

7. Spitzer A, Angel Y, Marudi O, Zeltser D, Saiag E, Goldshmidt H, et al. Association of a third dose of BNT162b2 vaccine with incidence of SARS-CoV-2 infection among health care workers in Israel. *JAMA*. 2022;327:341–9. <https://doi.org/10.1001/jama.2021.23641>
8. Abu-Raddad LJ, Chemaitelly H, Ayoub HH, AlMukdad S, Yassine HM, Al-Khatib HA, et al. Effect of mRNA vaccine boosters against SARS-CoV-2 Omicron infection in Qatar. *N Engl J Med*. 2022;386:1804–16. <https://doi.org/10.1056/NEJMoa2200797>
9. Su W, Wang H, Sun C, Li N, Guo X, Song Q, et al. The association between previous influenza vaccination and COVID-19 infection risk and severity: a systematic review and meta-analysis. *Am J Prev Med*. 2022;63:121–30. <https://doi.org/10.1016/j.amepre.2022.02.008>
10. Laing ED, Weiss CD, Samuels EC, Coggins SA, Wang W, Wang R, et al. Durability of antibody response and frequency of SARS-CoV-2 infection 6 months after COVID-19 vaccination in healthcare workers. *Emerg Infect Dis*. 2022;28:828–32. <https://doi.org/10.3201/eid2804.212037>

Address for correspondence: Chun-Hsien Yu, Department of Pediatrics, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, 289 Jianguo Rd, Xindian District, New Taipei City 23142, Taiwan; email: chryu@mail.tcu.edu.tw

## Three-Dose Primary Series of Inactivated COVID-19 Vaccine for Persons Living with HIV, Hong Kong

Denise Pui Chung Chan, Ngai Sze Wong, Bonnie C.K. Wong, Jacky M.C. Chan, Shui Shan Lee

Author affiliations: The Chinese University of Hong Kong, Hong Kong, China (D.P.C. Chan, N.S. Wong, S.S. Lee); Department of Health, Hong Kong (B.C.K. Wong); Princess Margaret Hospital, Hong Kong (J.M.C. Chan)

DOI: <https://doi.org/10.3201/eid2810.220691>

In a cohort of persons living with HIV in Hong Kong, surrogate virus neutralization testing for COVID-19 yielded a median level of 89% after the third dose of an inactivated COVID-19 vaccine, compared with 37% after the second dose. These results support using a 3-dose primary series for enhanced immune protection.

Worldwide, inactivated vaccines are most widely used to prevent SARS-CoV-2 infection and severe COVID-19 disease (1). Vaccination effectiveness is of particular importance for protecting persons at increased risk for severe diseases, notably immunocompromised patients, including persons living with HIV (PLHIV). As recently reported in a prospective study in Brazil (2), immunogenicity of inactivated vaccine is lower in PLHIV than in healthy adults. This lower protection is a cause for concern, especially in populations with high burden of HIV/AIDS and COVID-19. In Hong Kong, both inactivated and mRNA vaccines are available free for all eligible healthy and immunocompromised citizens. Immunocompromised persons have been prioritized for receiving a third, booster, dose, 3 months after completion of a 2-dose series of any COVID-19 vaccine. In a real-world study conducted prospectively on PLHIV in Hong Kong, we measured vaccine immunogenicity by the surrogate virus neutralization test (sVNT) to compare the responses after completion of 2 versus 3 doses of CoronaVac (Sinovac, <https://www.sinovac.com>), the same inactivated vaccine used in the Brazil study (2). Based on antibody-mediated blockage of ACE2-spike receptor binding domain (RBD) interaction, the sVNT results were used to assess the amplitude of neutralizing antibody responses against SARS-CoV-2 (3,4).

During April 2021–March 2022, a total of 122 PLHIV who had received CoronaVac were enrolled at 2 major HIV specialist clinics providing comprehensive HIV care, including antiretroviral therapy, in Hong Kong. Participants provided informed consent. We measured sVNT after completion of 2 or 3 doses of CoronaVac, in addition to transcribing demographic and clinical data collected during routine clinical follow-up appointments (Appendix, <https://wwwnc.cdc.gov/EID/article/28/10/22-0691-App1.pdf>). The median age of recruited PLHIV was 49 (IQR 40–56.5) years of age; most (86%) were male, all were receiving antiretroviral therapy, and the median latest CD4 count was 564.5/ $\mu$ L (IQR 394–733/ $\mu$ L) (Appendix Table 1). We included in the analyses a total of 132 sVNT measurements made within 90 days (median 48 days, IQR 24–70 days) of the second and within 90 days (median 33 days, IQR 28–53 days) of the third dose. We expressed results as percentage inhibition, using a cutoff of 30% for positive neutralizing response.

