

Lo scenario infettivologico emergente dalla  
co-circolazione di virus influenzali e SARS-CoV-2:  
implicazioni di salute pubblica

Massimo Galli

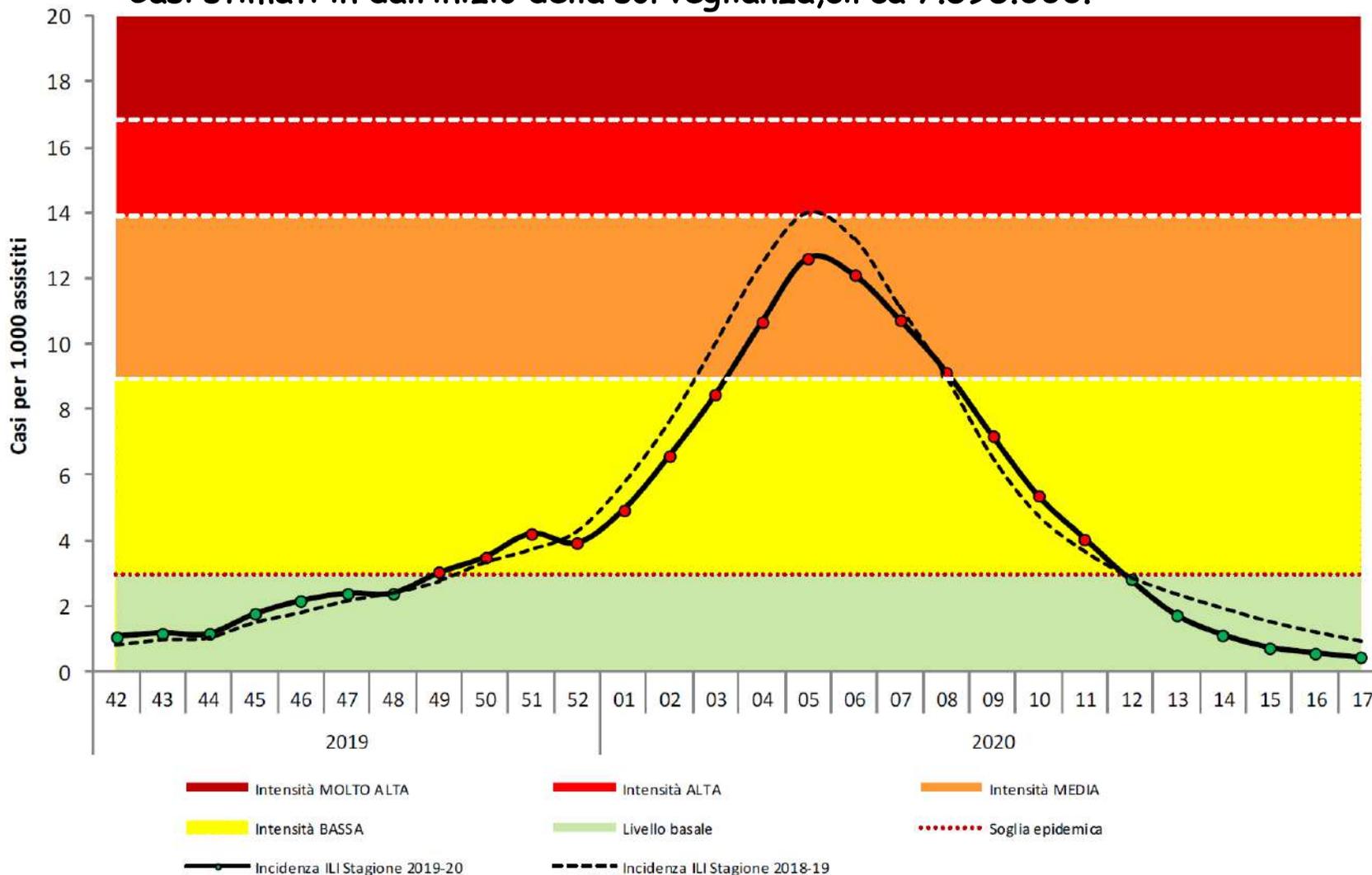
Clinica delle Malattie Infettive,  
DIBIC L. Sacco, UNIMI

