

# THE LANCET Microbe

## **Supplementary appendix 1**

This appendix formed part of the original submission and has been peer reviewed.  
We post it as supplied by the authors.

Supplement to: Acevedo-Rodriguez JG, Zamudio C, Kojima N, et al. Influenza incidence, lineages, and vaccine effectiveness estimates in Lima, Peru, 2023. *Lancet Microbe* 2024. [https://doi.org/10.1016/S2666-5247\(23\)00392-0](https://doi.org/10.1016/S2666-5247(23)00392-0)

## Supplemental Materials

### Vaccination status

The Peruvian scheme for influenza vaccination considers one seasonal (annual) dose for subjects older than 1 year; for children < 1 year, the recommendation is two doses at the 6<sup>th</sup> and 7<sup>th</sup> months of age.

Our definitions for influenza vaccination status considered that the seasonal 2022 and 2023 influenza vaccines became available at the Peruvian Ministry of Health facilities, including our sentinel sites, in May of each year.

The vaccine status for seasonal influenza had three categories: vaccinated, not vaccinated, and unknown. For the period considered in this report (January – September 2023), the vaccinated category applied to the following conditions:

- For patients between six months and one year of age, had they received two doses of influenza vaccine by the time of enrolment.
- For patients older than one year enrolled up to April 30<sup>th</sup>, 2023, had they received an influenza vaccine since May 1<sup>st</sup>, 2022, with at least 14 days between the dates of vaccination and onset of symptoms.
- For patients older than one year, enrolled between May 1<sup>st</sup>, 2023, and September 30<sup>th</sup>, 2023, had they received an influenza vaccine since May 1<sup>st</sup>, 2023, with at least 14 days between the dates of vaccination and onset of symptoms.

The primary data source to define vaccination status was the self-report of influenza vaccines and dates provided by patients at enrolment to the surveillance nurses (patients frequently receive a card after influenza vaccine administration).

A complementary data source was the Peruvian national digital immunization registry ([Acceder a tu carnet de vacunación contra la COVID-19 o del esquema regular - Servicio - Ministerio de Salud - Plataforma del Estado Peruano \(www.gob.pe\)](#)). Due to non-completed implementation, this registry could not be the primary data source for influenza vaccine. In contrast to almost 100% coverage for SARS-CoV-2 vaccination, records of the influenza vaccines remain limitedly registered in this digital system, notably for migrants and undocumented patients. In the national electronic immunization records, we could verify the self-reported vaccination in 64/77 (83%); we could not use that verification for those self-reported as unvaccinated. In 23 of 732 enrolled patients, vaccination information was self-reported as unknown. Finally, the VE analysis included patients >6 months of age.

## Incidence estimation

### Assumptions:

- All patients attended at the center were COVID-19-like illness (CLI).
- Enrolled patients are a random sample from the patients attended at the centers.
- Patients do not seek medical attention outside their assigned area.

### Statistical analysis:

We will consider the following notation:

- Number of non-enrolled CLI cases:  $n_u$
- Number of enrolled patients:  $n$
- Number of positive cases among enrolled patients:  $n_p$
- Proportion of positive cases among the enrolled cases:  $\hat{p}$

The number of non-enrolled positives cases is estimated by  $n_u \hat{p}$ . The point estimation of the incidence is:

$$\hat{\theta} = \frac{n_p + n_u \hat{p}}{N} = \frac{n_p + n_u \frac{n_p}{n}}{N}$$

where N is the population assigned at the health care centers. The population assigned to both centers is 91801.

