Public health impact of switching from a trivalent to a quadrivalent inactivated influenza vaccine in Ecuador

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Using a quadrivalent inactivated influenza vaccine (QIV) instead of a trivalent influenza vaccine (TIV) in the past influenza immunisation campaigns in Ecuador (2010-2019) would have prevented many illnesses and deaths caused by influenza and would have saved US$ 1.08 mln and US$ 2.25 mln from payer and societal perspectives, respectively.

Background

- In 2006, the Ministry of Public Health of Ecuador implemented the seasonal influenza vaccination programme with TIV supplied free of charge through annual campaigns.
- Although high-risk (HR) groups were vaccinated at a relatively high rate (77% in children aged <4 years, 69% in people aged ≥65 years, 81% among health workers, 52% among pregnant women and 94% among people with chronic diseases), the burden of the disease reported during influenza seasons between 2010 and 2019 was still substantial.
- Besides its impact on productivity, each year the disease resulted in an average of 591,661 consultations, 8,943 hospitalisations and 688 deaths.

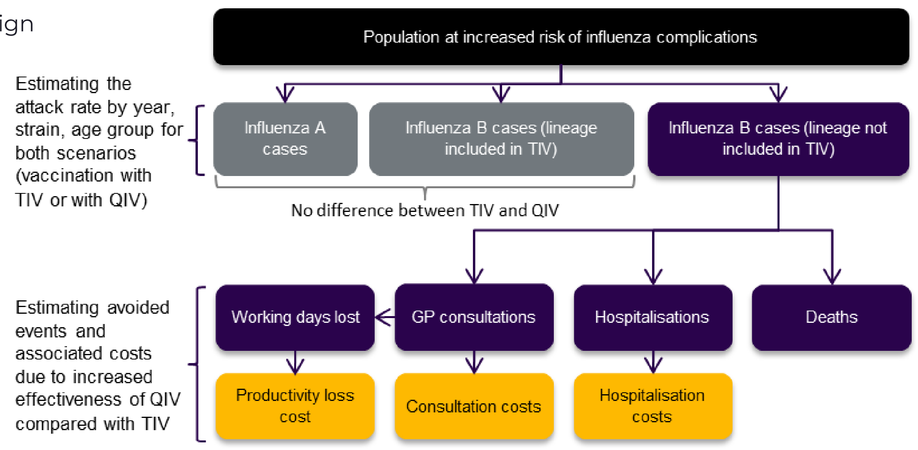
Objectives

- Our analysis compares the health and economic outcomes resulting from the use of QIV instead of TIV over the past ten influenza seasons (2010-2019) in the Ecuadorian population at high risk of influenza and its complications. The analysis was performed from the payer and societal perspectives.

Methods

- Based on a similar statistic model as the one published by Reed et al. in 2012[1], an estimation of the impact of a hypothetical scenario in which QIV replaced TIV in the previous 10 seasons (2010-2019) in Ecuador was made. The model structure is presented in Figure 1.
- The analysis was done for separate age groups to account for the heterogeneity of data and focus on recommended groups for vaccination i.e., children aged <4 years, elderly people aged ≥65 years, health workers, pregnant women, and people with chronic diseases.
- The impact of replacing TIV with QIV was calculated using data on the circulation of influenza viruses, vaccine coverage and its effectiveness, risk of influenza-related outcomes (medical visit consultations, hospitalisations, and deaths) and costs concerning influenza outcomes.
- Direct and indirect (due to workday loss) costs were estimated based on the most up-to-date local national statistics and validated by clinical experts.

Figure 1. Model design



Input data

- The distribution of circulating influenza strains in Ecuador was derived from the FluNet database[4]. Circulation of A lineage was based on Ecuador data, whereas the circulation of specific influenza B strains was based on Tropical South America data.
- Strains recommended for inclusion in TIV were based on WHO recommendations data[5].
- The strain and lineage distribution are presented in Table 1.