## Il 'conto' dell'influenza

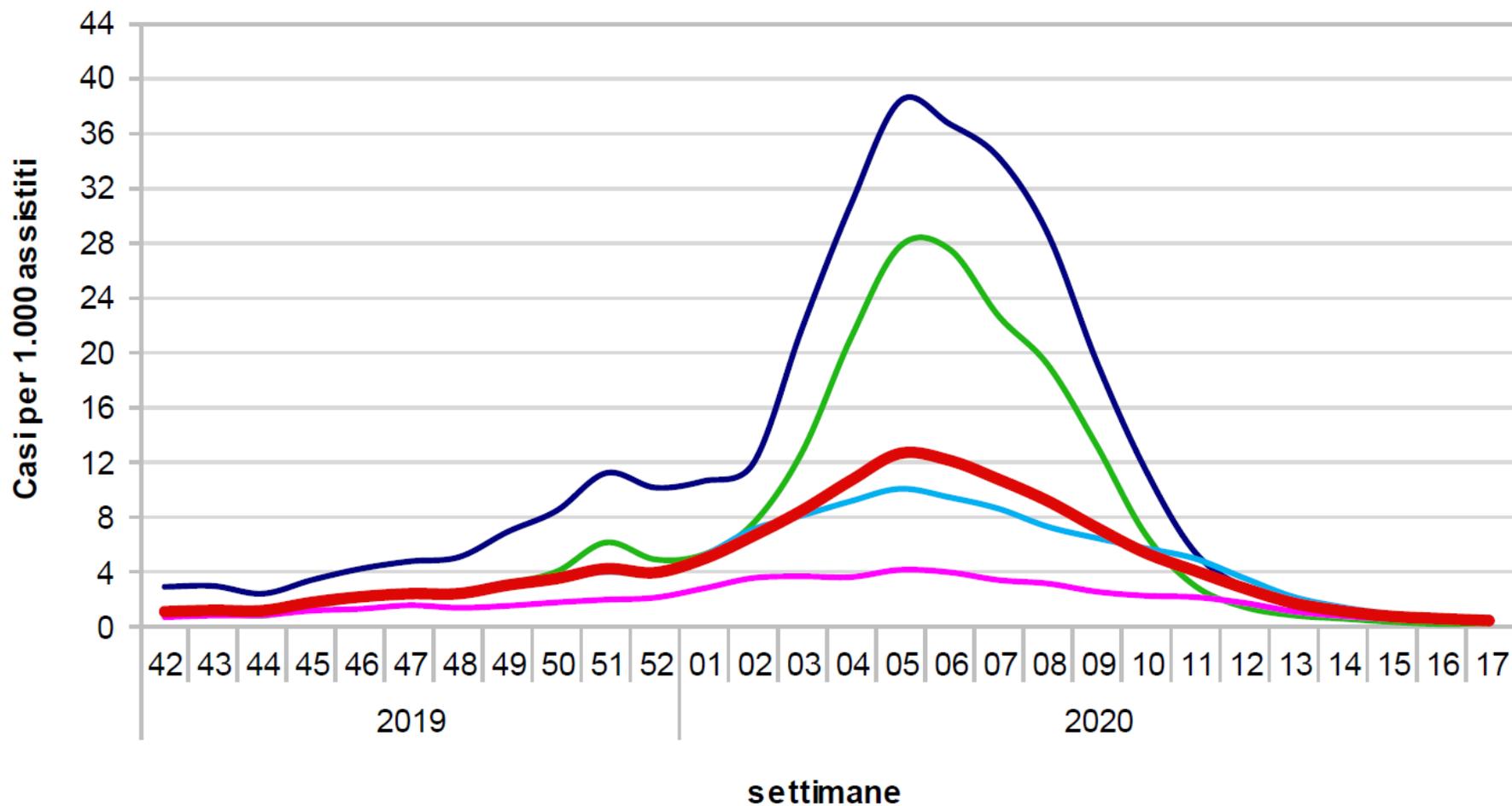
- I virus influenzali infettano annualmente tra il 5 e il 15% della popolazione adulta (da 350 milioni a 1 miliardo di persone) e 20-30% dei bambini.
- Ogni anno 3-5 milioni di casi presentano complicanze con una letalità di circa il 10% dei casi (250 a 500 mila persone, soprattutto bambini sotto i 5 anni, anziani e persone affette da malattie croniche).
- I decessi per influenza e le sue complicanze ogni anno in Italia sono mediamente 8000 .

# Stagione influenzale 2019-2020: una stagione a media intensità

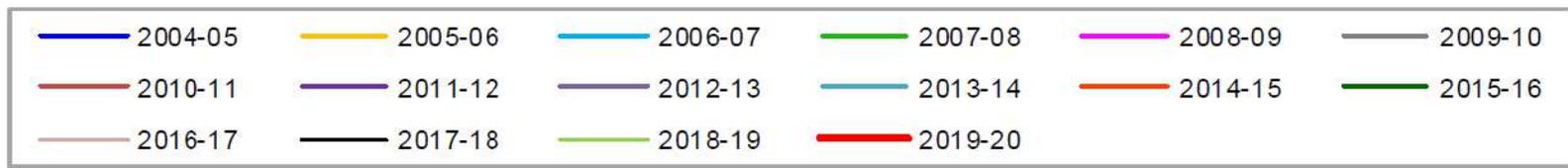
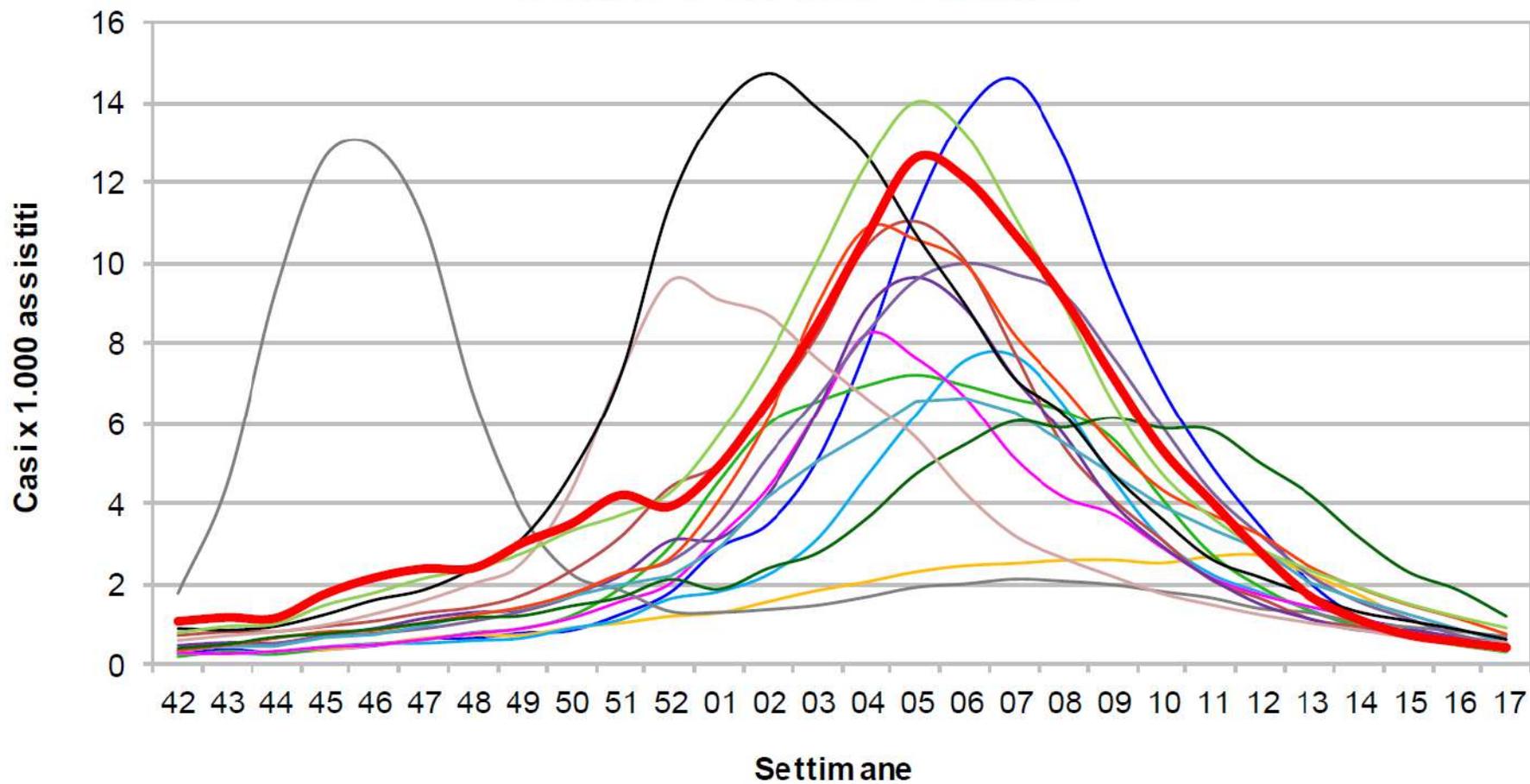
Casi stimati in dall'inizio della sorveglianza, circa 7.595.000.



