HIV and COVID-19 in 2021 and beyond

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Disclosure

I have received conference travel grants from:

- Pfizer, Meiji, Siam, Mylan, MSD, Janssen

Speaker Bureau

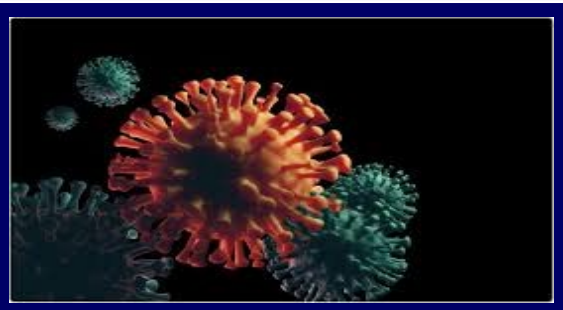
- Pfizer, Meiji, Mylan, Janssen, GSK, Zuellig Pharma

Outlines

- HIV and COVID-19 pandemics
- Interaction between HIV and SARS-CoV-2
- Clinical and treatment outcomes of COVID-19 among PLWH
- The impact of antiretroviral drugs
- COVID-19 and impact on HIV care
- COVID-19 vaccine for PLWH

HIV and COVID-19 pandemics

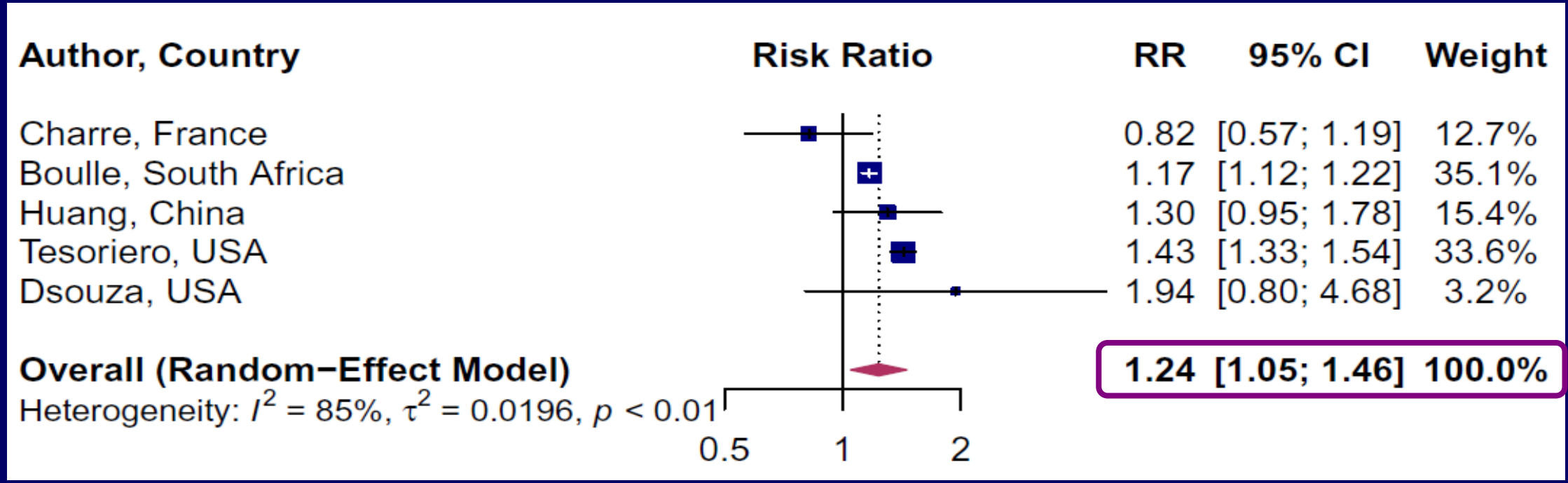
	HIV infection	COVID-19
Time emerged	April 1980	December 2019
Estimated total number of cases	80 million	204 million
Estimated annual new case	1.5 million	102 million
Estimated accumulated number of death	36 million	4 million
Estimated annual death	700,000	2 million
Sterile cure	?	Yes



UNAIDS 2021.
Worldometer 2021.

HIV and COVID-19 pandemics

- A systematic review and meta-analysis performed for published studies from January 1, 2020 to December 12, 2020.
- HIV-positive persons had a significantly higher risk of SARS-CoV-2 infection.



Ssentongo P, et al. Sci Rep 2021;11:6283.

HIV and COVID-19 pandemic

- The incidence rate of COVID-19 infection among PLWH differs by country.
- The US (0.8%) and Spain (1.8%) (based on PCR test)[1,2]
- China (0.68%) (based on both PCR and clinical diagnosis)[3]
- PLWH were more likely to be tested for COVID-19; HIV did not increase susceptibility to COVID-19, nor incidence of severe disease.[4]

COVID-19 Testing	PLWH	HIV-	OR (95% CI)*
Alive in 2020, n	30,981	76,745	--
Total tested, n (%)†	2599 (8.4)	4977 (6.5)	1.36 (1.29-1.43)
Total COVID-19+, n ▪ % of total alive	253 0.8	504 0.7	1.38 (1.18-1.61)

[1]Richardson S, et al. JAMA 2020;323:2052–9.
[2]Vizcarra P, et al. Lancet HIV 2020;7:e554–64.
[3]Guo W, et al. SSRN: China; 2020.
[4]AIDS 2020. Abstract LBPEC23.

