



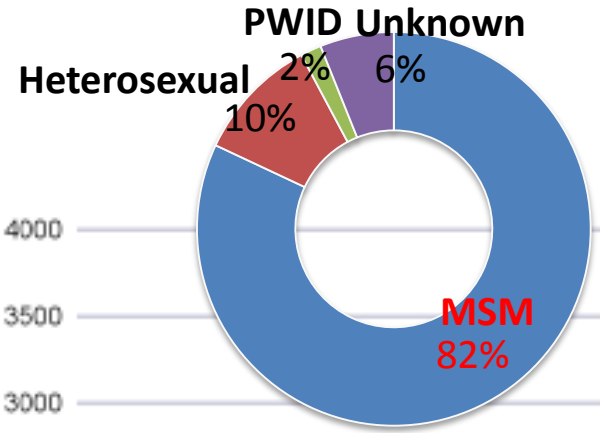
108年度藥事人員繼續教育課程

愛滋之治療預防新趨勢

北市聯醫仁愛院區內科部感染科 顧文瑋醫師

108年6月30日

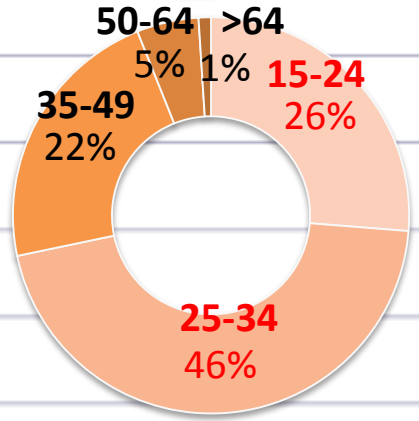
台灣愛滋疫情: 2017



Route of transmission for newly-diagnosed HIV cases in 2017

PLWH in Taiwan in 2017: 29,881

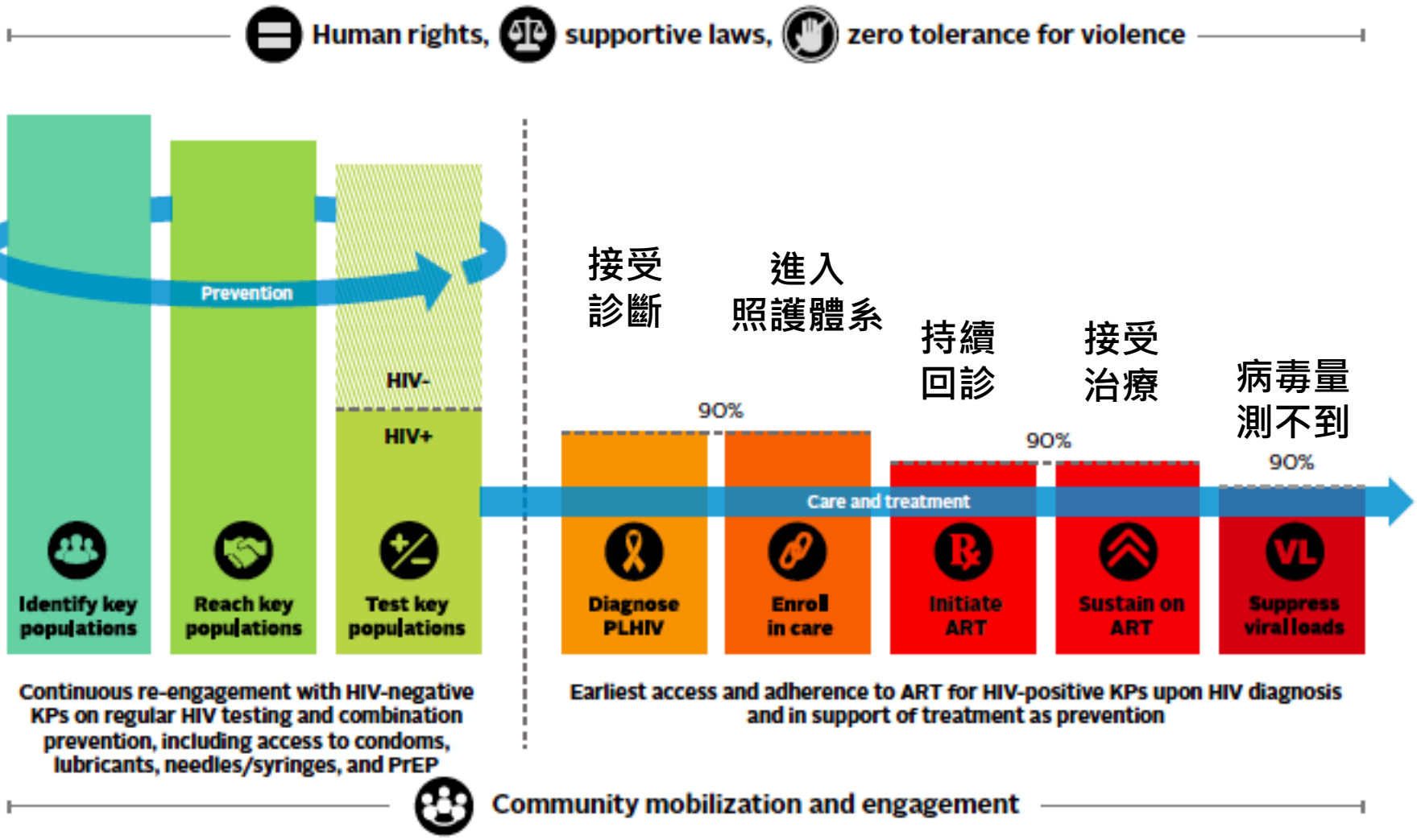
Prevalence: 126.8/100,000



Age distribution of newly-diagnosed HIV cases in 2017

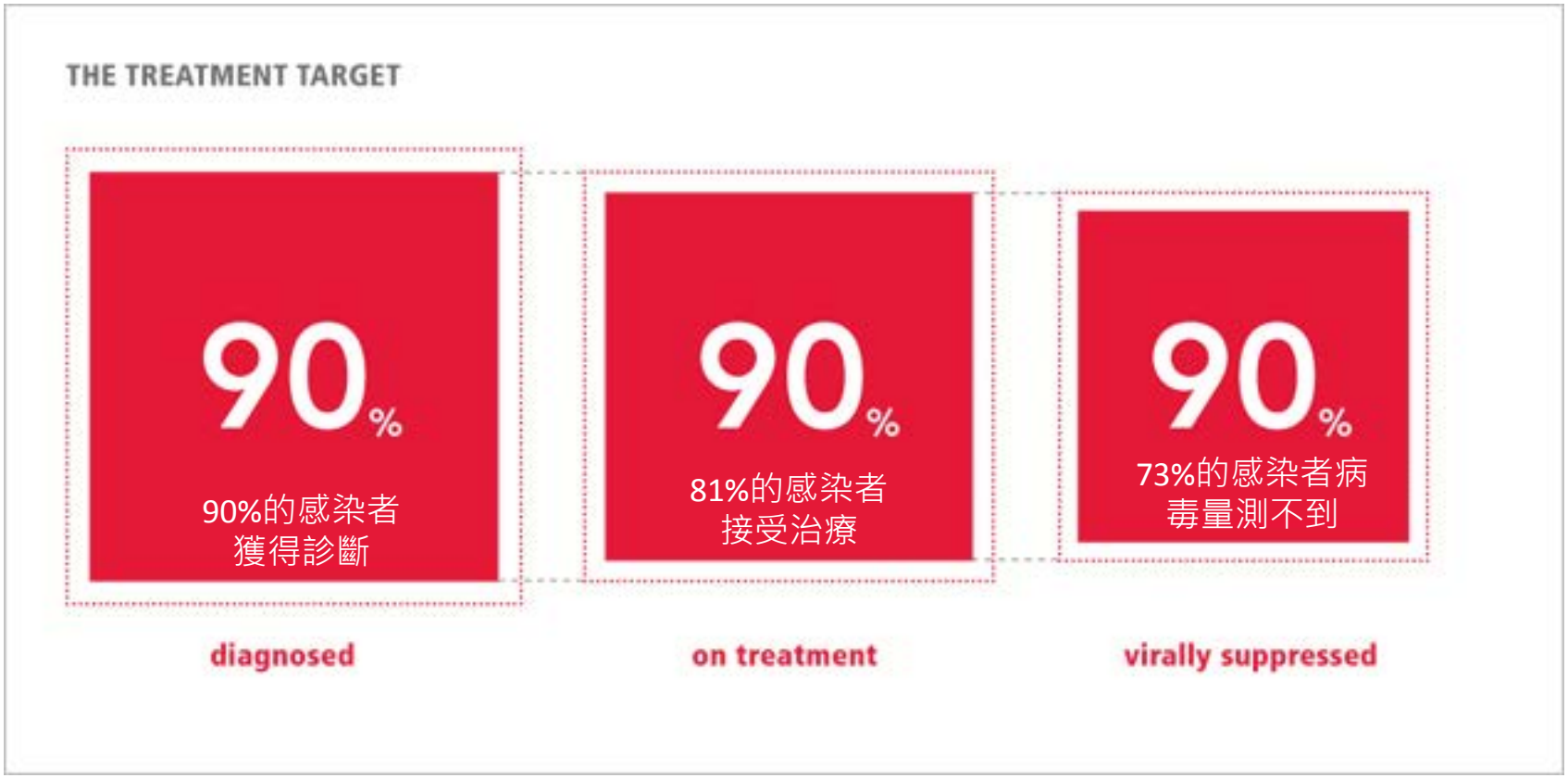
(As of Jan 2018)

什麼是HIV的預防與照顧階梯



FHI 360. HIV Cascade Framework for Key Populations. 2015

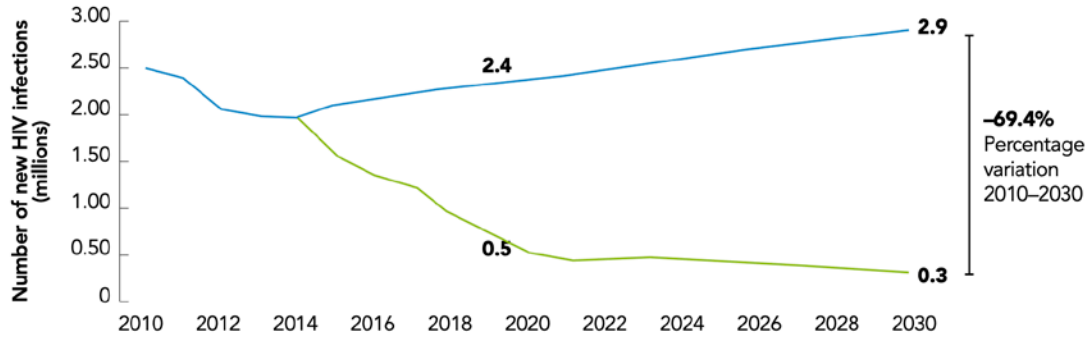
聯合國在2020預計 “90-90-90” 的目標



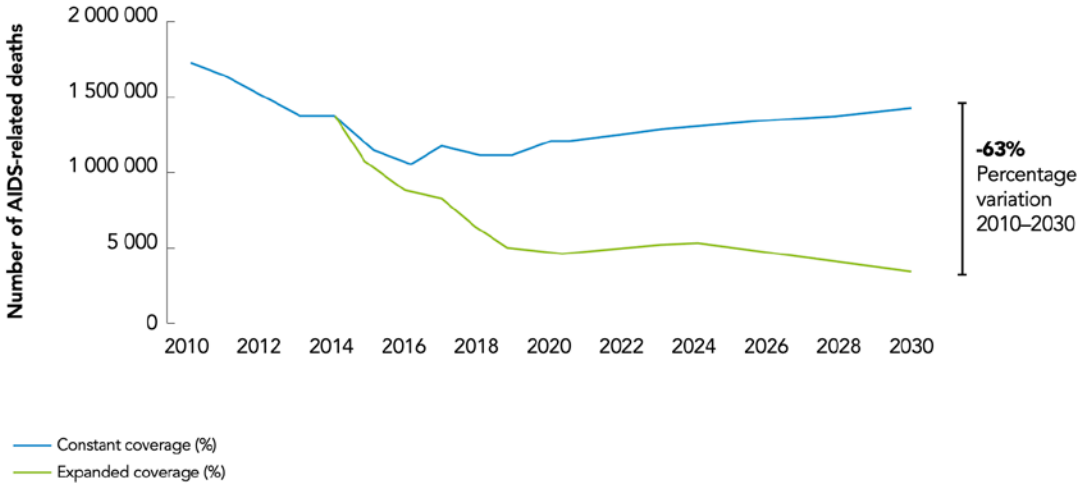
UNAIDS, 2014

達到90-90-90目標的好處

Ending AIDS scenario: new HIV infections (2010–2030)



Ending AIDS scenario: AIDS-related deaths (2010–2030)



UNAIDS, 2014

台灣愛滋照護階梯: 2017

2015	75%	79%	85%
2016	74%	84%	89%
2017	79%	87%	90%

Taiwan CDC.


愛滋篩檢
做自己的勇士
愛滋防治大使
黃士澤 醫師
提起勇氣，不再逃避
做自己的勇士
了解自我，爲健康拼下去
愛滋唾液快速自我篩檢服務
活動期間：105年9月1日至105年12月15日
活動網頁：http://hiva.cdc.gov.tw/oraltest
活動方式：請至試劑提供地點支付200元取得試劑。
完成篩檢後，請至活動網頁登錄並依步驟領回200元。
試劑提供地點
合作衛生局(試劑提供地點請參閱活動網頁)
民間團體
自動服務機(請準備50元硬幣4枚)
衛生福利部疾病管制署 TAIWAN CDC
www.cdc.gov.tw
1922防疫達人
www.facebook.com/TWCDC
Taiwan CDC LINE@
疫情通報及諮詢專線：1922
廣告


自我篩檢
愛自己也是一種
Rocker態度
愛滋防治大使
薛文琦 醫師
您曾因不安全性行為而有負擔嗎？
您可以掌握自身感染狀態
愛滋唾液快速自我篩檢服務
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廣告

疾管署愛滋自我篩檢計畫: 2018

Local Health Bureau
MSM Drop-in Centers

Vending Machines
Online Pay-at-pickup Service

https://hiva.cdc.gov.tw/oraltest/

“Time to Hit HIV, Early and Hard”

好處

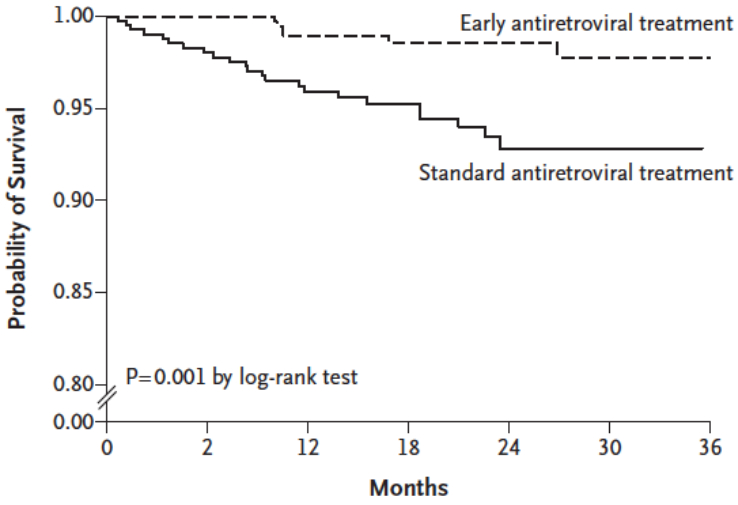
- 維持免疫功能
- 早期控制病毒複製
- 減低傳播風險

壞處

- 增加抗病毒藥物的毒性
- 減少病患藥物順從性
- 生活品質下降

何時該開始吃藥？CIPRA HT-001

- CIPRA HT-001 Trial
  - 自2005年開始於海地太子港的單一醫學中心所進行的RCT
  - 總共816人收案
  - **提前治療組 (early)**：CD4 200-350/cumm
  - **標準治療組 (standard)**：AIDS或是CD4 <200/cumm
- 試驗結果
  - 提前治療組相較標準治療組的**死亡率減少75% (6 vs. 23)，得到結核病的比率減少50% (18 vs. 36)**
  - 期中分析結果促使DSMB於2009年提前結束RCT

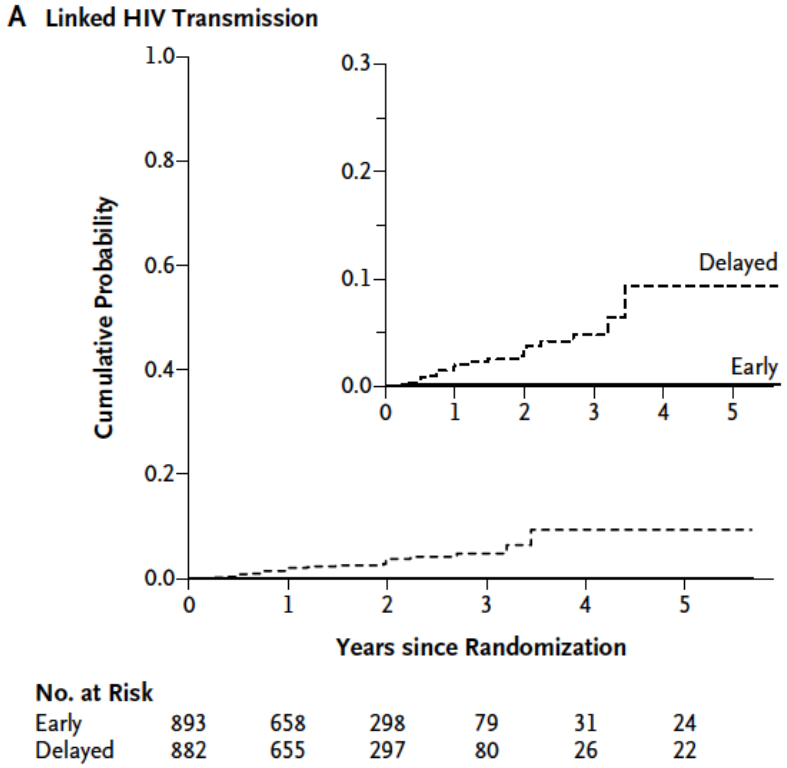


No. at Risk				
Early treatment	408	327	153	24
Standard treatment	408	309	137	22

Severe P et al. N Engl J Med 2010;363:257-65

何時該開始吃藥？HPTN 052

- HPTN 052 Trial
  - 2005-2010於非洲、南美、泰國的醫學中心所進行的RCT
  - 總共1763對serodiscordant的伴侶收案（98%為異性戀）
  - **提前治療組 (early)**：CD4 350-550/cumm
  - **延後治療組 (delayed)**：AIDS或是CD4 <250/cumm
- 試驗結果
  - 提前治療組相較延後治療組的**伴侶陽轉率減少了96% (1 vs. 27)**
  - 提前治療組相較延後治療組的**病患發生感染或死亡（主要為肺外結核）的比率減少41% (40 vs. 65)**

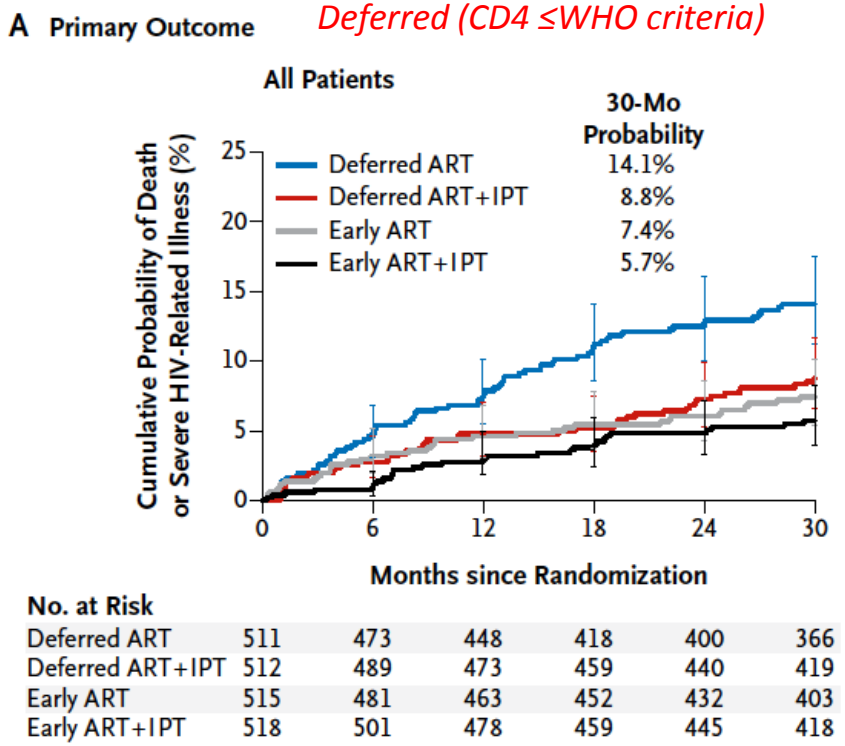


Cohen MS et al. N Engl J Med 2011;365:493-505

何時該開始吃藥？TEMPRANO

- 2008-2012於非洲象牙海岸的9個醫學中心所進行的RCT（2-by-2 factorial, 1:1 superiority trial）
- 總共收了2056位個案（41%的人收案時CD4 >500）
- 提前治療組相較延後治療組的病患發生**死亡或嚴重HIV相關疾病的比率降低了44%**
  - 結核病占42%, 侵襲性細菌感染占27%
  - 收案時CD4 >500者發生死亡或嚴重HIV相關疾病的比率也降低了44%

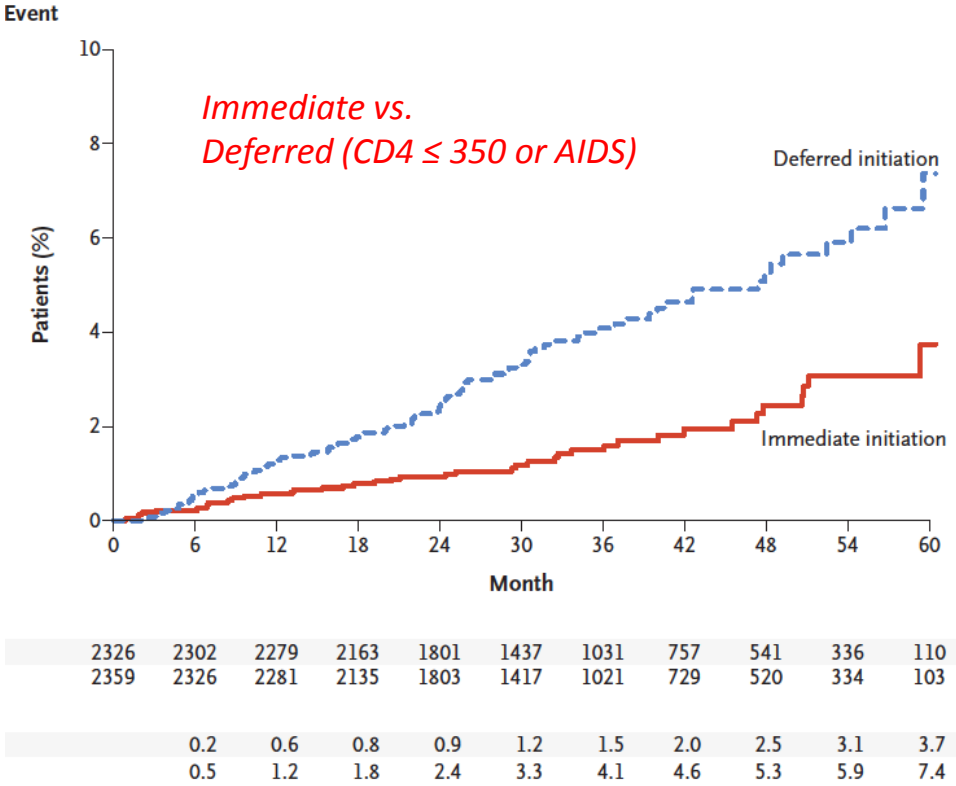
Early (immediately) vs.
Deferred (CD4 ≤WHO criteria)



Danel C et al. N Engl J Med 2015. 373:808-22.

何時該開始吃藥？START

- 2009-2013於全球35個國家215個研究中心進行的RCT
- 總共收了4685位個案
- 立即治療組相較延後治療組的病患發**生死亡或嚴重AIDS或非AIDS相關疾病的比率減少57% (0.6 vs. 1.38 per 100 patient-years)**
- 試驗安全委員會於2015年5月期中分析後建議延後治療組應全面開始接受治療



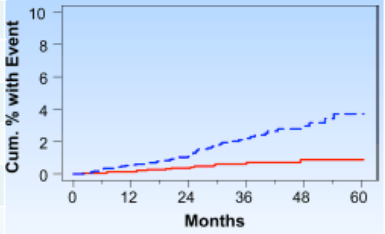
Lundgren JD et al. N Engl J Med 2015. 373:795-807.

何時該開始吃藥？START

Types of Serious AIDS Events

AIDS Events	Imm. ART	Def. ART
TB, pulm or extrapulm.*	6	20
Lymphoma, HL or NHL	3	10
Kaposi's sarcoma	1	11
PCP	1	5
Herpes zoster, diss.	0	3
Other**	3	1
Any Serious AIDS	14	50

0.2 vs. 0.72 /100 PY
(HR 0.28, CI: 0.15-0.5)

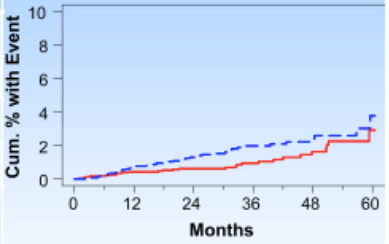


*: Participants from Africa: 16/26 (62%) of TB cases
**: Cervical carcinoma, extra-pulm. cryptococcosis, CMV, recurrent bacterial pneumonia

Types of Serious Non-AIDS Events

Non-AIDS Event	Imm. ART	Def. ART
Cancer, non-AIDS*	9	18
Cardiovascular disease*	12	14
Liver or renal disease	1	2
Death, other	7	13
Any Serious Non-AIDS	29	47

0.42 vs. 0.67 /100 PY
(HR 0.61, CI: 0.38-0.97)

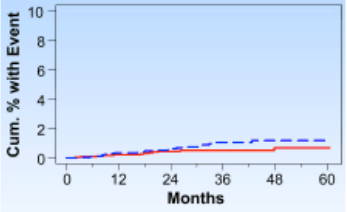


Participants from Australia, Europe, Israel and USA:
22/27 (81%) of cancer cases
19/26 (73%) of CVD cases

Causes of Death

Cause	Imm. ART	Def. ART
Accident/violence/suicide	4	6
AIDS, active disease	1	4
Cardiovascular disease	3	1
Non-AIDS cancer -HBV/HCV	1	1
Substance abuse	0	2
Other*	0	4
Unknown	3	3
Total	12	21

0.17 vs. 0.30 /100 PY
(HR 0.58, CI: 0.28-1.17)

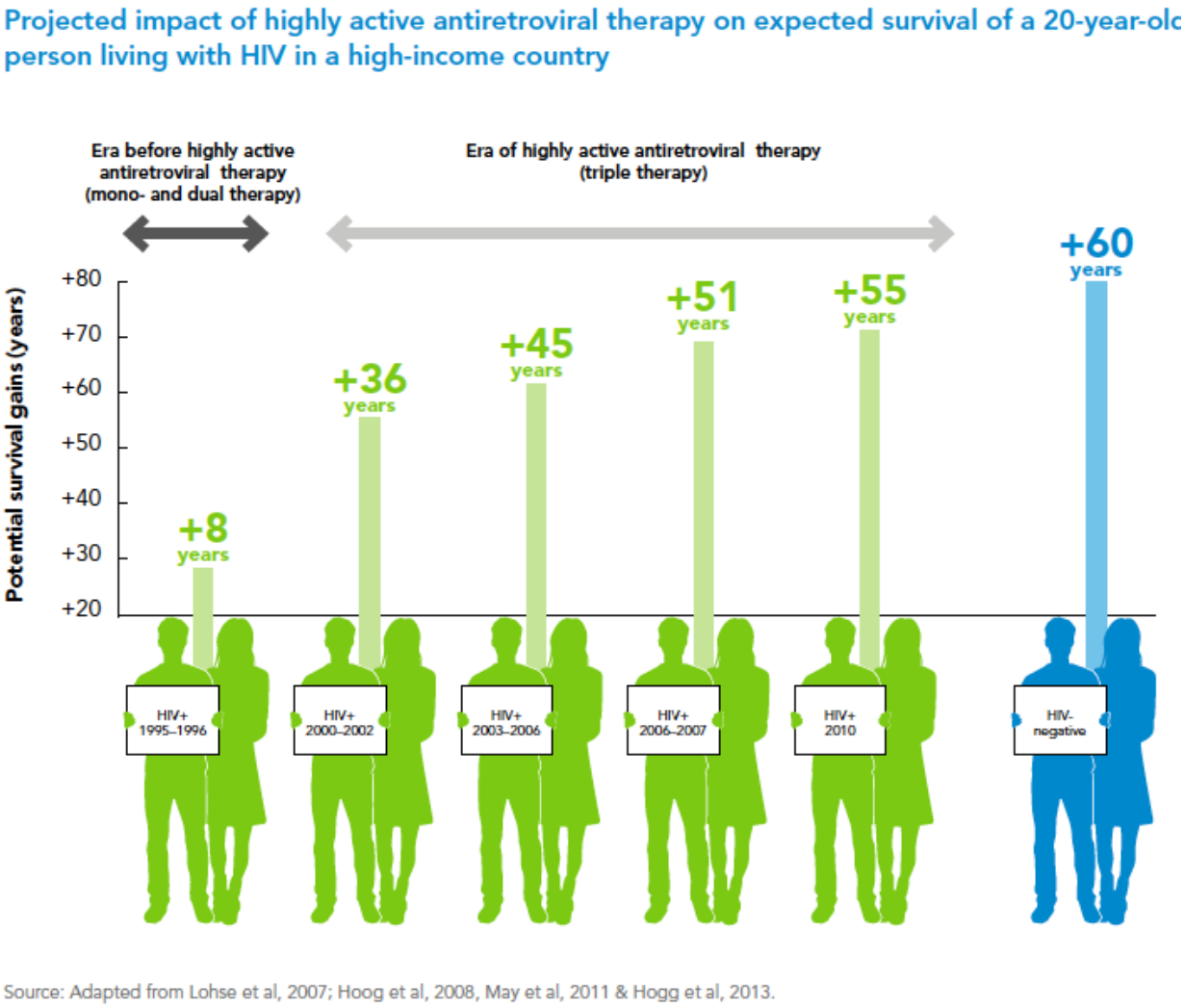


*Chronic viral hepatitis, renal failure, infection, diabetes mellitus

- 立即治療組相較延後治療組發生嚴重AIDS與非AIDS相關疾病的比率顯著較低，主要是來自**結核病**與**癌症**發生率的差異
- **68%**的事件發生在受試者**CD4 >500** 狀況下

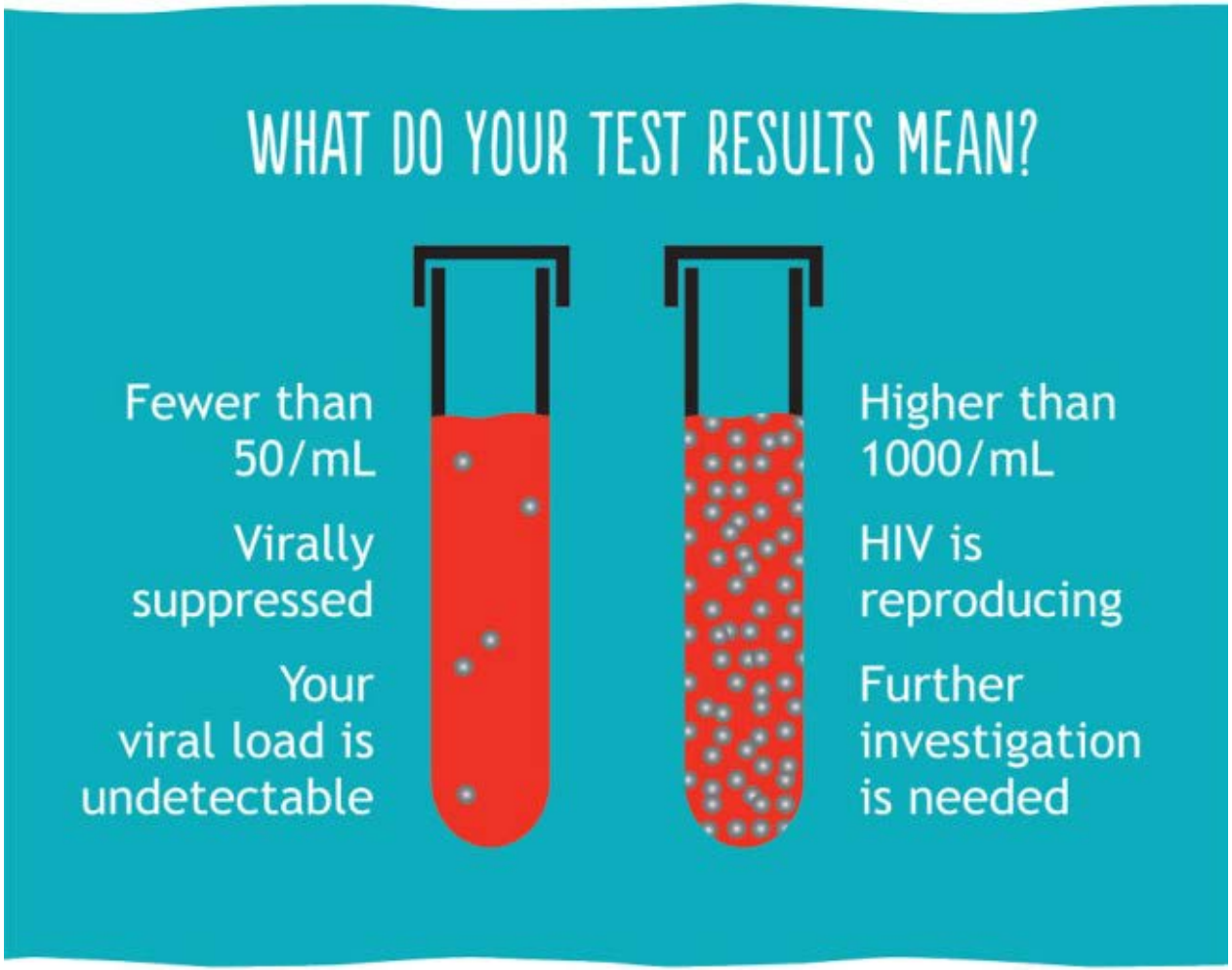
Lundgren JD et al. N Engl J Med 2015. 373:795-807.

