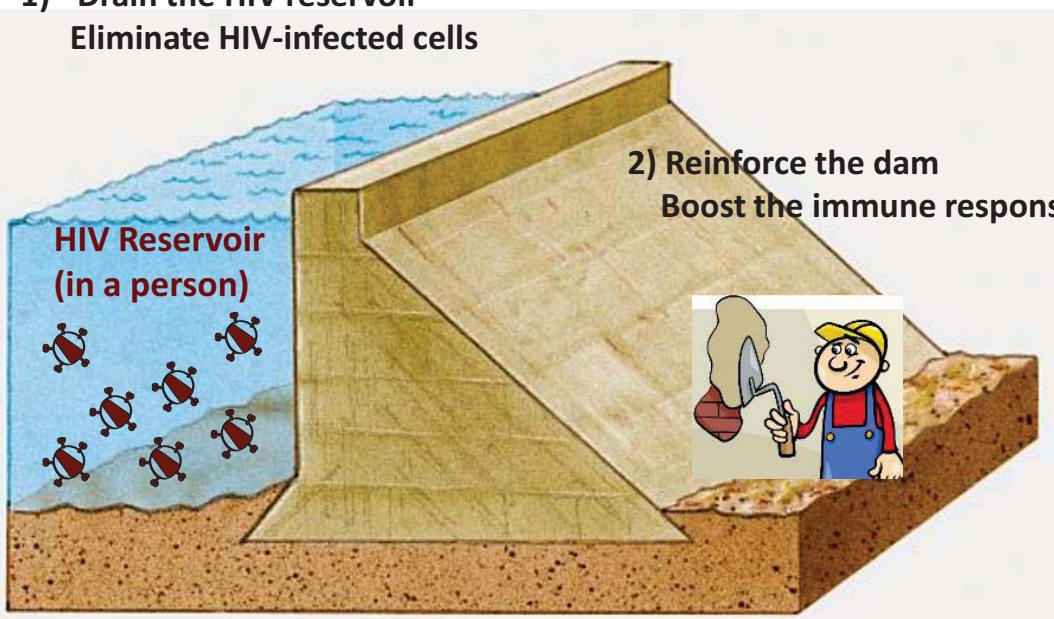
- 1) Drain the HIV reservoir
Eliminate HIV-infected cells



How Can We Prevent HIV From Rebounding Off of Therapy?



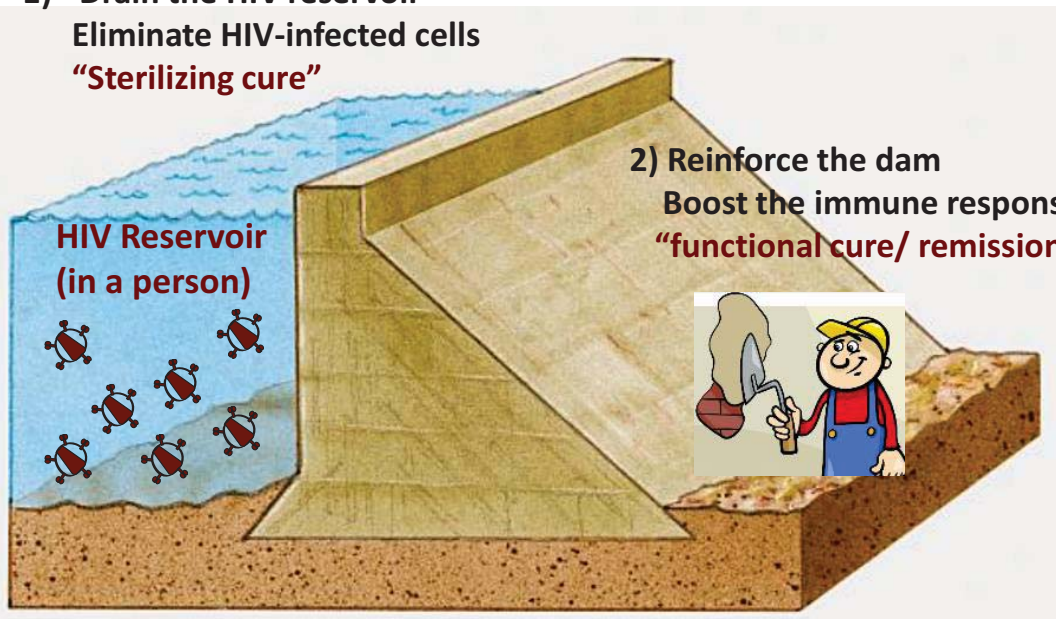
- 1) Drain the HIV reservoir
Eliminate HIV-infected cells



How Can We Prevent HIV From Rebounding Off of Therapy?



