Public health impact of switching from a trivalent to a quadrivalent inactivated influenza vaccine in the Dominican Republic

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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 the Dominican Republic (2010-2019) would have prevented many illnesses and deaths caused by influenza and would have saved RD$ 8.42 mln and RD$ 27.92 mln from payer and societal perspectives, respectively.

Background

- In 2006, the Ministry of Public Health of the Dominican Republic implemented the seasonal influenza vaccination program with TIV. Despite this, the vaccination rate among high-risk (HR) groups was relatively low (14% in children aged 0-1 years, 5% in people aged ≥65 years, 57% among health workers and 16% among pregnant women) with the burden of the disease reported during influenza seasons between 2010 and 2019 being substantial.
- Besides its impact on productivity, each year the disease resulted in an average of 404,251 consultations, 6,728 hospitalisations and 358 deaths.

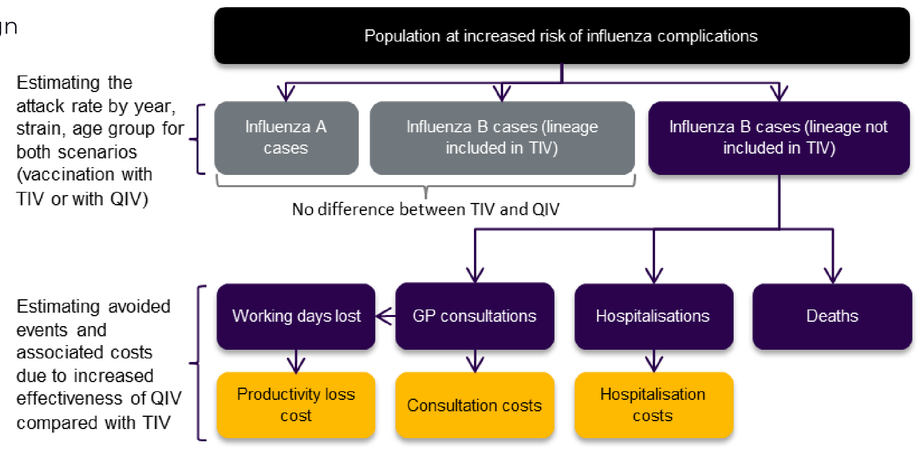
Objectives

- 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 Dominican Republic 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 on the impact of a hypothetical scenario in which QIV replaced TIV in the previous 10 seasons (2010-2019) in the Dominican Republic was made.
- 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 0-1 years, pregnant women, health workers, and elderly people aged 65+ years. The model structure is presented in Figure 1.
- 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 the Dominican Republic was derived from the FluNet database[8]. Circulation of A lineage and circulation of specific B strains (Victoria and Yamagata) for years 2016-2019 were based on Dominican Republic data, while circulation of specific influenza B strains for years 2010-2015 was based on Caribbean and Central America data.
- Strains recommended for inclusion in TIV were based on WHO recommendations data[4].
- 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	84.2%	15.40%	0.39%	Low
2011	Victoria	64.2%	34.06%	1.77%	Low
2012	Yamagata	88.2%	6.92%	4.84%	Medium
2013	Yamagata	90.9%	3.54%	5.55%	Medium
2014	Yamagata	68.6%	0.00%	31.43%	Null
2015	Yamagata	90.7%	0.12%	9.14%	Low
2016	Victoria	64.4%	8.45%	27.10%	High
2017	Victoria	41.3%	58.73%	0.00%	Null
2018	Victoria	88.7%	3.94%	7.39%	Medium
2019	Victoria	71.1%	3.33%	25.56%	High

*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 people at high risk in each year group was estimated using data from the Dominican Republic's National Statistics Office[5]. The number of health workers was based on Global Health Workforce Statistics[6].
- The size of the population, vaccine coverage and vaccine effectiveness were assumed constant over time.
- Attack rates were estimated based on data from the Tinoco et al. 2017[7] publication describing the influenza burden in Peru, as data for the Dominican Republic were missing. Attack rates were adjusted to specific seasons using the number of influenza cases reported from the Dominican Republic to FluNet each year[8].
- Rates of medical visits and hospitalisations related to influenza were based on Tinoco et al. 2017[7]
- Mortality rates were based on Centers for Disease Control and Prevention (CDC) influenza mortality rate data for the United States[9].
- Unit costs for medical visits and hospitalisation were based on the Dominican's Republic official data. From the payer (societal) perspective, the unit cost of a medical visit was RD$ 1,582 (RD$ 5,778) and the unit cost of influenza-related hospitalisation RD$ 42,673 (RD$ 48,824).
- The number of workdays lost per medical visit was based on Ecuador's National Statistics Office (INEC)[10] from the 2019 year.
- The model inputs were validated by local experts, and when available the use of local data were prioritised. They key model inputs are presented in Table 2.