愛滋病不再是世紀黑死病嘍



UNAIDS, The Gap Report, 2014.

病毒量測不到 = 良好控制


WHAT DO YOUR TEST RESULTS MEAN?
Fewer than 50/mL
Virally suppressed
Your viral load is undetectable
Higher than 1000/mL
HIV is reproducing
Further investigation is needed

治療即預防: 2016

- **PARTNER Study**
  - 2010-2014於西歐進行的前瞻性觀察性研究期中分析
  - 總共有1166對血清相異伴侶收案追蹤（340對男男性行為者、548對異性戀伴侶）
  - 受試者陽性伴侶病毒量皆 <200 copies/mL
  - 受試者伴侶間皆有進行沒有戴套的性行為
- 試驗結果
  - 估計追蹤期間發生過26,000無套肛交與36,000次陰道交
  - **共有11位受試者陽轉，但沒有任何一位是被陽性伴侶感染**
  - 繼續針對男男性行為者的相異伴侶繼續收案追蹤到2018年 (PARTNER2)

Rodger AJ et al. JAMA, 2016;316(2):1-11.

治療即預防: 2017

- **Opposite Attract Study**

- 於全球進行的前瞻性觀察性研究
- 總共有343對男男間性行為者血清相異伴侶收案追蹤
- 估計追蹤期間（591 CYFU）發生過16,889次無套肛交。HIV感染者的病毒量在95%追蹤期間都是測不到的。
- **共有3位受試者陽轉，但沒有任何一位是被陽性伴侶感染**

Bavinton BR, et al. Lancet HIV. 2018;5:e438-e447.

治療即預防: 2018

- **PARTNER-2 Study**
  - 2014-2018於西歐進行的多國多中心前瞻性觀察性研究
  - 總共有783對男男性行為者的血清相異伴侶收案追蹤（總共1596 CYFU）
  - 受試者陽性伴侶病毒量皆 <200 copies/mL
  - 受試者伴侶間皆有進行沒有戴套的性行為
  - 受試者陰性伴侶沒有使用 PEP 或是 PrEP

- 試驗結果
  - 估計追蹤期間發生過接近77,000無套肛交
  - **共有17位受試者陽轉，但沒有任何一位是被陽性伴侶感染**

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

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

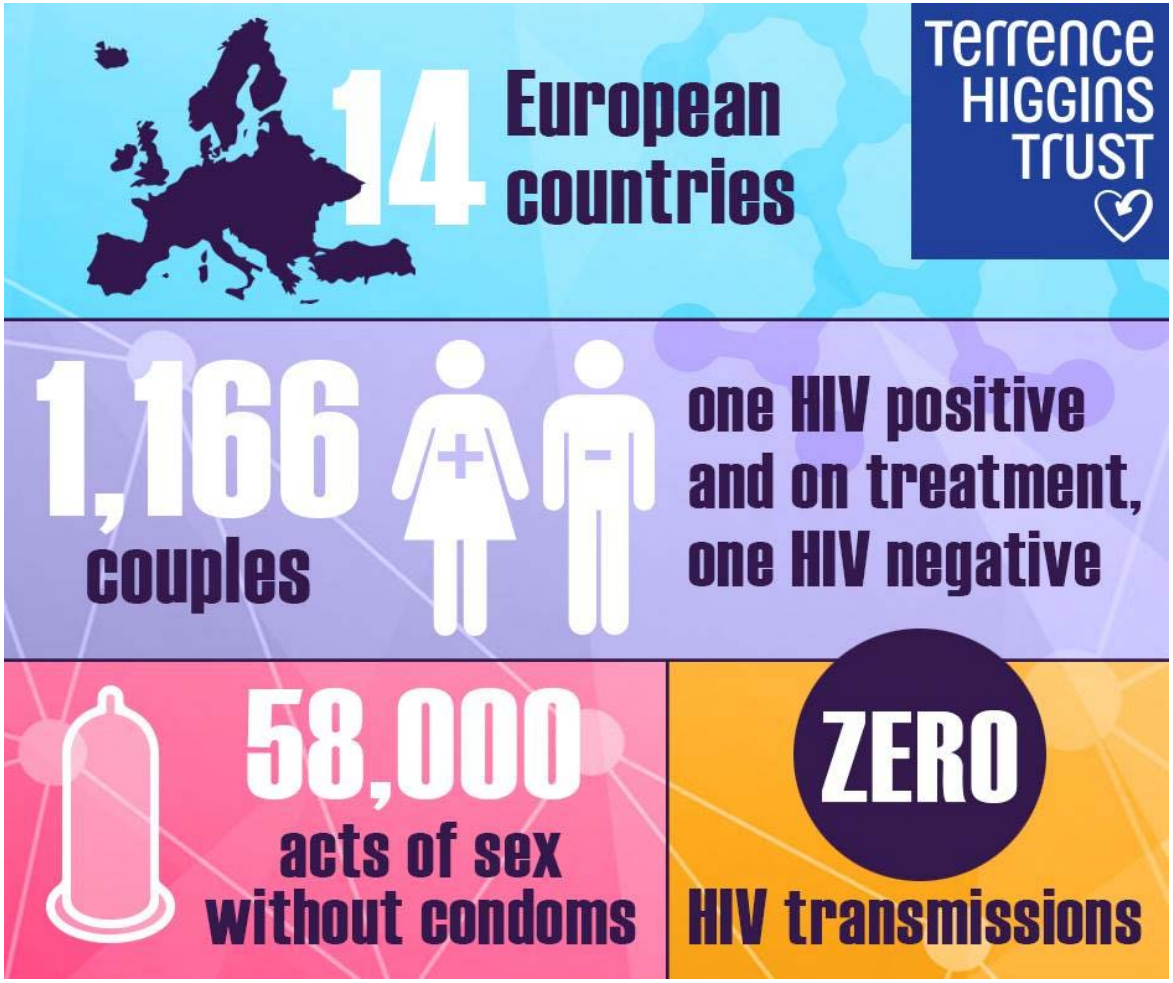
Sexual Behavior Reported by HIV-Negative Partner	Linked Transmissions, n	Upper 95% CI*	Condomless Sex Acts, n	CYFU
Any sex	0	0.23†	76991	1596
Anal sex	0	0.24	70743	1546
Insertive anal sex	0	0.27	52572	1345
Receptive anal sex without ejaculation	0	0.43	23153	867
Receptive anal sex with ejaculation	0	0.57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

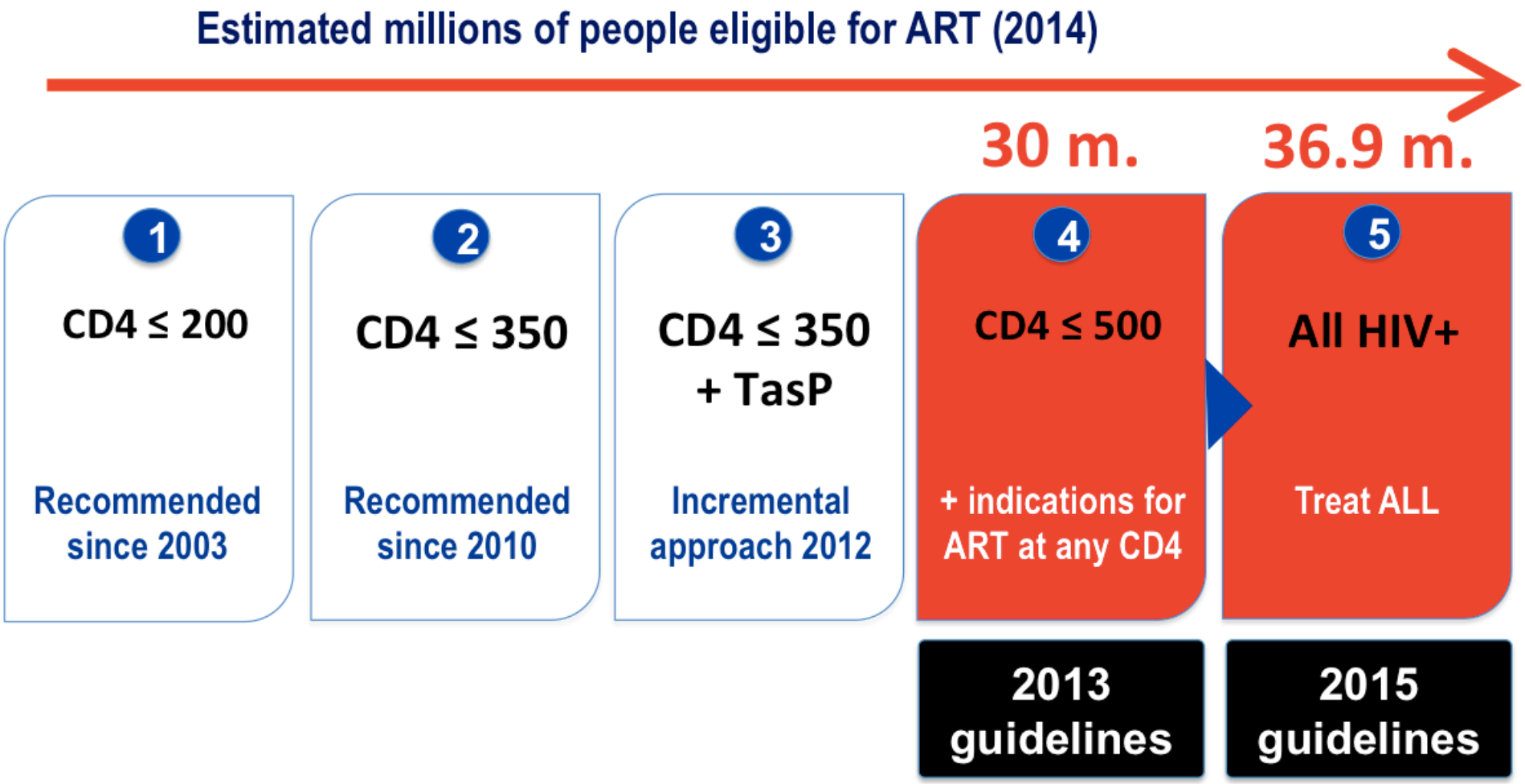
Rodger A, et al. AIDS 2018. Abstract WEAX0104LB.

病毒量測不到=沒有感染力

Undetectable = Untransmittable



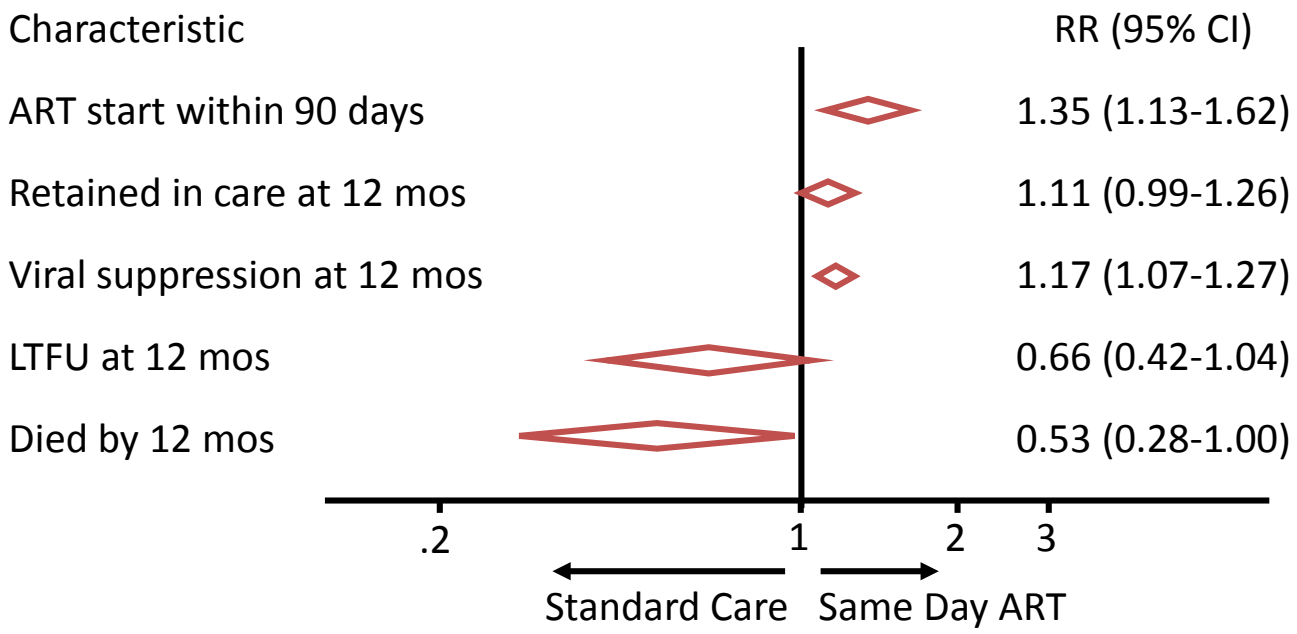
ART eligibility: 5 potential policy scenarios



World Health Organization

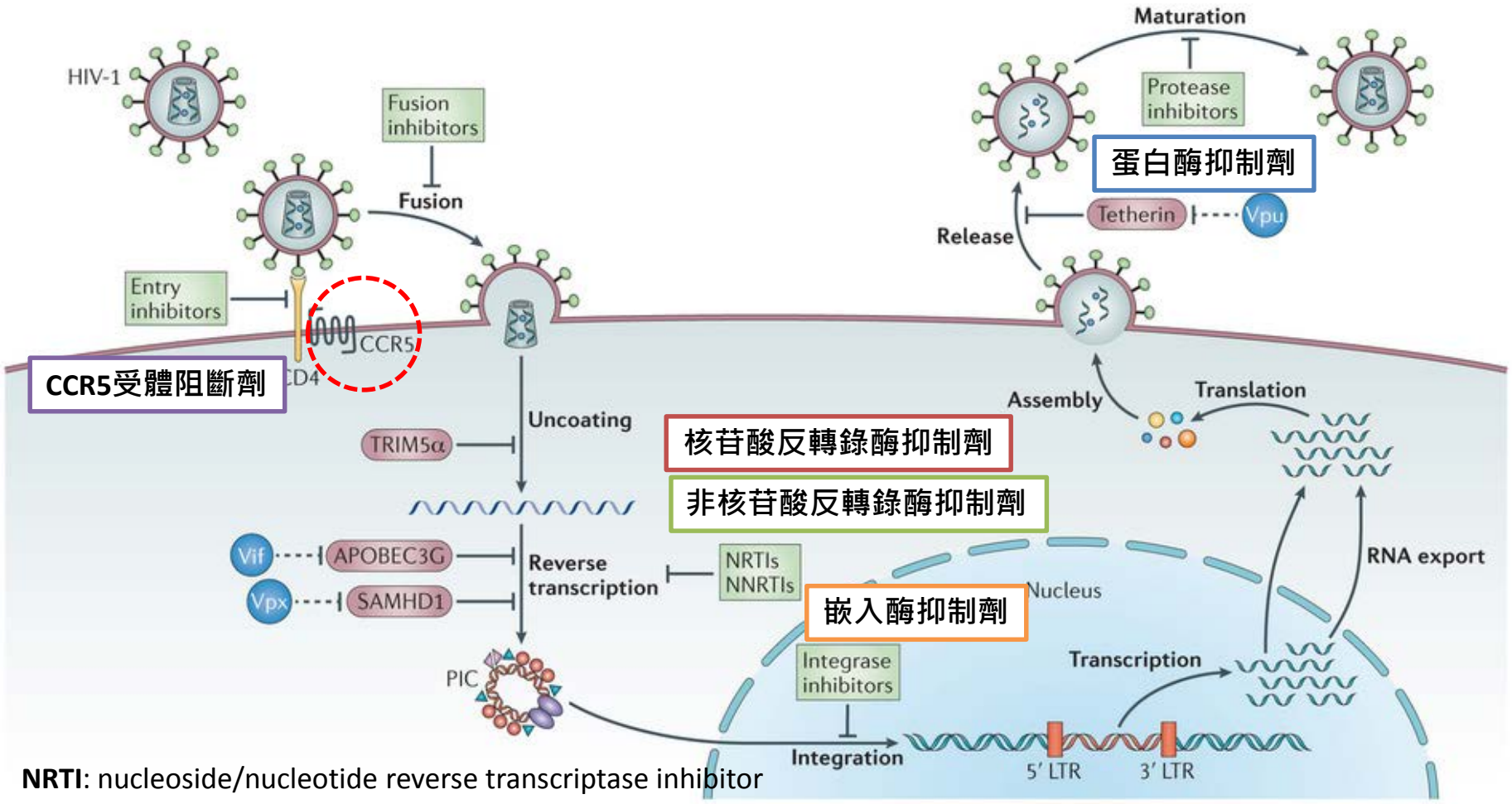
Improved Clinical Outcomes With Rapid ART Initiation

- Systematic review of ART initiation within 14 days of diagnosis across 4 randomized clinical trials
  - Compared with standard care, **same-day ART increased** likelihood of ART initiation in first 90 days, patient retention and viral suppression at 12 mos



Ford N, et al. AIDS. 2018;32:17-23.

HIV病毒複製與抗病毒藥物目標



NRTI: nucleoside/nucleotide reverse transcriptase inhibitor
NNRTI: non-nucleoside reverse transcriptase inhibitor
InSTI: integrase strand transfer inhibitor

Barre-Sinoussi F et al. Nat Rev Microbiol. 2013: 11:877

為什麼要三合一

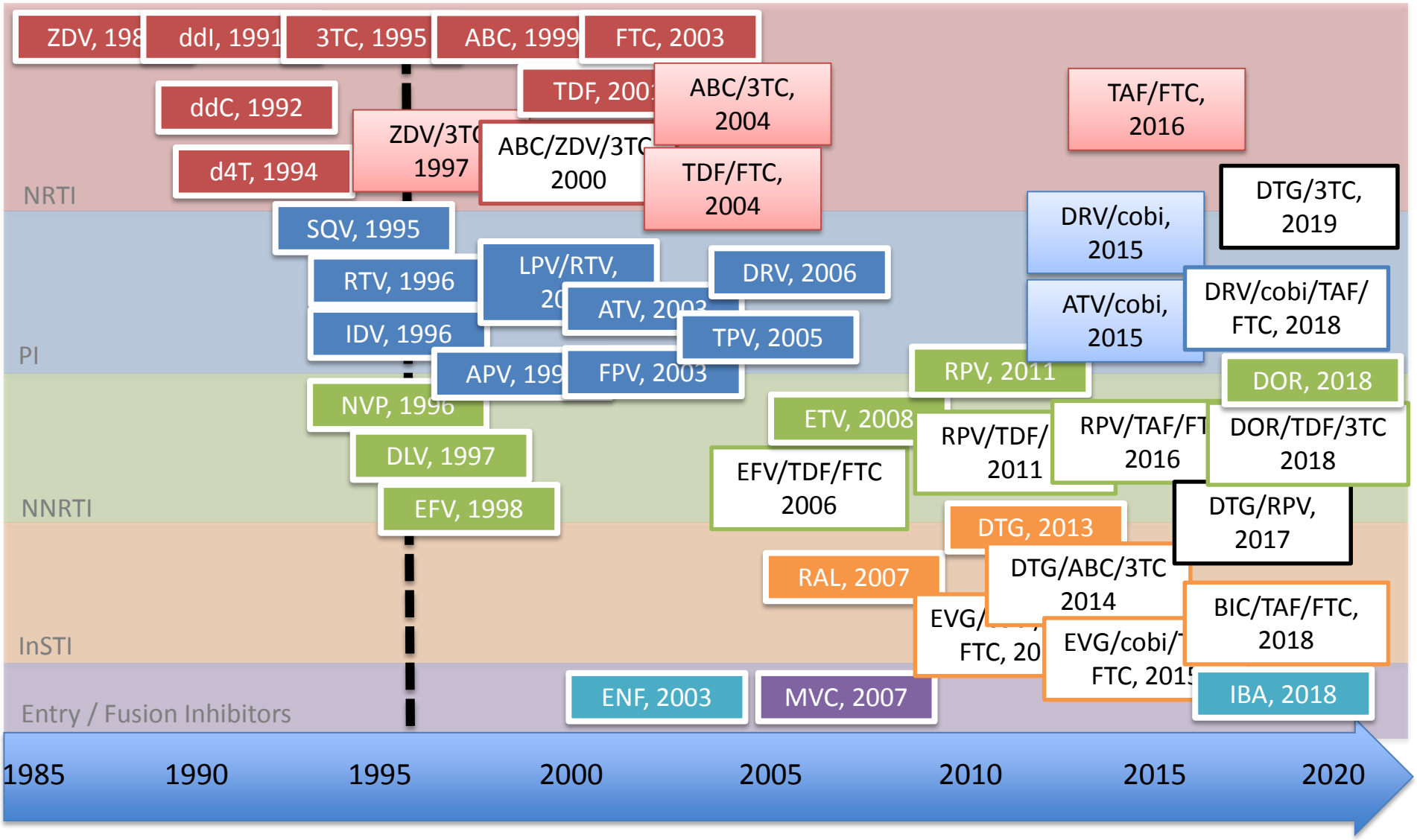
每天體內平均有
10^{10}個HIV病毒產生

使用三種藥物組合發生
抗藥性突變的機率就小於1

$$10^{10} \times \left[\frac{5}{10^5} \times \frac{5}{10^5} \times \frac{5}{10^5} \right] \approx 10^{-3}$$

每10,000個HIV病毒中有5個病毒
(也就是5×10^{-5}的機率) 會發生抗藥性的突變

抗病毒藥物的發展史 (Apr, 2019)



三合一抗病毒藥物組合的原則

核苷酸反轉錄酶抑制劑骨架
(NRTI Backbone)

- TDF/FTC (Truvada) 舒發泰
  TAF/FTC (Descovy)
- ABC/3TC (Kivexa) 克維滋
- ZDV/3TC (Combivir) 卡貝滋
- ddI 惠妥滋 + 3TC 速汰滋
- d4T 滋利特 + 3TC 速汰滋

+

非核苷酸反轉錄酶抑制劑 (NNRTI)
衛滋、希寧、恩臨

蛋白酶抑制劑 (PI)
快利佳、瑞塔滋、普利他/普澤力

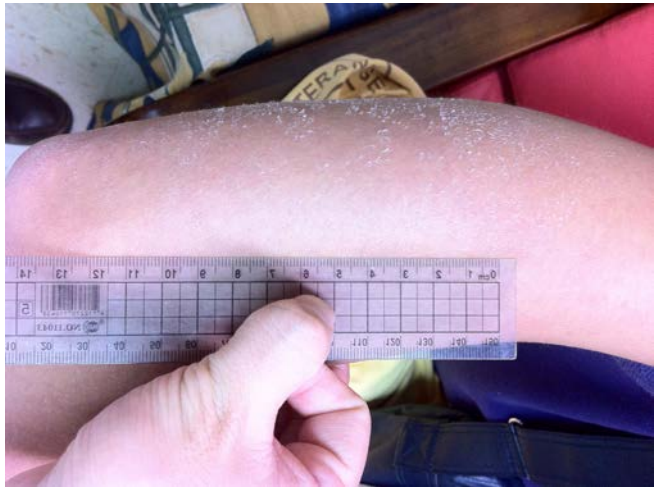
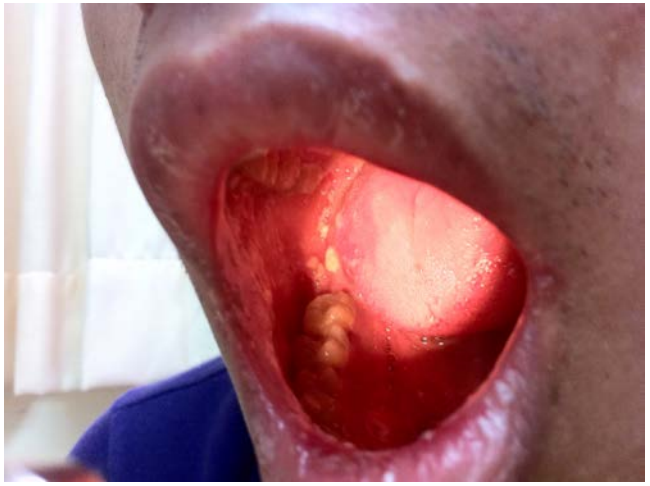
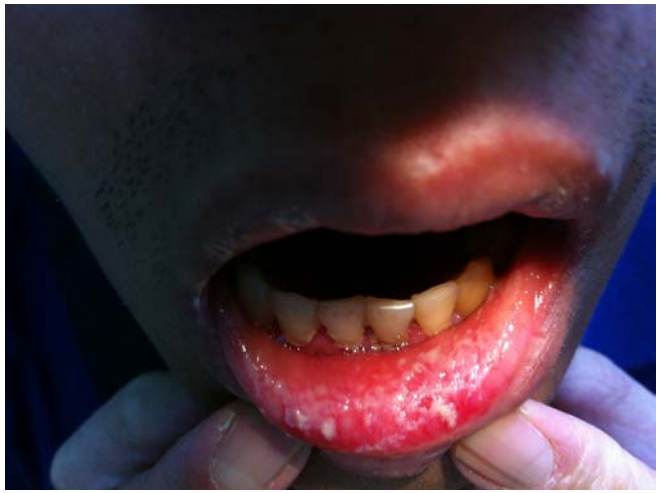
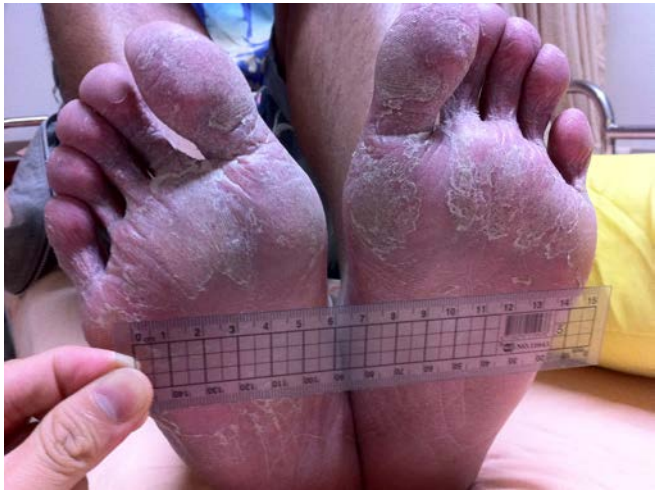
嵌入酶抑制劑 (InSTI)
宜昇瑞、汰威凱