The median sVNT level was 37% (IQR 24%–53%); 64% of participants tested positive (sVNT  $\geq$ 30%) after the second dose. After the third dose, the median sVNT rose to 89% (IQR 58%–95%; Mann-Whitney U = 648.5;

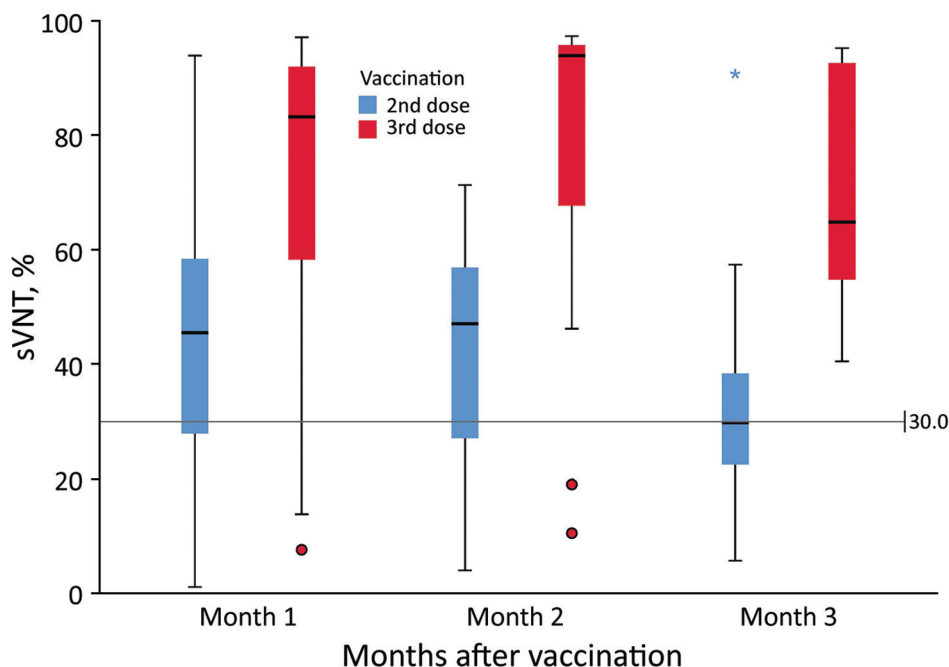
$p < 0.001$ ), paralleling a significantly higher percentage with sVNT positivity (91%; OR 5.67, 95% CI 1.86–17.33) (Figure). In multivariable linear regression, third-dose vaccination ( $B = 33.61$ ;  $p < 0.001$ ), days past respective dose ( $B = -0.17$ ;  $p = 0.047$ ), and latest CD4 count ( $B = 0.02$ ;  $p = 0.02$ ) were significant factors associated with high sVNT, whereas viral load suppression ( $< 200$ /mL) and age were not significant (Appendix Table 2).

Our immunogenicity results on the completion of a 2-dose schedule of CoronaVac in PLHIV were remarkably similar to those reported in Brazil (2). After 2 doses of CoronaVac, 28 PLHIV in Hong Kong had a median sVNT of 48% (IQR 30%–58%) after 27–55 days, compared with median sVNT of 46.2% (IQR 26.9%–69.7%) in Brazil after 41 days. The corresponding proportion of PLHIV with sVNT positivity ( $\geq 30\%$ ) was 79% after 27–55 days in our study and 71% after 41 days in the Brazil study.

Although effectiveness of inactivated COVID-19 vaccines has previously been shown in PLHIV (5), their moderate efficacy and waning immunogenicity after a standard 2-dose schedule pose challenges in developing vaccination strategy (1). Recent studies have demonstrated effectiveness and safety of 3 doses of inactivated COVID-19 vaccine in healthy adults (6). In this study, we have shown a stronger sVNT response after the third dose than the second dose, as has been reported for inactivated vaccines in healthy adults, including elderly persons (6,7). Our results provide data support for the effectiveness of a 3-dose primary series

of inactivated COVID-19 vaccine for all vaccinees, including PLHIV and immunocompromised hosts.

The anticipated suboptimal clinical outcome for PLHIV after COVID-19 has been shown in population-level studies (8) that called for prioritizing PLHIV for vaccination. With a high proportion of the global population receiving inactivated COVID-19 vaccines, we note a need to strategically adjust the regimen to attain a sustained and enhanced response in PLHIV. Routine administration of a 3-dose primary series of inactivated vaccines is a possible approach for reducing virus transmission and associated severe disease in healthy adults and PLHIV alike, as highlighted in guidance from the World Health Organization Strategic Advisory Group of Experts on Immunization ([https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE\\_recommendation-Sinovac-CoronaVac-2021.1](https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-Sinovac-CoronaVac-2021.1)) and the Centers for Disease Control and Prevention (<https://www.cdc.gov/hiv/basics/covid-19.html>). Recent studies have shown that the effectiveness of current COVID-19 vaccines against new variants, such as Omicron, could be reduced; immunogenicity was lower after 2 doses of inactivated vaccines than of mRNA vaccines (9). Further research is needed as the COVID-19 pandemic continues to evolve; in particular, the ongoing Ubuntu trial (<https://www.coronaviruspreventionnetwork.org>) may provide evidence for enhancing vaccination strategy for PLHIV amid the emergence of new variants.