Interaction between HIV and SARS-CoV-2

HIV infection	Potential outcome	COVID-19
CD4+ lymphopenia	Delayed SARS-CoV-2 clearance COVID-19 disease progression Risk for opportunistic infections	Lymphopenia (particularly CD4 lymphopenia)
Chronic inflammation induced prothrombotic conditions	Hypercoagulable state Thrombotic complications	Elevated levels of multiple proinflammatory cytokines

Gatechompol et al. AIDS Res Ther 2021;18:28.

Clinical presentations of COVID-19 in PLWH

Demographics

- Median age 40-60 years
- Men more than women
- Most of the PLWH with COVID-19 were on antiretroviral therapy and were virologically suppressed.
- High prevalence of comorbidities such as hypertension, diabetes and chronic kidney disease

Richardson S, et al. JAMA 2020;323:2052–9.
Guan WJ, et al. N Engl J Med 2020;382:1708–20.

Clinical presentations of COVID-19 in PLWH

Clinical manifestations

- The most common symptoms of COVID-19 detected were fever, cough or shortness of breath.
- The symptoms were similar to those reported in people without HIV.
- Most had mild to moderate severity of COVID-19.
- Risk factors for severe COVID-19 among PLWH were similar to those without HIV such as older age, obesity and comorbid medical conditions.

Ho HE, et al. J Infect Dis 2020;223:403–8.
Okoh AK, et al. J Acquir Immune Defic Syndr 2020;85:e4–5.
Shalev N, et al. Clin Infect Dis 2020;71:2294–7.
Suwanwongse K, et al. J Med Virol 2020;92:2387–9.

Clinical outcomes of COVID-19 in PLWH

Analysis of data from 39 US clinical centers in National COVID Cohort

Outcome	HIV-/SOT- (n = 501,416)	HIV+ Alone (n = 2932)	SOT+ Alone (n = 4633)	HIV+/SOT+ (n = 111)
Hospitalization, %	30.6	48.5	63.8	70.3
Invasive ventilation, %	1.9	5.5	9.9	≤ 20
Odds of hospitalization vs HIV-/SOT-				
▪ Adjusted OR estimate* (95% CI)	Ref	1.32 (1.22-1.43)	1.69 (1.58-1.81)	1.65 (1.06-2.56)
▪ *P* value		< .01	< .01	.03
	(n = 153,310)	**(n = 1421)**	**(n = 2956)**	**(n = 78)**
Odds of ventilation vs HIV-/SOT-				
▪ Adjusted OR estimate* (95% CI)	Ref	1.86 (1.56-2.22)	1.96 (1.74-2.12)	3.73 (2.08-6.67)
▪ *P* value		< .01	< .01	< .01

*Model adjusted for age, sex, race, ethnicity, study site, number of comorbidities.

CROI 2021 Abstract 103.

Clinical outcomes of COVID-19 in PLWH

Analysis of data from 39 US clinical centers in National COVID Cohort

- PLWH and SOT or both more likely to be hospitalized and receive mechanical ventilation with COVID-19
  - Increased risk of hospitalization independent of demographic factors in all groups

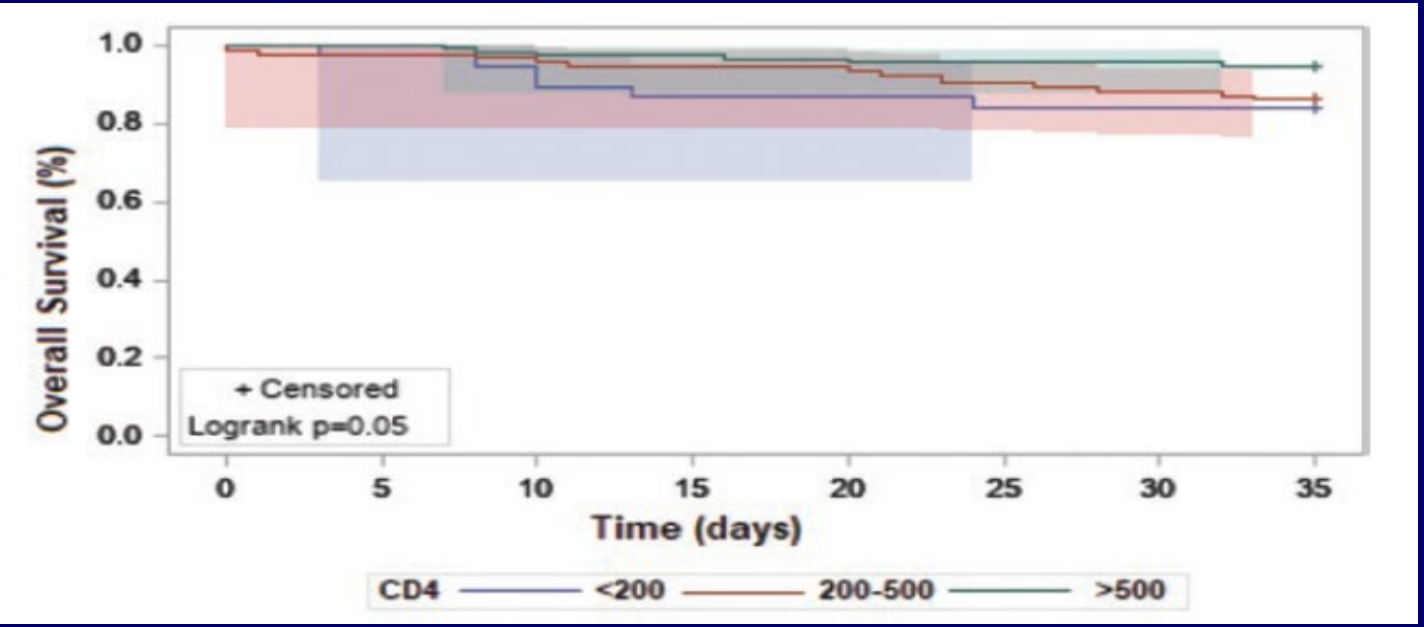
- Increased risk of hospitalization in immunosuppressed groups driven mainly by comorbid conditions
  - Higher odds of hospitalization in PLWH with history of cardiopulmonary (OR: 2.27; 95% CI: 1.58-3.26) and renal (OR: 2.28; 95% CI: 1.68-3.09) comorbidities