CCR5受體阻斷劑 (CCR5 Antogonist)
新特滋

核苷酸反轉錄酶抑制劑 (NRTI)

Zidovudine (AZT/ZDV)	**Retrovir** **立妥威** 	100 mg 3# BID	貧血、白血球降低、腸胃不適、乳酸代謝性酸中毒
Lamivudine (3TC)	**3TC 速汰滋** ***Epivir*** 	150 mg 2# QD or 1# BID	鮮少發生副作用，同時可以治療B型肝炎
AZT + 3TC 	**Combivir** **卡貝滋** ***Duovir, Zovilam*** **(300/150)**	1# BID	
Abacavir (ABC)	**Ziagen** **濟而剛** ***Abamat*** 	300 mg 2# QD or 1# BID	過敏反應 (可能致命)：發燒、皮疹、嘔吐、疲憊、咽喉痛、喘等 (HLA B*5701)。乳酸代謝性中毒
ABC + 3TC 	**Kivexa** **(600/300)** **克維滋**	1# QD	

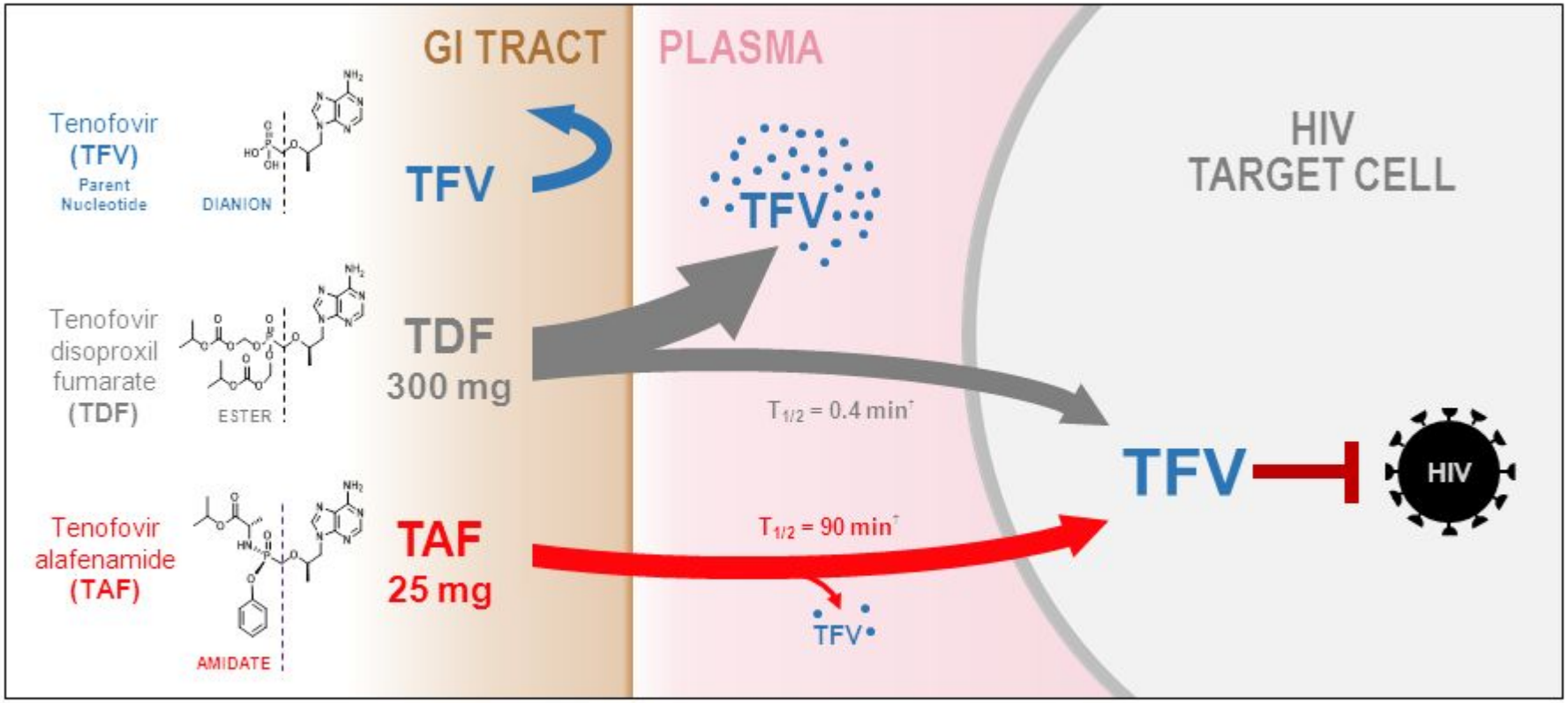
ABC引起的過敏反應

核苷酸反轉錄酶抑制劑 (NRTI)

Tenofovir *disoproxil fumarate* (TDF)	**Viread** **惠力妥** 	300 mg 1# QD	頭痛、腹瀉、無力、腎功能受損、骨質流失，同時可以治療B型肝炎
TDF + emtricitabine (FTC) 	**Truvada (300/200)** **舒發泰**	1# QD	可以作為暴露後預防性投藥 (pre-exposure prophylaxis, PrEP) 來預防HIV感染
Tefnofovir alafenamide (TAF)	**Genvoya (as STR)** **EVG/c/FTC/TAF (150/150/200/10)** **捷扶康**	1# QD with meal	頭痛、腹瀉、無力，同時可以治療B型肝炎
Didanosine (ddI)	**Videx** **惠妥滋** 	BW >60 Kg: 400 mg 1# QD BW <60 Kg: 250 mg 1# QD	胰臟炎、週邊神經炎、腸胃不適、腹瀉、乳酸代謝性酸中毒
Stavudine (d4T)	**Zerit** **滋利特** 	BW >60 Kg: 40 mg 1# BID BW <60 Kg: 30 mg 1# BID	週邊神經炎、乳酸代謝性酸中毒(可能致命)，脂肪易位

TDF v2.0: Tenofovir Alafenamide (TAF)



- **91% lower plasma TFV levels minimize renal and bone effects while maintaining high potency for suppressing HIV**

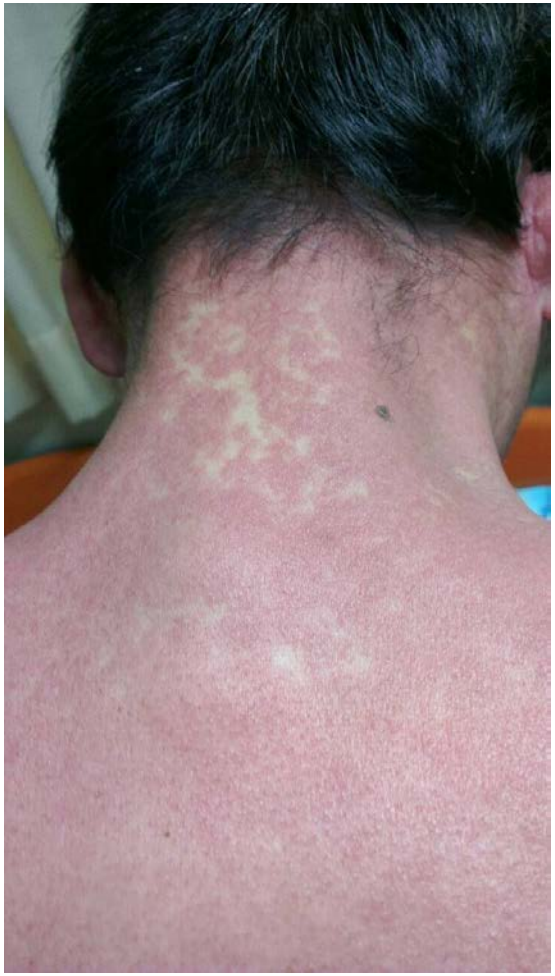
非核苷酸反轉錄酶抑制劑 (NNRTI)

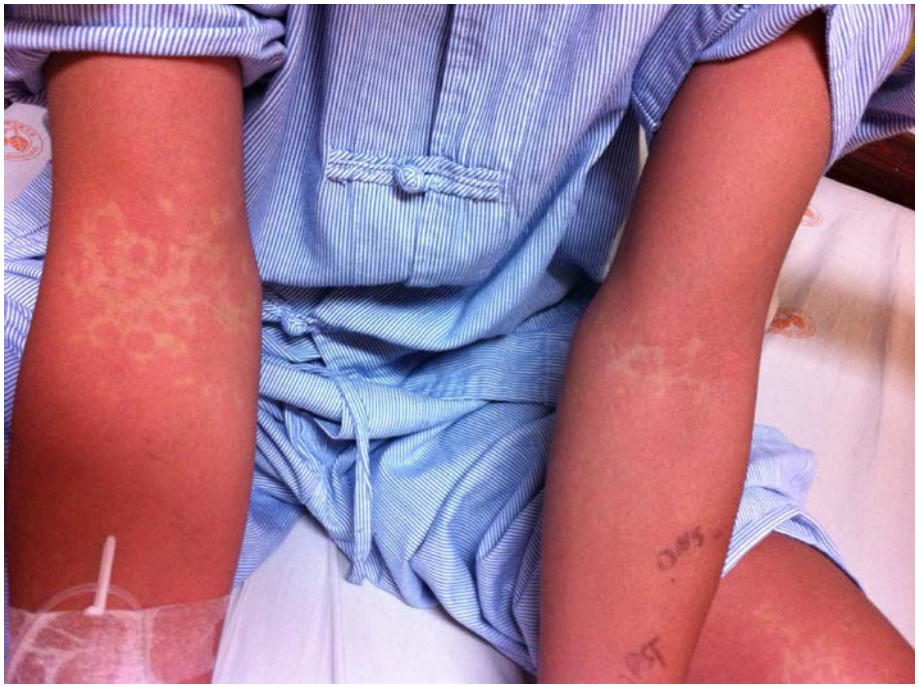
Nevirapine (NVP) 	**Viramune IR** **Viramune XR** **衛滋** ***Nevimat, Virapine***	*Lead-in (2 week):* 200 mg IR 1# QD *Full dose*: 200 mg IR 1# BID or 400 mg XR 1# QD	皮疹 (開始使用2-3週內)、肝功能異常、藥物性肝炎 (好發於高病毒量、治療前男性CD4 >400/cumm、女性CD4>250/cumm)
Efavirenz (EFV) 	**Stocrit** **希寧** ***Efamat, Efanzy, Immupnyn, Efavir***	600 mg 1# HS	皮疹 、肝功能異常、中樞神經系統症狀 (頭暈、嗜睡 、作夢、注意力不集中、幻想、失憶等)。 ~~孕婦於第一產程避免使用~~
Rilpivirine (RPV) 	**Edurant** **恩臨**	25 mg 1# QD	皮疹 、肝功能異常。（不適宜用於VL >100000 copies/ml, 尤其是CD4 <200的病患），和食物並用可以增加生體可用率，避免和制酸劑並用。

非核苷酸反轉錄酶抑制劑 (NNRTI)

Etravirine (ETR)	**Intelence** **英特萊** 	100 mg 2# BID	皮疹、腸胃不適 （適應症僅用於已用藥過產生抗藥性病人）

NVP引起的皮疹





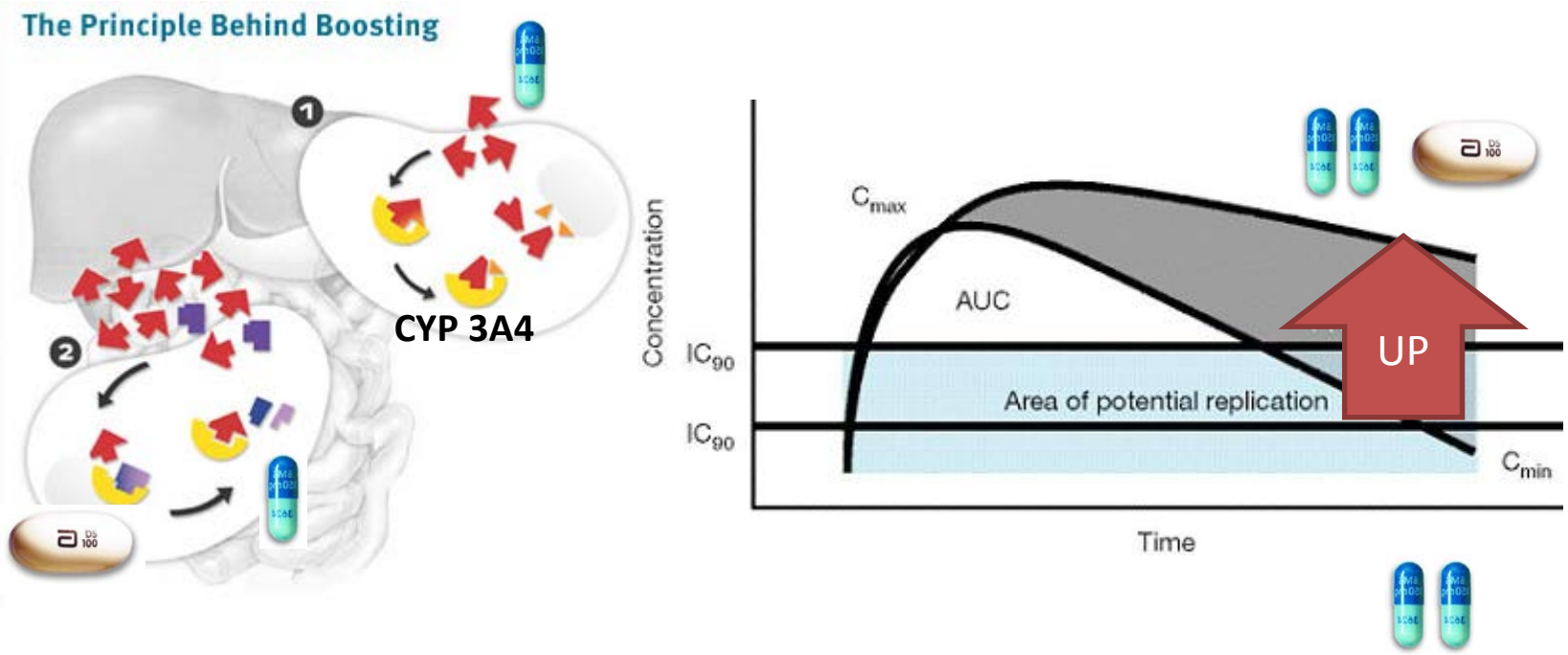
蛋白酶抑制劑 (PI)

Lopinavir/r (LPV/r) 	**Kaletra (200/50)** **快利佳**	2# BID or 4# QD in treatment-naïve patients	吸收不受食物或制酸劑影響。 副作用：腸胃不適、腹瀉、嘔吐、倦怠、肝功能異常、血糖上升、血脂肪上升、脂肪分布改變症候群
Atazanavir (ATV) 	**Reyataz 150** **Reyataz 200** **瑞塔滋**	150 mg 2# QD + ritonavir boost 100 mg 1# QD or 200 mg 2# QD	和食物並用可以增加生體可用率，避免和制酸劑並用。 副作用：膽紅素上升血糖上升、脂肪分布改變症候群、腎結石
Ritonavir (RTV) 	**Norvir** **諾億亞**	單顆100 mg 顆粒 目前不建議單獨使用，都是與其他PI併用，以增加其他PI血中濃度	和食物並用可以增加生體可用率。 副作用：腸胃不適、腹瀉、嘔吐、口唇及四肢發麻、血糖上升、血脂肪上升、脂肪分布改變症候群

蛋白酶抑制劑 (PI)

Darunavir (DRV) Darunavir/cobicistat (DRV/c) 	**Prezista 400** **Prezista 600** **普利他** **Prezcobix (800/150)** **普澤力**	400 mg 2# QD + ritonavir boost 100 mg 1# QD / 800/150 mg 1# QD in treatment-naïve pts 600 mg 1# BID + ritonavir boost 100 mg 1# BID in treatment-experienced pt	和食物並用可以增加生體可用率。吸收不受制酸劑影響。 副作用：肝毒性、血脂肪上升、頭痛、皮疹、含有sulfa成分。
Tipranavir (TPV) 	**Aptivus** **捷伏滋**	250 mg 2# BID + ritonavir boost 100 mg 2# BID in treatment-experienced pt	和食物並用可以增加生體可用率。副作用：肝炎、肝衰竭、凝血功能異常與顱內出血、皮疹、含有sulfa成分。中度或重度肝功能不全的病人禁用。 （適應症僅用於已用藥過產生抗藥性病人）

有加沒加「蠶寶寶」差哪裡？



http://www.natap.org/2006/EASL/EASL_01.htm
http://www.aegis.com/pubs/amfar/2004/AM040401.html

Cobicistat: A New Boosting Agent

- Small molecule with no HIV activity
  - No concern of drug resistance in pts with suboptimal virologic response
- Similar ↑ from BL in fasting TC and TGs compared with RTV when boosting same agent[1]
- **Inhibitor of CYP3A4; many drug–drug interactions**[2,3]
- Modest, rapid increase in serum Cr due to inhibition of tubular secretion[3]
  - Not associated with any change in actual GFR
  - Other drugs (including ARVs) have similar effect: DTG, RPV, RTV[4,5]
- Availability of cobicistat has allowed for development of new coformulated agents and regimens
  - EVG/c/FTC/TDF (Stribild), EVG/c/FTC/TAF (Genvoya)
  - ATV/c (), DRV/c (Precobix), DRV/c/FTC/TAF

1. Gallant JE, et al. J Infect Dis. 2013;208:32-39. 2. DHHS Guidelines February 2013.
3. TDF/FTC/EVG/COBI [package insert]. 4. RPV [package insert]. 5. DTG [package insert].

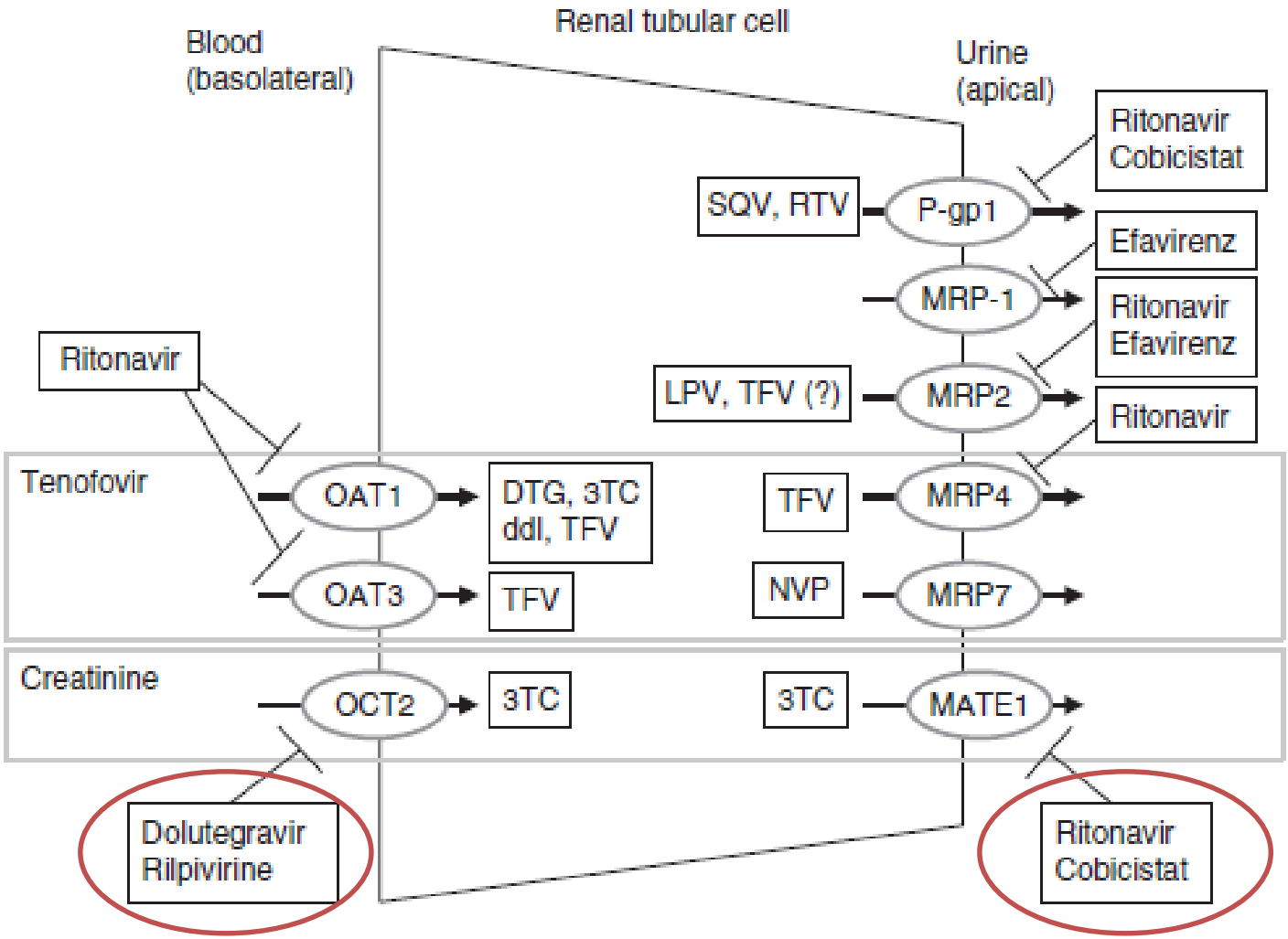
Potential Drug-drug Interactions With Cobicistat and Ritonavir

- Both inhibit **CYP3A** and **P-gp**; RTV also an inducer of CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, or UGT1A1
- There is **no interaction** between COBI and **methadone**

Agents That Have Interactions With RTV and/or COBI	
▪ Analgesics	▪ Contraceptives
▪ Antiarrhythmics	▪ Digoxin
▪ Anticancer agents	▪ Glucocorticoids
▪ Anticoagulants	▪ **Methamphetamine**
▪ Anticonvulsants	▪ **PDE5 inhibitors**
▪ **Antidepressants**	▪ **Rifabutin**
▪ Beta-blockers	▪ Sedatives/hypnotics
▪ **Clarithromycin**	▪ **Statins**

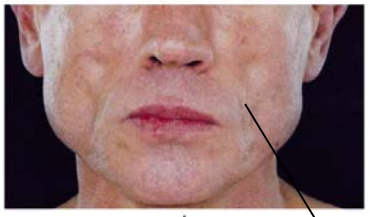
Marzolini C, et al. J Antimicrob Chemother. 2016;71:1755-1758.
COBI [package insert]. RTV [package insert].

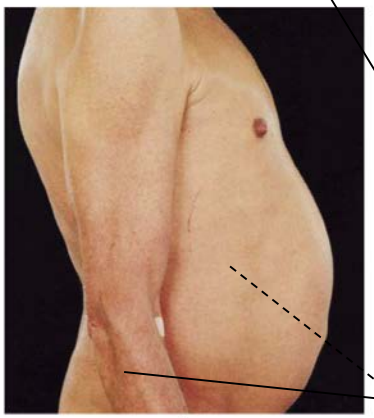
Decreased Tubular Secretion of Creatinine via Inhibition of MATE-1

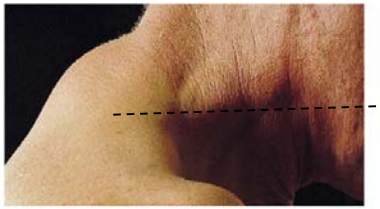


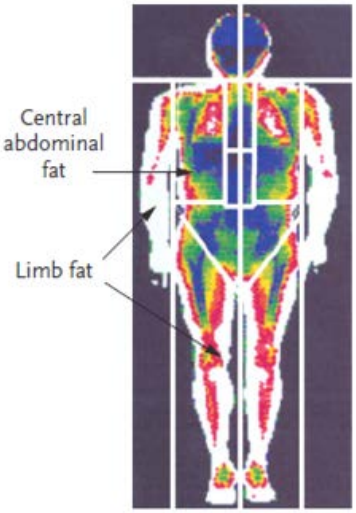
Yombi et al. *AIDS*. 2014;28:621-632.

脂肪分布改變症候群









Lipodystrophy

Lipoatrophy 脂肪萎縮 (d4T/ZDV)
wasting of face, limb, buttock

Lipohypertrophy 脂肪增生 (boosted PI?)
fat accumulation in abdomen, breast, and posterior neck

Grinspoon S et al. N Engl J Med 2005;352:48-62

嵌入酶抑制劑 (InSTI)

Raltegravir (RAL) 	**Isentress 宜昇瑞**	400 mg 1# BID	噁心、頭痛、腹瀉、發燒、CK上升。要避免與含有Mg^{2+}或Al^{3+}的胃藥同時服用、惡化憂鬱症狀（少見）
Elvitegravir (EVG)	**Genvoya (as STR) EVG/c/FTC/TAF (150/150/200/10) 捷扶康**	1# QD with meal	噁心、腹瀉、頭痛、要避免與含有Mg^{2+}或Al^{3+}的胃藥同時服用、惡化憂鬱症狀（少見）、需與食物並用
Dolutegravir (DTG) 	**Tivicay 汰威凱**	InSTI-naïve: 50 mg 1# QD InSTI-experienced: 50 mg 1# BID	失眠、頭痛、皮疹。要避免與含有Mg^{2+}或Al^{3+}的胃藥同時服用、惡化憂鬱症狀（少見）孕婦於第一產程避免使用

CCR5受器阻斷劑 (CCR5 Antagonist)

Maraviroc (MVC)  	**Celsentri** **(150, 300)** **新特滋**	標準劑量 (包括 NVP, RAL, TPV/r): 300 mg 1# BID Strong CYP3A4 inhibitors +/- CYP3A4 inducers (all PIs except TPV/r): 150 mg 1# BID Strong CYP3A4 inducers (EFV, ETR, RIF w/o PIs)： 300 mg 2# BID	噁心、頭痛、腹瀉、倦怠、姿勢性低血壓、肝毒性與過敏反應。 用藥前必須先進行 R5/X4 tropism test

疾管署建議優先給付用藥

ZDV/3TC 卡貝滋
+ RAL or DTG
+ NVP or EFV or RPV
+ LPV/r or ATV/r or ATV (400) or DRV/r

TDF/FTC 舒發泰
+ NVP or EFV

ABC/3TC 克維滋
+ NVP or EFV

SEP 2017

TDF/FTC/EFV 亞翠佩
TDF/FTC/RPV 康普萊
ABC/3TC/DTG 三恩美
TAF/FTC/EVG/c 捷扶康

ZDV/3TC 卡貝滋
+ RAL or DTG
+ NVP or EFV or RPV
+ LPV/r or ATV/r or ATV (400)
+ DRV/r or DRV/c

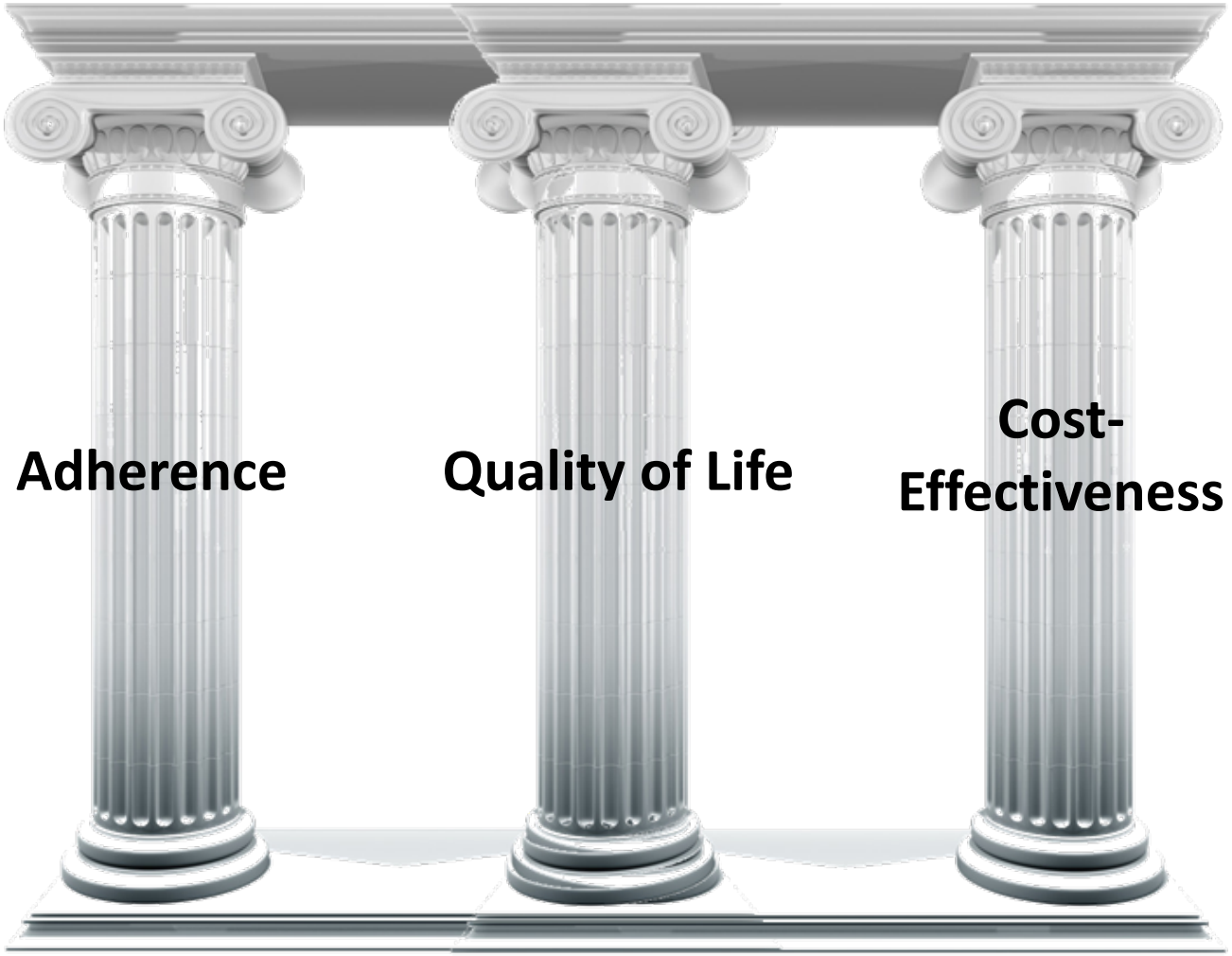
TDF/FTC 舒發泰 or TDF/3TC
+ NVP

ABC/3TC 克維滋
+ EFV

各國對於初次接受治療者的建議組合

NNRTI-based	PI-based	InSTI-based
WHO / Jul 2018		
TDF/FTC/EFV or TDF/3TC/EFV *(in pregnancy desiring women)*	(second-line only)	**TDF/3TC/DTG**
DHHS (US) / Oct 2018	(Partially) NRTI-sparing: **DRV/r + 3TC** or **DRV/r + RAL** or **DTG + 3TC**	
TDF/FTC/EFV or TDF/3TC/EFV TAF/FTC + EFV TDF/FTC/RPV or TAF/FTC/RPV TDF/3TC/DOR or TAF/FTC + DOR	TDF/FTC or TAF/FTC + DRV/c or DRV/r TDF/FTC or TAF/FTC + ATV/c or ATV/r ABC/3TC + DRV/c or DRV/r	**TAF/FTC/BIC** **ABC/3TC/DTG** **TDF/FTC or TAF/FTC + DTG** TAF/FTC/EVG/c or TDF/FTC/EVG/c **TDF/FTC or TAF/FTC + RAL** ABC/3TC + RAL
IAS-USA (US) / Jul 2018		
TDF/FTC/EFV TDF/FTC/RPV or TAF/FTC/RPV	TDF/FTC or TAF/FTC + DRV/c or DRV/r	**TAF/FTC/BIC** **ABC/3TC/DTG** **TAF/FTC + DTG** TAF/FTC/EVG/c or TDF/FTC/EVG/c TDF/FTC + RAL or TAF/FTC + RAL
EACS (EU) / Oct 2017	NRTI-sparing: **DRV/r or DRV/c + RAL**	
TDF/FTC/RPV or TAF/FTC/RPV ABC/3TC + EFV TDF/FTC/EFV	**TDF/FTC or TAF/FTC + DRV/r or DRV/c** TDF/FTC or TAF/FTC + ATV/c or ATV/r ABC/3TC + ATV/c or ATV/r ABC/3TC + DRV/c or DRV/r	**ABC/3TC/DTG** **TDF/FTC or TAF/FTC + DTG** **TDF/FTC/EVG/c or TAF/FTC/EVG/c** **TDF/FTC or TAF/FTC + RAL** ABC/3TC + RAL