**Figure.** Distribution of sVNT by month after second and third doses of CoronaVac vaccine (Sinovac, <https://www.sinovac.com>) among persons living with HIV, Hong Kong. Horizontal lines inside boxes indicate medians, box tops and bottoms indicate 25th and 75th percentiles, and error bars indicate high and low values excluding outliers. Blue asterisk and red dots indicate outliers. Gray line indicates cutoff of 30% for positive neutralizing response. sVNT, surrogate virus neutralization test.

## Acknowledgments

We thank the clinical team for assistance in recruitment, blood sampling, and data management. We thank Eric Poon and Samantha So for laboratory assistance.

This work was supported by Health and Medical Research Fund Commissioned Research on the Novel Coronavirus Disease (grant COVID1903008-Project A) and Council for the AIDS Trust Fund (grant MSS358R).

## About the Author

Dr. Chan is a research fellow at the Chinese University of Hong Kong, Hong Kong, China. Her research interests include emerging viral infections and vaccine studies.

## References

1. Mallapaty S. China's COVID vaccines have been crucial – now immunity is waning. *Nature*. 2021;598:398–9. <https://doi.org/10.1038/d41586-021-02796-w>
2. Netto LC, Ibrahim KY, Picone CM, Alves APPS, Aniceto EV, Santiago MR, et al. Safety and immunogenicity of CoronaVac in people living with HIV: a prospective cohort study. *Lancet HIV*. 2022; 9:e323–31. [https://doi.org/10.1016/S2352-3018\(22\)00033-9](https://doi.org/10.1016/S2352-3018(22)00033-9)
3. Tan CW, Chia WN, Qin X, Liu P, Chen MI, Tiu C, et al. A SARS-CoV-2 surrogate virus neutralization test based on antibody-mediated blockage of ACE2-spike protein-protein interaction. *Nat Biotechnol*. 2020;38:1073–8. <https://doi.org/10.1038/s41587-020-0631-z>
4. Wong NS, Wong BCK, Chan JMC, Wong KH, Tsang OTY, Mok CKP, et al. Surrogate neutralization responses following severe acute respiratory syndrome coronavirus 2 vaccination in people with HIV: comparison between inactivated and mRNA vaccine. *AIDS*. 2022;36:1255–64. <https://doi.org/10.1097/QAD.0000000000003237>
5. Feng Y, Zhang Y, He Z, Huang H, Tian X, Wang G, et al. Immunogenicity of an inactivated SARS-CoV-2 vaccine in people living with HIV-1: a non-randomized cohort study. *EClinicalMedicine*. 2022;43:101226. <https://doi.org/10.1016/j.eclinm.2021.101226>
6. Zeng G, Wu Q, Pan H, Li M, Yang J, Wang L, et al. Immunogenicity and safety of a third dose of CoronaVac, and immune persistence of a two-dose schedule, in healthy adults: interim results from two single-centre, double-blind, randomised, placebo-controlled phase 2 clinical trials. *Lancet Infect Dis*. 2022;22:483–95. [https://doi.org/10.1016/S1473-3099\(21\)00681-2](https://doi.org/10.1016/S1473-3099(21)00681-2)
7. Liang XM, Xu QY, Jia ZJ, Wu MJ, Liu YY, Lin LR, et al. A third dose of an inactivated vaccine dramatically increased the levels and decay times of anti-SARS-CoV-2 antibodies, but disappointingly declined again: a prospective, longitudinal, cohort study at 18 serial time points over 368 days. *Front Immunol*. 2022;13:876037. <https://doi.org/10.3389/fimmu.2022.876037>
8. Boffito M, Waters L. More evidence for worse COVID-19 outcomes in people with HIV. *Lancet HIV*. 2021;8:e661–2. [https://doi.org/10.1016/S2352-3018\(21\)00272-1](https://doi.org/10.1016/S2352-3018(21)00272-1)
9. Cheng SMS, Mok CKP, Leung YWY, Ng SS, Chan KCK, Ko FW, et al. Neutralizing antibodies against the SARS-CoV-2 Omicron variant BA.1 following homologous and heterologous CoronaVac or BNT162b2 vaccination. *Nat Med*. 2022;28:486–9. <https://doi.org/10.1038/s41591-022-01704-7>