## Incidenza delle sindromi influenzali in Italia per classi di età. Stagione 2019 - 2020

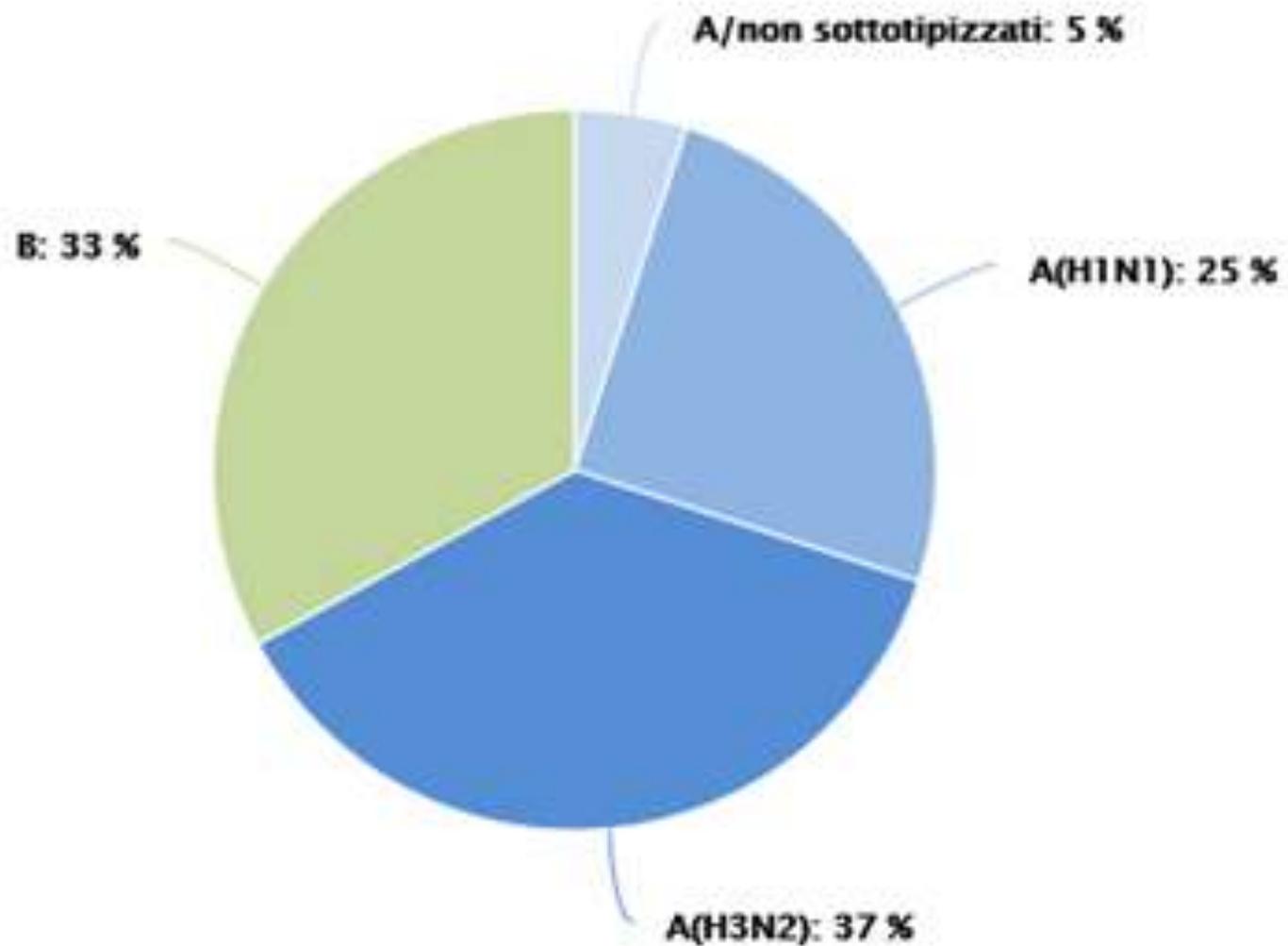


## Incidenza delle sindromi influenzali (ILI) in Italia. Stagioni 2004/05 - 2019/20

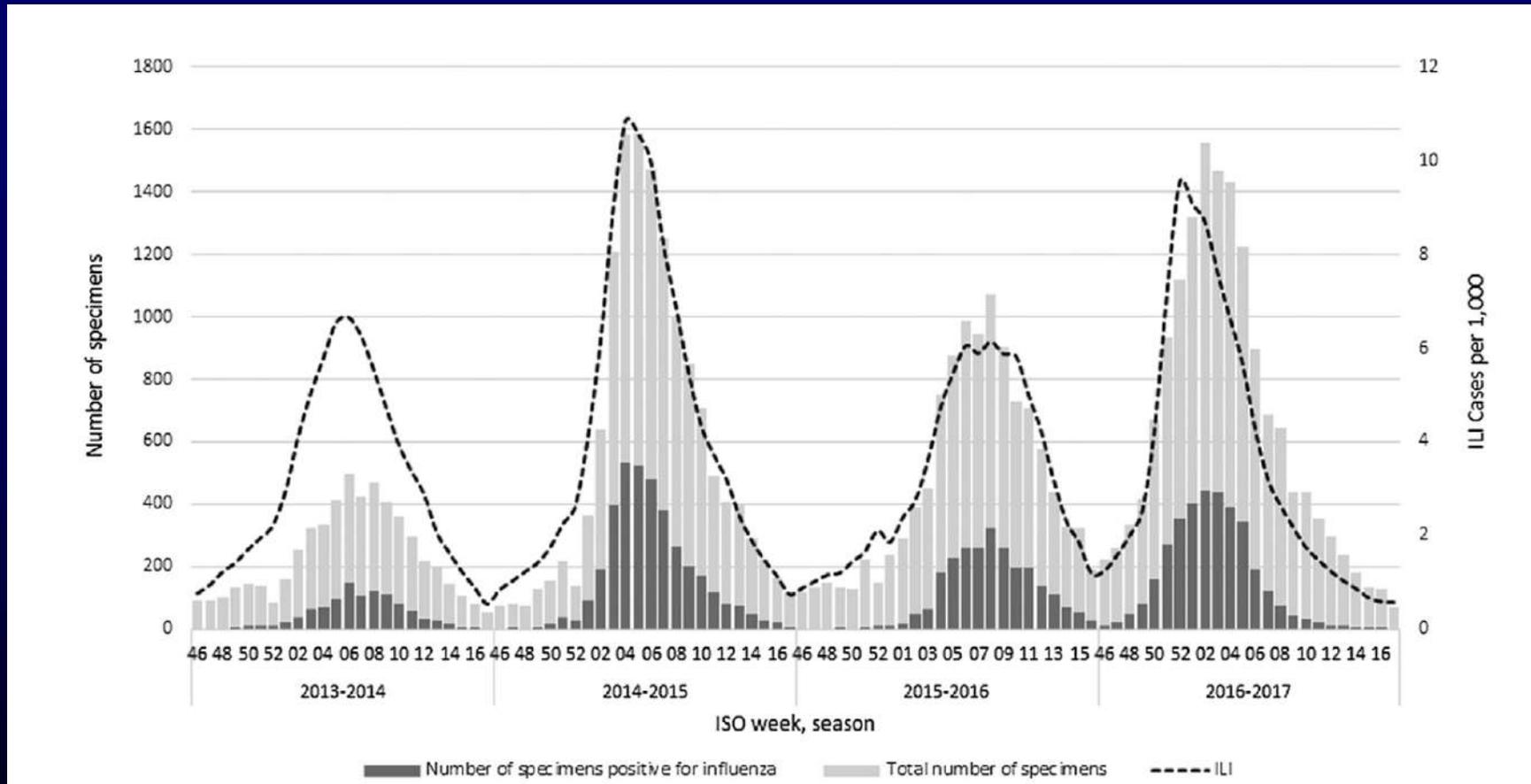


# Proporzione di campioni positivi per tipo/sottotipo segnalati

(settimane 46/2019-17/2020)



**Total number of specimens, number of positive specimens for influenza and ILI cases (per 1,000 inhabitants) by week and season. Italy, 2013/14, 2014/15, 2015/16 and 2016/17 season.**





Contents lists available at [ScienceDirect](#)

## International Journal of Infectious Diseases

journal homepage: [www.elsevier.com/locate/ijid](http://www.elsevier.com/locate/ijid)