References

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11. National Statistical Office of the Dominican Republic.
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Table 2. Model inputs

	0-1y	2-17y HR	18-49y HR	50-64y HR	65+y
Population size	388,152	3,107,809	4,635,516	1,153,132	641,072
Vaccination coverage, %	13.94%	0.00%	0.99%	0.55%	4.98%
VE[a] against influenza A, %	59.00%	60. 63%	61.00%	61.00%	58.00%
VE[a] against matched B, %	66.00%	74.94%	77.00%	73.00%	69.00%
VE[a] against mismatched B	44.00%	50.50%	52.00%	49.00%	47.00%
VE[a] against B [QIV]	66.00%	74.94%	77.00%	73.00%	69.00%
Attack rate in unvaccinated individuals	21.40%	17.93%	5.10%	5.10%	3.60%
Medical visit rate[b]	13,800	7,489	1,900	2,100	1,600
Hospitalisation rate[b]	480	57	40	80	60
Mortality rate[b]	1.71	0.73	1.20	3.59	37.24
Number of workdays lost per medical visit[c, d]	3.5	3.9	6.7	3.0	3.9
Productivity loss per workday lost costs [RD $]			1,297		

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 Dominican Republic's employment pattern [11, 12].

Results

- The results by group and outcome are detailed in Table 3. Over the 2010-2019 period, QIV would have prevented 4,393 influenza cases, around 96 influenza-related hospitalisations and 4 deaths compared to TIV used in the Dominican Republic.
- QIV would have reduced influenza costs by RD$ 8.42 mln from the payer perspective and more than tripled (i.e., RD$ 27.92 mln) from the societal perspective.
- Over a 10-year period, societal costs represent 70% of the total potential savings. Work absenteeism and patient co-payment of medical services highlight the need to adopt such a perspective.

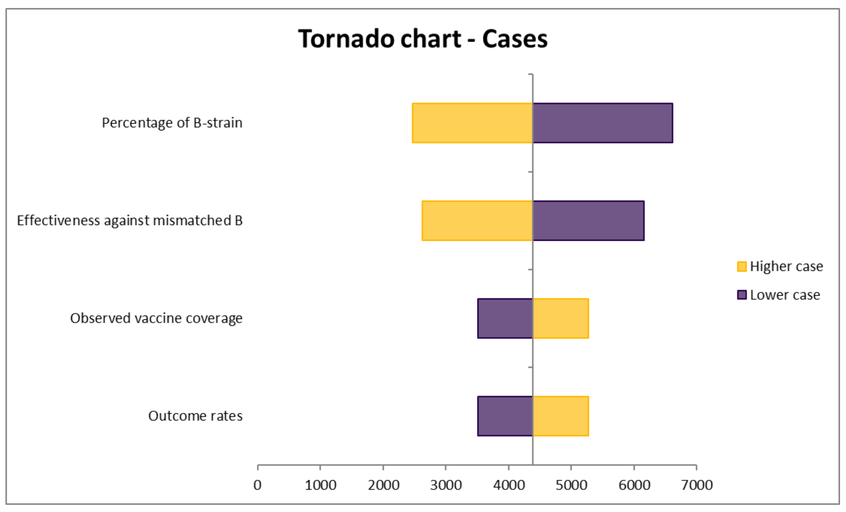
Table 3. Influenza related events & associated costs avoided with QIV per year, in thousands of RD$

	2010	2011	2012	2013	2015	2016	2018	2019	Over 10 years*
% of mismatched cases	2.44%	4.94%	58.82%	38.96%	1.24%	76.23%	65.22%	88.46%	-
The number of additional events avoided:									
Influenza cases	4	47	118	117	1	3,561	215	330	4,393
GP consultations	3	30	74	73	1	2,222	134	206	2,742
Hospitalisations	0	1	3	3	0	77	5	7	96
Workdays saved	9	105	261	259	2	7,878	475	729	9,719
Deaths	0	0	0	0	0	4	0	0	4
Costs saved [RD$] – payer perspective									
GP Consultations	4	47	116	116	1	3,515	212	325	4,337
Hospitalisations	4	44	110	109	1	3,307	200	306	4,080
Total savings	8	91	226	225	2	6,822	412	631	8,417
Costs saved [RD$] – societal perspective									
GP Consultations	15	171	426	423	3	12,841	775	1,188	15,842
Hospitalisations	4	50	125	125	1	3,784	228	350	4,668
Workdays Saved	7	80	199	198	2	6,005	362	556	7,408
Total savings	27	301	750	745	6	22,630	1,366	2,094	27,919

* Results for the years 2014 and 2017 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 2,467 and 6,617.

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.
- Additionally, reducing the number of influenza cases would diminish the burden on the health care system in influenza season, which would allow for more attention to other diseases.
- To achieve a higher effect, the replacement of TIV with QIV should accompany the spread of the vaccination in the Dominican Republic.

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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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