Impact of 2018/19 influenza vaccination in older adults, based on primary care, hospitalizations and influenza associated mortality in Spain

I-MOVE / I-MOVE+ annual meeting

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Background

- Vaccination is the most effective public health intervention to reduce the burden of seasonal influenza and its associated complications among older adults (>64 years)

- It is important to evaluate the benefits of influenza vaccination programs, in terms of numbers of influenza averted events

Objective:

Quantifying the number of influenza related events in primary care, hospitalizations and influenza associated mortality in older adults, prevented by the IV program in season 2018/19 in Spain

Data source:
Spanish Influenza surveillance systems

	Events	Data Source
Mild influenza	• Medically attended influenza confirmed cases (**MAICC**)	**Spanish Influenza Sentinel Surveillance System (SISSS). Primary Care**
Severe influenza	• Hospitalized Confirmed Influenza Cases (**Hosp**)	**Surveillance of Hospitalized Confirmed influenza cases (Hosp).**
Severe influenza	• Severe Hospitalized Confirmed Influenza Cases (**SHCIC**) • **ICU admissions** in SHCIC	**Surveillance of Severe Hospitalized Confirmed influenza cases (SHCIC)**
Influenza mortality	• **Deaths** in SHCIC	
Influenza mortality	• Influenza attributable **deaths**	**FluMOMO model**

Methodology

- Common protocol within the I-MOVE+ project
- We compared the number of influenza events observed in the population with influenza vaccination program (n) to the estimated number that would have occurred without the vaccination programme (N).

Observed events (n) + **Averted events** (NAE) = **Events in a population without influenza vaccination program** (N)

Number of averted events

$$NAE = n * \left(\frac{VC * VE}{1 - VC * VE} \right)$$

- Number of observed events
- Influenza vaccine coverage
- Influenza vaccine effectiveness

Prevented fraction

$$PF = \left(\frac{NAE}{NAE + n} \right)$$

Number Needed to Vaccine

$$NNV = \left(\frac{pop}{VE * (NAE + n)} \right)$$

Spanish Influenza Sentinel Surveillance System in primary care (SISSS)

By week

Number of reported ILI x (**Positives** / **Samples**) = **Medically attended influenza-confirmed cases (MAICC)**

Weekly % positives

Sum over (w40 – w20)

By season

$$\frac{\text{Medically attended influenza-confirmed cases (MAICC)}}{\text{SISSS catchment population}} = \text{MAICC rate x 100,000}$$

Extrapolation

x population in Spain

Total number of Medically attended influenza-confirmed cases in Primary Care in Spain

95% CI were calculated using Monte-Carlo simulations

Hospitals from **19 Spanish regions** reporting:

Surveillance of Hospitalized (Hosp) and Severe Hospitalized Confirmed influenza cases (SHCIC)

- **All influenza hospitalizations (since 2017/18)**
- **Severe hospitalized influenza confirmed cases**
- **ICU admissions among SHCIC**
- **Influenza deaths among SHCIC**

Regional estimates → (heterogenous reporting, clinical testing practice, % rapid test…)

$$\frac{\text{Number of reported cases}}{\text{Catchment population}} = \text{•Hosp rate •SHCIC rate •ICU rate •Death rate}$$

→ x regional population → **No. of estimated cases in region**

Beta-binomial method

$$X_i \setminus p_i \sim Bin(n_i, p_i)$$
$$p_i \sim Beta(\mu, \Theta), \text{ i.i.d}$$
$$p_i = \frac{x_i}{n_i} \;;\; i = 1 \ldots 19 \text{ regions}$$

Pooling of over dispersed data

$\hat{\mu}$=mean event rate
$\hat{\Theta}$=measure of the variation in p

National estimates

Total number of cases in Spain:
- **Hospitalizations**
- **Severe hospitalizations**
- **ICU admissions**
- **Deaths**

$$= \frac{1}{\textit{\% of influenza testing in hospitals}} \times \text{No. of estimated cases in Spain}$$

Pooled rates x 100,000 (Hosp, SHCIC, ICU, death)

← x population in Spain

Estimation of influenza-attributable mortality in hospitals

Input data sources

- **All-cause mortality**
  Computerized civil registers (92% Spanish population)
- **Influenza activity**
  (Goldstein index: weekly ILI rates x laboratory positivity rates)
- **Extreme ambient temperatures**
  National Oceanic and Atmospheric Administration (NOAA)

Statistical analysis

FluMOMO model

multiplicative Poisson regression time-series model

Number of IA deaths and IAM rates:

- All ages
- Age group (0-4, 5-14, 15-64 and >64 years)