Advantages of STR



單藥錠處方 Single-Tablet Regimen (STR)

2006
Atripla 亞翠佩
(TDF/FTC/EFV)
123

2011
Complera 康普萊
(TDF/FTC/RPV)
GSI

2012
Stribild "Quad Pill"
(TDF/FTC/EVG/Cobi)
GSI

2014
Triumeq 三恩美
(ABC/3TC/DTG)
572 Tri

2015
Genvoya 捷扶康
(TAF/FTC/EVG/Cobi)
GSI

2016
Odefsey
(TAF/FTC/RPV)
GSI

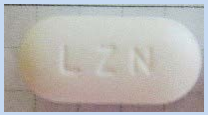
2017
Symtuza
(TAF/FTC/DRV/Cobi)
J G

2018
Biktarvy
(TAF/FTC/BIC)
9883

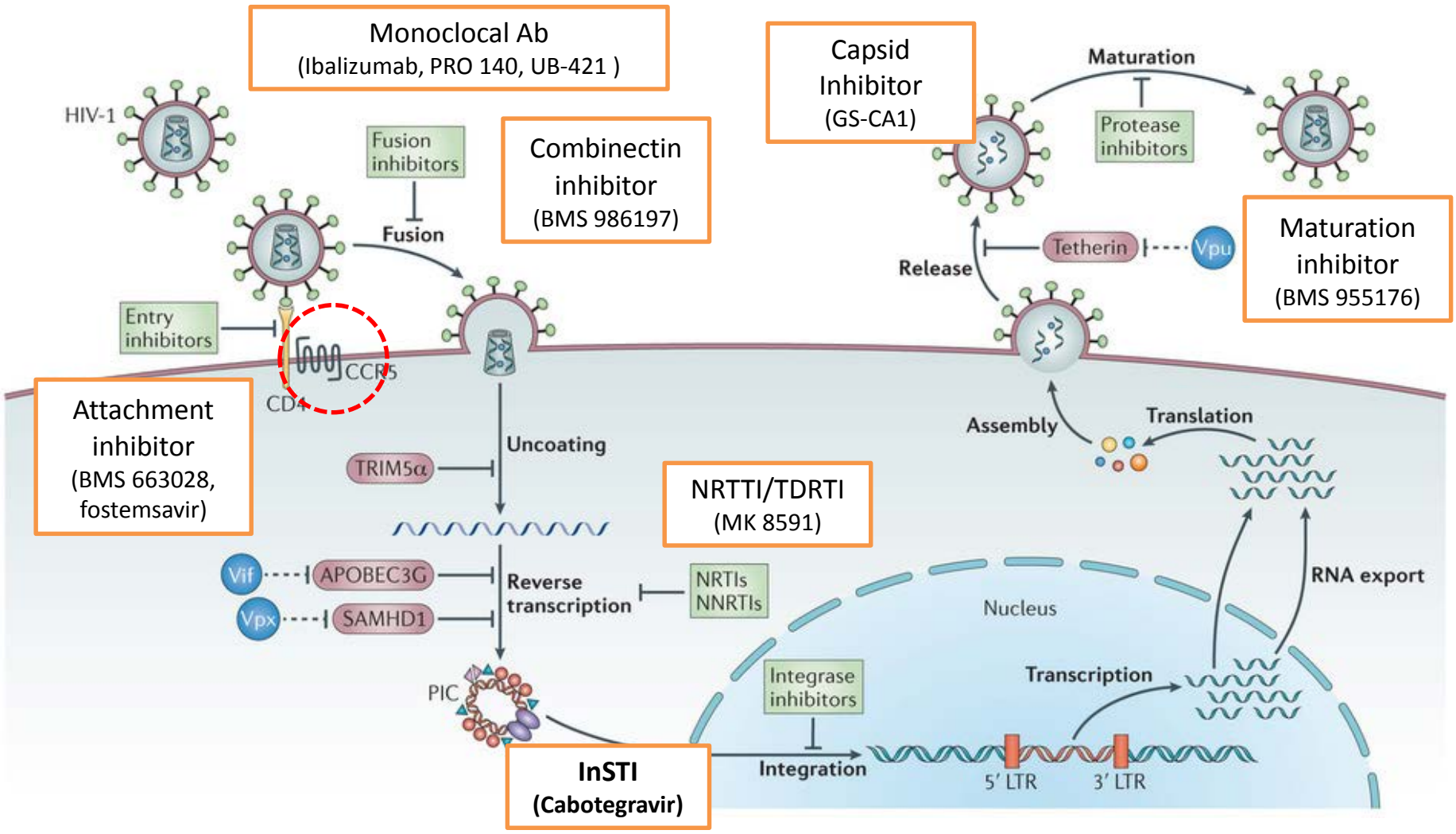
2018
Delstrigo
(TDF/3TC/DOR)
776

2017
Juluca
(DTG/RPV)
SV J3T

2019
Dovato
(DTG/3TC)
SV 137

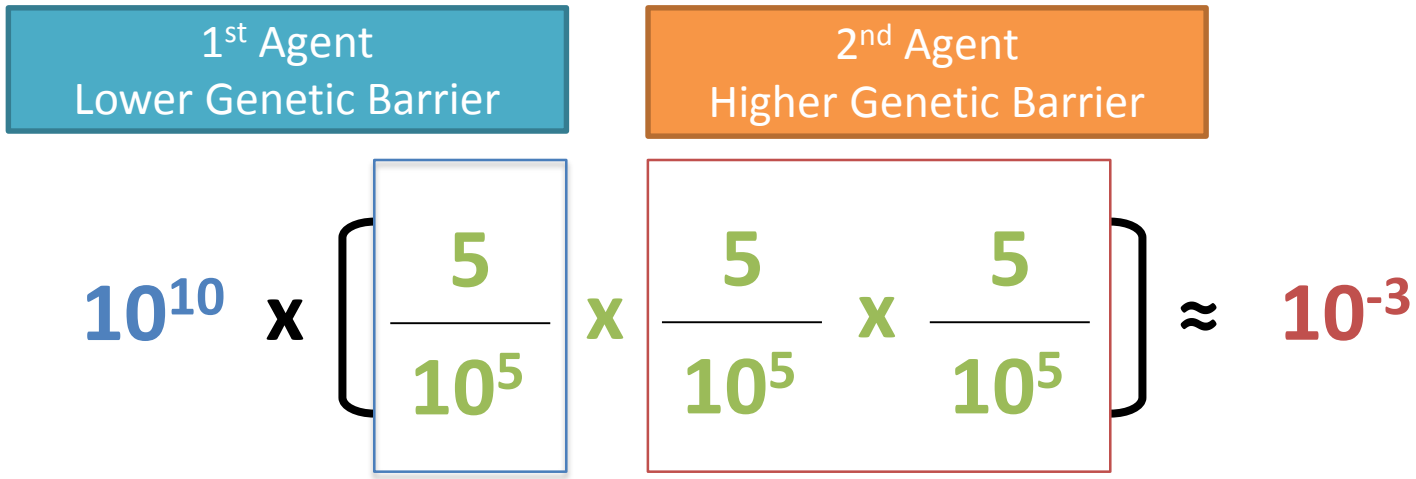
TDF/FTC/EFV 	***Atripla* 亞翠佩 (300/200/600)**	1# QN	頭痛、腹瀉、無力、腎功能受損、骨質流失、皮疹 、肝功能異常、中樞神經系統症狀 (頭暈、嗜睡 、作夢、注意力不集中、幻想、失憶等)
TDF/FTC/RPV 	***Complera* 康普萊 (300/200/25)**	1# QD with meal	頭痛、腹瀉、無力、腎功能受損、骨質流失、不適宜VL >100,000 copies/ml，尤其是CD4 <200的病患，需與食物並用、避免和制酸劑並用
ABC/3TC/DTG 	***Triumeq* 三恩美 (600/300/50)**	1# QD	不適宜HBV帶原者，須注意過敏反應 (可能致命)：發燒、皮疹、嘔吐、疲憊、咽喉痛、喘等 (HLA B*5701)、要避免與含有Mg^{2+}或Al^{3+}的胃藥同時服用、惡化憂鬱症狀（少見）。孕婦於第一產程避免使用
EVG/c/FTC/TAF 	**Genvoya 捷扶康 (150/150/200/10)**	1# QD with meal	噁心、腹瀉、頭痛、要避免與含有Mg^{2+}或Al^{3+}的胃藥同時服用、惡化憂鬱症狀（少見）、需與食物並用
ZDV/3TC/NVP 	***Duovir-N, Trezav* 倍歐滅-N (300/150/200)**	1# BID *Lead-in:* *AZT/3TC/NVP 1# QD + AZT/3TC 1# QD*	貧血、白血球降低、腸胃不適、乳酸代謝性酸中毒、不適宜HBV帶原者、初次治療開始需分開lead-in，初次治療不適宜治療前男性CD4 >400、女性CD4>250

正在研發的新抗病毒藥物



Barre-Sinoussi F et al. Nat Rev Microbiol. 2013: 11:877

打破傳統三合一的觀念?

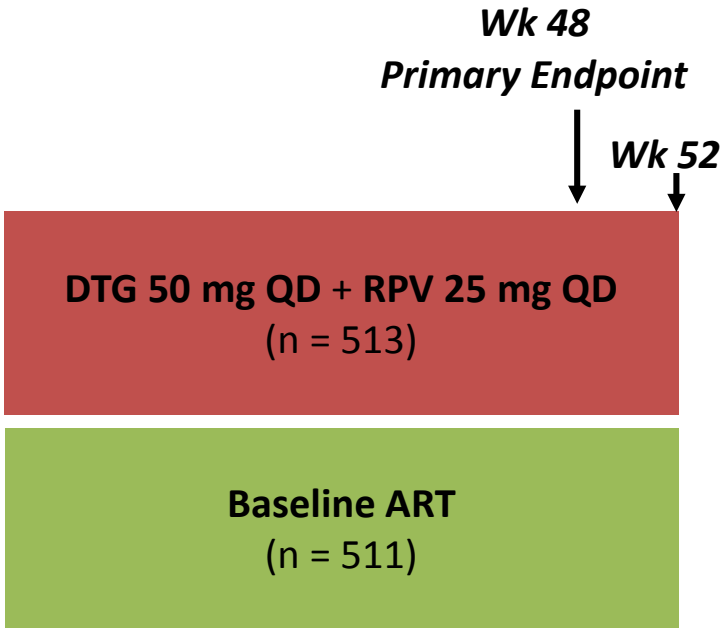


NNRTI (EFV)	Boosted PI (LPV/r)
Single NRTI (3TC)	Boosted PI (LPV/r, ATV/r, DRV/r)
InSTI (RAL)	Boosted PI (DRV/r)
NNRTI (RPV)	InSTI (DTG)
Single NRTI (3TC)	InSTI (DTG)

SWORD 1 & 2: Switch From Suppressive ART to DTG + RPV Dual Therapy

- Randomized, open-label, multicenter phase III trials

Adult pts on stable ART* ≥ 6 mos with baseline HIV-1 RNA < 50 copies/mL; no previous virologic failure or current HBV infection (N = 1024)



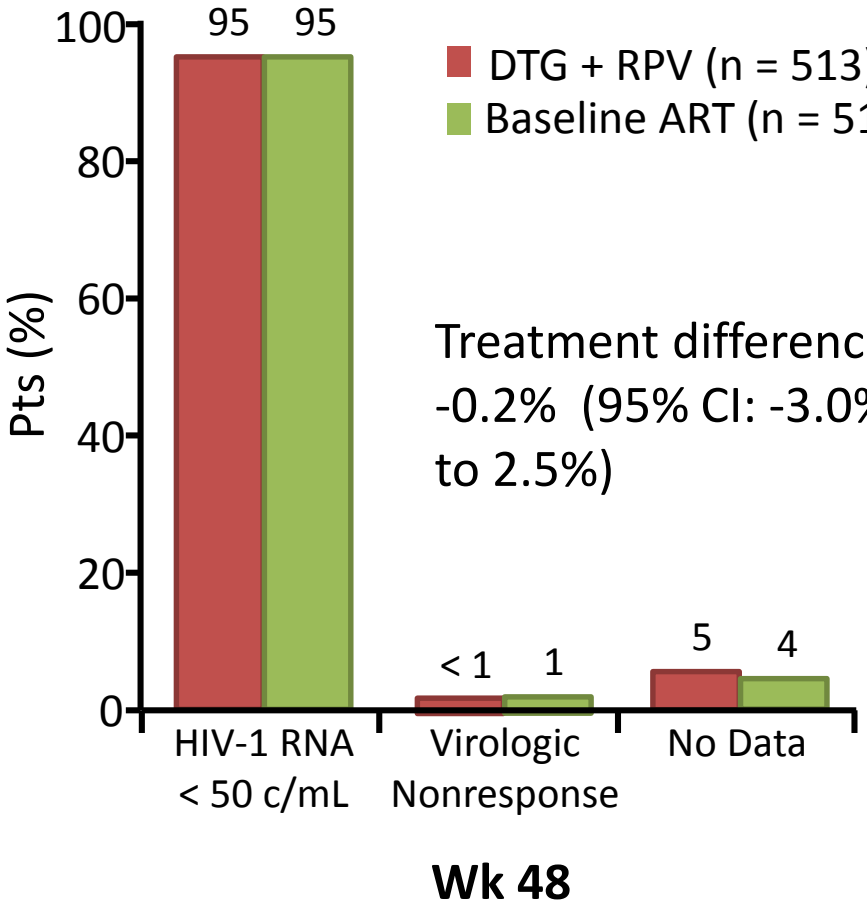
Pts continued or switched to DTG + RPV through Wk 148

*Comprising an INSTI, NNRTI, or PI plus 2 NRTIs.

- 70% to 73% of pts receiving TDF at baseline

Llibre JM, et al. CROI 2017. Abstract 44LB.

SWORD 1 & 2: 48週研究結果



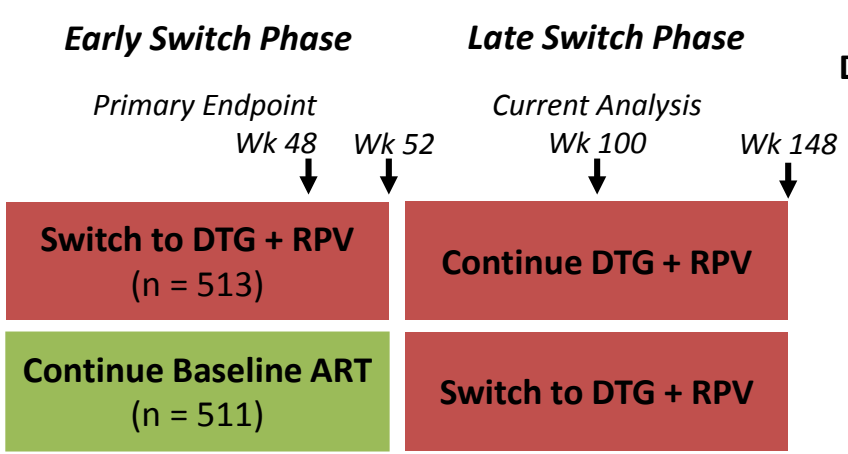
- 1 pt with confirmed criteria for virologic withdrawal at Wk 36 in DTG + RPV arm had K101K/E
  - Documented nonadherence at VF
  - Resuppressed with continued DTG + RPV
  - No INSTI resistance

Llibre JM, et al. CROI 2017. Abstract 44LB. Slide credit: Clinical Care Options

SWORD 1 & 2: 100週研究結果

- Parallel, randomized, open-label, multicenter phase III noninferiority studies[1,2]

Adults on stable ART (INSTI, NNRTI, or PI + 2 NRTIs) with HIV-1 RNA < 50 copies/mL for ≥ 6 mos at screening; no previous VF or current HBV infection (N = 1024)



Virologic Response With DTG + RPV by FDA Snapshot
(HIV-1 RNA < 50 copies/mL at Wk 100)

89%

93%

DTG dosed 50 mg PO QD; RPV dosed 25 mg PO QD.
*70% to 73% of patients receiving TDF at baseline.

- Primary endpoint: HIV-1 RNA < 50 copies/mL maintained in 95% of patients in each arm at Wk 48; adjusted treatment difference: -0.2% (95% CI: -3.0 to 2.5)[2]
- 10/990 (1%) confirmed virologic withdrawals through Wk 100 (Treatment-emergent NNRTI resistance mutations documented in 3/10, all from early switch arm)

1. Aboud M, et al. AIDS 2018. Abstract THPEB047. 2. Llibre JM, et al. Lancet. 2018;391:839-849.

SWORD 1 & 2: 100週研究結果

P Value for Change From BL in Mean Serum Concentration	Early Switch		Late Switch
	Wk 48	Wk 100	Wk 100
Osteocalcin	< .001	< .001	< .001
Bone-specific alkaline phosphatase	< .001	< .001	< .001
Procollagen 1 N-terminal propeptide	< .001	-	.05
Type 1 collagen-C telopeptide	< .001	< .001	.05

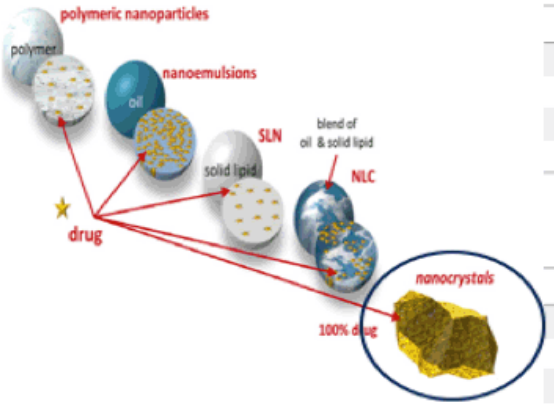
- All bone turnover markers significantly lower at Wk 100 vs BL except procollagen 1 N-terminal propeptide in early switch arm

- No changes in lipid levels (total cholesterol, LDL-C, HDL-C, triglycerides, total cholesterol:HDL-C ratio) or atherogenesis and inflammation biomarkers at Wk 100 vs BL in either group

- Early switch group maintained improvements in markers of renal tubular function (urine retinol-binding protein/creatinine ratio and urine β_2-microglobulin/creatinine ratio) observed from BL to Wk 48 through Wk 100

Aboud M, et al. AIDS 2018. Abstract THPEB047.

新劑型研發: Nano顆粒長效劑型針劑



R H. Müller, et al. European Journal of Pharmaceutics and Biopharmaceutics 78 (2011) 1-9

GSK744 200mg/mL

Component	Function
GSK1265744A (d50 ~200 nm)	Active
Mannitol	Tonicity agent
Surfactant System	Wetting/Stabilizer
Water for Injection	Solvent

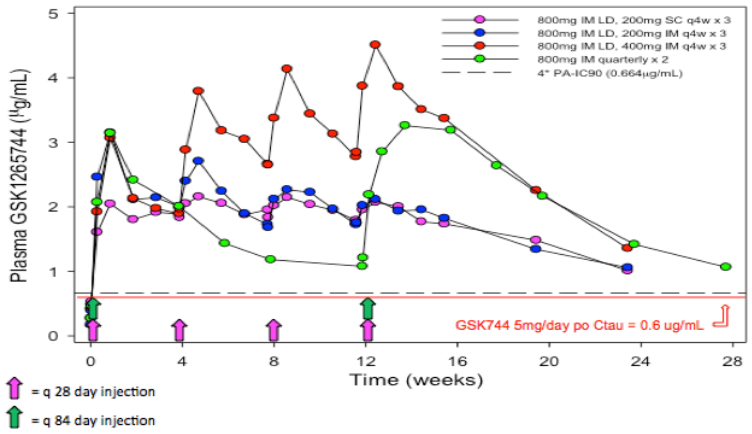
cabotegravir

TMC278 300mg/mL

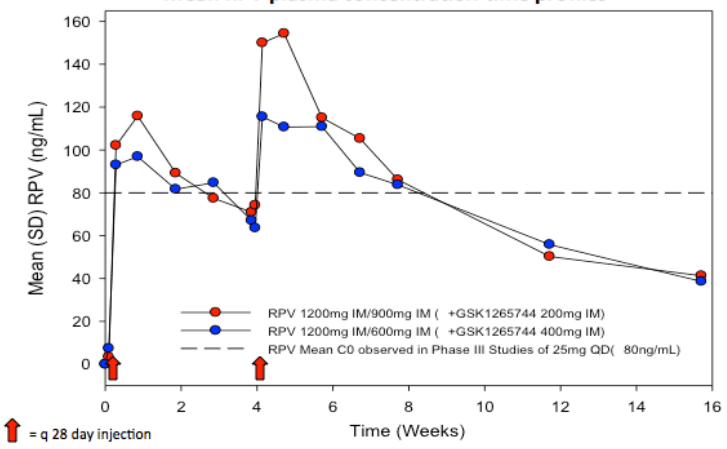
Component	Function
TMC278 (d50 ~200 nm)	Active
Glucose	Tonicity agent
Surfactant System	Wetting/Stabilizer
Water for Injection	Solvent

rilpivirine

Mean GSK744 plasma concentration-time profiles



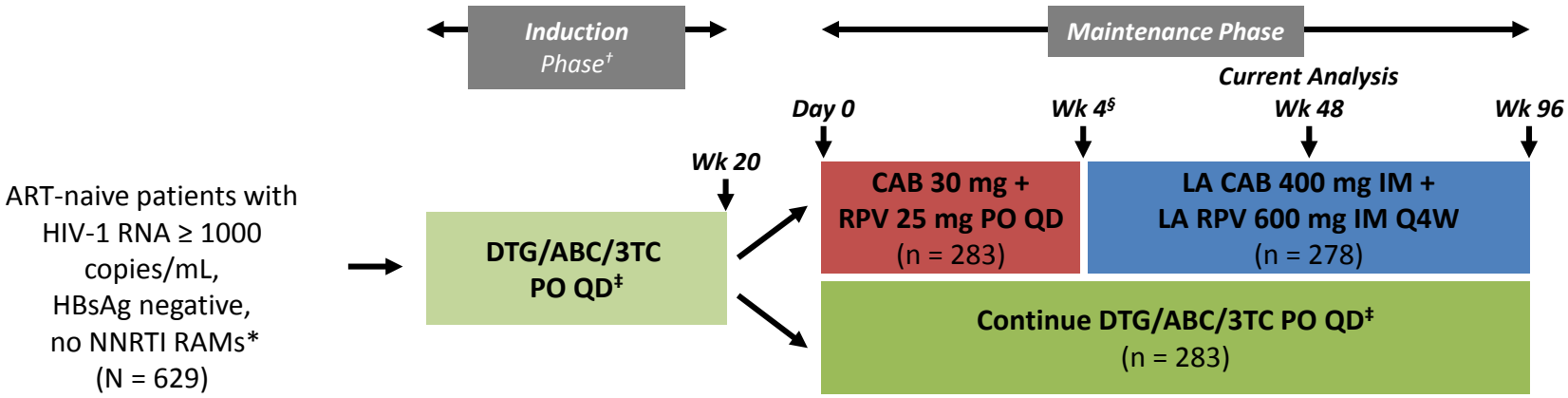
Mean RPV plasma concentration-time profiles



Spreen W et al. IAS 2013, Abstract WEAB0103.

FLAIR: Long-Acting CAB + RPV Maintenance After DTG/ABC/3TC Induction

- Multicenter, randomized, open-label phase III noninferiority trial



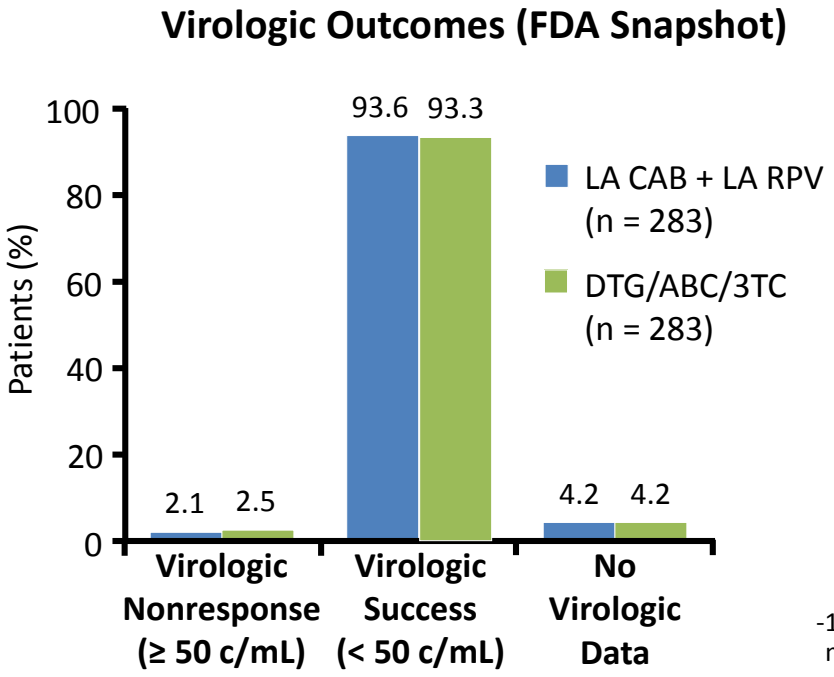
*K103N permitted. †Patients with HIV-1 RNA < 50 copies/mL from Wk 16 to Wk 20 continued to maintenance phase. ‡Alternative, non-ABC NRTIs permitted for intolerance or HLA-B*5701 positivity. §Loading dose: LA CAB 600 mg IM + LA RPV 900 mg IM; regular dosing begun at Wk 8.

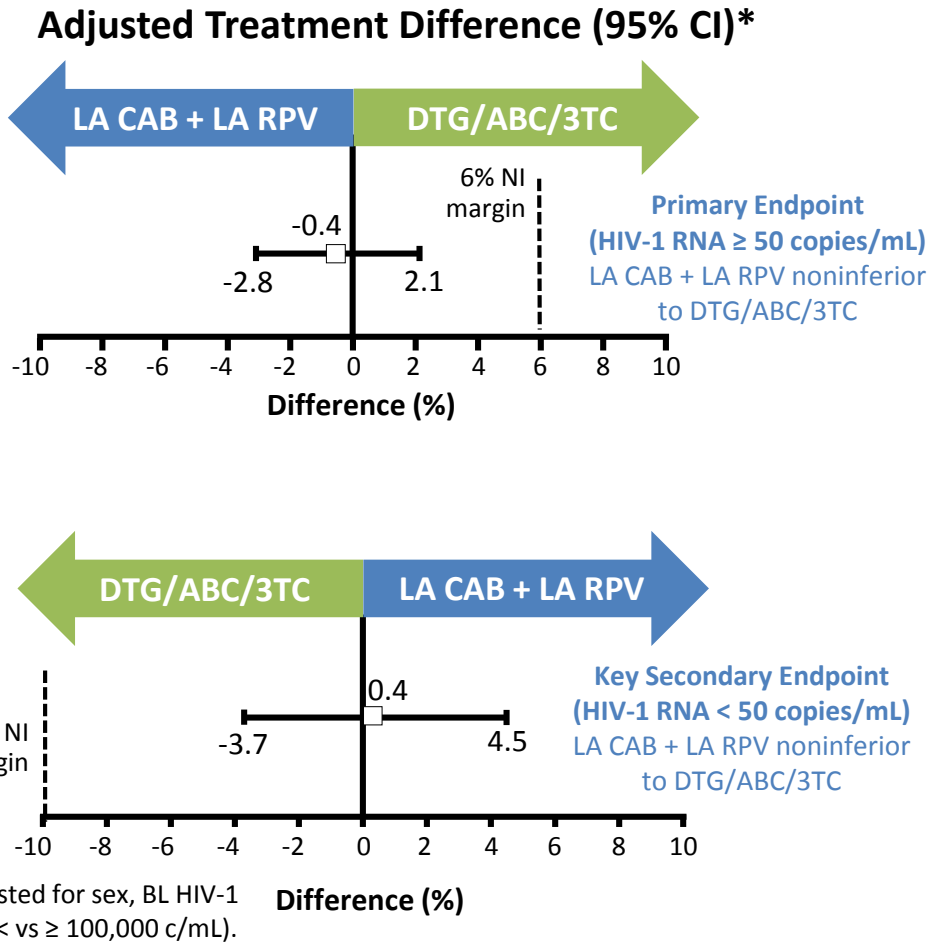
Primary endpoint: HIV-1 RNA ≥ 50 copies/mL at Wk 48 by FDA Snapshot (6% noninferiority margin)

Secondary endpoints: HIV-1 RNA < 50 copies/mL at Wk 48 by FDA Snapshot, resistance at confirmed virologic failure, safety and tolerability, patient-reported outcomes

Orkin et al. CROI 2019. Abstr 140LB. NCT02938520.