CROI 2021 Abstract 103.

Clinical outcomes of COVID-19 in PLWH

The study of 286 PLWH with COVID-19 from 36 US centers

- 94.3% on ART; 88.7% with HIV virologic suppression
- Older age, chronic lung disease, hypertension, and lower CD4+ counts associated with decreased survival
- No association between ART or lack of viral suppression and COVID-19 outcomes



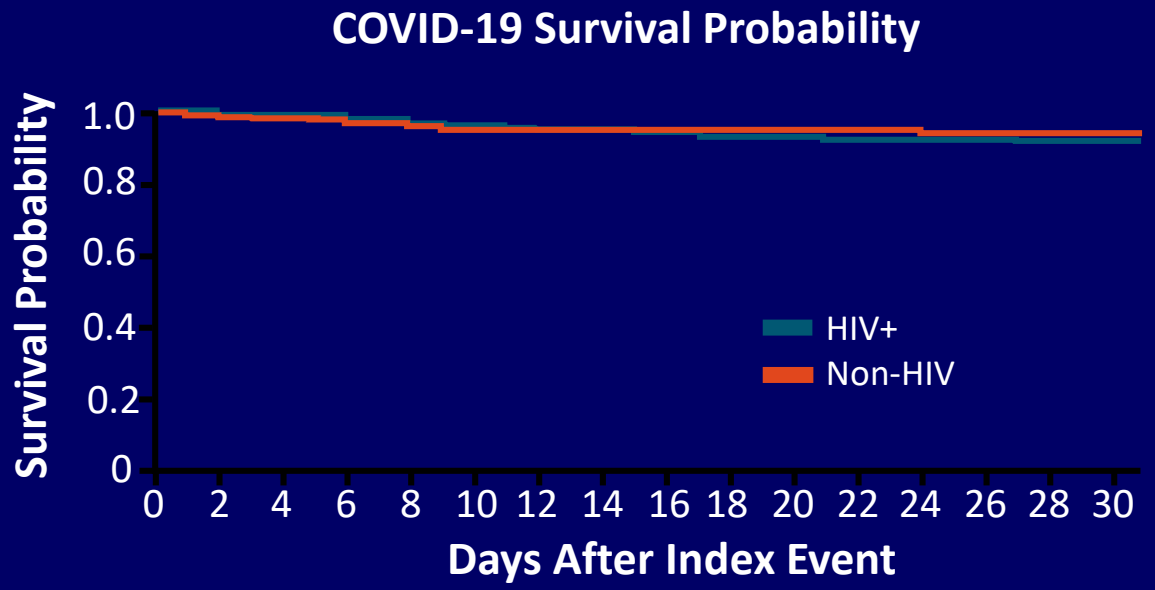
Dandachi D, et al. Clin Infect Dis 2020 Sep [Epub].

Clinical outcomes of COVID-19 in PLWH

Outcomes of COVID-19 in PLWH: Multicenter Research Network

- COVID-19–positive patients with HIV (n = 404) compared with a propensity-matched cohort of patients without HIV (n = 49,763)

- After 1:1 matching (BMI, diabetes, hypertension, chronic lung diseases, chronic kidney disease, race, history of nicotine dependence and sex), mortality no longer significantly different with vs. without HIV (risk ratio: 1.33; 95% CI: 0.69-2.57).