Number of Influenza-attributable deaths in >64 y in Spain

x **53%** of all deaths in Spain occur in hospitals *

Number of Influenza-attributable hospital deaths in >64 y in Spain

* Jiménez-Puente 2006. Distribution and Trend of Deaths within the Hospital Environment in Spain during the 1997-2003 period

Influenza Vaccine Effectiveness (IVE)

Pooled VE results from 2018/19 I-MOVE studies; >64 years old

Type/subtype	Primary Care VE (95% CI)	Hospital VE (95% CI)
A(H1N1)pdm09	63 (38; 78)	38 (15; 55)
A(H3N2)	20 (-20; 46)	10 (-13; 28)

Weighting by country-specific influenza virus circulation

Influenza virus distribution in Spain (SISSS)

Influenza type/subtype	Proportion (%)
A(H1N1)pdm09	36.3
A(H3N2)	61.2
B	0

Pooled VE in 2018/19, weighted by influenza virus distribution in Spain

	Primary Care VE (95% CI)	Hospital VE (95% CI)
VE for Spain; all A virus	**35.9 (13.9; 57.9)**	**20.4 (5.6; 35.6)**

Influenza vaccine coverage in ≥64 yrs (%)

Data source	Season			
	2015-16	2016-17	2017-18	2018-19
Spanish Ministry of Health	56.1	55.5	55.7	54.4

Impact results based on primary care averted MAICC

	Medically attended influenza confirmed cases (MAICC)	
	Estimate (95% CI)	
ILI incidence rate (per 100,000 pop)	668	(624 – 712)
% influenza positive	48.5	
Population >64 y	8 995 937	
Number of observed MAICC (n)	29125	(27214 -31069)
Influenza VC (%)	54.4	
Influenza VE (%)	35.9	(13.9 – 57.9)
Number of averted MAICC	**7021**	(1396 - 12389)
Averted rate (MAICC/10^5)	**78.1**	(15.5 - 137.7)
Number needed to vaccinate (NNV)	**692**	(385 - 2802)
Prevented fraction (PF)	**19.5%**	(4.5% - 29,8%)

Preliminary results

Impact results based on severe influenza averted events

	Hospitalizations		Severe Influenza Hospitalizations (SHCIC)		ICU Admission among SHCIC	
	Estimate (95% CI)		Estimate (95% CI)		Estimate (95% CI)	
Number of events observed (n)	48487		14511		2430	
Influenza VC (%)	54.4		54.4		54.4	
Influenza VE (%)	20	(6 – 36)	20	(6 – 36)	74	(42 – 88)
Number of averted events (NAE)	**2523**	(325 – 4692)	**1790**	(235 – 3319)	**1640**	(745 – 2251)
Averted rate (NAE/10^5)	**28.0**	(3.6 - 52.2)	**19.9**	(2.6 - 36.9)	**18.2**	(8.3 - 25.0)
Number needed to vaccinate (NNV)	**1913**	(988 – 9532)	**2700**	(1388 – 13039)	**2983**	(2170 – 6527)
Prevented fraction (PF)	**11.0%**	(1.6% -18.6%)	**11.0%**	(1.6% -18.6%)	**40.3%**	(23.4% - 48.1%)

Preliminary results

Pooled I-MOVE VE in 2018/19, weighted by influenza virus distribution in Spain

VE against ICU admission in patients hospitalized with influenza (Casado, 2018. CMAJ)

Impact results based on Influenza deaths averted in hospitals

	Deaths confirmed with influenza (SHCIC)		Influenza-attributable deaths in hospitals (FluMOMO)	
	Estimate (95% CI)		Estimate (95% CI)	
Number of events observed (n)	3343		2812	
Influenza VC (%)	54.4		54.4	
Influenza VE (%)	70	(34 – 87)	70	(34 – 87)
Number of averted events (NAE)	2042	(725 – 2983)	1730	(604 -2511)
Averted rate (NAE/10^5)	22.7	(8.1 – 33.2)	19.2	(6.7 – 27.9)
Number needed to vaccinate (NNV)	2395	(1636 – 6557)	2826	(1944 – 7927)
Prevented fraction (PF)	38.0%	(17.9% - 47.1%)	38.1%	(17.6% 47.2%)

All-cause influenza-atrributable deaths (FluMOMO)	% of total deaths in hospitals *	All-cause IA deaths in hospitals
5305	53%	2812