FLAIR: Efficacy at Wk 48 in ITT-E Population





Orkin et al. CROI 2019. Abstr 140LB. NCT02938520.

FLAIR: Safety

AEs, n (%)	LA CAB + LA RPV (n = 283)	DTG/ABC/3TC (n = 283)
AEs in ≥ 10% of patients		
▪ Any event (per patient)	246 (87)	225 (80)
• Nasopharyngitis	56 (20)	48 (17)
• Headache	39 (14)	21 (7)
• Upper RTI	38 (13)	28 (10)
• Diarrhea	32 (11)	25 (9)
Drug-related AEs in ≥ 3% of patients		
▪ Any event (per patient)	79 (28)*	28 (10)
• Headache	14 (5)	4 (1)
• Pyrexia	13 (5)	0
Drug-related serious AEs	1 (< 1)†	0
AEs leading to d/c	9 (3)	4 (1)

*94% (74/79) were grade 1/2. †Right knee monoarthritis.

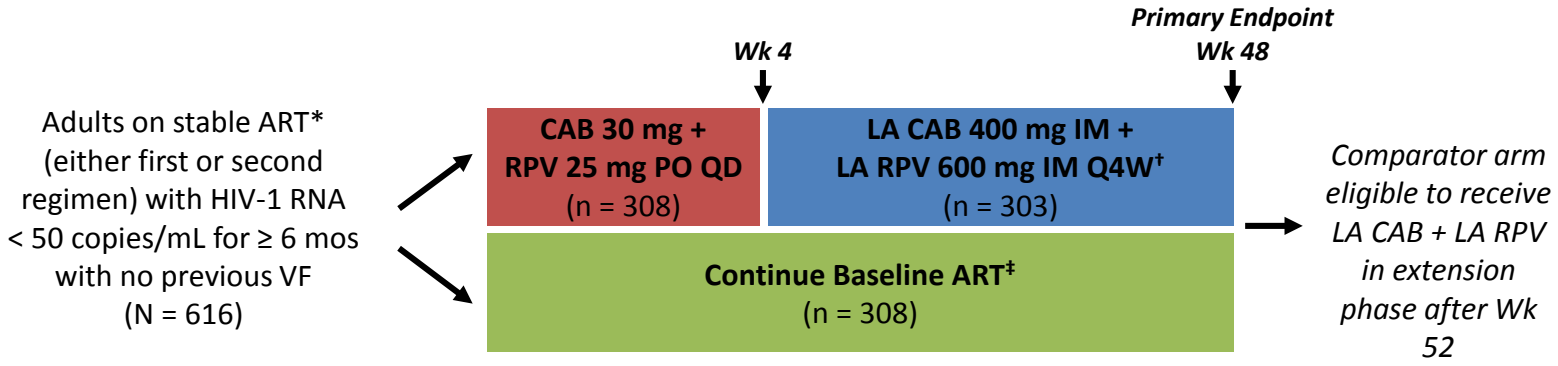
Injection-Site Reactions	LA CAB + LA RPV (n = 283)
Patients receiving injections, n	278
Injections given, n	7704
ISR events, n (%)	2203 (28.6)
▪ Pain	1879 (85.3)
▪ Nodule	86 (3.9)
▪ Induration	82 (3.7)
▪ Swelling	38 (1.7)
▪ Warmth	38 (1.7)
▪ Grade 3 ISR pain	12 (< 1.0)
Median duration of ISRs, days	3
Patients with ISR leading to d/c, n (%)	2 (< 1.0)

- 99% of ISRs were grade 1/2, 88% resolved within 7 days

Orkin et al. CROI 2019. Abstr 140LB. NCT02938520.

ATLAS: Switch to LA CAB + RPV vs Continued 3-Drug ART in Virologically Suppressed Adults

- Multicenter, randomized, open-label phase III noninferiority trial

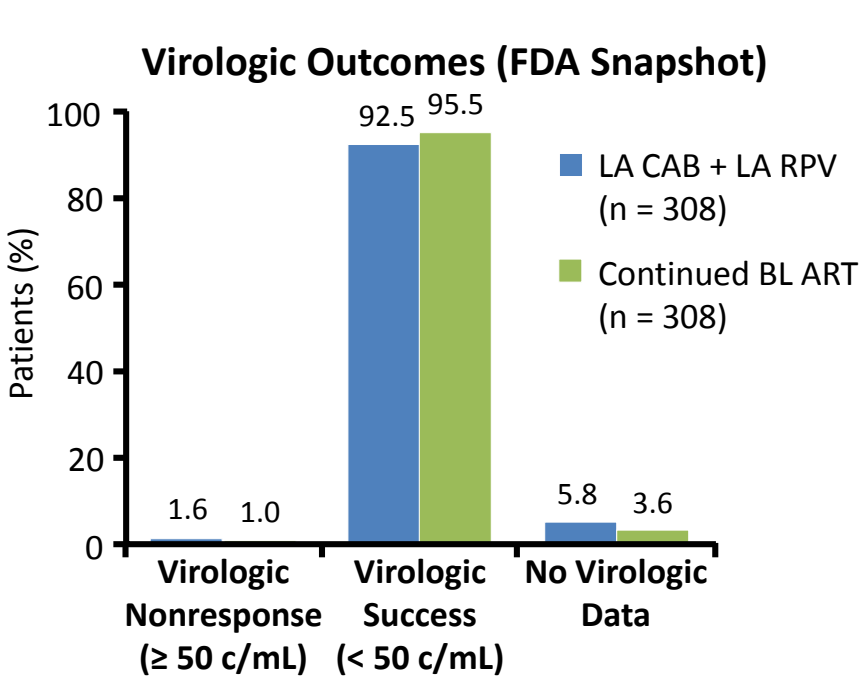


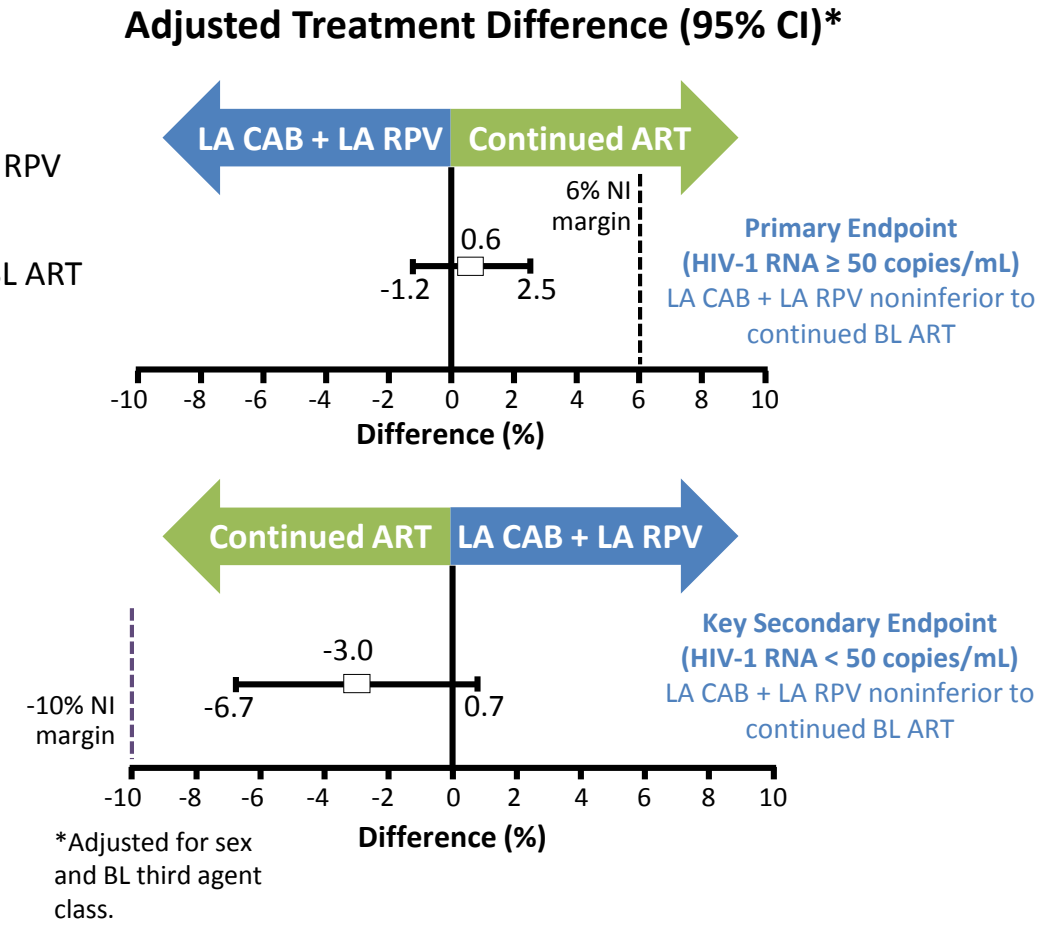
*Permitted baseline regimens: 2 NRTIs + INSTI (except DTG/ABC/3TC), NNRTI, or boosted PI (or unboosted ATV).
†Loading dose: LA CAB 600 mg IM + LA RPV 900 mg IM; regular dosing begun at Wk 8.

- Primary endpoint: HIV-1 RNA ≥ 50 copies/mL at Wk 48 by FDA Snapshot (6% noninferiority margin)
- Secondary endpoints: HIV-1 RNA < 50 copies/mL at Wk 48 by FDA Snapshot, resistance at confirmed virologic failure, safety and tolerability, patient-reported outcomes

Swindells et al. CROI 2019. Abstr 139. NCT02951052.

ATLAS: Efficacy at Wk 48 in ITT-E Population





Swindells et al. CROI 2019. Abstr 139. NCT02951052.

ATLAS: Safety

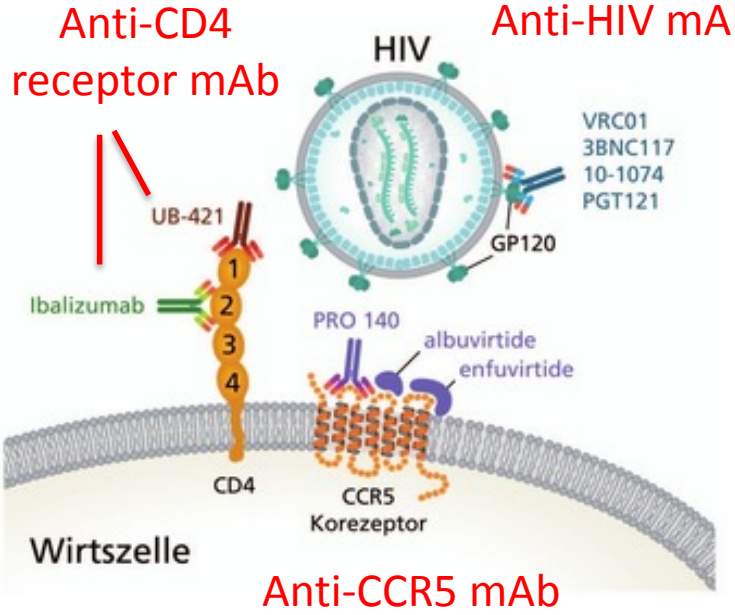
AEs, n (%)	LA CAB + LA RPV (n = 308)	Continued BL ART (n = 308)
AEs in ≥ 10% of patients		
▪ Any event (per patient)	264 (86)	220 (71)
• Nasopharyngitis	52 (17)	42 (14)
• Upper RTI	32 (10)	25 (8)
• Headache	34 (11)	17 (6)
Drug-related AEs in ≥ 3% of patients		
▪ Any event (per patient)	88 (29)*	8 (3)
• Fatigue	11 (4)	0
• Pyrexia	11 (4)	0
• Headache	11 (4)	0
• Nausea	11 (4)	0
AEs leading to d/c	10 (3)	5 (2)

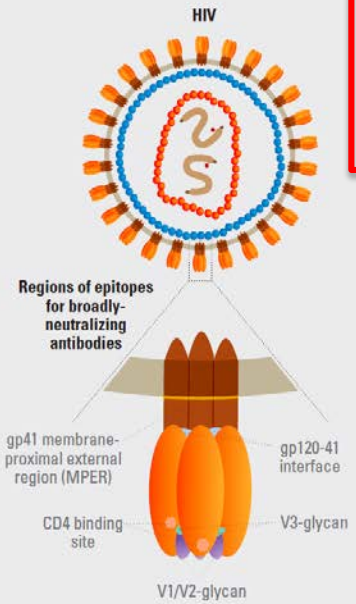
*95% (84/88) were grade 1/2.

Injection-Site Reactions	LA CAB + LA RPV (n = 308)
Patients receiving injections, n	303
Injections given, n	6978
ISR events, n (%)	1460 (20.9)
▪ Pain	1208 (82.7)
▪ Nodule	54 (3.7)
▪ Induration	54 (3.7)
▪ Swelling	48 (3.3)
▪ Grade 3 ISR pain	20 (1.7)
Median duration of ISRs, days	3
Patients with ISR leading to d/c, n (%)	4 (1.3)

- 99% of ISRs were grade 1/2, 88% resolved within 7 days

Swindells et al. CROI 2019. Abstr 139. NCT02951052.

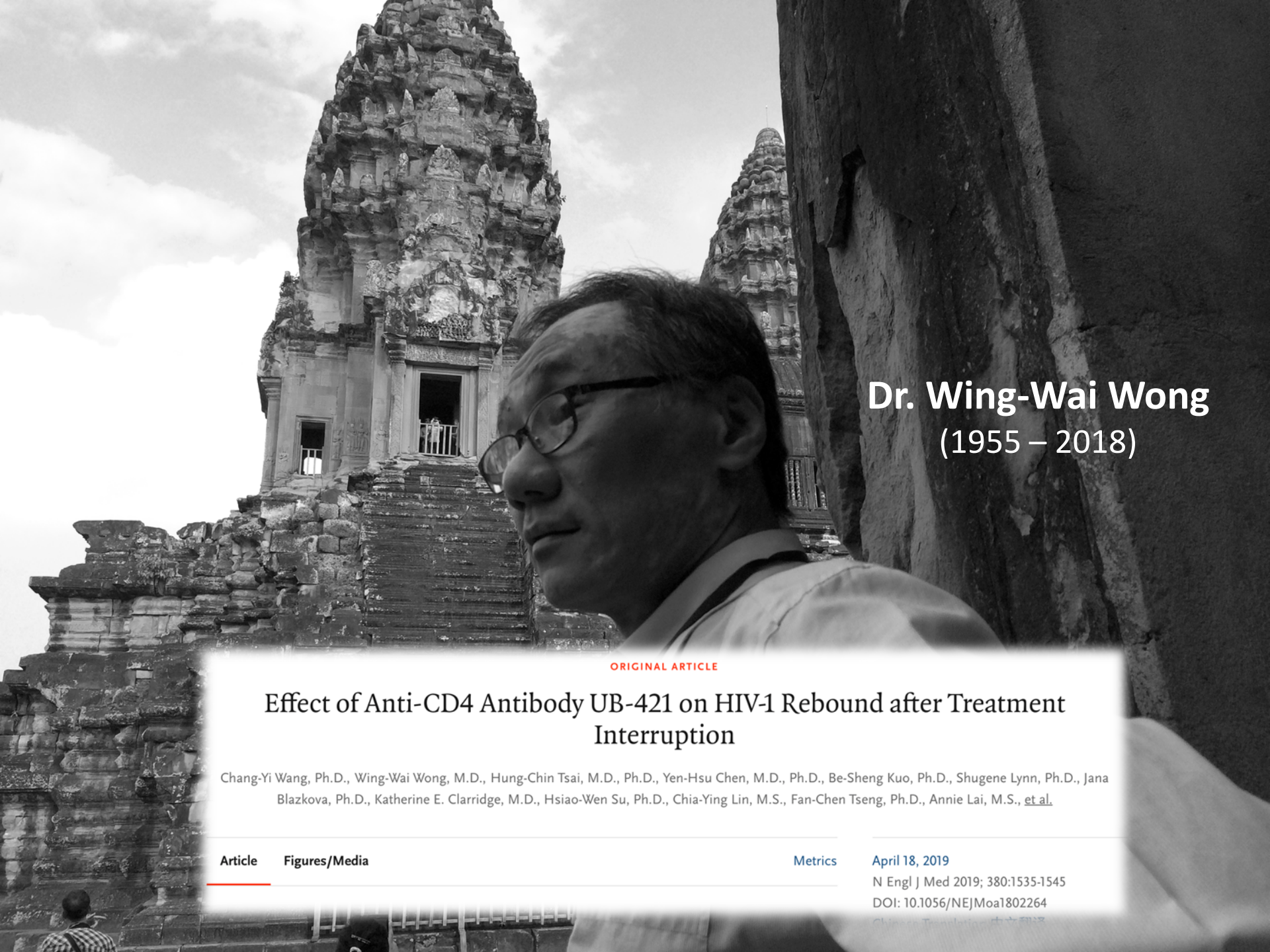




Most of today's licensed effective vaccines teach the body how to make antibodies that defend against infection. These potent immune responses could be a key to HIV vaccine-induced protection. Scientists in this complex field continue to make strides.

HIV trimer target	Antibody	Research highlights
CD4 binding site	3BNC117	Well-tolerated and enhanced anti-HIV antibody-based responses in a Phase I dose- escalation study in people living with HIV and HIV-negative individuals. Further early-phase trials for prevention ongoing and planned in combination with other antibodies.
	VRC01	Two large-scale proof-of-concept trials are testing VRC01 infusions in HIV-negative cisgender men and transgender men and women who have sex with men (North and South America) and HIV-negative women (sub-Saharan Africa). Two Phase I studies of VR01 and VRC01LS, delivered via intravenous infusions (IV) and subcutaneous (SC) routes, are ongoing and planned in the US with HIV-negative participants. One ongoing Phase I single-dose study is evaluating VRC01LS as treatment in participants living with HIV.
	VRC07-523	Two Phase I studies are ongoing and planned of VRC07-523LS administered via IV and/or SC in people living with HIV (US) and HIV-negative individuals (South Africa).
	N6	Identified in early studies as exceptionally broad and potent, capable of neutralizing 98% of strains. Currently in cell-line development for clinical trials.
gp41 membrane proximal external region (MPER)	10e8	Planned for clinical trials.
gp120-41 interface	8ANC195	Not yet planned for clinical trials.
V1/V2-glycan	CAP256-VRC26	Planned Phase I study will test CAP256-VRC26.25LS, delivered via SC or IV routes, in people living with HIV and HIV-negative individuals (South Africa).
	PGDM1400	Identified in animal studies as exceptionally broad and potent with cross-clade neutralization coverage of 83% at low doses. In cell-line development for clinical trials.
	PG9	Ongoing Phase I trial establishing safety and optimal doses of AAV vector gene-transfer approach in HIV-negative adult males (UK).
V3-glycan	PGT121	Ongoing Phase I study, delivering antibody via IV routes in HIV-negative individuals (US).
	10-1074	Phase I open-label trial evaluating safety and antiretroviral effects in both people living with HIV and HIV-negative individuals demonstrated safety and suppressed viremia in most participants living with HIV.
Combinations	3BNC117+10-1074	Phase I study testing antibody combination as prophylaxis in HIV-negative individuals has concluded recruitment and final data collection is underway (US).
	CAP256-VRC26 +PGT121 CAP256-VRC26 +VRC07	Phase II studies planned in HIV-negative individuals, contingent upon safety profile and immune response data in Phase I clinical trials of individual antibodies (South Africa).

Lewis S, et al. CROI 2017. Abstract 449LB. Lalezari J, et al. CROI 2017. Abstract 437.
Wang C-Y, et al. CROI 2017. Abstract 450LB.



Dr. Wing-Wai Wong
(1955 – 2018)

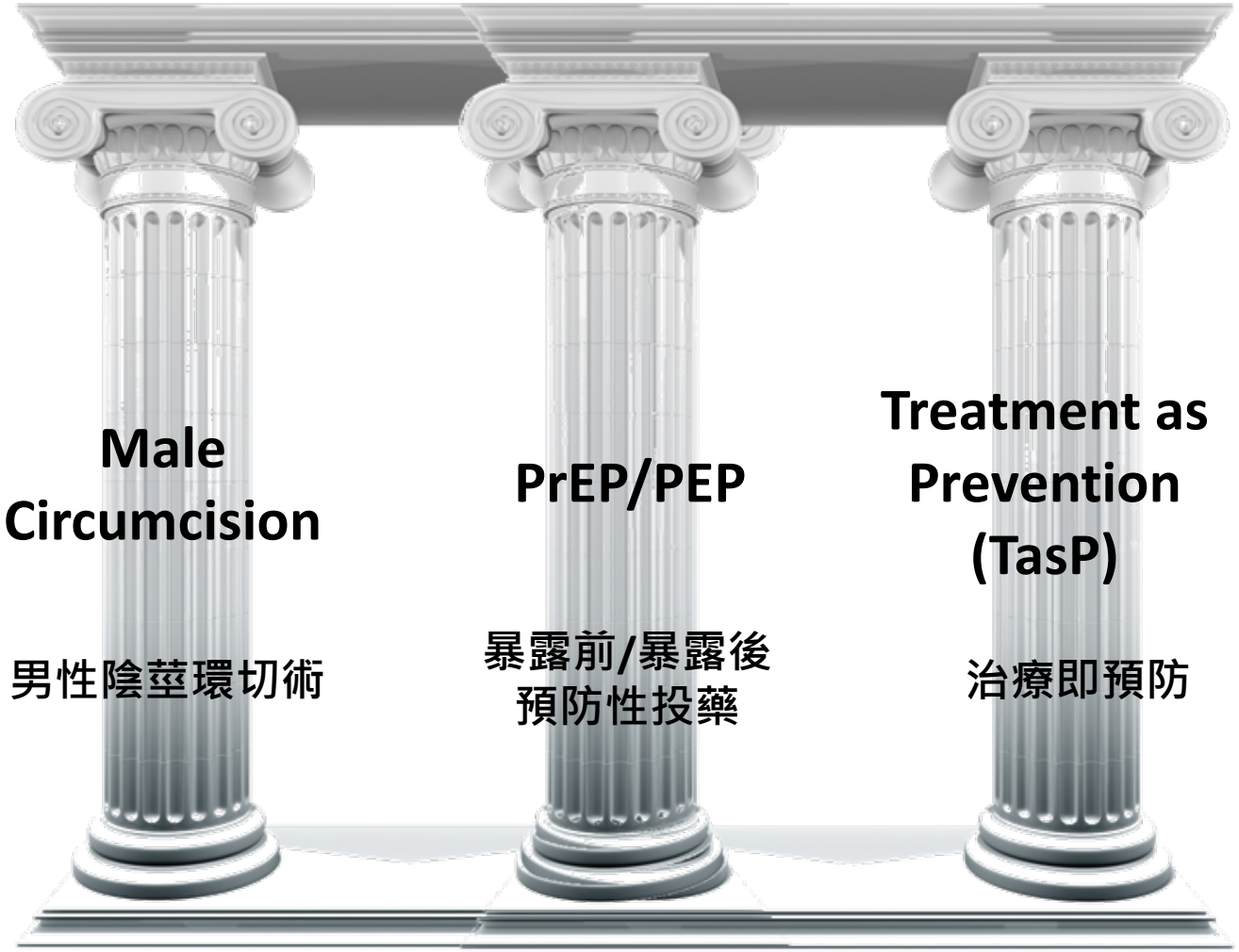
ORIGINAL ARTICLE

Effect of Anti-CD4 Antibody UB-421 on HIV-1 Rebound after Treatment Interruption

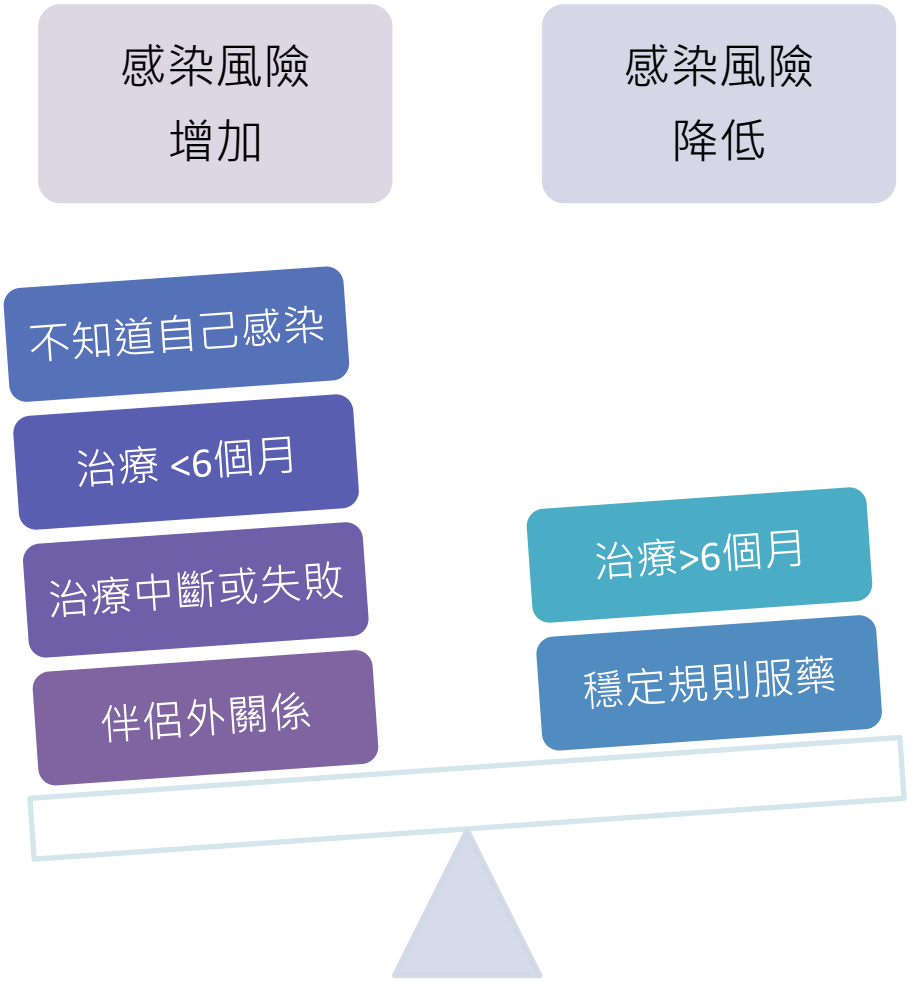
Chang-Yi Wang, Ph.D., Wing-Wai Wong, M.D., Hung-Chin Tsai, M.D., Ph.D., Yen-Hsu Chen, M.D., Ph.D., Be-Sheng Kuo, Ph.D., Shugene Lynn, Ph.D., Jana Blazkova, Ph.D., Katherine E. Clarridge, M.D., Hsiao-Wen Su, Ph.D., Chia-Ying Lin, M.S., Fan-Chen Tseng, Ph.D., Annie Lai, M.S., et al.

April 18, 2019
N Engl J Med 2019; 380:1535-1545
DOI: 10.1056/NEJMoa1802264

新一代愛滋預防策略：Prevention 2.0



但只有「治療即預防」是不夠的...