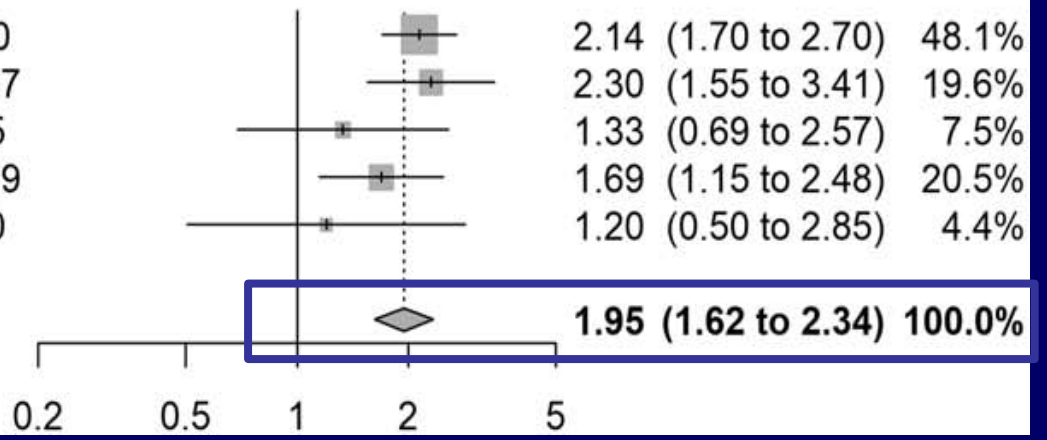
Hadi YB, et al. AIDS 2020;34:F3-F8.

Clinical outcomes of COVID-19 in PLWH

Meta-analysis of studies describing COVID-19 outcomes in PLWH

Study	Country	HIV+ N	HIV+ C19 Death	HIV- N	HIV- C19 Death	HR	95%-CI	Weight
Boulle	ZA	540552	3978 115	2920380	18330 510	2.14	(1.70 to 2.70)	48.1%
Bhaskaran	UK	27480	n/a 25	17282905	n/a 14857	2.30	(1.55 to 3.41)	19.6%
Hadi	US	n/a	404 20	n/a	404 15	1.33	(0.69 to 2.57)	7.5%
Geretti	UK	n/a	122 30	n/a	47470 13969	1.69	(1.15 to 2.48)	20.5%
Karmen-Tuohy	US	n/a	21 6	n/a	42 10	1.20	(0.50 to 2.85)	4.4%
Random effects model						**1.95**	**(1.62 to 2.34)**	**100.0%**

Heterogeneity: I^2 = 8%, τ^2 = 0.0042, p = 0.36



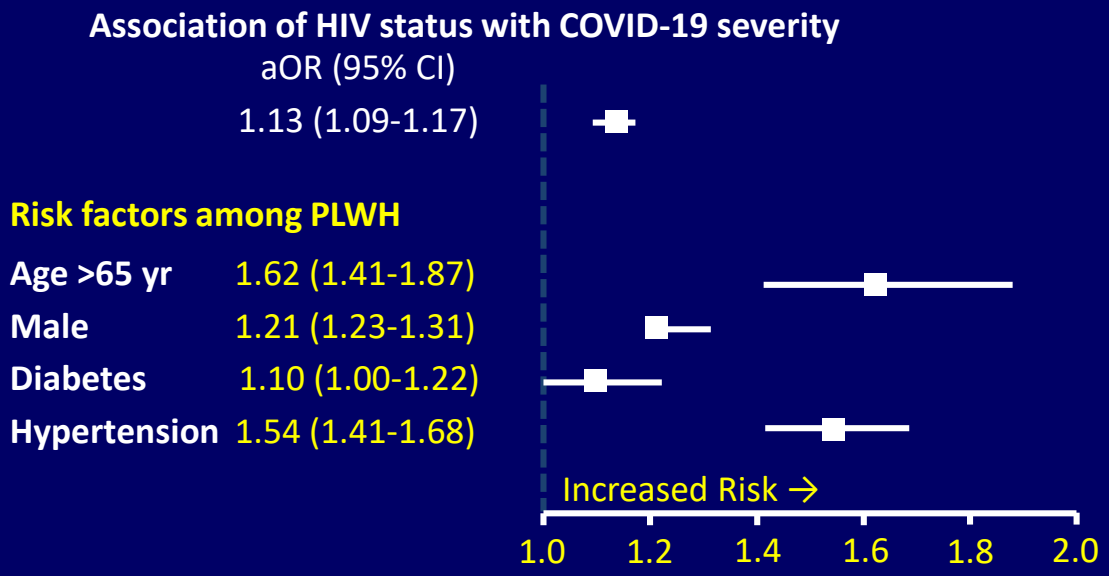
- Risk of death remained elevated for PLWH in a subgroup analysis of hospitalized cohorts (hazard ratio 1.60, 95%CI: 1.12–2.27)
- There were insufficient data on the effect of CD4+ T-cell count and HIV viral load on COVID-19 outcomes.

