**The Effects of the Attributable Fraction and the Duration of Symptoms on Burden Estimates of Influenza-Associated Respiratory Illnesses in a High HIV-Prevalence Setting, South Africa, 2013-2015 (Supplementary Material)**

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**METHODS**

**Statistical analysis**

*Rates of influenza-associated respiratory hospitalizations and outpatient consultations*

The equation used to estimate the rates of influenza-associated SARI (used for either SARI-10 or SARI-7 cases) hospitalization is provided below:

 (1)

Where  is the estimated age-specific rate of influenza-associated SARI hospitalization in age group *i*; is the age-specific number of SARI cases enrolled; 7/5 is the coefficient used to adjust for non-enrolment over weekends;  is the age-specific proportion of all eligible SARI cases that were enrolled (obtained from study logs); *HUSSARI* is the proportion of SARI cases that sought care at the surveillance site over the total number of SARI cases that sought care to any hospital obtained from healthcare utilization surveys (HUS) conducted in the catchment areas of the surveillance sites [[[1]](#endnote-1),[[2]](#endnote-2)]; is the observed age-specific influenza detection rate among SARI cases tested; is the age-specific influenza-virus AF among SARI cases estimated at the same sentinel sites during the same study period [[[3]](#endnote-3)]; and *Popi* is the age-specific mid-year population at risk [[[4]](#endnote-4)]. For this analysis we assumed that the number of admission during weekends was the same as during working days as reported in previous studies conducted in South Africa [[[5]](#endnote-5)].

The same approach was used to estimate the rates of influenza-associated SCRI (used for either SCRI-10 or SCRI-7 cases) hospitalizations.

The equation used to estimate the rates of influenza-associated ILI consultations is provided below:

 (2)

Where  is the estimated age-specific rate of influenza-associated ILI outpatient consultations in age group *i*; is the age specific rate of SARI-10 hospitalization (adjusted for non-enrollment and healthcare seeking behavior as obtained in equation 1); *Z* is the proportion of SARI-10 cases that sought outpatient care before hospitalization; *X* is ratio of ILI consultation referred to hospital to the total number of ILI consultations obtained from ILI surveillance over the study period;  is the proportion of ILI cases in age group *i* over the total number of ILI cases after adjusting for non-enrolment;  is the proportion of SARI cases in age group *i* over the total number of SARI cases after adjusting for non-enrolment; is the observed age-specific influenza detection rate among ILI cases tested; and is the age-specific influenza virus AF among ILI cases estimated at the same sentinel sites within the study period [3].

**RESULTS**

**Table S1: Estimated mean annual rates of and relative risk associated with HIV-infection for influenza-associated severe respiratory illness hospitalization (any duration of symptoms), Klerksdorp and Pietermaritzburg, South Africa, 2013-2015.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Age group**  **(in years)** | **Influenza-associated severe respiratory illness hospitalization ratesa**  **(95% CI)** | | | **RR HIV-infected vs. HIV-uninfected**  **(95% CI)** |
| **All** | **HIV-infected** | **HIV-uninfected** |
| **Unadjustedb** | | | | |
| <1 | 470.6 (395.4-552.7) | 720.4 (91.7-2736.6) | 468.4 (395.8-553.9) | 1.6 (0.4-6.5) |
| 1-4 | 119.0 (101.0-140.6) | 550.2 (305.3-980.6) | 110.9 (92.9-131.6) | 4.7 (2.6-8.6) |
| 5-24 | 20.4 (15.7-24.6) | 108.2 (78.8-150.3) | 14.0 (10.9-17.7) | 7.7 (5.2-11.3) |
| 25-44 | 80.5 (72.2-89.6) | 235.3 (208.7-262.8) | 12.9 (9.2-17.9) | 18.1 (12.9-25.3) |
| 45-64 | 110.2 (96.1-125.7) | 417.6 (356.1-488.1) | 36.8 (27.8-47.2) | 11.4 (8.5-15.4) |
| ≥65 | 193.9 (157.9-236.0) | 1133.6 (664.7-1772.4) | 163.7 (130.6-203.9) | 6.8 (4.1-11.3) |
| <5d | 189.3 (168.2-212.6) | 569.1 (303.0-929.9) | 182.9 (161.6-205.6) | 3.7 (2.2-6.3) |
| ≥5e | 63.6 (59.2-68.3) | 258.9 (237.0-282.2) | 24.7 (21.8-28.1) | 11.3 (9.6-13.4) |
| Allf | 77.7 (73.1-82.6) | 258.2 (236.0-280.8) | 45.5 (41.6-49.5) | 9.8 (8.4-11.4) |
| **AF-adjustedc** | | | | |
| <1 | 436.8 (365.3-517.1) | 674.6 (11.6-2136.6) | 434.7 (361.6-501.2) | 1.7 (0.4-7.0) |
| 1-4 | 103.1 (85.9-122.9) | 494.9 (273.5-924.6) | 95.7 (78.5-114.3) | 5.1 (2.7-9.4) |
| 5-24 | 16.8 (13.5-20.7) | 95.9 (64.9-131.1) | 11.0 (8.3-14.4) | 8.7 (5.7-13.4) |
| 25-44 | 69.3 (61.5-77.7) | 206.6 (182.8-233.7) | 9.6 (6.4-13.9) | 21.5 (14.5-31.7) |
| 45-64 | 95.5 (82.1-109.6) | 366.5 (308.3-431.9) | 30.7 (22.5-40.2) | 11.8 (8.6-16.3) |
| ≥65 | 173.7 (140.4-214.7) | 1027.3 (617.1-1695.8) | 146.3 (114.6-183.8) | 6.8 (4.0-11.7) |
| <5d | 169.7 (149.7-191.7) | 514.7 (274.2-880.1) | 164.0 (144.1-185.8) | 3.9 (2.2-6.8) |
| ≥5e | 54.8 (50.7-59.1) | 227.7 (206.8-249.2) | 20.5 (17.8-23.4) | 12.2 (10.2-14.7) |
| Allf | 67.7 (63.4-72.2) | 227.2 (207.2-248.9) | 39.2 (35.6-42.9) | 10.4 (8.8-12.2) |

Abbreviations: CI: confidence intervals; RR: relative risk; HIV: human immunodeficiency virus.

a Rates expressed per 100,000 population.

b Estimated rates without adjustment for the attributable fraction.

c Estimated rates adjusted by the attributable fraction.

d Relative risk adjusted by age within the following categories: <1 and 1-4 years.

e Relative risk adjusted by age within the following categories: 5-24, 25-44, 45-64 and ≥65 years.

f Relative risk adjusted by age within the following categories: <1, 1-4, 5-24, 25-44, 45-64 and ≥65 years.

**Figure S1: HIV prevalence among patients with mild or severe respiratory illness, Klerksdorp and Pietermaritzburg, South Africa, 2013-2015. A: Influenza-like illness; B: Severe acute respiratory illness (symptom duration ≤10 days); C: Severe chronic respiratory illness (symptom duration >10 days).**



**Figure S2: Overall unadjusted and AF-adjusted mean annual influenza-associated severe respiratory illness hospitalization rates (any duration of symptoms) by age group, Klerksdorp and Pietermaritzburg, South Africa, 2013-2015.**



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