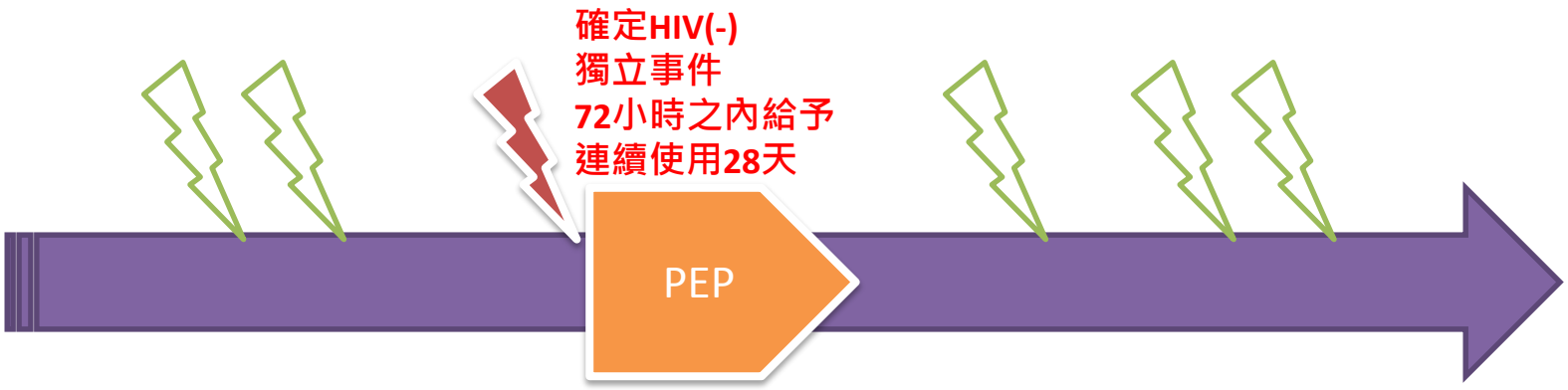


感染初期的病毒是最脆弱的

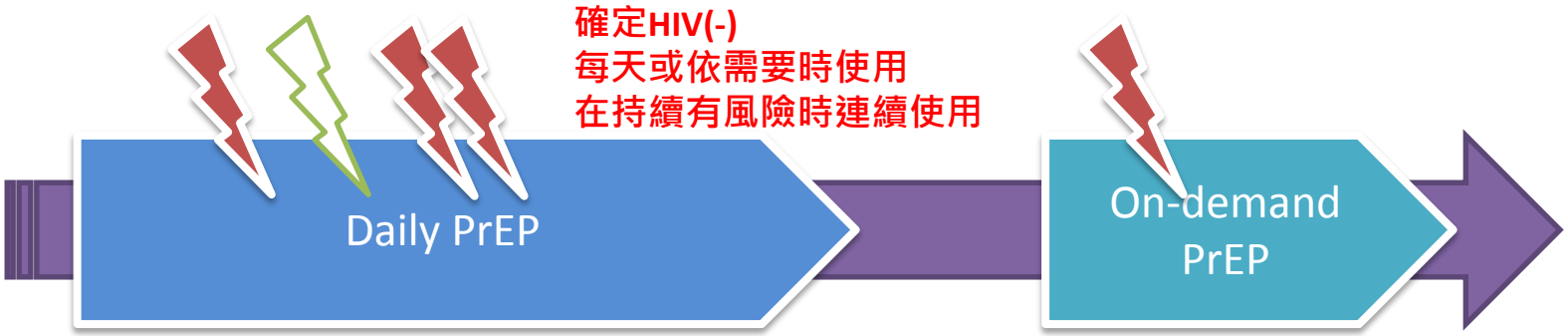
Garcia-Lerma JG et al. Trends Pharmacol Sci 2010;31: 74

預防性投藥的使用時機

暴露後預防性投藥 (PEP)



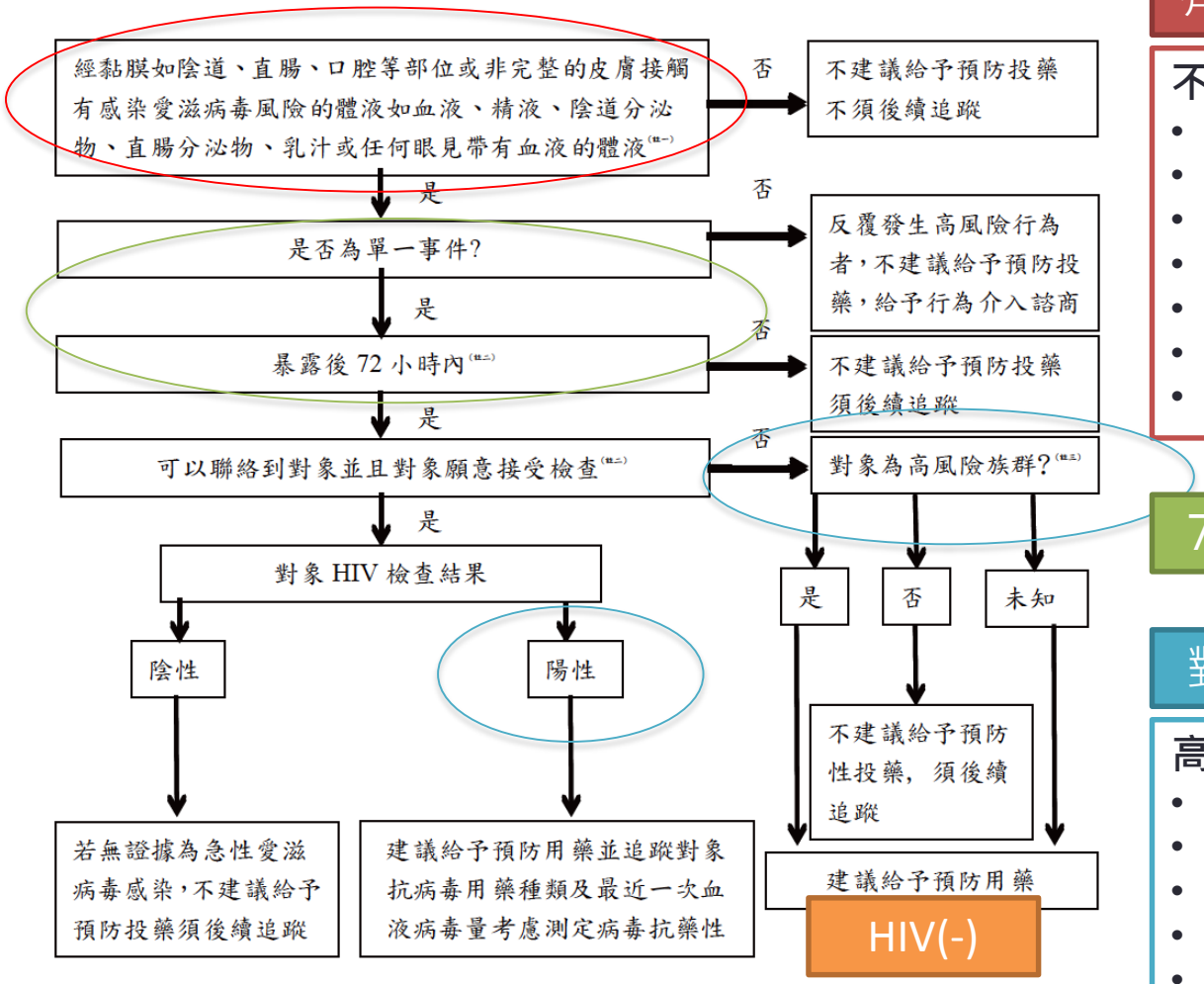
暴露前預防性投藥 (PrEP)



抗反轉錄病毒藥物的不同用途

	Pre-Exposure Prophylaxis 暴露前預防性投藥	Post-Exposure Prophylaxis 暴露後預防性投藥	Combined Antiretroviral Therapy 抗反轉錄病毒療法
縮寫	PrEP	PEP	cART
目的	>90%	>80%	治療HIV感染 壓制病毒複製
使用對象	HIV 陰性者 常常有暴露的風險	HIV 陰性者 偶爾有暴露的風險	HIV 陽性者
使用時機	每天使用 依需要時使用	發生危險暴露後 72 小時之內	確定診斷感染HIV後
使用藥物	二合一抗病毒藥物組合 **TDF/FTC (舒發泰)**	標準三合一 抗病毒藥物組合	標準三合一 抗病毒藥物組合
服藥次數	一天一次一顆 事前兩顆、事後兩顆	一天一次或兩次 顆粒不定	一天一次或兩次
使用時間	不一定 依風險高低決定	28天	終生服藥不間斷
費用來源	自費	自費	健保給付

台灣愛滋病學會nPEP指引：評估流程



有風險的暴露

不具有風險的暴露

- 輕吻（無黏膜或皮膚傷口）
- 口對口接觸（無黏膜與皮膚傷口）
- 用手撫慰生殖器（無黏膜或皮膚傷口）
- 口- 陰道性交（無可見血液）
- 咬傷（無可見血液）
- 口- 陰莖性交?（插入方）
- 口- 肛門?（無可見血液）

72小時之內發生單一事件

對象是高風險或HIV帶原者

高風險族群

- 多重性伴侶者
- 性傳染病者
- 雙性或男男間性行為者
- 共用針頭者
- 性工作者或性-毒品交易者

愛滋病檢驗治療指引第五版

台灣愛滋病學會nPEP指引：檢查時程

	基礎值	暴露後 4-6週	暴露後 3個月	暴露後 6個月
HIV Ag/Ab combo	V	V	V	(V)**
CBC/DC	(V)	(V)		
AST/ALT	V	V		
BUN/Crea	V	V		
VDRL/RPR, TPHA	V	V		(V)
HBsAg, anti-HBs, (anti-HBc)	V			V
Anti- HCV	V			V
Pregnancy test (urine/blood)	V	V		

If ZDV used

After Tx

- ****若暴露後anti-HCV 陽轉，則anti-HIV追蹤延長至 6個月**
- 暴露者無保護性抗體((serum anti-HBs <10mIU/mL)且對象為B肝感染者建議盡快(暴露後24小時內)給予HBIG及第一劑HBV疫苗(施打在不同部位)，並於1-2個月及6個月完成第二劑和第三劑疫苗；暴露者無保護性抗體但對象未知是否為B肝感染者，除非確定為疫苗不反應者，建議仍要施打HBV疫苗
- HCV antibody 一旦為陽性需檢查HCV RNA並與專科醫師討論後續治療

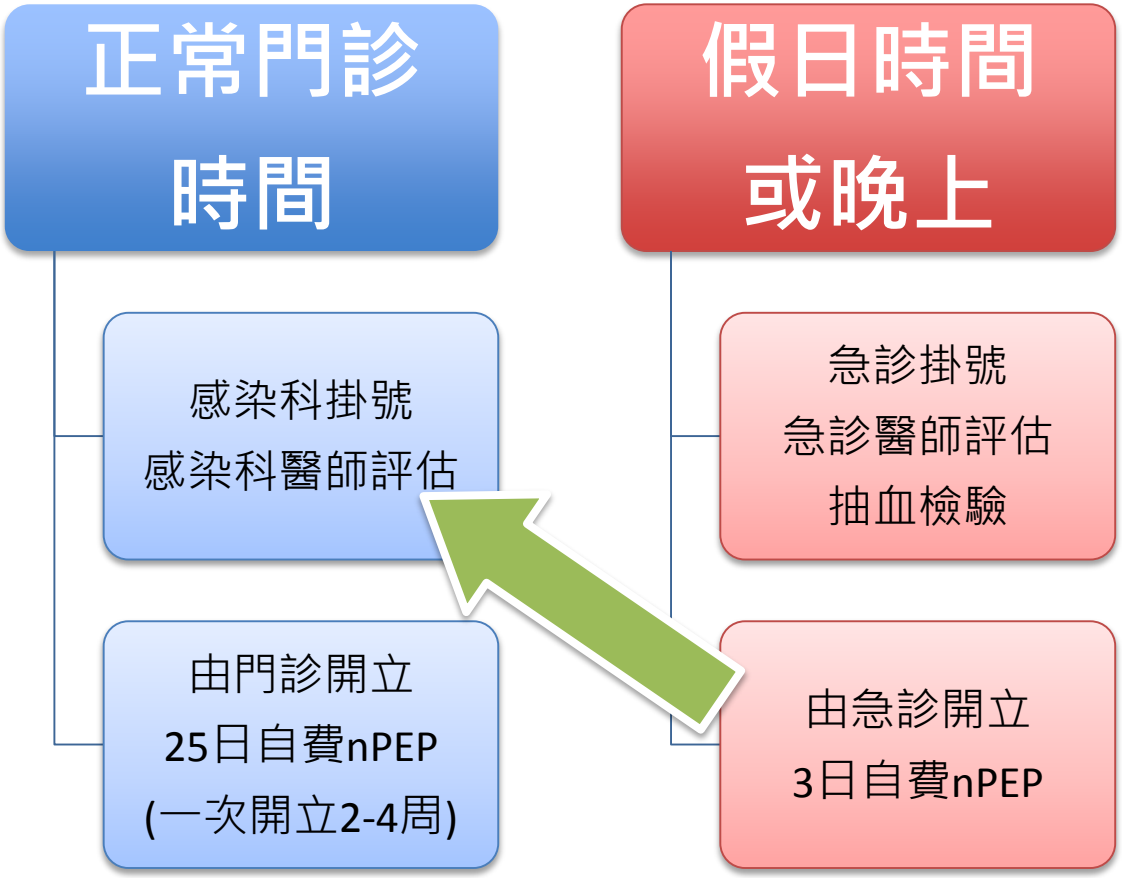
愛滋病檢驗治療指引第五版

台灣愛滋病學會nPEP指引：建議處方

藥物種類	第三種藥物（3rd agent）	骨幹藥物（Backbone agent）
優先建議		
	Dolutegravir 50 mg 每日一次 口服	TDF/FTC* 300/200 mg 每日一次 口服
	Raltegravir 400 mg 每日兩次 口服	
	Darunavir 800 mg + ritonavir 100 mg 每日一次 口服	
替代處方		
	Lopinavir/ritonavir 800/200 mg 每日一次 口服	TDF 300 mg + Lamivudine 300 mg 每日一次 口服
	Rilpivirine 25 mg 每日一次 口服	Zidovidine/Lamivudine 300/150 mg 每日兩次 口服
	Atazanavir 300 mg + + ritonavir 100 mg 每日一次 口服	Abacavir***/Lamivudine 600/300 mg 每日一次 口服
	Efavirenz** 600 mg 每日一次 口服	

愛滋病檢驗治療指引第五版

台北榮總nPEP開立流程



Nevirapine

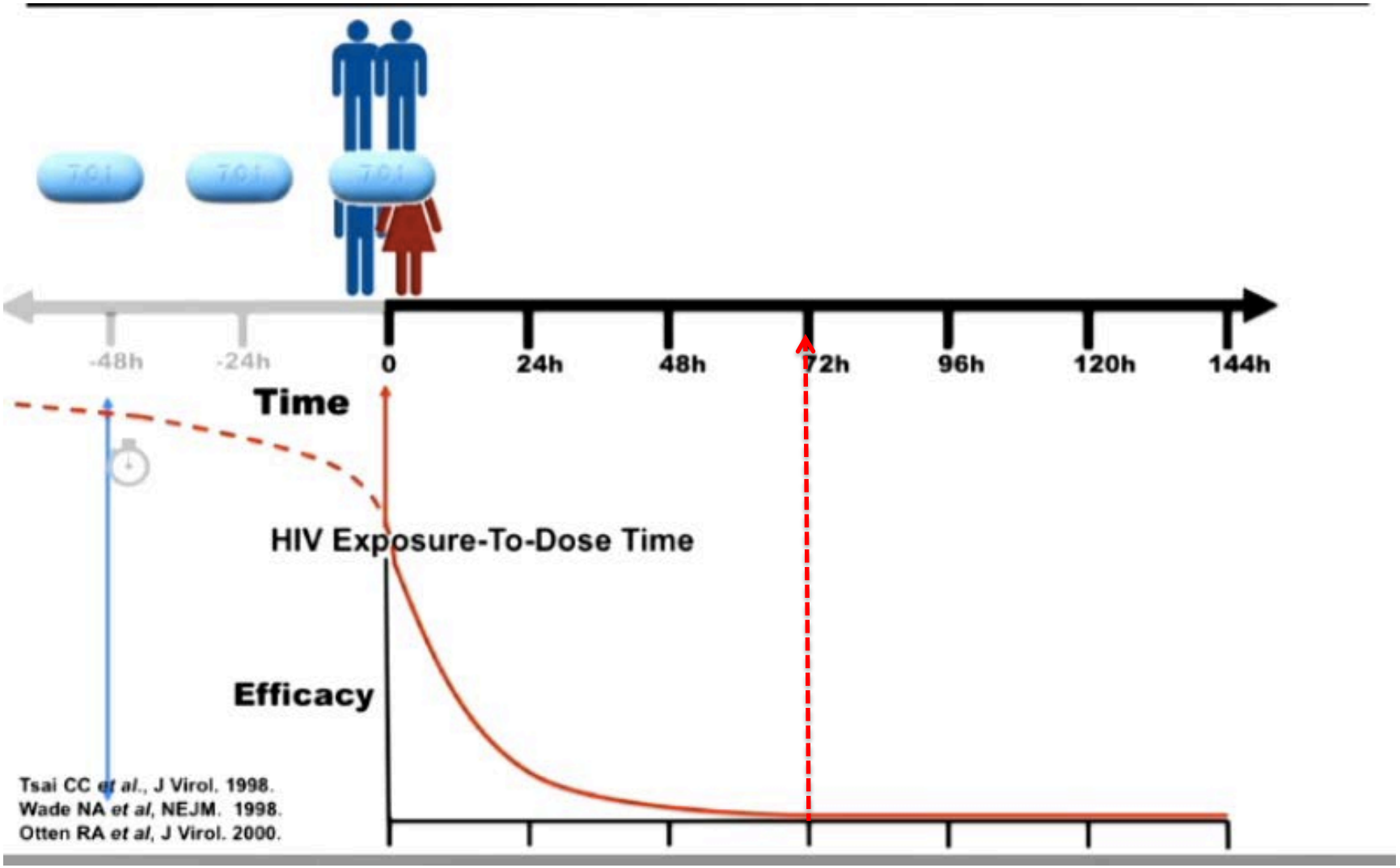
TAF

台北榮總nPEP常用的組合

藥物組合	每日 服藥次數	每日 顆粒數	副作用	服藥限制	每日 藥價
Combivir + EFV	2	3	☹☹☹	睡前	185
Combivir +RPV	2	3	☹	飯後	387
Atripla	1	1	☹☹	睡前	437
Combivir + RAL	2	4	☹	X	468
Combivir + DTG	2	3	☹	X	474
Complera	1	1	☺☺	飯後	496
Triumeq	1	1	☺	X	513
Truvada + RAL	2	3	☺☺	X	765
Truvada + DTG	1	2	☺	X	771

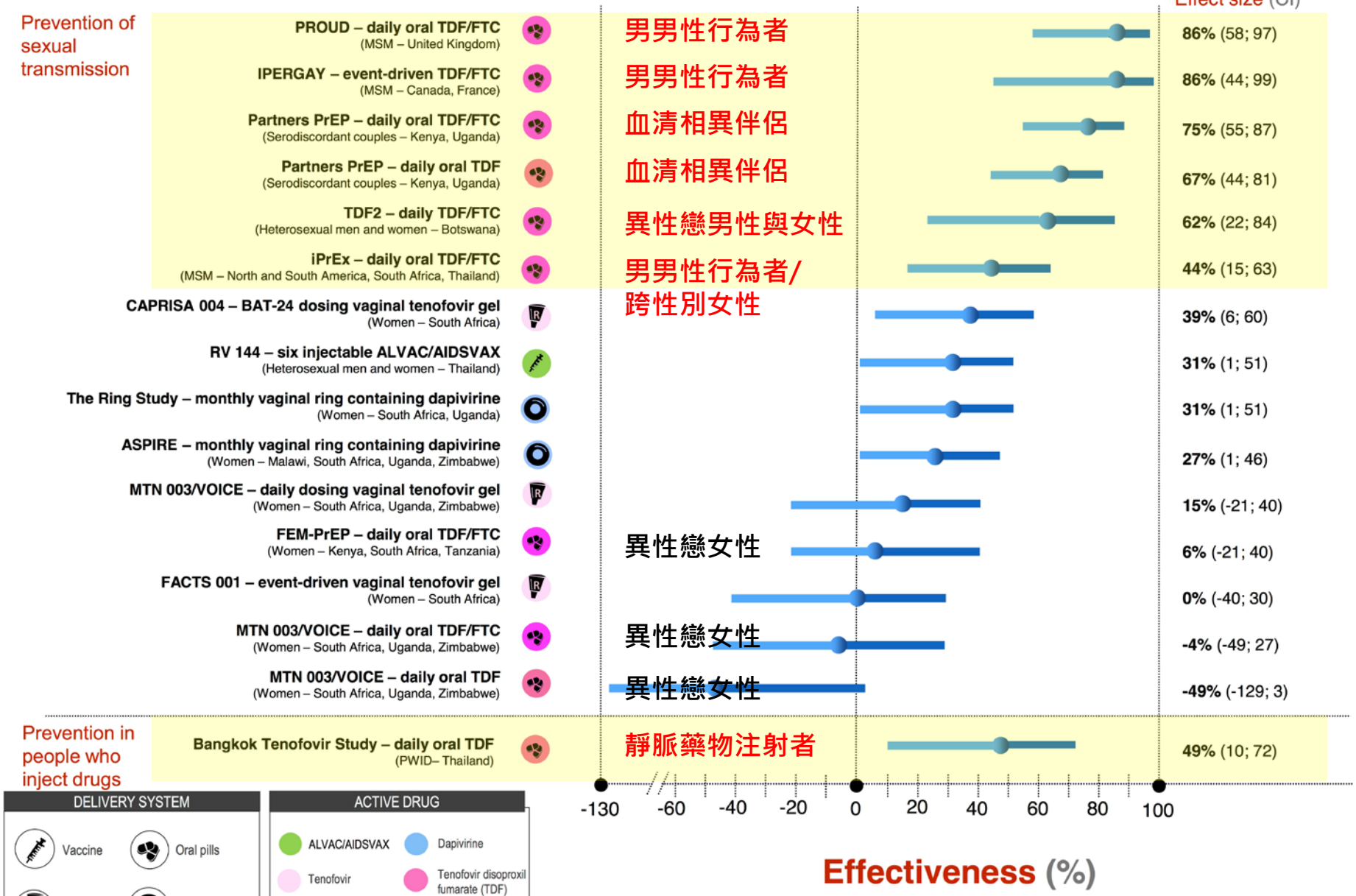
EFV: efavirenz; RPV: rilpivirine; RAL: raltegravir; DTG: dolutegravir

暴露前 vs. 暴露後預防性投藥



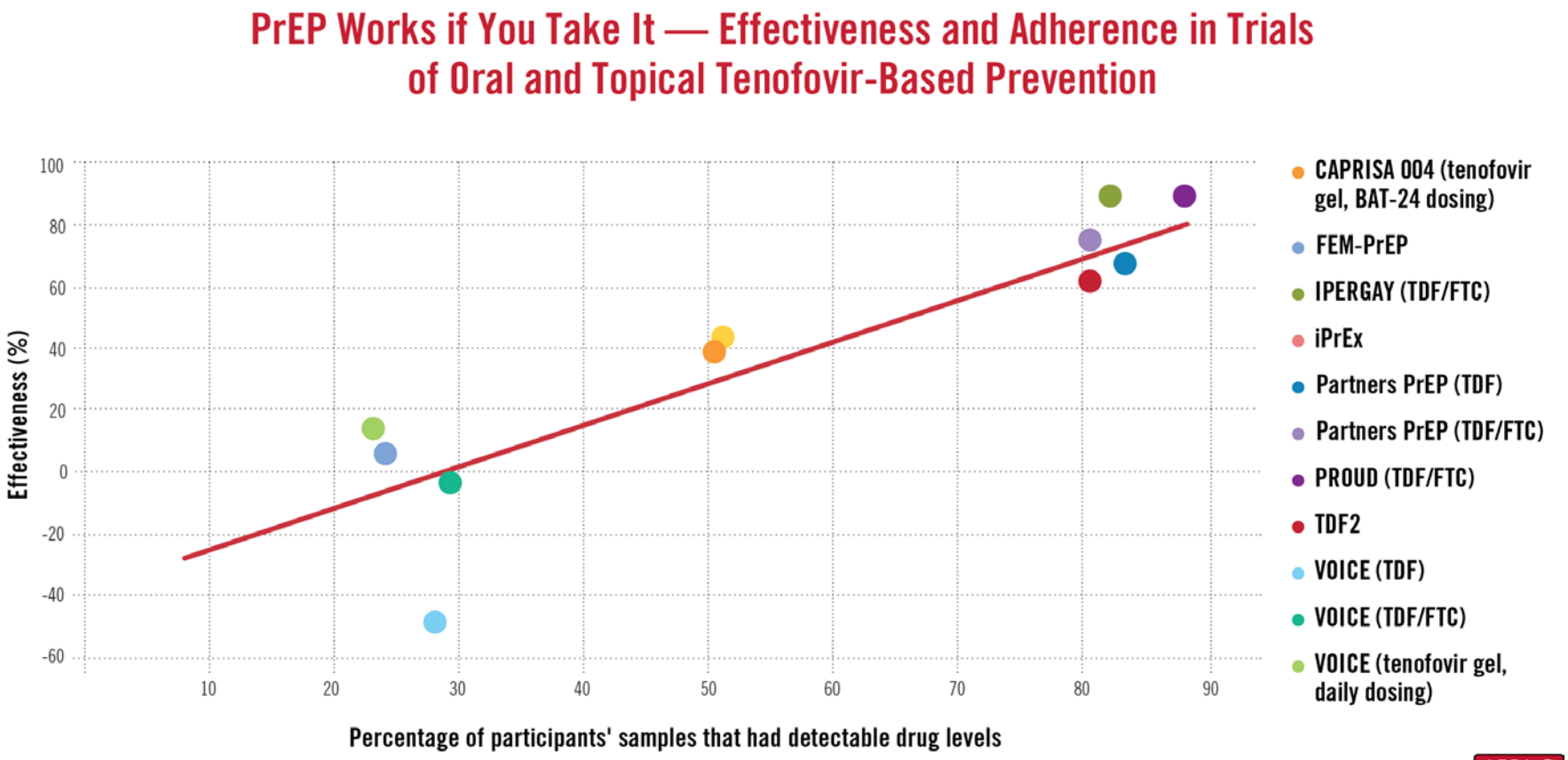
Clinical Trial Evidence for HIV Prevention Options (February 2016)