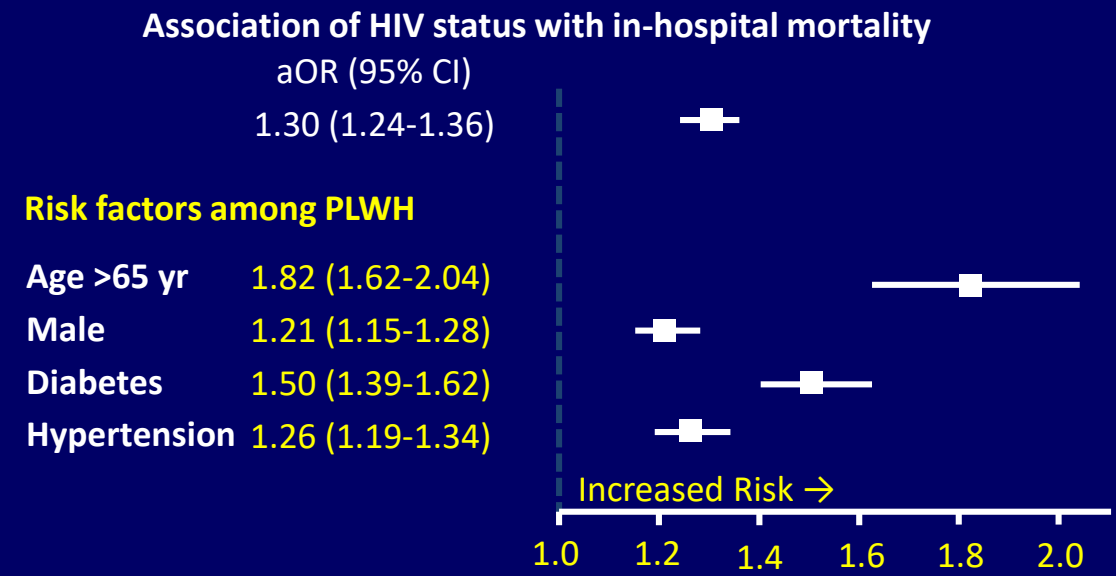
Mellor MM, et al. AIDS 2021;35:F1–F10.

Clinical outcomes of COVID-19 in PLWH

Data from WHO Global Clinical Platform for COVID-19 2020-2021

- 168,649 patients from 24 countries with known HIV status hospitalized with suspected or confirmed COVID-19
- 15,552 (9.2%) with HIV infection; information on ART available for 40% of PLWH
- Among PLWH: mean age 45.5 yr, 37.1% male, 94.6% from South Africa