Table 1. List of strains included in TIV and distribution of influenza lineages and strains of influenza by year

Season	B lineage in TIV	Influenza A	B / Victoria	B / Yamagata	B lineage mismatch*
2010	Victoria	100.0%	0.00%	0.00%	Null
2011	Victoria	99.9%	0.13%	0.00%	Null
2012	Yamagata	55.9%	2.21%	41.94%	Low
2013	Yamagata	92.8%	4.03%	3.17%	Medium
2014	Yamagata	51.0%	13.24%	35.80%	Low
2015	Yamagata	82.0%	0.72%	17.32%	Low
2016	Victoria	90.7%	3.92%	5.41%	Medium
2017	Victoria	72.3%	11.37%	16.36%	Medium
2018	Victoria	89.1%	2.40%	8.52%	High
2019	Victoria	92.2%	4.92%	2.89%	Medium

*High: Mismatch>66%, Medium: 33%<Mismatch<66%, Low: Mismatch<33%, Complete: 100%, Null: 0%

- Vaccine efficacy and coverage rates were based on Clements et al. 2014[2] and national statistics published by the Pan American Health Organization (PAHO), respectively[3].
- The proportion of HR people in each year group was estimated using data from Ecuador's National Statistics Office[6] and Epidemiological Surveillance 1994-2017[7], the number of health workers was based on Global Health Workforce Statistics[8].
- The size of the population, vaccine coverage and vaccine effectiveness were assumed constant over time.
- Attack rates were estimated based on data from Tinoco et al. 2017[9] describing the influenza burden in Peru, as data for Ecuador were missing. Attack rates were adjusted to specific seasons using the number of influenza cases reported from Ecuador to FluNet each year[4].
- Rates of medical visits, hospitalisations and mortality related to influenza were sourced from Peruvian data and assumed to be similar to the Ecuadorian context[9,10].
- Unit costs for medical visits and consultations were estimated based on Ecuadorian data[11]. It was assumed that the medical visit cost consists of 70% general practitioner (GP) visit consultation cost and 30% emergency department (ED) consultation cost. The hospitalisation cost consists of 90% of hospitalisation in the regular ward and 10% in the intensive care unit.
- The unit cost of a medical visit was assumed to be US$ 30.39, and the unit cost of influenza-related hospitalisation was estimated at US$ 726.15
- The number of workdays lost per medical visit was based on Ecuador's National Statistics Office (INEC)[12] from the year 2019.
- The model inputs were validated by local experts. They key model inputs are presented in Table 2.

Table 2. Model inputs

	0-1y	2-4y	5-11 HR	12-17 HR	18-49 HR	50-64 HR	≥65 years
Population size	672,042	1,009,562	46,465	39,827	620,948	132,863	1,105,992
Vaccination coverage, %	76.7 %	76.70%	94.00%	94.00%	69.70%	90.70%	68.50%
VE[a] against influenza A, %	59.00%	59.00%	61.00%	61.00%	61.00%	61.00%	58.00%
VE[a] against matched B, %	66.00%	66.00%	77.00%	77.00%	77.00%	73.00%	69.00%
VE[a] against mismatched B	44.00%	44.00%	52.00%	52.00%	52.00%	49.00%	47.00%
VE[a] against B [QIV]	66.00%	66.00%	77.00%	77.00%	77.00%	73.00%	69.00%
Attack rate in unvaccinated individuals	21.40%	25.60%	20.40%	11.20%	5.10%	5.10%	3.60%
Medical visit rate[b]	13,800	13,100	9,700	3,400	1,900	2,100	1,600
Hospitalisation rate[b]	480	220	40	22	40	80	60
Mortality rate[b]	1.91	0.73	0.73	0.40	1.57	9.54	29.73
Number of workdays lost per medical visit	3.5[c]	3.9[c]	3.9[c]	3.9[c]	6.7	3.0	3.9
Productivity loss per workday lost costs [US $][d]	21.5	21.5	21.5	21.5	21.5	21.5	21.5

HR – High risk; [a] Vaccine efficacy; [b] Per 100,000 general population; [c] Caregiver workdays losses included; [d] Workdays lost were further adjusted by the national employment rate to account for the Ecuadorian employment pattern[13].

Results

- The results by group and outcome are detailed in Table 3. Over the 2010-2019 period, QIV would have prevented 42,325 influenza cases, around 549 influenza related hospitalisations and 29 deaths compared to TIV used in Ecuador.
- QIV would have reduced influenza costs by US$ 1.08 mln from the payer perspective and more than doubled i.e., US$ 2.25mln from the societal perspective.
- The productivity loss costs were significant, as each medical visit was related to at least 3 days of absenteeism due to influenza and its recuperation.
- Most (27%) of the prevented influenza cases were avoided in 2017 due to relatively high B circulation and mismatch.