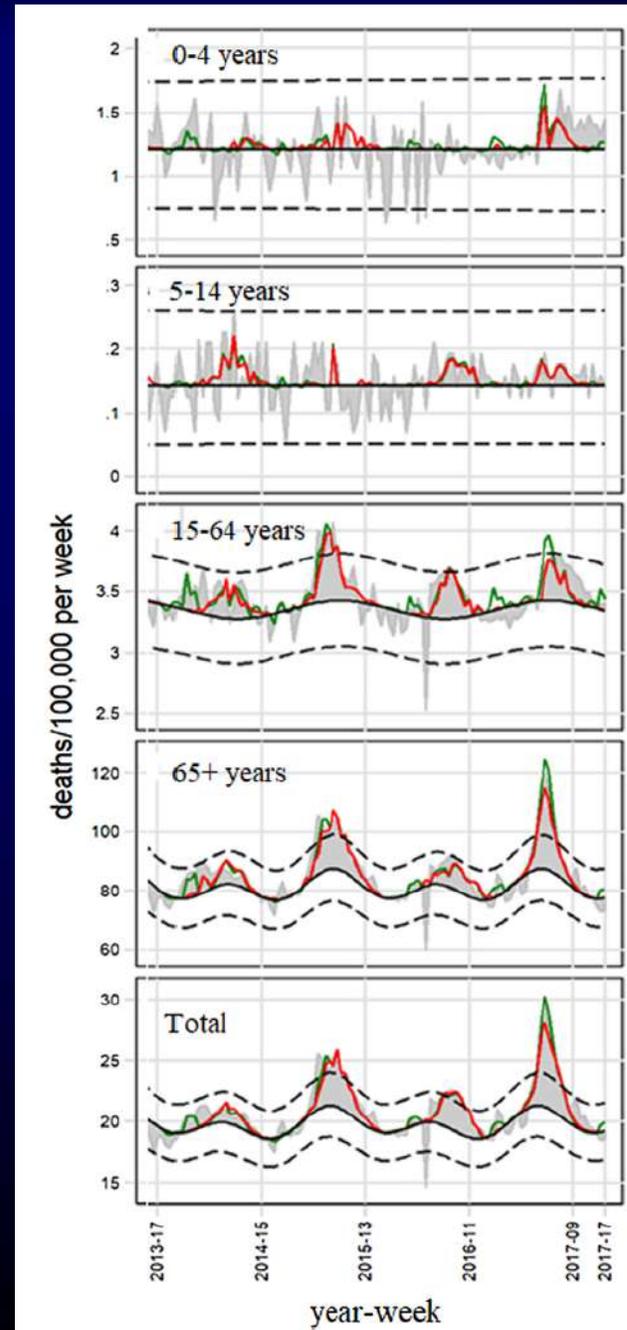
Investigating the impact of influenza on excess mortality in all ages in Italy during recent seasons (2013/14–2016/17 seasons)



- We estimated excess deaths of 7,027, 20,259, 15,801 and 24,981 attributable to influenza epidemics in the 2013/14, 2014/15, 2015/16 and 2016/17, respectively, using the Goldstein index.
- The average annual mortality excess rate per 100,000 ranged from 11.6 to 41.2 with most of the influenza associated deaths per year registered among the elderly.
- However children less than 5 years old also reported a relevant influenza attributable excess death rate in the 2014/15 and 2016/17 seasons (1.05/100,000 and 1.54/100,000 respectively).