Bertagnolio. IAS HIV Science 2021. Abstr PEBLB20

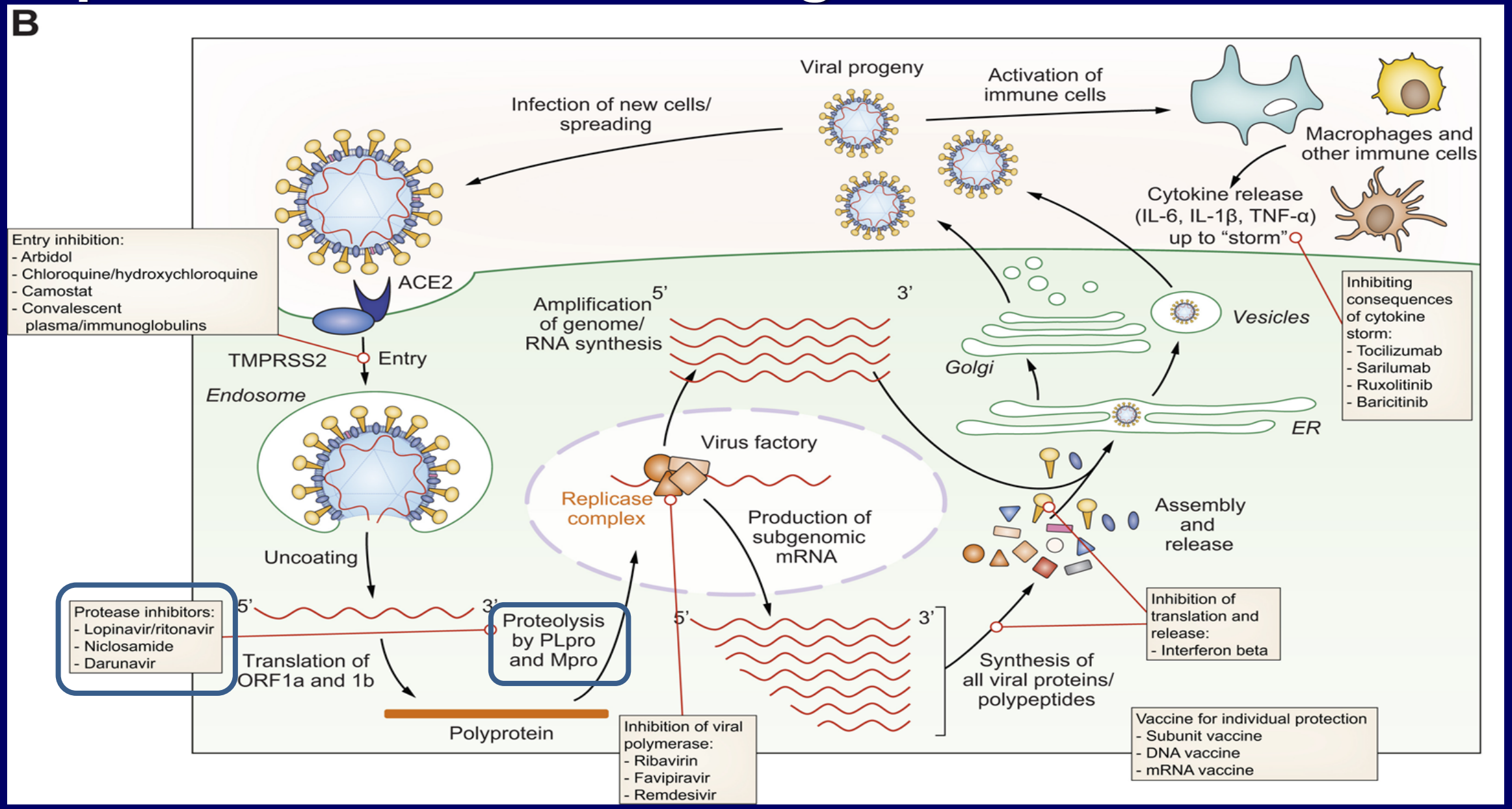
Slide credit: clinicaloptions.com

Clinical outcomes of COVID-19 in PLWH

CDC and NIH guidance summary

- Older adults and those with underlying medical conditions are at highest risk of life-threatening COVID-19.
- PLWH not receiving effective ART or with low CD4+ cell counts may also be at increased risk for severe disease.
- Recommendations for treatment in PWH are the same as those for the general population.
- In persons with advanced HIV and suspected or documented COVID-19, HIV-associated OIs should be considered in the differential diagnosis of febrile illness.
- Pay attention to potential DDIs and overlapping toxicities among COVID-19 treatments, ARV medications, and other co-medications

Impact of antiretroviral drugs



Asselah T, et al. J Hepatol 2021;74:168-184.

Impact of antiretroviral drugs

Lopinavir/ritonavir

- Lopinavir-ritonavir has been shown to have in vitro antiviral activity against beta-coronaviruses such as SARS-CoV, and MERS-CoV.
- Several observational studies and case reports demonstrated that the clinical benefit of LPV/r among COVID-19 patients was inconclusive.
- Three RCTs demonstrated lack of clinical benefits of LPV/r.

IDSA guidelines 2021.
Gatechompol et al. AIDS Res Ther 2021;18:28.
Cao B, et al. N Engl J Med 2020;382:1787–99.
Horby PW, et al. Lancet 2020;396:1345–52.
Pan H, et al. N Engl J Med 2021;384:497–511.

Impact of antiretroviral drugs

Lopinavir/ritonavir (cont.)

- Patients receiving LPV/r had a shorter stay in the ICU than those receiving standard of care (-5 days; CI [-9 – 0]).

Darunavir/ritonavir

- No in-vitro activity against SARS-CoV-2
- PLWH receiving a darunavir-containing regimen were not protected from COVID-19 in a case series.

IDSA guidelines 2021.
Cao B, et al. N Engl J Med 2020;382:1787-99.
Riva A, et al. Pharmacol Res 2020;157:104826.

Impact of antiretroviral drugs

Thai guidelines 2021

ฉบับปรับปรุง วันที่ 4 สิงหาคม พ.ศ. 2564 สำหรับแพทย์และบุคลากรสาธารณสุข

แนวทางเวชปฏิบัติ การวินิจฉัย ดูแลรักษา และป้องกันการติดเชื้อในโรงพยาบาล กรณีโรคติดเชื้อไวรัสโคโรนา 2019 (COVID-19)

7. ข้อมูลการศึกษา boosted lopinavir/ritonavir (LPV/r) ส่วนใหญ่ที่ทำในต่างประเทศ มีผู้ป่วยในการศึกษาจำนวนมาก ให้ผลตรงกันว่ายานี้มีประโยชน์ไม่ชัดเจนในการลดอัตราการตาย แต่ช่วยลดระยะเวลาที่อยู่ในหอผู้ป่วยวิกฤตได้ และไม่มีข้อมูลเกี่ยวกับ darunavir/ritonavir มากพอ

Impact of antiretroviral drugs

Tenofovir

- Has in-vitro activity against SARS-CoV-2
- A prospective cohort in Spain observed a higher rate of COVID-19 infection among PLWH on TAF or TDF.
- A case series demonstrated that tenofovir-based ART did not provide any clinical benefit against COVID-19 among PLWH.
- PREVENIR/Sapris-Sero Substudy: IgG Spike Seroprevalence suggests that TDF/FTC PrEP does not reduce risk of SARS-CoV-2 infection.

Gatechompol et al. AIDS Res Ther 2021;18:28.
Vizcarra P, et al. Lancet HIV 2020;7:e554–64.
Shalev N, et al. Clin Infect Dis 2020;71:2294–7.
Byrd KM, et al. J Int AIDS Soc 2020;23:e25573.
Delaugerre, et al. IAS HIV Science 2021. Abstr OAC0201.

COVID-19 and impact on HIV care

Risk of care interruption, especially ART interruption

- Affecting 17.7 million people receiving ART
- 10% increase in deaths among PLWH in low- and middle-income countries over 5 years
- Strict quarantine measures and transportation lock downs
- Shortage of ART
- Diversion of HIV care to COVID-19 care among HCWs

WHO. Disruption in HIV, Hepatitis and STI services due to COVID-19 2020.
Gatechompol et al. AIDS Res Ther 2021;18:28.

COVID-19 and impact on HIV care

Impact beyond HIV care

- Emergency services
- Urgent blood transfusions
- Routine immunization
- Dental services
- Rehabilitation services
- Non-communicable disease care
- Family planning
- Surgery
- Sexually-transmitted infection diagnosis and treatment

WHO. Disruption in HIV, Hepatitis and STI services due to COVID-19 2020.