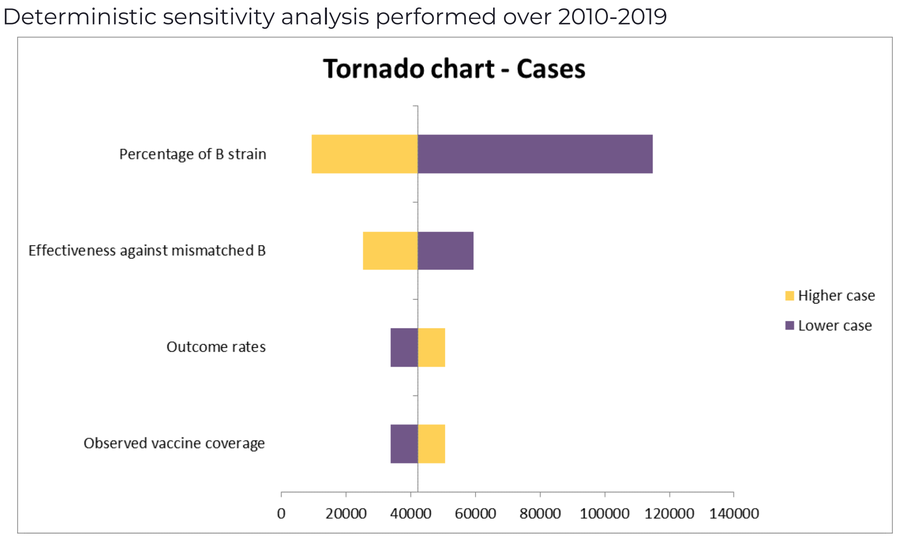
Table 3. Influenza related events & associated costs avoided with QIV per year

	2012	2013	2014	2015	2016	2017	2018	2019	Over 10 years*
% of mismatched cases	5.00%	56.00%	27.00%	4.00%	58.00%	59.00%	78.00%	37.00%	-
The number of additional events avoided									
Influenza cases	1,247	7,024	3,833	132	7,115	11,386	9,139	2,448	42,325
GP consultations	662	3,729	2,035	70	3,777	6,044	4,852	1,300	22,470
Workdays saved	2,567	14,456	7,889	272	14,643	23,431	18,808	5,038	87,105
Hospitalisations	16	91	50	2	92	148	119	32	549
Deaths	1	2	7	0	5	8	5	2	29
Costs saved [US$]									
GP consultations	20,126	113,327	61,845	2,135	114,794	183,689	147,440	39,495	682,851
Workdays saved	34,484	194,180	105,968	3,658	196,695	314,742	252,632	67,673	1,170,033
Hospitalisations	11,754	66,189	36,121	1,247	67,046	107,284	86,113	23,067	398,821
Payer perspectve	31,880	179,516	97,966	3,382	181,840	290,973	233,553	62,563	1,081,673
Societal perspective	66,365	373,695	203,934	7,040	378,535	605,715	486,185	130,236	2,251,705

* Results for the years 2010 and 2011 are not reported, as there was no mismatch between influenza lineage included in TIV and therefore QIV posed no gain in comparison

- A deterministic sensitivity analysis was performed over the study period for the total number of influenza cases avoided.
- All but one inputs were tested +/-20% from the base case, namely the ranges for effectiveness against mismatched B were based on Clements et al. 2014[2]
- Key drivers were the percentage of B strain, effectiveness against mismatched B, observed vaccine coverage, and the variation in the influenza-related outcome rates (attack rate, GP visits, hospitalisation rate, death rate). Cases avoided varied between 9,430 and 114,773.

Figure 2. Deterministic sensitivity analysis performed over 2010-2019



Conclusions

- Protection against a larger number of circulating influenza strains offered by QIV would reduce the number of influenza infections and consequently its impact on the health care system and work absenteeism when compared to TIV.
- The results suggest that switching from TIV to QIV in the past influenza immunisation campaigns in Ecuador would have prevented many illnesses and deaths caused by influenza and reduced health care resource use, leading to substantial savings

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Disclosure of COI:

1. Londono S, Garcia W, and Botero L are Sanofi employees and as such may be eligible for stock options.
2. Zerda I, Gorecki M, and Clay E have no conflict of interest to declare

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