## Excess mortality for winter seasons 2013/14, 2014/15, 2015/16 and 2016/17.

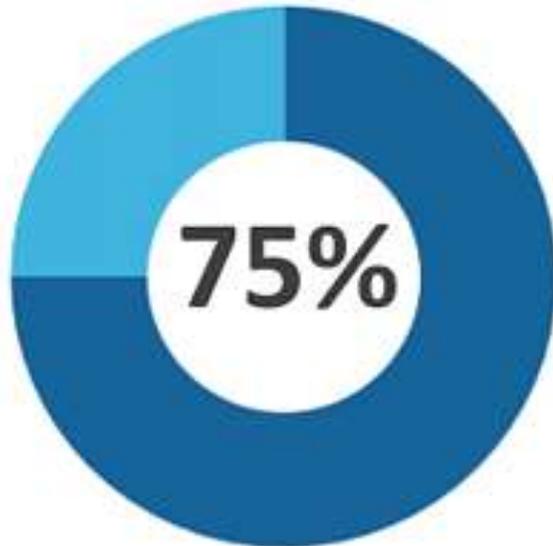
Black line represents the baseline. Dotted line the 95% confidence interval. The shaded grey areas represent deviations in expected deaths from the estimated baseline. The red curves indicate mortality attributable to influenza activity, using the Goldstein index (ILI x % of positive specimens) as the IA indicator, and the green curves indicate effect of IA + extreme temperatures



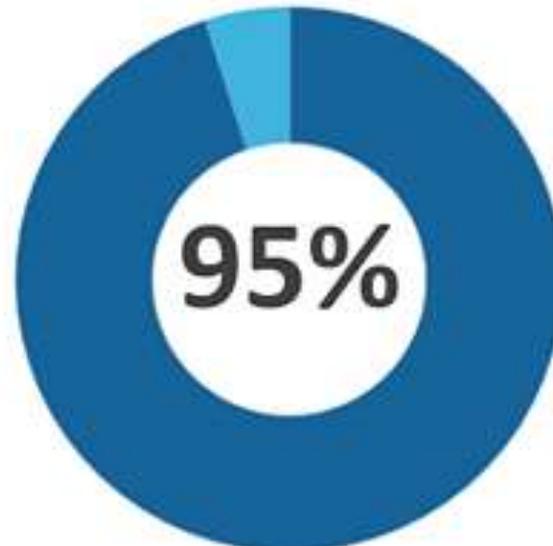
# Obiettivi di copertura per la vaccinazione antinfluenzale

OBIETTIVI DI COPERTURA PER TUTTI I GRUPPI TARGET

Obiettivo minimo



Obiettivo ottimale



## Copertura vaccino Antinfluenzale negli anziani (età $\geq 65$ anni)

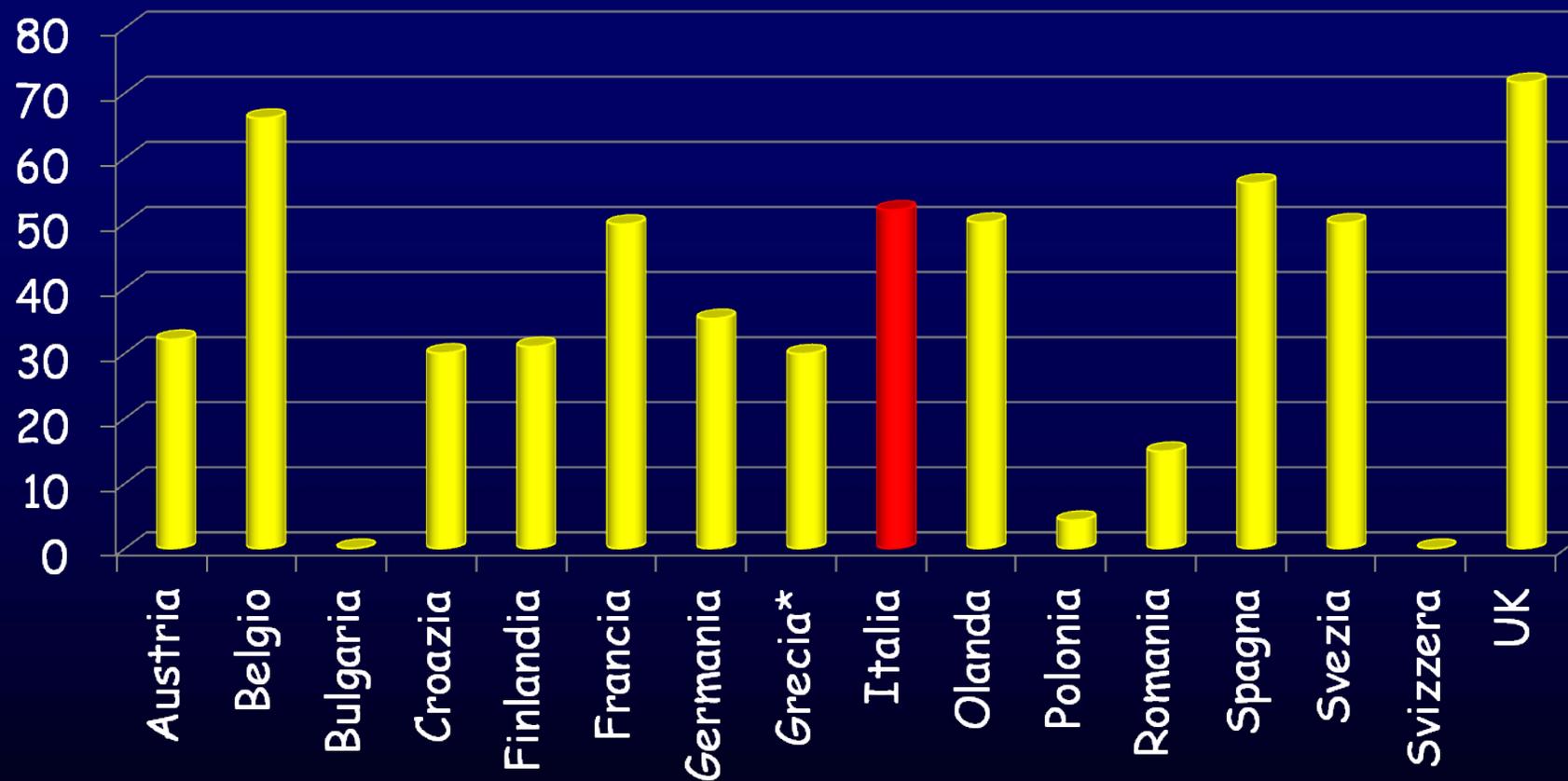


dato nazionale 54,6 (per 100 abitanti - 2019-2020)