On the other hand, the variance of the estimator is approximated by the sum of: a) the variance of the number of observed cases and the variance of the un (approximately) observed cases:

$$\widehat{Var}(\hat{\theta}) = \widehat{Var}\left(\frac{n_p + n_u \frac{n_p}{n}}{N}\right) = \frac{\left(1 + \frac{n_u}{n}\right)^2 n^2 \hat{p}(1 - \hat{p})}{N^2}$$

An interval estimation for the incidence is given by:

$$\hat{\theta} \mp z_{1-\alpha/2} \sqrt{\widehat{Var}(\hat{\theta})}$$

On the other hand, let  $c$  be the proportion of persons that are assigned the health center and use it. Then a proposed plug-in estimator of the incidence is:

$$\hat{\varphi} = \frac{n_p + n_u \hat{p}}{\hat{c}N} = \frac{\hat{\theta}}{\hat{c}}$$

where  $\hat{c}$  is the estimated proportion of persons that are assigned the health care center and seek attention there.

The variance of the estimator in the log scale is given by:

$$Var(log(\hat{\varphi})) = Var(log(\hat{\theta})) + Var(log(\hat{c}))$$

By the delta's method

$$Var(log(\hat{\theta})) \approx Var(\hat{\theta}) \frac{1}{\hat{\theta}^2}$$

Similarly

$$Var(log(\hat{c})) \approx Var(\hat{c}) \frac{1}{\hat{c}^2} = \frac{c(1-c)}{m} \frac{1}{c^2} = \frac{(1-c)}{cm}$$

where  $m$  is the sample size of the study to estimate  $c$ . Then

$$\widehat{Var}(log(\hat{\varphi})) = \widehat{Var}(\hat{\theta}) \frac{1}{\hat{\theta}^2} + \frac{(1-\hat{c})}{\hat{c}m}$$

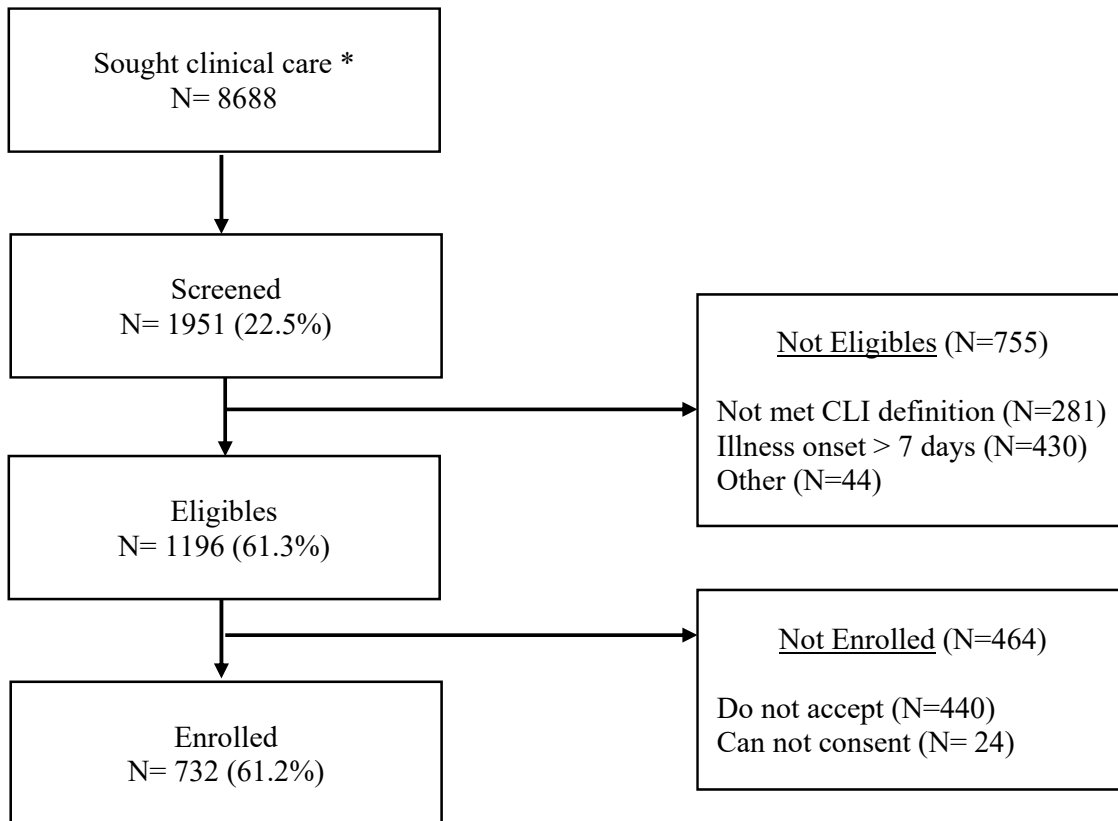
Then a confidence interval for  $\varphi$  is computed by