COVID-19 and impact on HIV care

Strategies to mitigate care disruptions

- ARV multi-month dispensing policy
- Telemedicine platforms
- Toll-free hotlines
- Community sample collection and community ART deliveries
- Triaging to identify priorities
- Task shifting
- Strategies to maintain HCWs' physical and mental health
- Redirecting patients to other facilities

WHO. Disruption in HIV, Hepatitis and STI services due to COVID-19 2020.
Gatechompol et al. AIDS Res Ther 2021;18:28.

COVID-19 vaccine for PLWH

The 4 available types of COVID-19 vaccine

Whole virus
Inactivated virus

Sinopharm
BBIBP-CorV

SinoVac
CoronaVac

Bharat Biotech
Covaxin

Protein subunit
Virus-like particles

Novavax
NVX – Cov2373

Nucleic acid
Encapsulated mRNA

Moderna
mRNA – 1273

BioNTech/Pfizer
BNT162b2

Viral vector

Oxford/AstraZeneca
ChAdOx1/AZD222
(Covidshield)

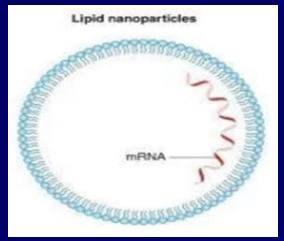
Johnson & Johnson
JNJ-78436735/Ad26.Cov2S

Gamaleya (Sputnik)
Sputnik V/Gam-Covid-Vac

Zembe L, UNAIDS 2021.

COVID-19 vaccine for PLWH

COVID-19 mRNA vaccine efficacy trials that recruited PLWH



- Pfizer study recruited at 196 people with stable HIV infection
  - Whole study VE of 95% (symptomatic infection)
  - Safety/efficacy results for PLWH not included in primary analysis

- Moderna study recruited 176 people with HIV infection
  - Whole study VE 0f 94% (symptomatic infection)
  - Efficacy in PLWH: 0 cases in vaccine group (n = 80) and 1 case in placebo group (n = 76); No safety concerns

Zembe L, UNAIDS 2021.
Polack FP, et al. N Engl J Med 2020;383:2603-15.
Baden LR, et al. N Engl J Med 2021;384:403-16.

COVID-19 vaccine for PLWH

COVID-19 viral vector vaccine efficacy trials that recruited PLWH

- Oxford/AstraZeneca studies recruited 160 people with HIV infection in the UK and South Africa
  - Whole study VE of 70% (symptomatic infection)
  - Safety/efficacy results for PLWH not reported in the article

- Janssen (Johnson & Johnson) vaccine study recruited 1218 people with HIV infection (2.8% of all participants)
  - Whole study VE of 66% (symptomatic infection)
  - 2 cases of COVID 19 in the vaccine and 4 in the placebo recipients; No safety concerns

Zembe L, UNAIDS 2021.
Voysey M, et al. Lancet 2021;397:99-111.
Sadoff J, et al. N Engl J Med 2021;384:1824-35.

COVID-19 vaccine for PLWH

COVID-19 subunit vaccine efficacy trials that recruited PLWH

- Novavax vaccine study against the B.1.351 Variant in South Africa
  - Whole study VE of 60% (symptomatic infection)
  - Included 148 PLWH
  - Covid-19 was observed in 4 of 76 participants in the vaccine group and in 2 of 72 participants in the placebo group.
  - No safety concerns

Shinde B, et al. N Engl J Med 2021;384:1899-909.

COVID-19 vaccine for PLWH

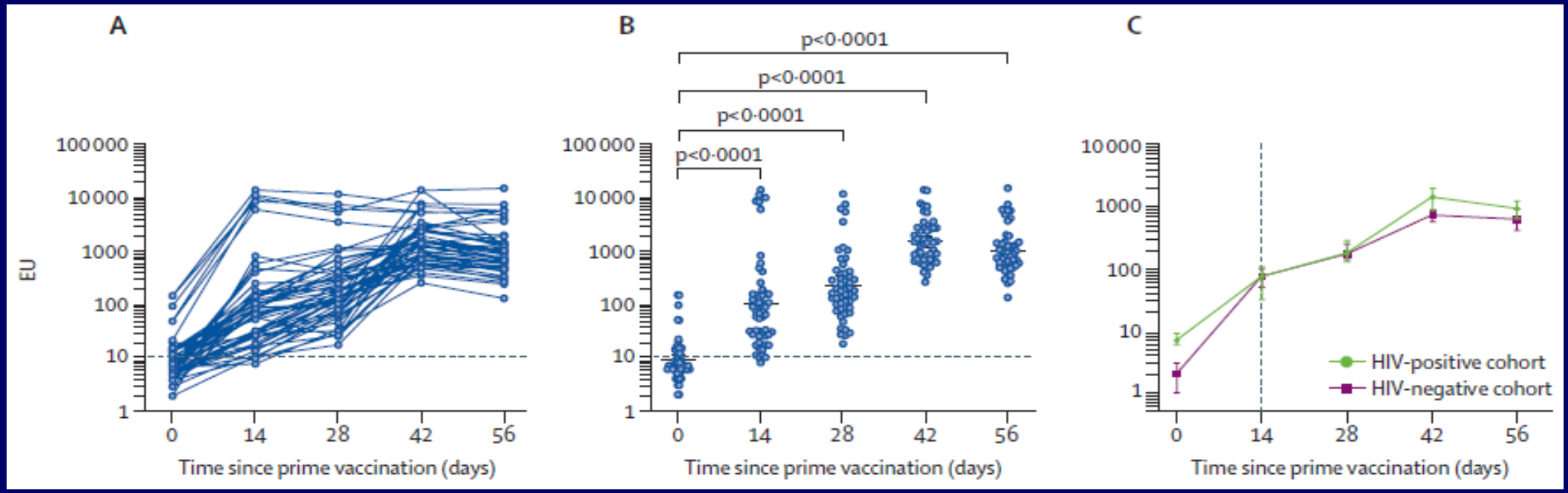
COVID-19 viral vector vaccine efficacy trials that recruited PLWH