0-40 41-50 50,1-60 60,1-70

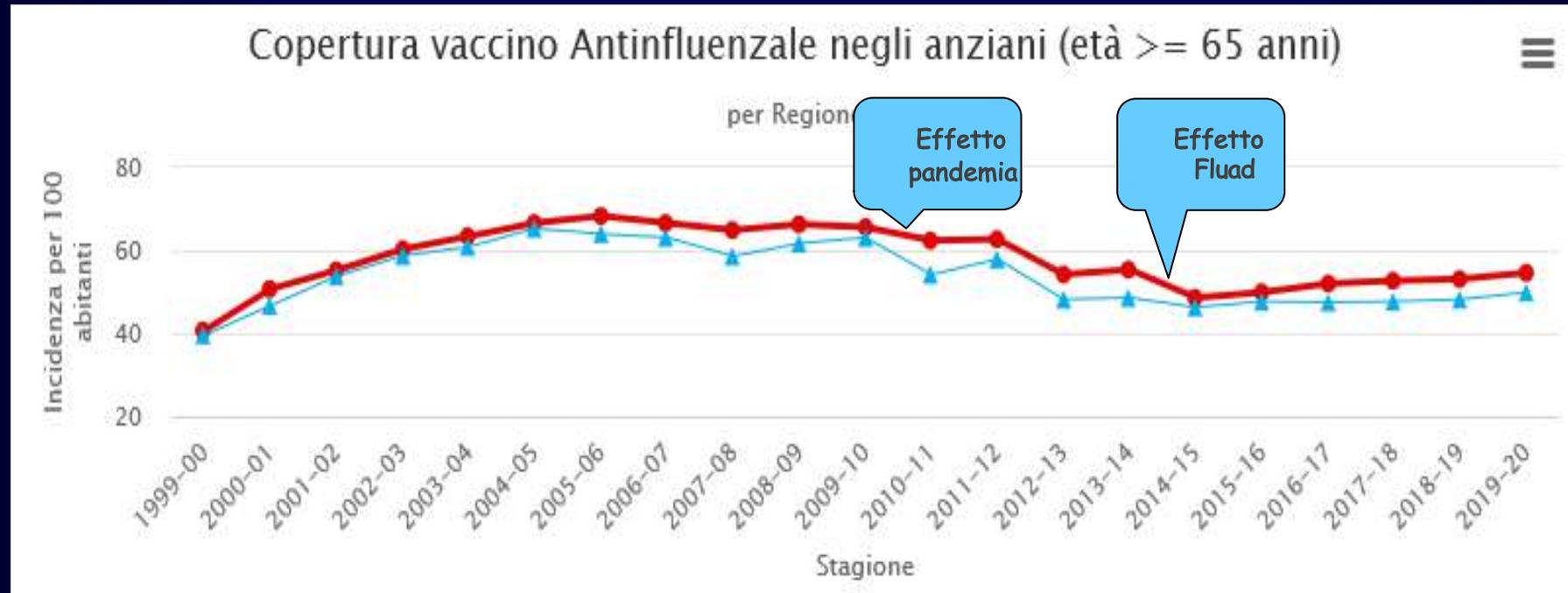
## Copertura vaccinale per influenza in Europa nei >65 anni. Dati più recenti disponibili al 2017



\*intera popolazione

*Sheikh et al. Vaccine 2018:4979-92.*

## Anziani e vaccinazione antinfluenzale in Italia e in Lombardia



## **Knowledge and attitudes on influenza vaccination among Italian physicians specialized in respiratory infections: an Italian Respiratory Society (SIP/IRS) web-based survey**

- 144 (8.1%) completed the survey (97 men; median age 59 years).
- 81% recommended vaccination to all their patients
- two thirds of respondents considered influenza vaccination safe for immunocompromised patients.
- More than 50% of respondents underwent seasonal influenza vaccination in 2015 and 68% declared the intention to undergo vaccination in 2016 epidemic season.
- Reasons for having vaccination mainly referred to 'protect oneself from influenza' (63%), 'protect patients' (31%) or household members' (6%).
- The main reasons for vaccination refusal were 'lack of time' (45%), 'concerns about side effects' (22%), 'do not get influenza easily and/or not afraid of influenza infection' (22%) and 'disagreement with indication of vaccination for HCWs' (9%).

Review

Lower vaccine uptake amongst older individuals living alone: A systematic review and meta-analysis of social determinants of vaccine uptake



Anu Jain<sup>a,\*</sup>, A.J. van Hoek<sup>a,b</sup>, Delia Boccia<sup>a</sup>, Sara L. Thomas<sup>a</sup>

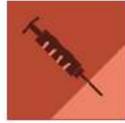
<sup>a</sup> Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK

<sup>b</sup> Immunisation, Hepatitis and Blood Safety Department, Public Health England, 61 Colindale Avenue, London NW9 5EQ, UK

- Higher SIV uptake was reported for individuals **not living alone** (summary odds ratios (OR) = 1.39 (95% confidence interval (CI): 1.16-1.68).
- Lower SIV uptake was observed in **immigrants and in more deprived areas**: summary OR = 0.57 (95%CI: 0.47-0.68) and risk ratio = 0.93 (95%CI: 0.92-0.94) respectively.
- Higher SIV uptake was associated with **higher income** (OR = 1.26 (95%CI: 1.08-1.47)) and **higher education** (OR = 1.05 (95%CI: 1-1.11)) in adequately adjusted studies.

# Can influenza vaccine modify COVID-19 clinical course?

- It was found that of influenza vaccination was associated with lower risk of COVID-19 infection and influenza vaccination rate was 93.9% among 5940 of non-COVID-19 vs. 6.1% among 384 COVID-19 positive cases.  
*Jehi L, et al. Chest 2020.*  
<https://doi.org/10.1016/j.chest.2020.05.580>
- In addition, 10% increase in influenza vaccination coverage was associated with a statistically significant 28% reduction in COVID-19 death rate in the elderly.  
*Zanettini C, et al. MedRxiv 2020;*  
<https://doi.org/10.1101/2020.06.24.20129817>
- In a pre-print study of 92,664 COVID-19 patients of which about one-third received influenza vaccine. Influenza vaccinated patients had 8% lower odds of intensive care unit admission, 18% lower odds of requiring mechanical ventilation and 17% lower odds of death  
*Fink G, et al. n.d. doi:10.1101/2020.06.29.20142505*