AVAC
Global Advocacy for HIV Prevention

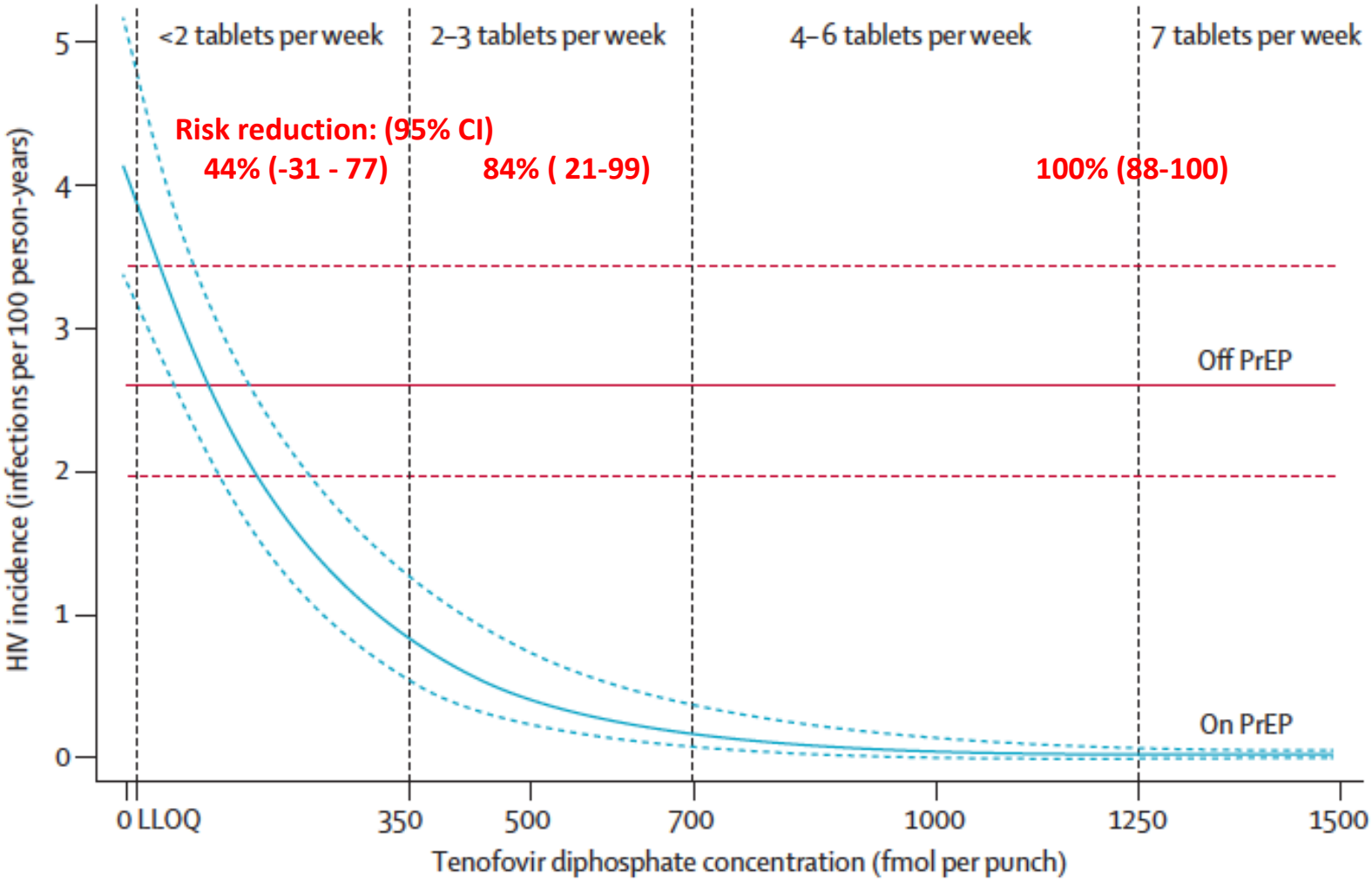


Adapted from: Salim S. Abdool Karim, CAPRISA

使用PrEP的順從度決定保護效果

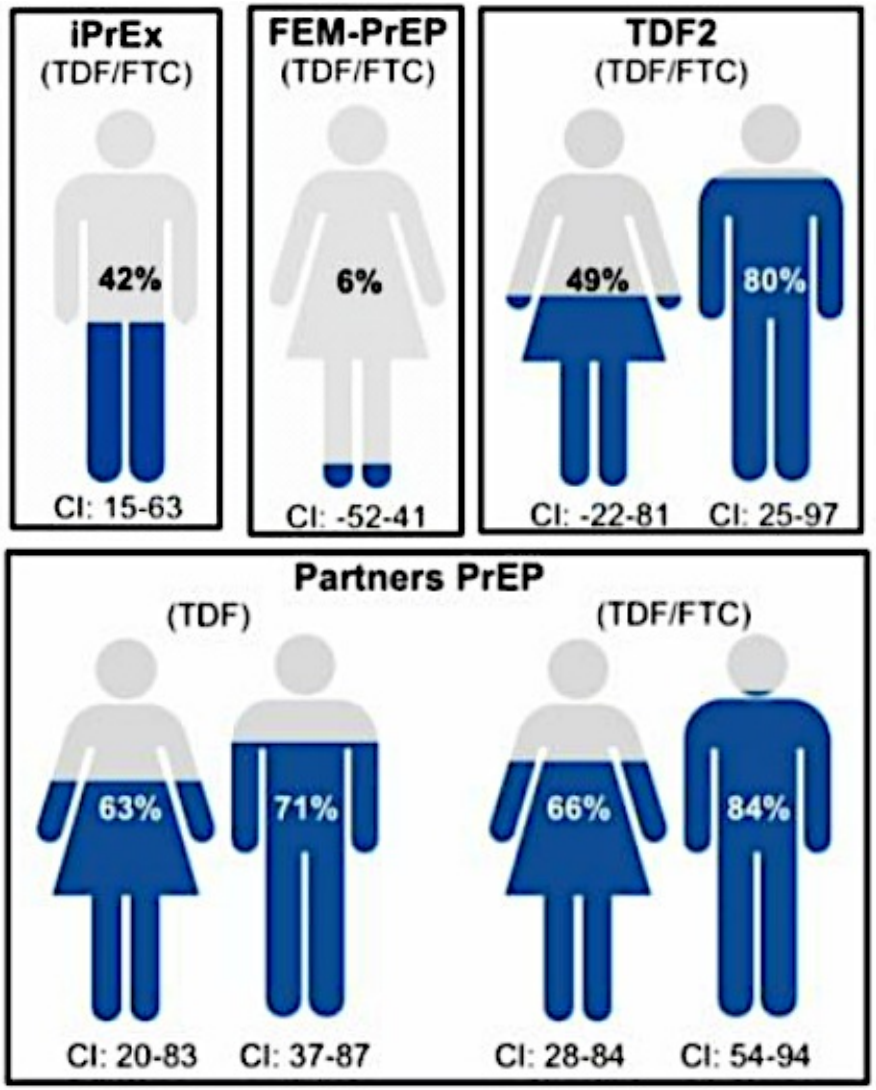


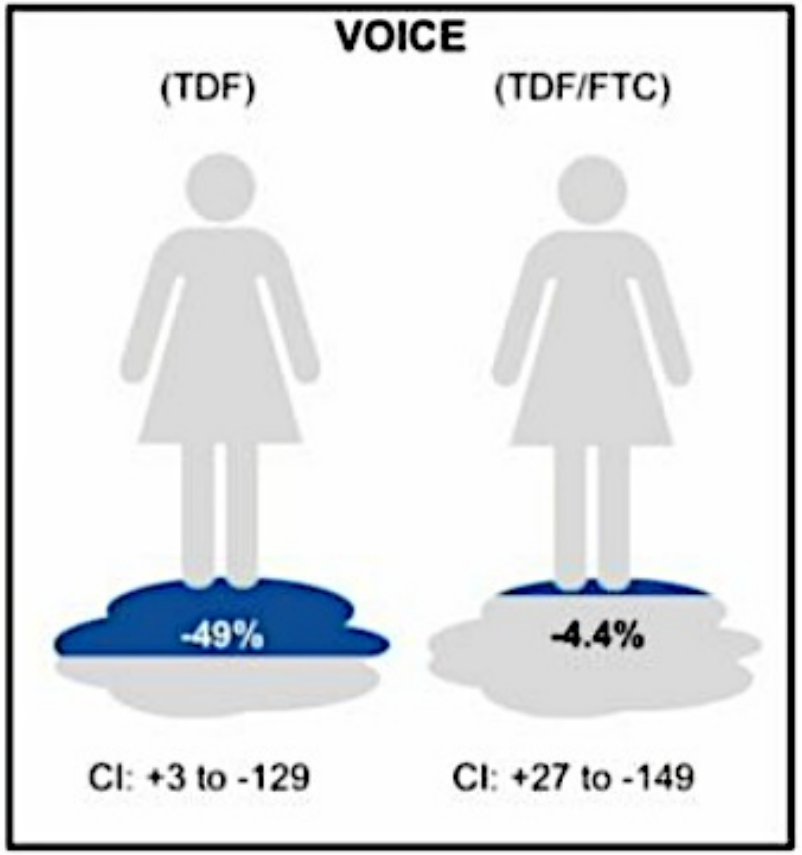
順從度與保護力：iPrEx-OLE



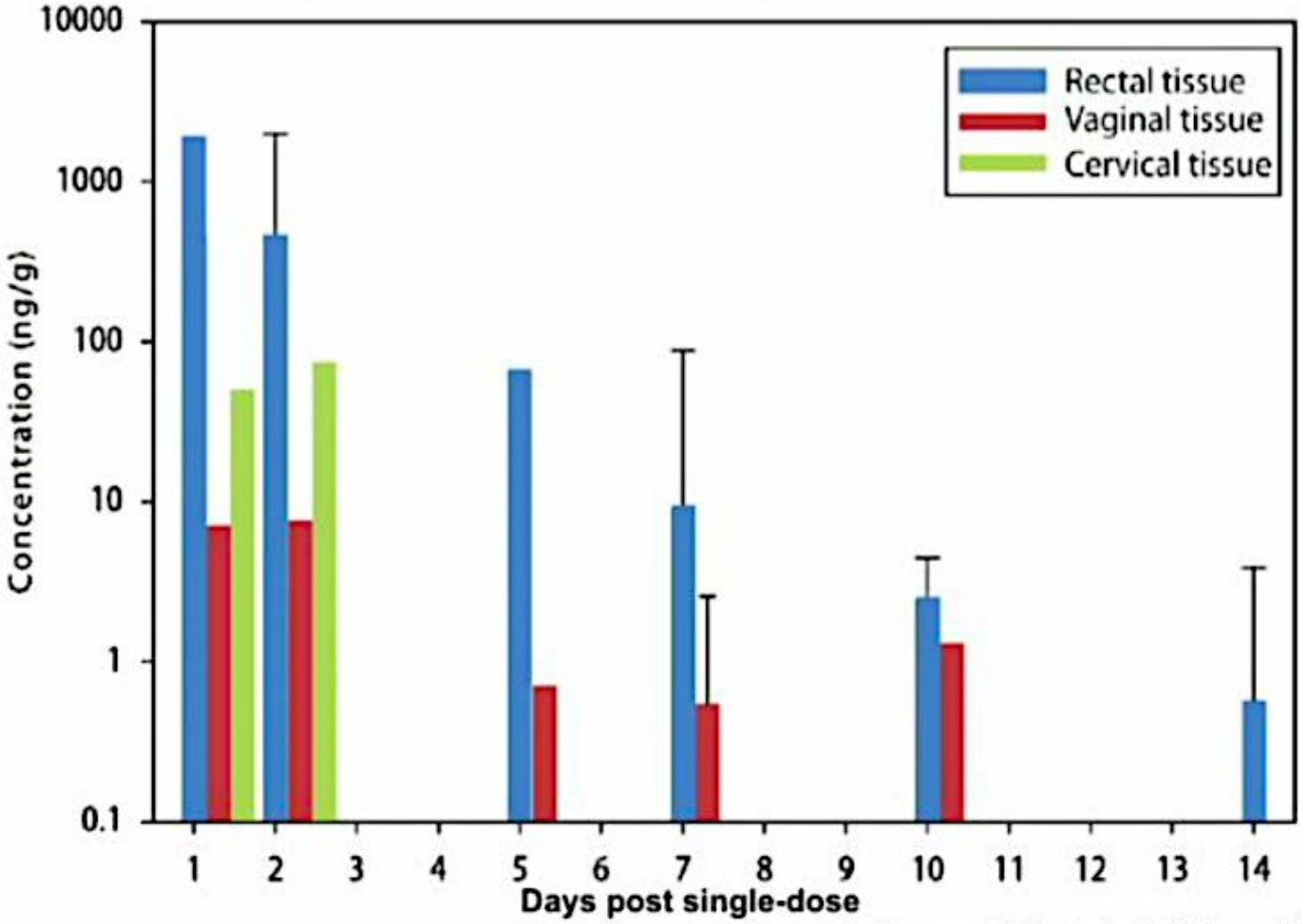
Grant R, et al. AIDS 2014. Abstract TUAC0105LB.

口服PrEP保護效果為何男女有別





口服TDF在組織的濃度大大不同



Patterson KB *et al.* Sci Transl Med. 2011.

暴露前預防性投藥: 亞洲現況

Updated September 2018

Regulatory Status of TRUVADA and generic TDF/FTC for PrEP

TRUVADA & generic TDF/FTC approved for prevention

Belgium, Canada, Czech Republic, England, France, Germany, Greece, Ireland, Israel, Italy, Kenya, Lesotho*, Netherlands, Nigeria, Portugal, Scotland, Slovenia, South Africa, Spain, Swaziland*, Sweden, Thailand, United States, Wales, Zimbabwe

TRUVADA approved for prevention

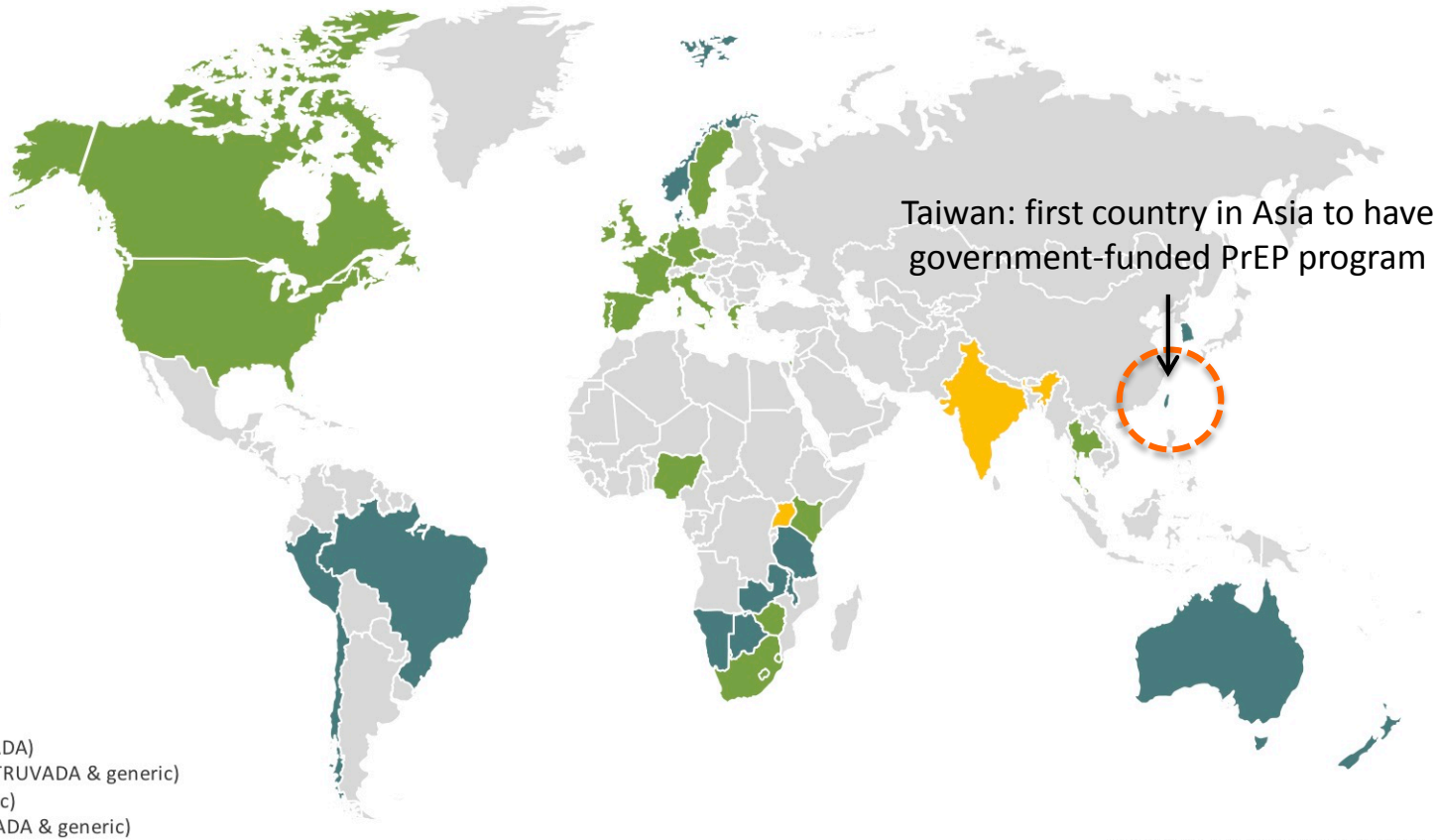
Australia, Bahamas, Barbados, Botswana, Brazil, Chile, Denmark, Malawi, Namibia, New Zealand, Norway, Peru, South Korea, Taiwan, Tanzania, Zambia

Generic TDF/FTC approved for prevention

India, Uganda

Regulatory application submitted for a prevention indication for TDF/FTC

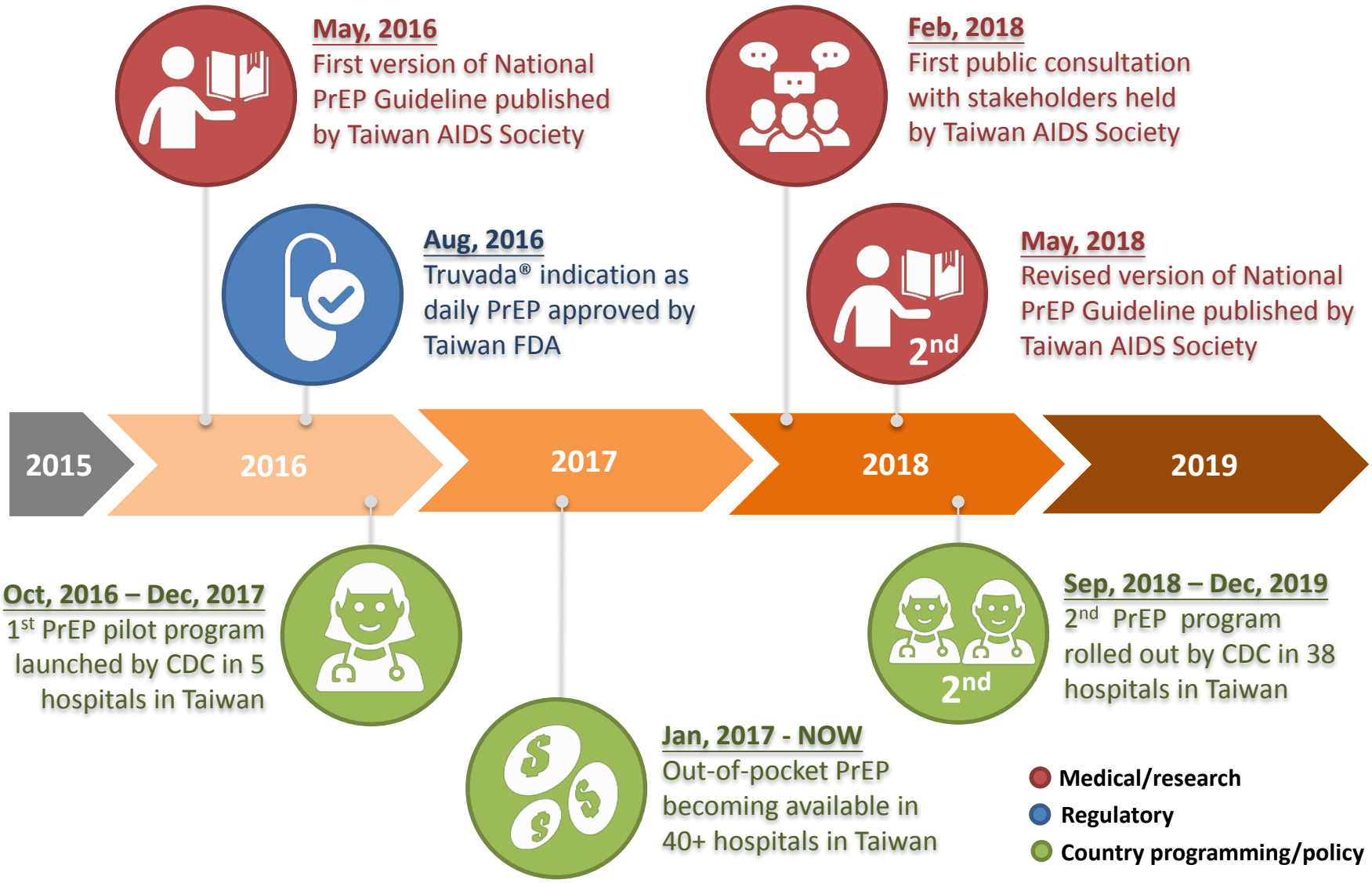
Botswana (generic), Cote d'Ivoire (generic), Ecuador (TRUVADA), Hong Kong (TRUVADA), Mexico (TRUVADA), Mozambique (TRUVADA & generic), Senegal (generic), Ukraine (TRUVADA & generic)



**Approved via import license from South Africa.*

AVAC

台灣推動暴露前預防性投藥進程



台灣暴露前口服預防性投藥使用指引: 2016

"The panel recommends people at substantial risk of HIV infection to take daily oral tenofovir (TDF) 300 mg / emtricitabine (FTC) 200 mg fixed-dose combination as additional prevention measures."

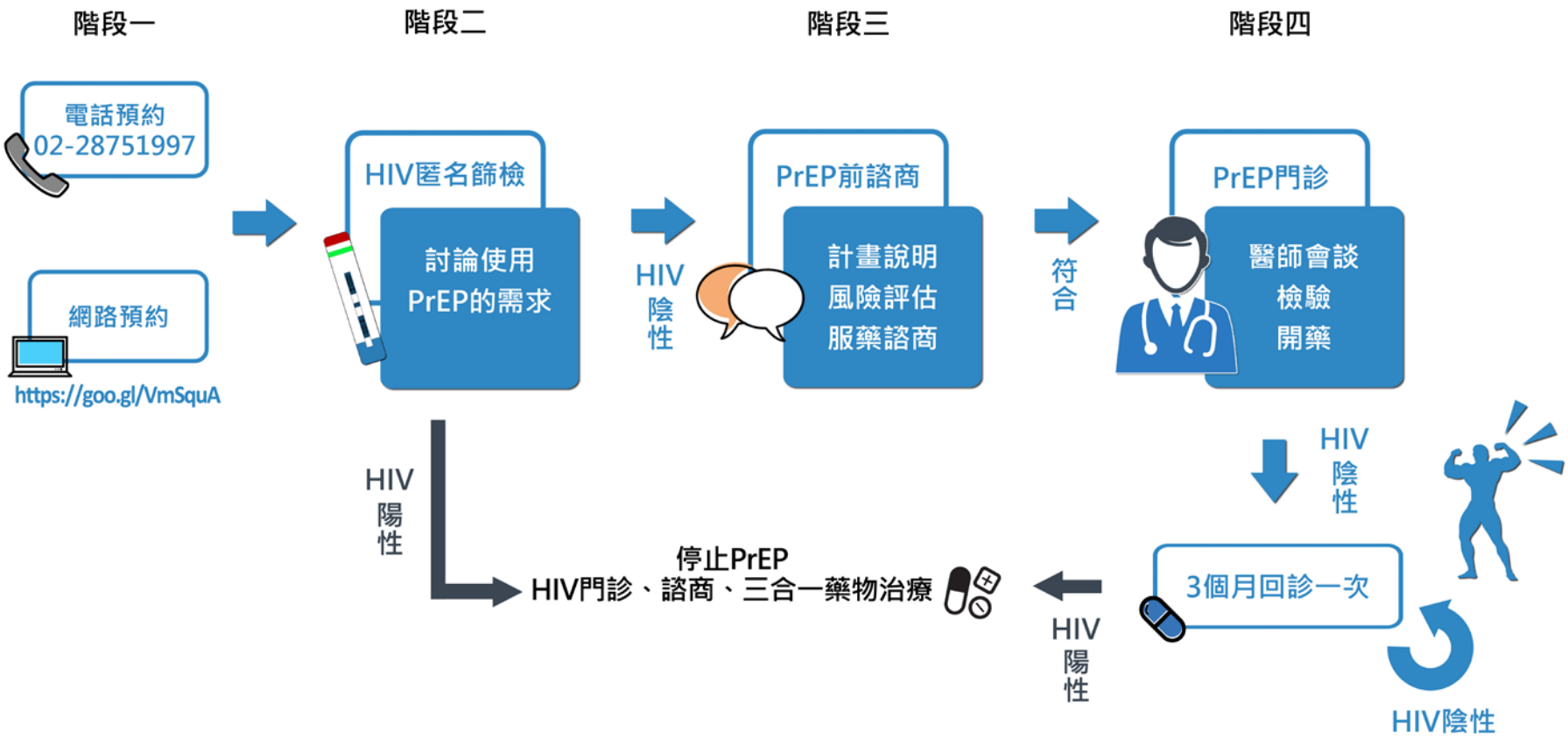
Key Populations	Dosing Schedule	Level of Evidence	Grading of Recommendations
Men who have sex with men (MSM) / Transgender women (TGW)	**Daily**	High	Strongly recommended
HIV-negative partner of heterosexual serodiscordant couples	**Daily**	High	Strongly recommended
People who inject drug (PWID)	**Daily**	High	Weakly recommended
Heterosexual men and women	**Daily**	Moderate	Weakly recommended

http://www.aids-care.org.tw/DB/News/file/254-1.pdf

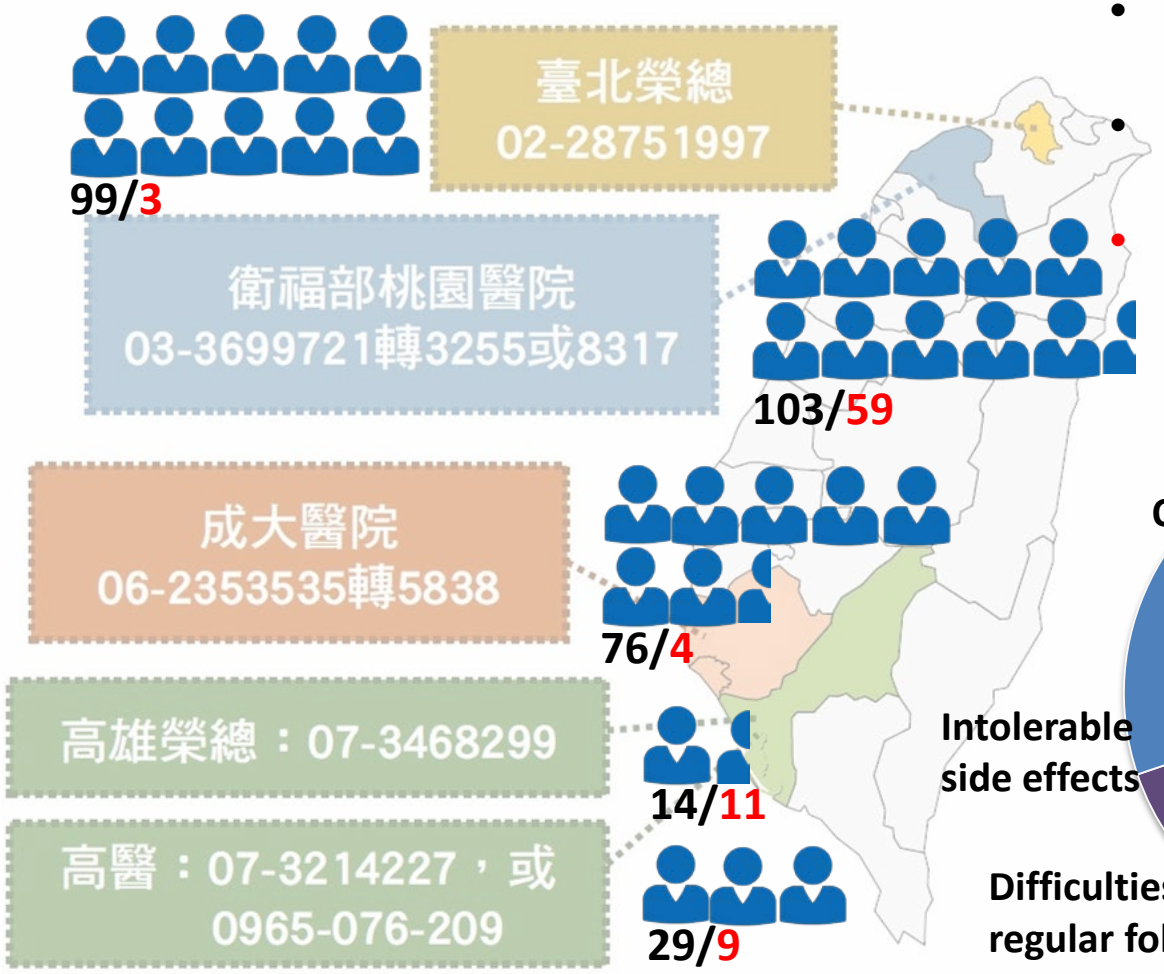
“預防愛滋的新選擇”

https://www.youtube.com/watch?v=kh-Me2VOxmA

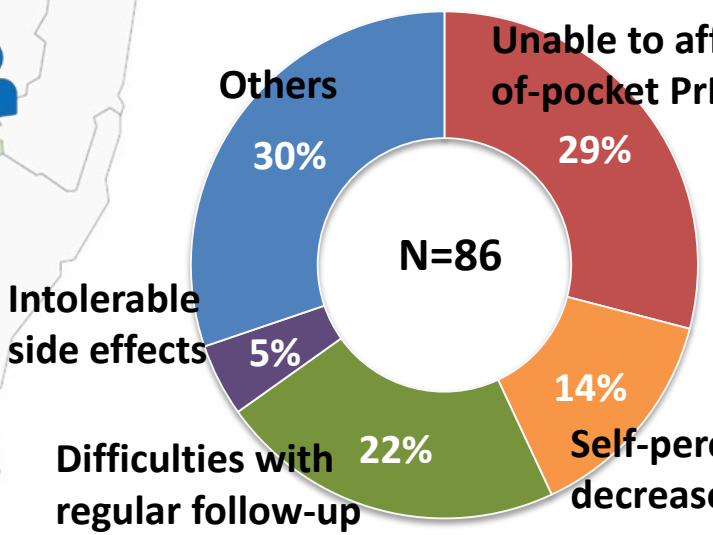
台灣疾管署PrEP前驅計畫：以北榮為例



疾管署PrEP前驅計畫: 2016-2017



- Median duration of PrEP use: 93 days (range: 21-285 days)
- 74 clients used daily (24.5%) vs. 228 used non-daily (75.5%)
- 86 clients withdrawn from the program



Taiwan CDC. Unpublished data

2018年台灣暴露前預防性投藥使用指引

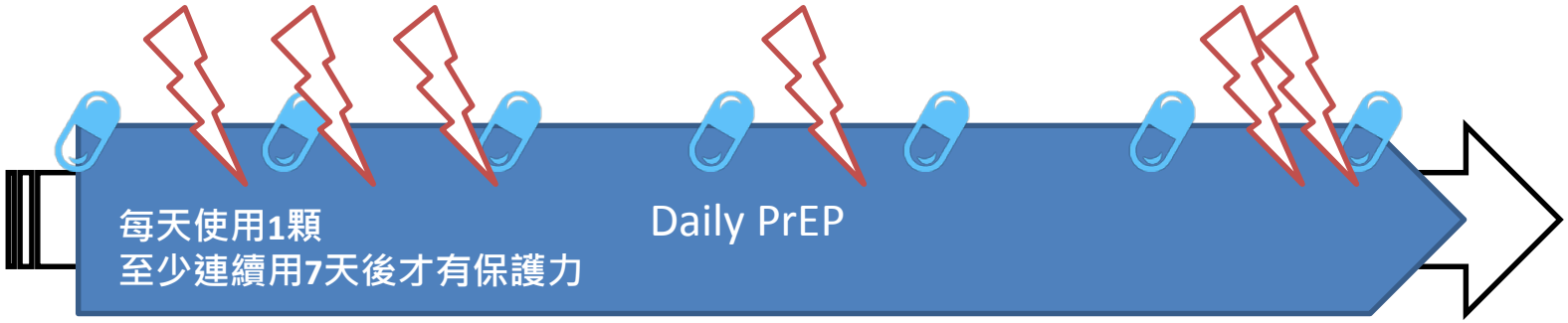
“The panel recommends people at substantial risk of HIV infection to take oral tenofovir (TDF) 300 mg / emtricitabine (FTC) 200 mg fixed-dose combination as additional prevention measures.”