Address for correspondence: Shui Shan Lee, Stanley Ho Centre for Emerging Infectious Diseases, Postgraduate Education Centre, Prince of Wales Hospital, Shatin, Hong Kong, China; email: sslee@cuhk.edu.hk

## Rickettsial Infections Causing Acute Febrile Illness in Urban Slums, Brazil

John B. Fournier,<sup>1</sup> Lucas S. Blanton,<sup>1</sup> Nivison Nery Jr., Elsie A. Wunder Jr., Federico Costa, Mitermayer G. Reis, Guilherme S. Ribeiro, David H. Walker, Albert I. Ko

Author affiliations: Yale School of Public Health, New Haven, Connecticut, USA (J.B. Fournier, E.A. Wunder Jr., F. Costa, M.G. Reis, A.I. Ko); University of Texas Medical Branch, Galveston, Texas, USA (L.S. Blanton, D.H. Walker); Fundação Oswaldo Cruz, Salvador, Brazil (N. Nery Jr., F. Costa, M.G. Reis, G.S. Ribeiro, A.I. Ko); Universidade Federal da Bahia, Salvador (N. Nery Jr., F. Costa, M.G. Reis, G.S. Ribeiro)

DOI: <https://doi.org/10.3201/eid2810.220497>

We conducted enhanced acute febrile illness surveillance in an urban slum community in Salvador, Brazil. We found that rickettsial infection accounted for 3.5% of urgent care visits for acute fever. Our results suggest that rickettsiae might be an underrecognized, treatable cause of acute febrile illness in impoverished urban populations in Brazil.

*Rickettsia* spp. are small, obligately intracellular, gram-negative bacilli. The genus includes the spotted fever group rickettsiae (SFGR) and typhus group rickettsiae (TGR). SFGR and TGR are underrecognized causes of acute febrile illness (AFI) worldwide, particularly in the tropics, because clinical manifestations of rickettsial infections are often indistinguishable from those of other endemic infections (1). Recent studies have suggested that SFGR profiles in Brazil might be shifting toward

<sup>1</sup>These authors contributed equally to this article.

# Three-Dose Primary Series of Inactivated COVID-19 Vaccine for Persons Living with HIV, Hong Kong

## Appendix

### Data Analysis

This is a prospective study with subject recruitment at two out of three major public HIV specialist clinics in Hong Kong. PLHIV aged 18 or above attending either clinic, receive at least two doses of CoronaVac, at least one sample collected within 90 days from either the second or third dose, and not diagnosed with COVID-19 before blood sampling were included in this study. The sVNT level within 90 days following the second dose was compared with the third dose by Mann-Whitney U test, while difference of neutralizing antibody positivity (sVNT  $\geq 30\%$ ) in the two time points was compared in the univariable logistic regression model. The association between each independent factor and sVNT level was examined in univariable linear regression, and the factors significantly associated with sVNT level were included in the multivariable linear regression. All statistical analyses were performed in SPSS Statistics 25 (<https://www.ibm.com/products/spss-statistics>). Complete case analysis was performed.

**Appendix Table 1.** Characteristics of PLHIV receiving CoronaVac inactivated vaccine, Hong Kong

Characteristic	n (%)
Sex, n = 116	
F	16 (14)
M	100 (86)
Median age (IQR), n = 117	49 (40–56.5)
Median nadir/baseline CD4, cells/ $\mu$ L (IQR), n = 99	203 (54–338)
Median latest CD4, cells/ $\mu$ L (IQR), n = 100	564.5 (394–733)
Latest viral load status, n = 100	
$\geq 200$ copies/mL	4 (4)
$< 200$ copies/mL	96 (96)
On antiretroviral therapy at blood sampling	
No	0 (0)
Yes	122 (100)

\*Values are no. (%) except as indicated. IQR, interquartile range; PLHIV, persons living with HIV.

**Appendix Table 2.** Factors associated with sVNT level in study of PLHIV receiving CoronaVac inactivated vaccine, Hong Kong\*

Characteristic	Univariable linear regression			Multivariable linear regression		
	B	Beta	p value	B	Beta	p value
Male sex (female coded as 0)	-3.12	-0.04	0.65	/		
Age at sampling (year-old)	0.27	0.11	0.21	/		
Third dose vaccination (second dose vaccination coded as 0)	34.11	0.58	<0.001†	33.61	0.546	<0.001†
Days from respective dose	-0.24	-0.21	0.01†	-0.17	-0.156	0.047†
Latest CD4 count (cells/ $\mu$ L)	0.02	0.20	0.04†	0.02	0.182	0.02†
Viral load suppression (<200/mL) (viral load $\geq$ 200/mL coded as 0)	16.89	0.12	0.22	/		
Constant (for multivariable linear regression)	/			38.47		<0.001†

\*B, unstandardized coefficients; Beta, standardized coefficients.

†p<0.05