Article

# The Association between Influenza and Pneumococcal Vaccinations and SARS-CoV-2 Infection: Data from the EPICOVID19 Web-Based Survey

Marianna Noale <sup>1,\*</sup>, Caterina Trevisan <sup>1,2</sup>, Stefania Maggi <sup>1</sup>, Raffaele Antonelli Incalzi <sup>3</sup>, Claudio Pedone <sup>3</sup>, Mauro Di Bari <sup>4</sup>, Fulvio Adorni <sup>5</sup>, Nithiya Jesuthasan <sup>5</sup>, Aleksandra Sojic <sup>5</sup>, Massimo Galli <sup>6</sup>, Andrea Giacomelli <sup>6</sup>, Sabrina Molinaro <sup>7</sup>, Fabrizio Bianchi <sup>8</sup>, Claudio Mastroianni <sup>9</sup>, Federica Prinelli <sup>5</sup> and on behalf of the EPICOVID19 Working Group

- Influenza and anti-pneumococcal vaccinations were received, respectively, by 16% and 2% of those <65 years, and by 53% and 13% of those >65 years.
- SARS-CoV-2 NPS testing was reported by 6680 participants.
- Anti-pneumococcal and influenza vaccinations were associated with a decreased probability of a SARS-CoV-2 NPS positive test in the younger participants (OR = 0.61, 95% CI 0.41–0.91; OR = 0.85, 95%CI 0.74–0.98; respectively).
- A significantly lower probability of a positive test result was detected in the individuals >65 years who received anti-pneumococcal vaccination (OR = 0.56, 95%CI 0.33–0.95).

Brief Report

## Influenza Vaccination and Risk of SARS-CoV-2 Infection in a Cohort of Health Workers

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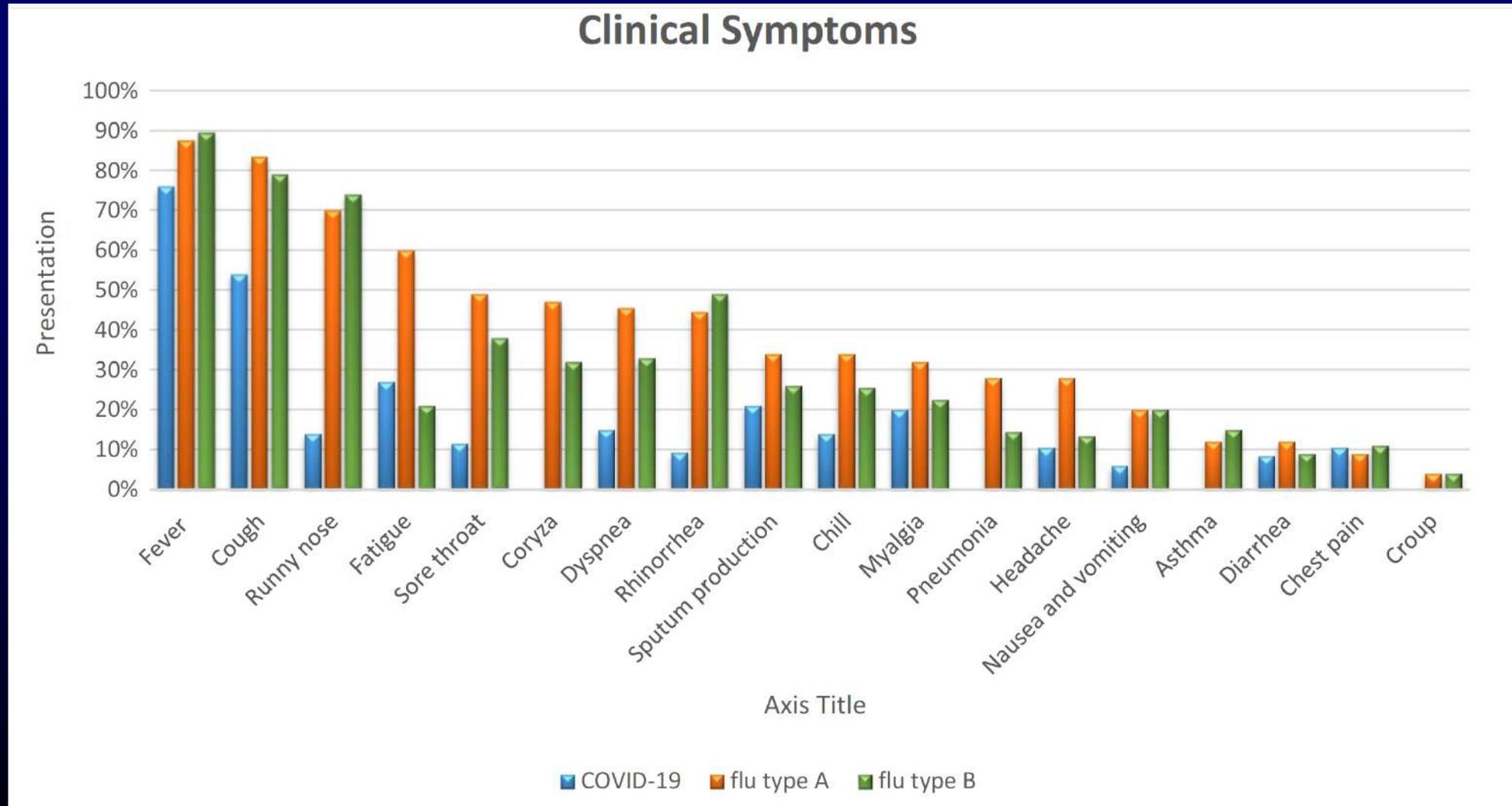


**Abstract:** Vaccines may induce positive non-specific immune responses to other pathogens. This study aims to evaluate if influenza vaccination in the 2019–2020 season had any effect on the risk of SARS-CoV-2 confirmed infection in a cohort of health workers. During the first SARS-CoV-2 epidemic wave in Spain, between March and May 2020, a cohort of 11,201 health workers was highly tested by RT-qPCR and/or rapid antibody test when the infection was suspected. Later in June, 8665 of them were tested for total antibodies in serum. A total of 890 (7.9%) health workers were laboratory-confirmed for SARS-CoV-2 infection by any type of test, while no case of influenza was detected. The adjusted odds ratio between 2019–2020 influenza vaccination and SARS-CoV-2 confirmed infection was the same (1.07; 95% CI, 0.92–1.24) in both comparisons of positive testers with all others (cohort design) and with negative testers (test-negative design). Among symptomatic patients tested by RT-qPCR, the comparison of positive cases and negative controls showed an adjusted odds ratio of 0.86 (95% CI, 0.68–1.08). These results suggest that influenza vaccination does not significantly modify the risk of SARS-CoV-2 infection. The development of specific vaccines against SARS-CoV-2 is urgent.