Preliminary results

Impact results based on Influenza deaths averted in hospitals

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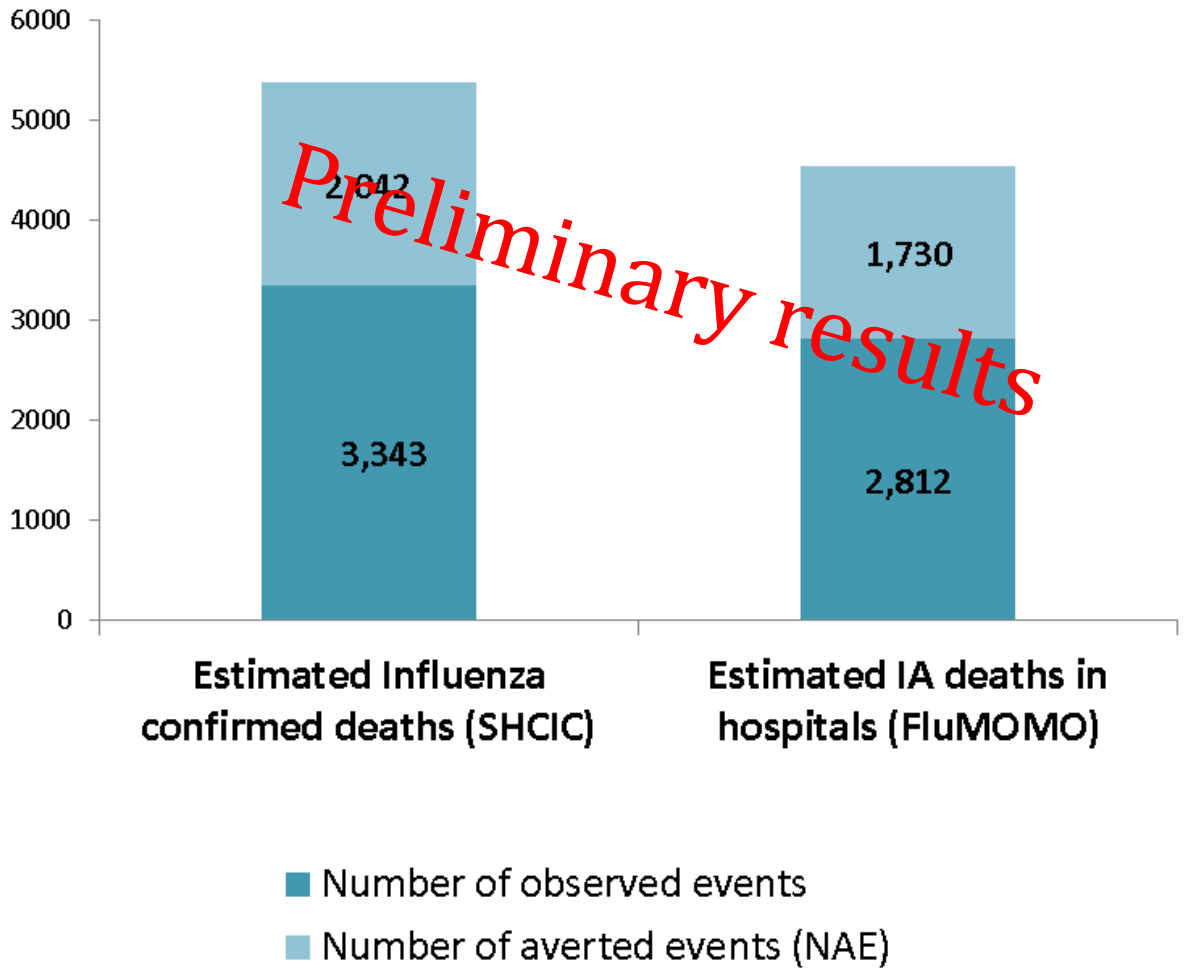
Preliminary results

VE against death in patients hospitalized with influenza. (Casado, 2018. CMAJ)

Influenza mortality in hospitals



Limitations

- Multiplier to estimate de number of severe influenza events in Spain is based on the frequency of influenza testing in two reference hospitals belonging to two Spanish regions (out of nineteen)
- The estimation of deaths occurred in hospital is based on a previous study from 2006 in Spain
- Influenza VE against UCI and deaths in hospitals is based on one study in Spain
- Measuring the impact assuming no indirect effect
- The role of previous immunity is not accounted

Conclusions

- Influenza vaccination was able to prevent 20% MAICC, 11% hospitalizations, 40% ICU admissions and 38% influenza related deaths in the season 2018/19
- Comparable estimations of influenza mortality prevented in hospitals using different data sources (SHCIC surveillance and population-based model FluMOMO)
- Even with suboptimal VE and VC among the elderly, our results suggest that IV programs considerably reduce the burden of influenza-related outcomes
- Quantifying the benefit of annual vaccination in terms of influenza events prevented each season may contribute to the public health challenge of increasing vaccine coverage and will be key to strengthen communication with the general public and decision makers

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Thanks for your attention!