1) Drain the HIV reservoir
Eliminate HIV-infected cells
“Sterilizing cure”



Therapeutic Strategies which Aim to Cure HIV Infection



‘Kick and kill’ – reactivate latent HIV with drugs and kill with immune system



Gene therapy to delete HIV out of cells



Gene therapy to make cells resistant to HIV



Vaccines / Immunotherapies – enhance immune responses to control virus

- ‘Block and lock’ – permanently silence HIV expression (force into deeper latency)

Thank you



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隱私保密的重要性

【AIDS名單外洩】3千筆AIDS個資遭po上網 北市聯醫驚爆醜聞

- 經過多年的努力，AIDS（人類後天免疫缺乏症候群）雖然無法完全治癒，也不再是可怕的絕症，為保護病患，政府早在1990年時就公告禁止任何AIDS患者個資遭公開。
- 但本刊日前接獲報料，指網路竟然出現一份人數多達3千餘筆的台灣愛滋病患個資供人下載，而將資料放上網路的竟然就是主管單位台北市立聯合醫院昆明防治中心，目前該筆資料到底有多少人下載已不可考，但防治中心負責管制資料卻帶頭違法，有關單位應主動調查，保障患者權益。

鏡週刊 2018/6/20

無恥12醫師公開胡病歷

- 包括民進黨立委林進興在內及台中醫界聯盟代表高大成共十二位醫師昨召開記者會，公布台中市長胡志強的「病歷表解析」證明胡再度中風機率高，並聲稱資料是從台中榮總流出，由於涉及違反《醫師法》，台中市衛生局將對榮總及與會醫生蒐證後開罰。
- 台灣醫療改革基金會執行長劉梅君痛斥：「公開病人的資料違背醫學倫理及行政倫理，全民應予唾棄！政治人物為選舉打壓對手，不惜洩露病人私密資料，就是一種失德行為！」民眾陳小姐受訪時對十二名醫師在記者會上的表現不敢恭維，她說：「如果遇到這種事，一定會換醫院換醫師看診。」曾先生更是痛罵：「把病人隱私看得無關重要的醫師太沒有醫德了。」

蘋果日報 2005/11/30

大陸愛滋病患隱私暴露事件

- 全國30省份275位愛滋病感染者稱接到了詐騙電話，愛滋病感染者的個人信息疑似被大面積泄露。
- 騙子自稱是政府部門或衛生局的工作人員，將給愛滋病感染者發放補助。
- 電話交流中，愛滋病感染者們發現詐騙者事先已掌握他們的個人信息，包括真實姓名、身份證號、聯繫方式、戶籍信息、確診時間、隨訪的醫院或區縣疾控等等。

隱私保密相關法令

- 《個人資料保護法》第六條等也規範，有關醫療、基因、性生活、健康檢查及犯罪前科之個人資料，不得蒐集、處理或利用。但有下列情形之一者，不在此限：
 - 一、法律明文規定。
 - 二、公務機關執行法定職務或非公務機關履行法定義務必要範圍內，且事前或事後有適當安全維護措施。
 - 三、當事人自行公開或其他已合法公開之個人資料。
 - 四、公務機關或學術研究機構基於醫療、衛生或犯罪預防之目的，為統計或學術研究而有必要，且資料經過提供者處理後或經蒐集者依其揭露方式無從識別特定之當事人。
 - 五、為協助公務機關執行法定職務或非公務機關履行法定義務必要範圍內，且事前或事後有適當安全維護措施。
 - 六、經當事人書面同意。

隱私保密相關法令

- 《人類免疫缺乏病毒傳染防治及感染者權益保障條例》第十四條規定，「主管機關、醫事構人員及其他因業務知悉感染者之姓名及病歷等有關資料者，除依法律規定或基於防治需要外，對該項資料，不得洩漏。」
- 醫師法二十三條「醫師對於因業務知悉或持有他人病情或健康資訊，不得無故洩漏」

Thank you