Key Populations	Dosing Schedule	Level of Evidence	Grading of Recommendations
Men who have sex with men (MSM) / Transgender women (TGW)	Daily	High	Strongly recommended
Men who have sex with men (MSM) / Transgender women (TGW)	**On-Demand**	**High**	**Weakly recommended**
HIV-negative partner of heterosexual serodiscordant couples	Daily	High	Strongly recommended
People who inject drug (PWID)	Daily	High	Weakly recommended
Heterosexual men and women	Daily	Moderate	Weakly recommended

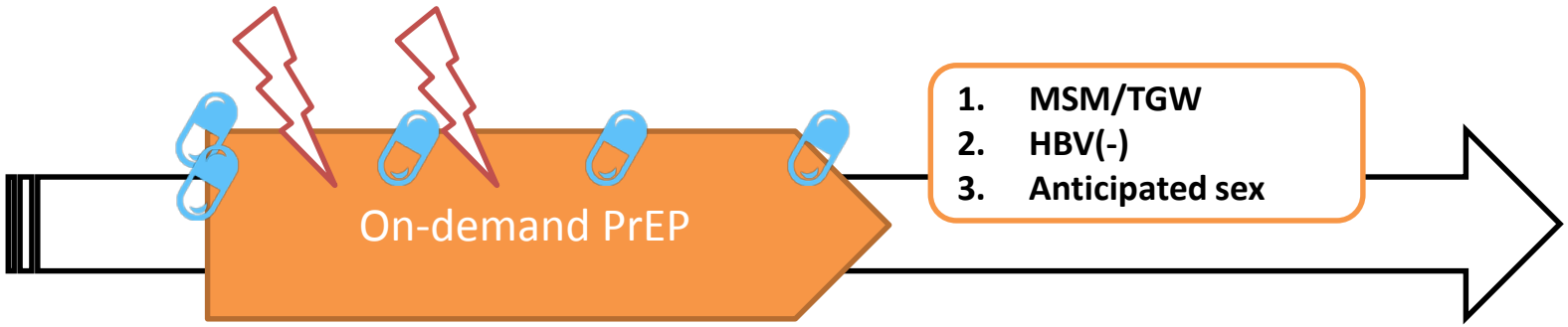
http://www.aids-care.org.tw/index.asp

兩種暴露前預防性投藥的使用時機

每天服用的暴露前預防性投藥 (Daily PrEP)



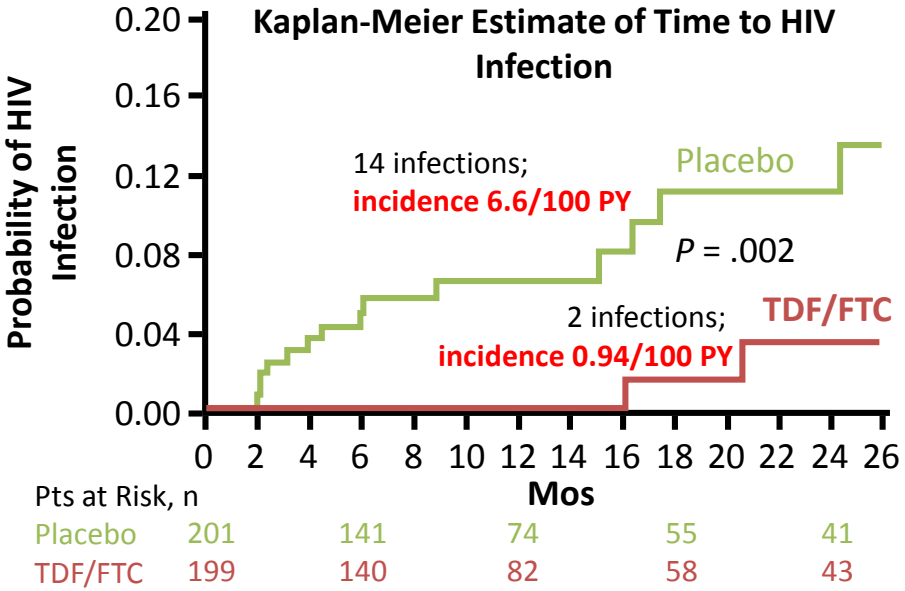
依需要時使用的暴露前預防性投藥 (On-demand PrEP)



性行為前當天 x2顆
每隔24小時 x1顆
一直到性行為後連續兩天

「依需要時使用」暴露前預防性投藥

- Randomized double-blind trial of **event-driven oral TDF/FTC* (n = 199)** vs **placebo (n = 201)** (both with prevention services) in France
  - 2 tablets taken 2-24 hrs before sex
  - 1 tablet 24 hrs after sex
  - 1 tablet 48 hrs after first event-driven dose
- Primary endpoint: HIV seroconversion
- **86% reduction in risk** seen in PrEP arm (95% CI: 40% to 99%, *P* = .002)
  - Number needed to treat for 1 yr to prevent 1 infection: 18
  - Median of **16 pills taken per mo** in each arm
- **High rate of STIs seen in both groups (33% vs. 32%)**
- **Frequent recreational drug use in the past 12 months in both groups (44% vs. 48%)**

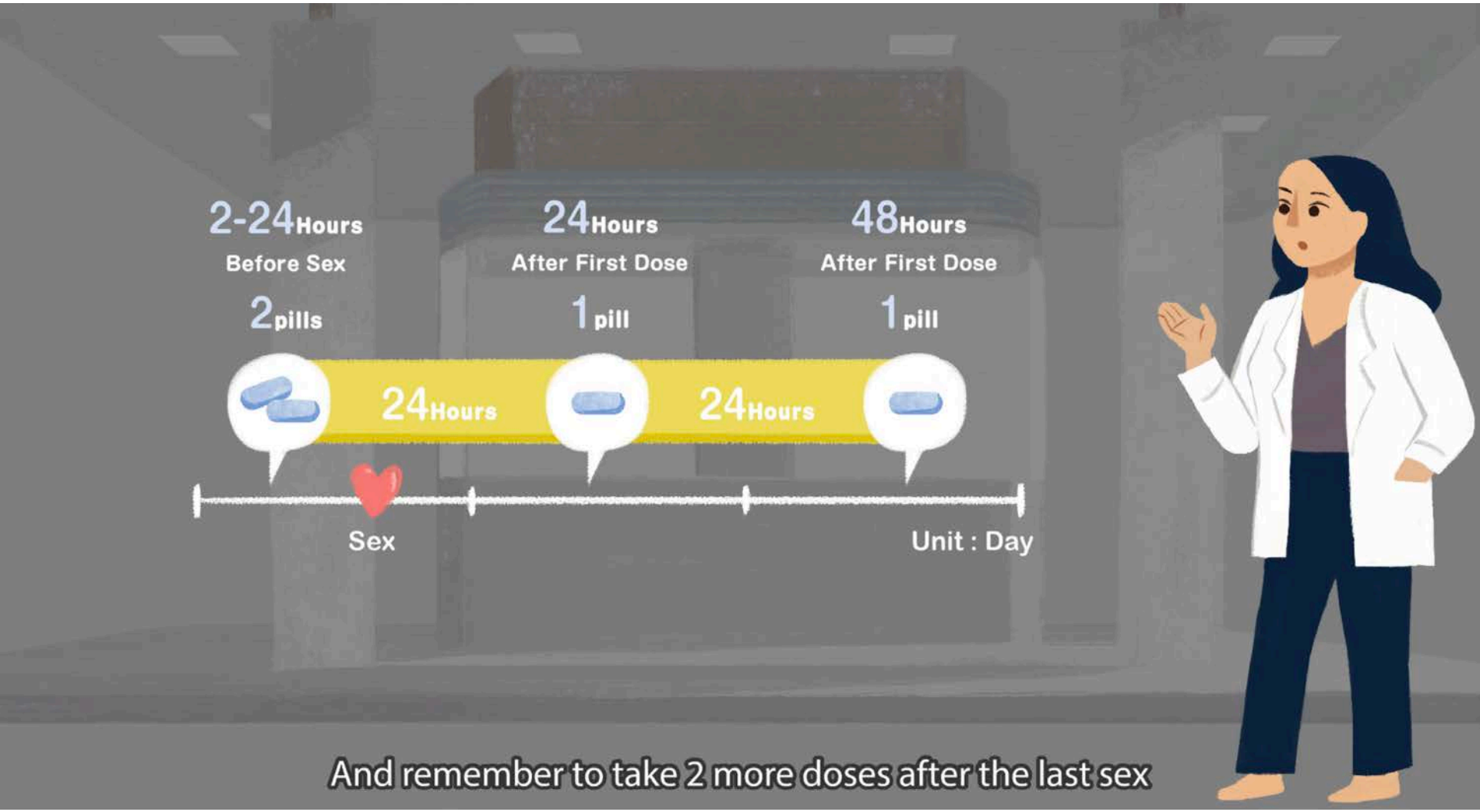


- In pts with infection, no TFV found in serum in last 2 visits
- 4 cases of acute HCV infection noted among lab abnormalities
- DSMB stopped trial early and recommended all participants start PrEP

*On-demand PrEP strategy not FDA approved.

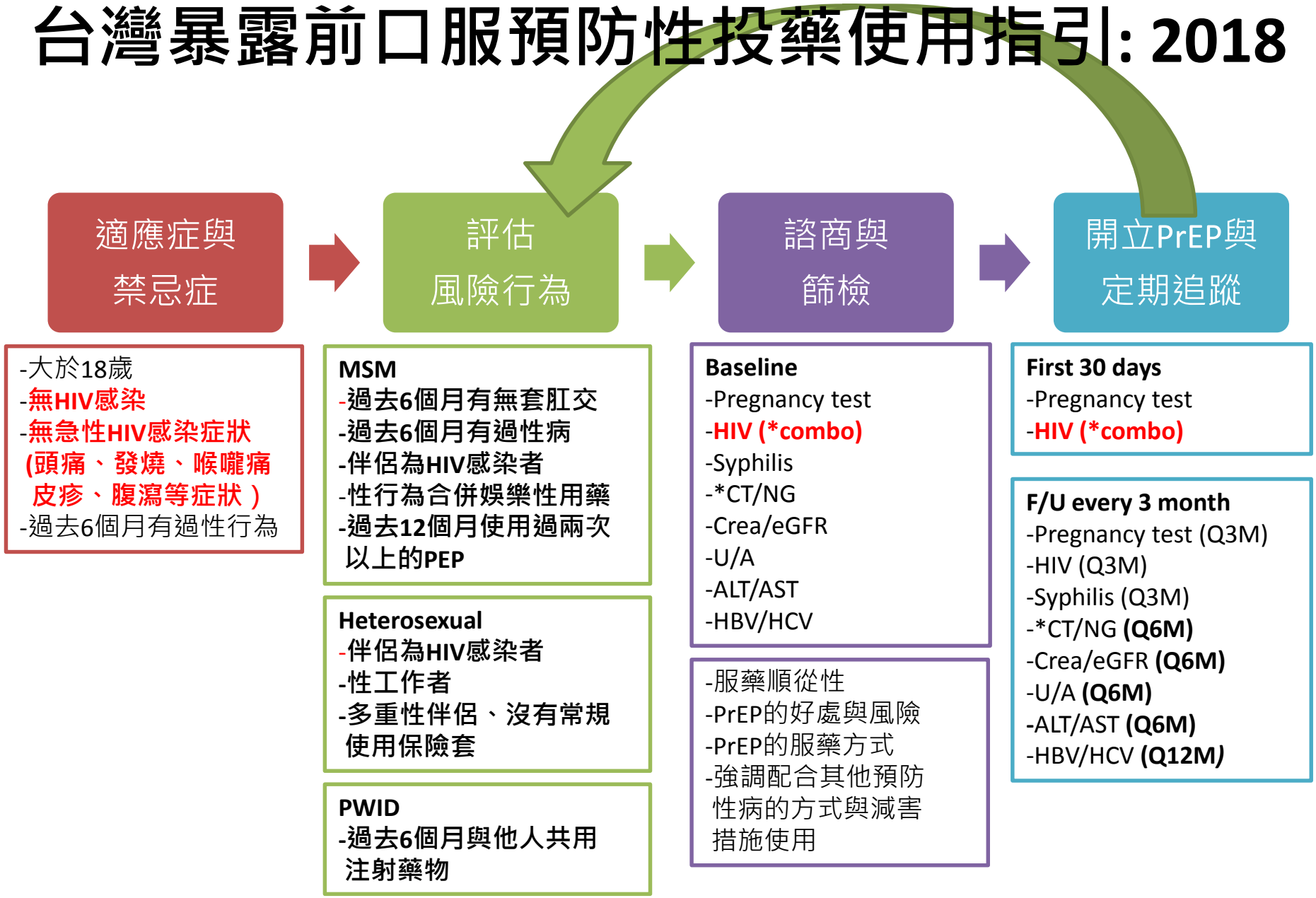
Molina JM, et al. N Eng J Med. 2015;373:2237-46.

“暴露前預防性投藥的新吃法”



https://www.youtube.com/watch?v=s21OOILKfhc

台灣暴露前口服預防性投藥使用指引: 2018



http://www.aids-care.org.tw/DB/News/file/254-1.pdf

疾管署公費PrEP計畫: 2018-2019

台北榮總、市立聯醫昆明院區、
台北馬偕、台大醫院 (4)

部立桃園 (1)

東元醫院 (1)

新竹台大、新竹馬偕 (2)

為恭醫院 (1)

台中榮總、中山附醫 (2)

彰化彰基、員林彰基 (2)

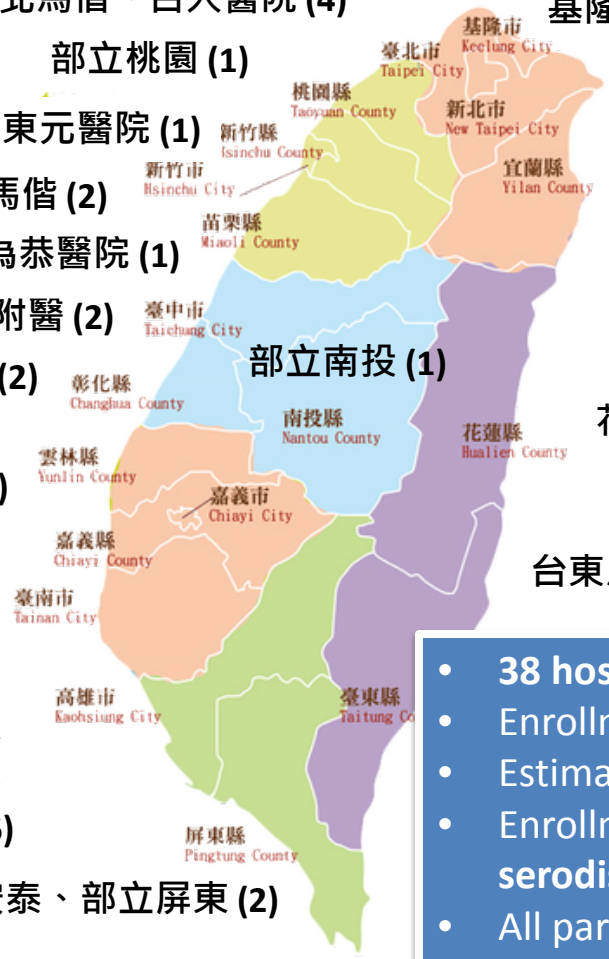
雲林若瑟 (1)

大林慈濟、嘉義長庚 (2)

台南成大、台南奇美 (2)

市立民生 (HERO)、高醫附醫、
鳳山李嘉文泌尿科診所、
高雄榮總、市立小港、
七賢高美泌尿科診所 (6)

屏東安泰、部立屏東 (2)



部立南投 (1)

基隆長庚、三總基隆民眾診療處 (2)

亞東醫院、新店耕莘、淡水馬偕 (3)

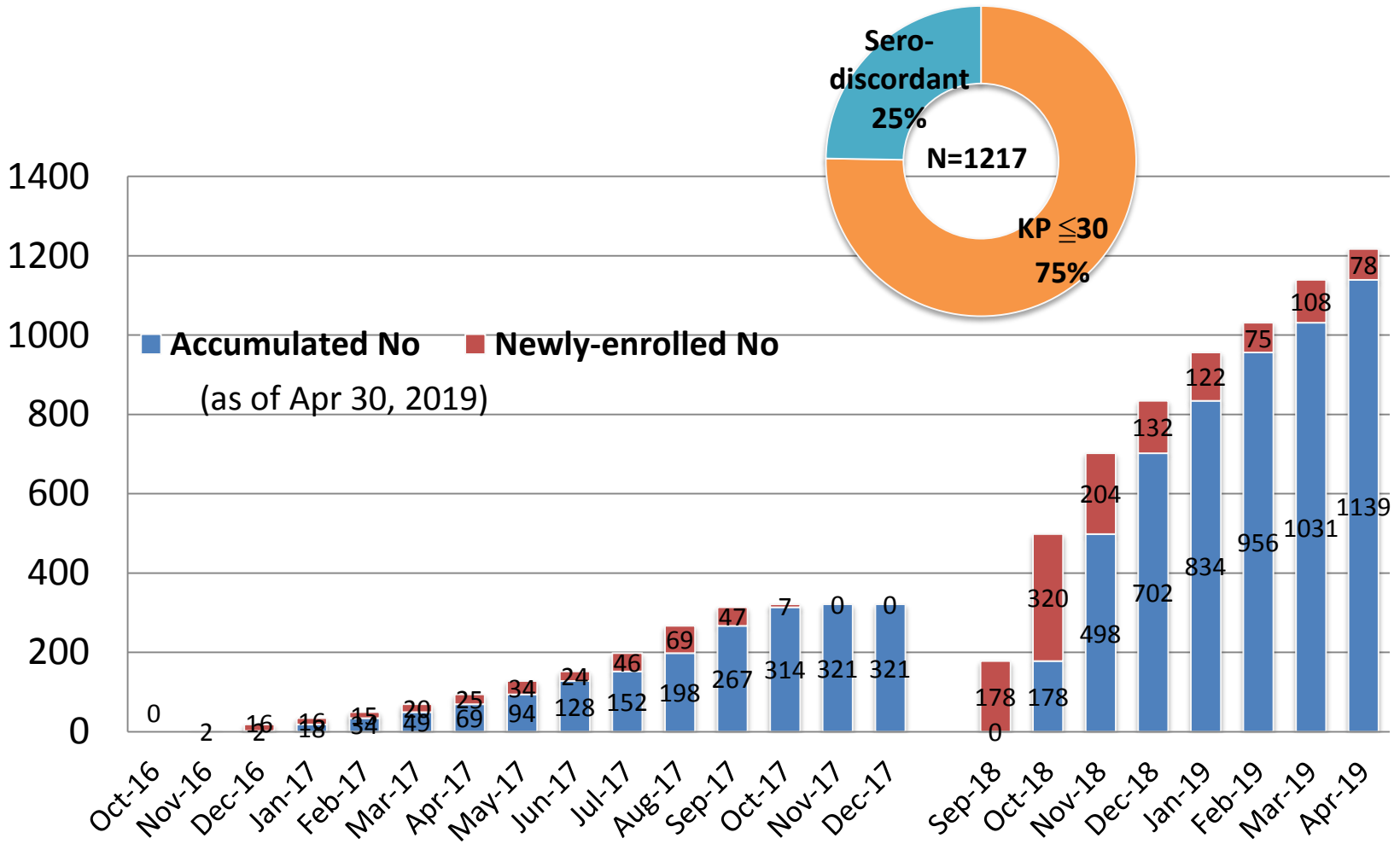
羅東聖母、羅東博愛、陽大附醫 (3)

花蓮慈濟、花蓮門諾 (2)

台東馬偕 (1)

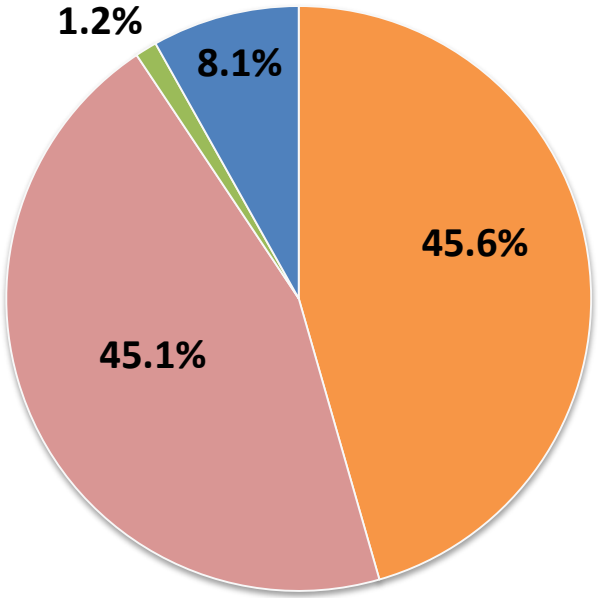
- **38 hospitals** throughout Taiwan
- Enrollment period: **Sep 2018 - Dec 2019**
- Estimated number of enrollment: **2,000**
- Enrollment criteria: **KP ≤30 years, serodiscordant couple**
- All participants were provided **free TDF/FTC for 12 months (up to 360 tablets)**

疾管署公費PrEP計畫: 收案趨勢



Taiwan CDC. Unpublished data

疾管署公費PrEP計畫: 上個月使用方式



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

N= 909
(as of JAN 23, 2019)

Daily vs. 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%

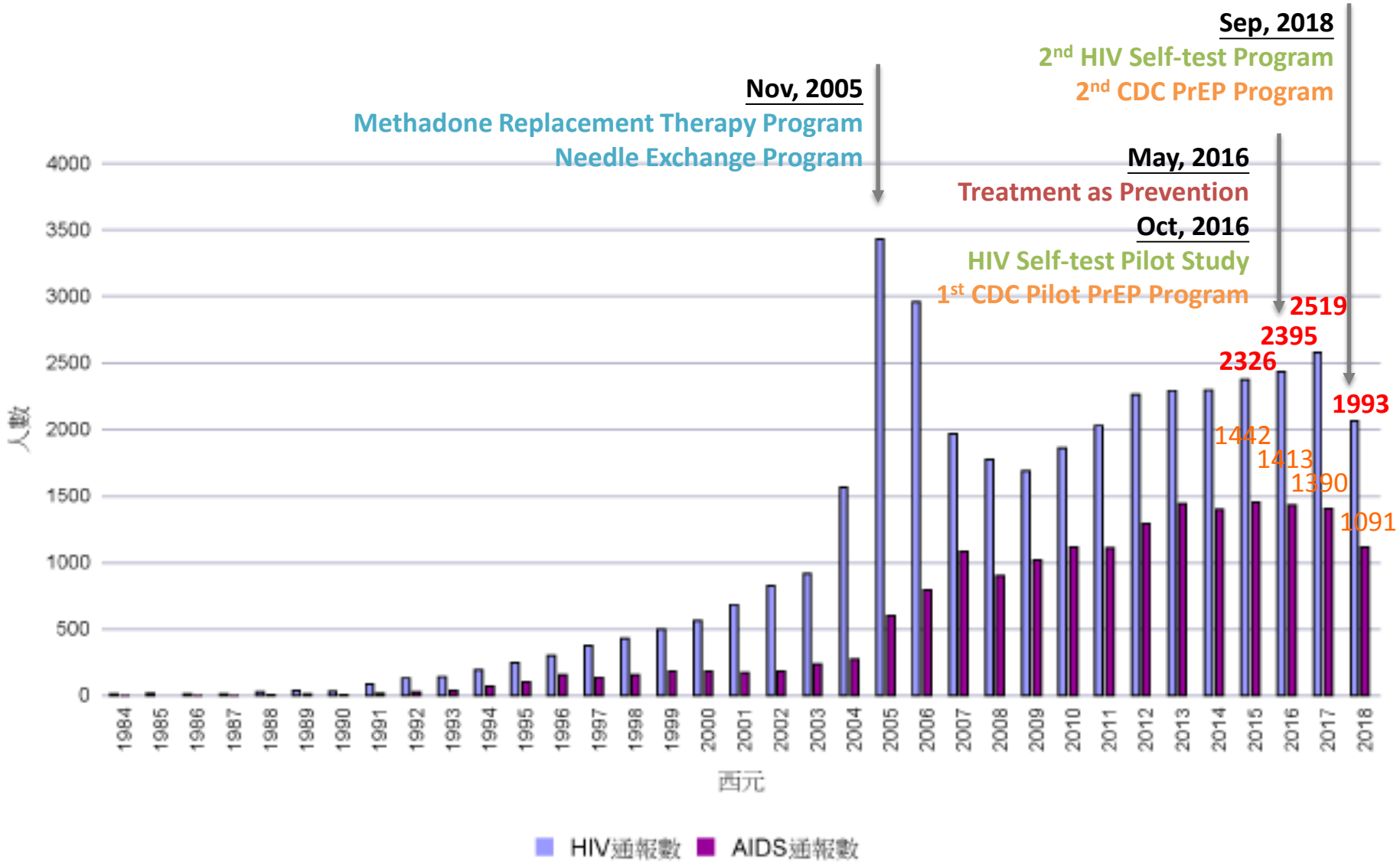
Taiwan CDC. Unpublished data

台灣愛滋照護階梯: 2018

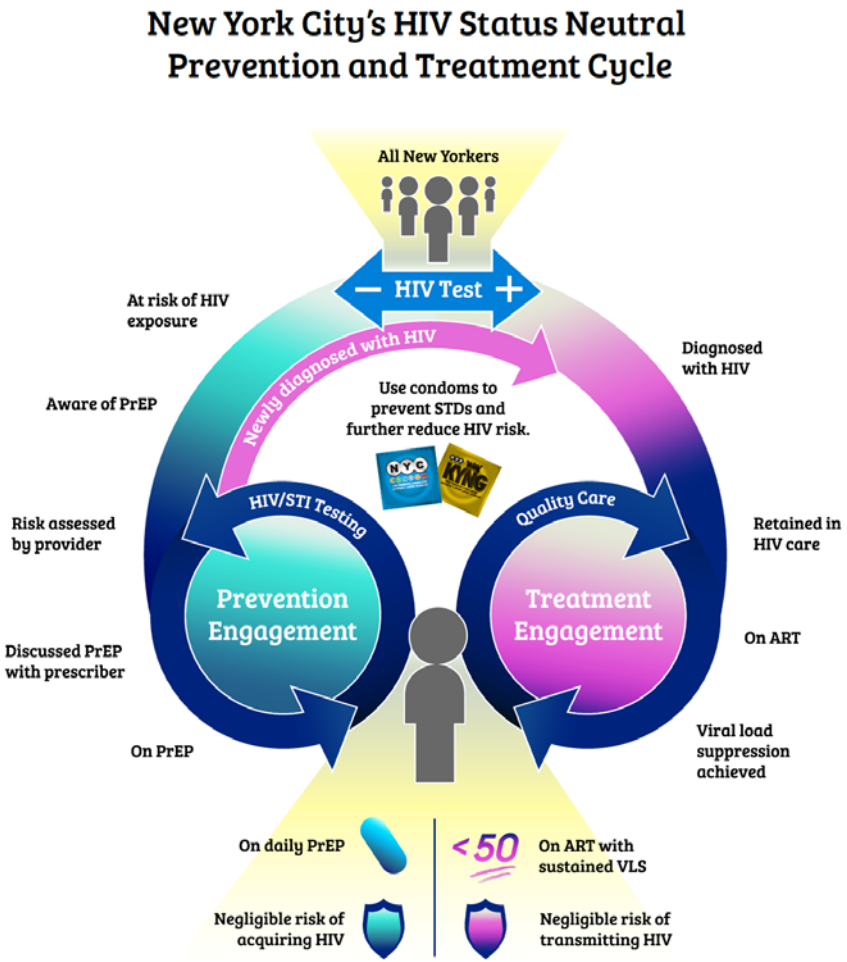
2015	75%	79%	85%
2016	74%	84%	89%
2017	79%	87%	90%
2018	**84%**	**88%**	**94%**

Taiwan CDC.

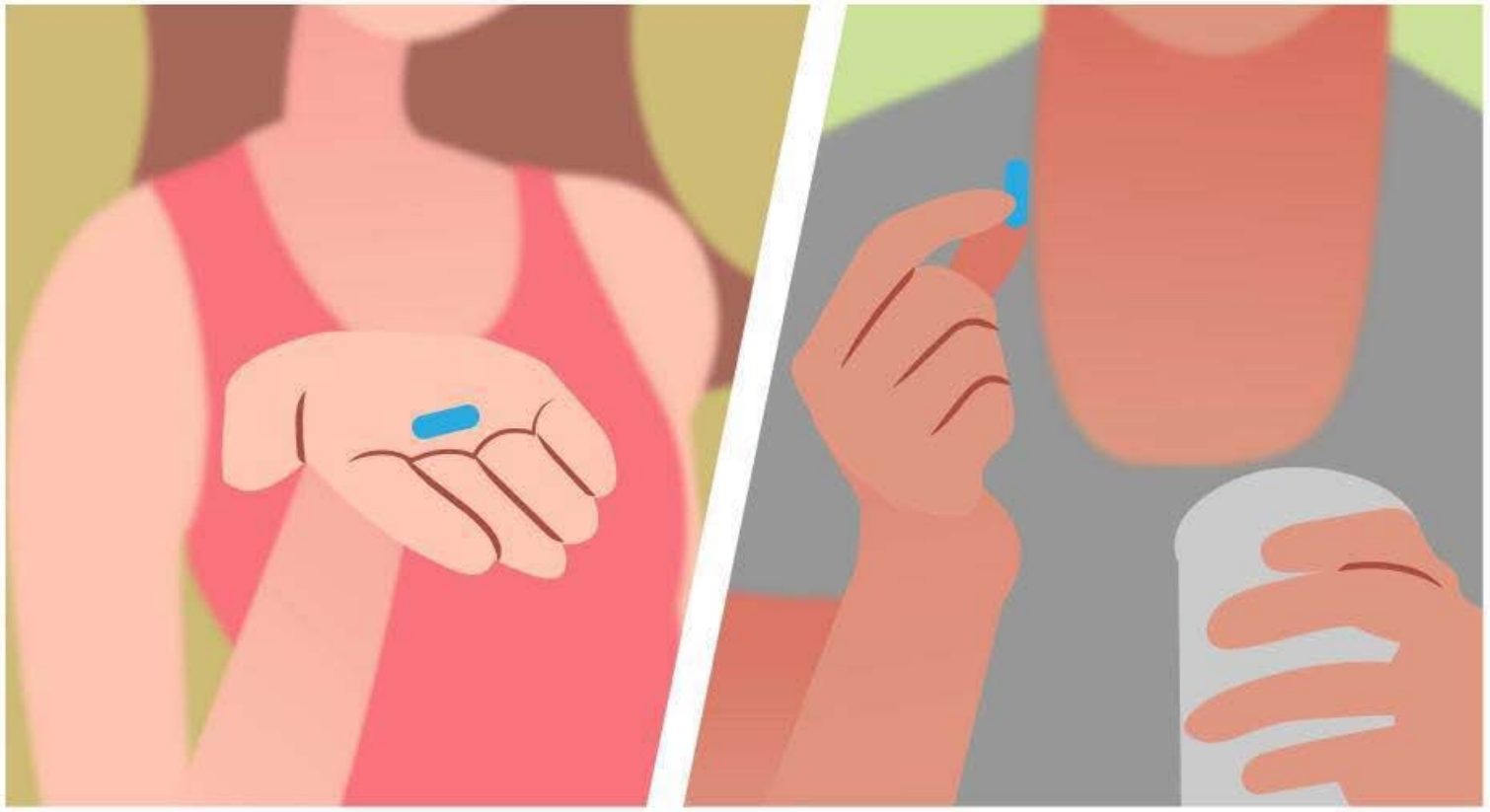
台灣愛滋疫情: 2018


Sep, 2018
2nd HIV Self-test Program
2nd CDC PrEP Program
Nov, 2005
Methadone Replacement Therapy Program
Needle Exchange Program
May, 2016
Treatment as Prevention
Oct, 2016
HIV Self-test Pilot Study
1st CDC Pilot PrEP Program
2519
2395
2326
1993
1442
1413
1390
1091
4000
3500
3000
2500
2000
1500
1000
500
0
人數
1984 1985 1986 1987 1988 1989 1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018
西元
HIV通報數
AIDS通報數

美國紐約的策略



Daskalakis DC. CROI 2017. Plenary Session



“Put the power in the people, put the pill in their palms.” – Sheena McCormack

THANK YOU

PROUD & IPERGAY: 追蹤研究結果

- **IPERGAY:** randomized, double-blind, placebo-controlled study of event-driven FTC/TDF PO PrEP for uninfected, high-risk MSM in France and Canada (N = 400)
  - Previous findings: HIV incidence/100 PY, FTC/TDF vs placebo groups 0.91 vs 6.60 (*P* = .002; 86% reduction in HIV incidence with event-driven FTC/TDF); median pills/mo: 15[1]
  - **Substudy of 269 pts using ≤ 15 pills/mo** with reported PrEP use systematically/often during intercourse: HIV incidence/100 PY, FTC/TDF vs placebo groups **0 vs 9.3 (*P* = .013)**[2]
- **PROUD:** randomized, open-label study of immediate vs deferred FTC/TDF PO QD PrEP for uninfected, high-risk MSM in England (N = 544)[3]
  - Current analysis: post deferred phase, in which all pts offered PrEP

HIV Incidence/100 PY (Infections/PY)[4]	Immediate PrEP	Deferred PrEP	*P* Value
Deferred phase (Yr 1)	1.6 (4/254)	9.4 (21/223)	NR
Post deferred phase (Yrs 2-4)	**1.2 (5/424)**	**0.3 (1/356)***	**.18**

*Significant difference in HIV incidence observed for deferred group pts in deferred vs post deferred phases (*P* < .0001).

1. Molina JM, et al. N Engl J Med. 2015;373:2237-2246. 2. Antoni G, et al. IAS 2017. Abstract TUAC0102.
3. McCormack S, et al. Lancet. 2016;387:53-60. 4. White E, et al. IAS 2017. Abstract TUAC0101.