- **Safety and immunogenicity of the ChAdOx1 nCoV-19 (AZD1222) vaccine in PLWH**
  - **Single-arm open-label vaccination substudy within the protocol of the larger phase 2/3 trial COV002**
  - **Eligible participants were required to be on antiretroviral therapy (ART), with undetectable plasma HIV viral load (<50 copies per mL), and CD4 counts of more than 350 cells per µL.**
  - **54 participants with HIV (all male, median age 42.5 years [IQR 37.2–49.8])**

Frater J, et al. Lancet HIV 2021 June [Epub].

COVID-19 vaccine for PLWH

- **Safety and immunogenicity of the ChAdOx1 nCoV-19 (AZD1222) vaccine in PLWH**
  - **Similar rates of local and systemic reactions as HIV-negative participants**
  - **No correlation between anti-spike IgG response at day 56 and CD4 cell count or age.**



Frater J, et al. Lancet HIV 2021 June [Epub].

COVID-19 vaccine for PLWH

Points to consider

- The available data so far are limited
- Unknown the effect size of low CD4 cell count or high HIV VL
- HIV affects T cell responses more than B cell responses.
- All currently available COVID 19 vaccines contain some of the genetic material from SARS-CoV-2 but not the whole live virus.
- There is no reason to think these vaccines will be less safe for people with HIV.

Zembe L, UNAIDS 2021.

COVID-19 vaccine for PLWH

แนวทางการฉีดวัคซีนโควิด-19 ในผู้ติดเชื้อเอชไอวี

จัดทำโดย : กองโรคเอดส์และโรคติดต่อทางเพศสัมพันธ์ กรมควบคุมโรค

วันที่ 1 มิถุนายน 2564

ผู้ติดเชื้อเอชไอวีเป็นกลุ่มผู้มีภาวะภูมิคุ้มกันบกพร่องซึ่งเสี่ยงต่อการติดเชื้อโควิด-19 และเกิดอาการของการติดเชื้อโควิด-19 รุนแรงได้ ผลงานวิจัยต่างๆ พบว่าในผู้ที่มี CD4 < 350 cells/mm^3 จะเกิดอาการรุนแรงเมื่อติดเชื้อโควิด-19 มากกว่าผู้ที่มี CD4 สูง ถึง 3 เท่า ดังนั้นผู้ติดเชื้อเอชไอวี จึงควรได้รับการฉีดวัคซีนเพื่อป้องกันอาการรุนแรงจากการติดเชื้อโควิด-19 [1] [2]

ผู้ที่สามารถฉีดวัคซีนโควิด-19 ได้ [1] [2]

- ผู้ติดเชื้อเอชไอวีทุกรายสามารถเข้ารับบริการฉีดวัคซีนได้โดยไม่ต้องคำนึงถึงระดับ CD4 หรือปริมาณไวรัสในเลือด
- ในผู้ที่มีระดับ CD4 < 200 cells/mm^3 หรือ มีปริมาณไวรัสในเลือดสูง ควรได้รับการพิจารณาเข้ารับบริการฉีดวัคซีนก่อน แต่ควรให้แพทย์ผู้ดูแลรักษาเป็นผู้พิจารณาอาการแสดงทางคลินิก ณ ขณะนั้นของผู้ติดเชื้อว่าจะสามารถฉีดวัคซีนได้หรือไม่

วัคซีนโควิด-19 ที่ผู้ติดเชื้อสามารถใช้ได้ [3]

ในปัจจุบันมีวัคซีนโควิด-19 ที่ผลิตจากหลายบริษัท มีกรรมวิธีการผลิตที่แตกต่างกัน ซึ่งวัคซีนโควิด-19 ที่เข้ามาในประเทศไทยทุกชนิดสามารถใช้ได้กับผู้ติดเชื้อเอชไอวี ได้แก่ Sinovac, AstraZeneca, Pfizer, Moderna, Johnson&Johnson เป็นต้น โดยยังไม่มีรายงานการเกิดปฏิกิริยาระหว่างวัคซีนโควิด-19 กับยาต้านไวรัสเอชไอวีที่ผู้ติดเชื้อรับประทานอยู่เป็นประจำ


คณะแพทยศาสตร์ มหาวิทยาลัยธรรมศาสตร์
Q&A
Thai AIDS Society
TAS
มหาวิทยาลัยธรรมศาสตร์
THAMMASAT UNIVERSITY
คณะแพทยศาสตร์
30th
MOVE
ANNIVERSARY
FACULTY OF MEDICINE
THAMMASAT UNIVERSITY