$$log(\hat{\varphi}) \mp z_{1-\alpha/2} \sqrt{\widehat{Var}(log(\hat{\varphi}))}$$

### Results:

In order to estimate  $c$ , we used data from a community survey study that was conducted between July 24<sup>th</sup> and October 6<sup>th</sup> 2023 had 839 participants. Among the survey participants, 646 (77.0%) reported CLI related symptoms in the previous six months. Among those, 527 (81.6%) reported seeking health care for the episode of CLI related symptoms at any health care service, including pharmacies. Finally, among those who reported use of any health care service during the episode of CLI related symptoms, 164 (31.1%) used the assigned health care center. Using this data, we estimate  $c$  by  $\hat{c} = 164/646$ . and compute the annual incidence in the Supplemental Table.

Supplemental Table 1. Flow diagram of recruitment and enrollment from patients with COVID-19-like illness seeking clinical care in two primary health centers in Lima, Peru, January 1 to September 30, 2023.



\*From health centers reports

Supplemental Table 2. Influenza test results and seasonal vaccination status among enrolled patients presenting in two primary care centers with COVID-19-like illness in Lima, Peru, by selected characteristics, January 1 to September 30, 2023

Characteristic	Enrolled Patients		Influenza negative, no. (%)
	Total no.	Influenza positive, no. (%)	
<b>Overall</b>	<b>732</b>	<b>106 (14.5)</b>	<b>626 (85.5)</b>
<b>Age in years</b>			
<5	134	6 (4.5)	128 (95.5)
5–59	523	93 (17.8)	430 (82.2)
≥60	75	7 (9.3)	68 (90.7)
<b>Sex</b>			
Male	256	48 (18.7)	208 (81.3)
Female	476	58 (12.2)	418 (87.8)
<b>Preexisting conditions<sup>†</sup></b>			
One or more condition	145	20 (13.8)	125 (86.2)
No preexisting conditions	587	86 (14.6)	501 (85.4)
<b>Vaccination status*</b>			
Do not know	23	5 (21.7)	18 (78.3)
No	632	91 (14.4)	541 (85.6)
Yes	77	10 (13)	67 (87)

<sup>†</sup>Pre-existing conditions: pregnancy, diabetes mellitus, hypertension, asthma, chronic

hepatopathy, chronic neurological, hematological, pulmonary or renal disease,

immunodeficiency (including HIV), cardiovascular or cerebrovascular disease, cancer, Down

syndrome and other relevant conditions.

\*Vaccinated status: Patients who reported the age-recommended doses and date-appropriate

seasonal vaccine, until >14 days before enrollment, were considered vaccinated. In the

national electronic immunization records, we could verify the self-reported vaccination in

64/77 (83%); we could not use that verification for those self-reported as unvaccinated (632).

In 23 of 732 enrolled patients, vaccination information as self-reported was unknown.

Supplemental Table 3. Estimated annual incidence per 1000 habitants.

	Influenza (IC 95%)	Influenza A (IC 95%)	Influenza B (IC 95%)
2023*	72.17 (57.91 - 89.95)	53.79 (42.03 - 68.84)	18.38 (12.41 - 27.24)

\*Enrolled between January 1 and September 30, 2023

September 2023