**Keywords:** SARS-CoV-2; COVID-19; influenza vaccination; health workers; pandemic

- The adjusted odds ratio between 2019–2020 influenza vaccination and SARS-CoV-2 confirmed infection was the same (1.07; 95% CI, 0.92–1.24) in both comparisons of positive testers with all others (cohort design) and with negative testers (test-negative design)
- Among symptomatic patients tested by RT-qPCR, the comparison of positive cases and negative controls showed an adjusted odds ratio of 0.86 (95% CI, 0.68–1.08).
- **These results suggest that influenza vaccination does not significantly modify the risk of SARS-CoV-2 infection.**

# Meta-analysis on symptoms presentation of patients with confirmed COVID-19, influenza type A and influenza type B



## Comparison of influenza type A and B with COVID-19: A global systematic review and meta-analysis on clinical, laboratory and radiographic findings

- Most of the patients with COVID-19 had abnormal chest radiology (84%,  $p < 0.001$ ) in comparison to influenza type A (57%,  $p < 0.001$ ) and B (33%,  $p < 0.001$ ).
- The incubation period in COVID-19 (6.4 days estimated) was longer than influenza type A (3.4 days).
- Likewise, the duration of hospitalization in COVID-19 patients (14 days) was longer than influenza type A (6.5 days) and influenza type B (6.7 days).
- Case fatality rate of hospitalized patients in COVID-19 (6.5%,  $p < 0.001$ ), influenza type A (6%,  $p < 0.001$ ) and influenza type B was 3% ( $p < 0.001$ ).

Original Paper

## Self-Reported Symptoms of SARS-CoV-2 Infection in a Nonhospitalized Population in Italy: Cross-Sectional Study of the EPICOID19 Web-Based Survey

	Negative, No (%) 3,536 (80.5) <sup>c</sup>	Positive, No (%) 856 (19.5) <sup>c</sup>	aOR (95% CI)	P-value
Fever	518 (14.6)	444 (51.9)	2.46 (1.98 to 3.05)	<.001
Myalgia	961 (27.2)	527 (61.6)	1.45 (1.17 to 1.80)	.001
Olfactory and/or taste disorders	291 (8.2)	507 (59.2)	10.32 (8.39 to 12.70)	<.001
Cough	984 (27.8)	466 (54.4)	1.28 (1.03 to 1.58)	.023
Shortness of breath	335 (9.5)	182 (21.3)	0.89 (0.67 to 1.18)	.403
Chest pain	386 (10.9)	206 (24.1)	0.92 (0.70 to 1.20)	.538
Tachycardia	354 (10.0)	165 (19.3)	0.93 (0.70 to 1.23)	.610
Gastrointestinal disturbances	817 (23.1)	382 (44.6)	1.20 (0.98 to 1.48)	.082
Conjunctivitis	351 (9.9)	156 (18.2)	1.11 (0.85 to 1.45)	.450
Sore throat/rhinorrea	1,332 (37.7)	415 (48.5)	0.87 (0.71 to 1.07)	.181
Headache	1,213 (34.3)	485 (56.7)	1.18 (0.95 to 1.45)	.128

*After controlling for sex, age, education, smoking habit, and number of co-morbidities*

## Symptoms reported by anti SARS CoV 2 antibodies positive subjects in Castiglione d'Adda

	IgG negative/doubt (n=3225)	IgG positive (n=918)	Total Sample (n=4143)
<b>Symptomatic : n (%)</b>			
- fever	500 (15.5%)	491 (53.5%)	991 (23.9%)
- cough	430 (13.3%)	259 (28.2%)	689 (16.6%)
- anosmia	93 ( 2.9%)	267 (29.1%)	360 ( 8.7%)
- dysgeusia	103 ( 3.2%)	311 (33.9%)	414 (10.0%)
- dispnea	128 ( 4.0%)	135 (14.7%)	263 ( 6.3%)
- rash	54 ( 1.7%)	46 ( 5.0%)	100 ( 2.4%)
- arthromyalgia	242 ( 7.5%)	258 (28.1%)	500 (12.1%)
At least one of the above:	878 (27.1%)	638 (69.5%)	1516 (36.6%)
Other symptoms	290 ( 9.0%)	227 (24.7%)	517 (12.5%)

## Influenza and COVID-19: What does co-existence mean?

### Surveillance

#### Recommendations:

- Enhance global surveillance of ILI and pneumonia with unknown aetiology
- Maintain influenza virus sharing and extend to SARS-CoV-2 to aid rapid detection of new potential pandemic strains and determination of vaccine composition
- Include diagnostic results for influenza and SARS-CoV-2 (plus other respiratory viral infections if available) in all reported ILI outbreaks
- Have sentinel sites participate in national, regional and international influenza virus and SARS-CoV-2 monitoring systems with data posted on appropriate reporting platforms
- Extend surveillance to co-infections, particularly for known respiratory pathogens causing complications, such as pneumococcal *S pneumoniae* or *S aureus*.

# Influenza and COVID-19: What does co-existence mean?

## Vaccination and antiviral use

### Recommendations:

- Increase seasonal influenza vaccination coverage for high-risk groups (eg older adults) and healthcare workers, as recommended by WHO and other health organizations
- Prepare for prophylaxis or early influenza antiviral treatment, particularly for high-risk groups, during influenza epidemics
- Increase pneumococcal vaccination coverage

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Abbreviations: ILI, influenza-like illness; WHO, World Health Organization.



# *Ministero della Salute*

DIREZIONE GENERALE DELLA PREVENZIONE SANITARIA  
Ufficio 5 Prevenzione delle Malattie Trasmissibili e Profilassi Internazionale

Nella prossima stagione influenzale 2020/2021, non è esclusa una co-circolazione di virus influenzali e SARS-CoV-2, pertanto, si rende necessario ribadire l'importanza della vaccinazione antinfluenzale, in particolare nei soggetti ad alto rischio di tutte le età, per semplificare la diagnosi e la gestione dei casi sospetti, dati i sintomi simili tra Covid-19 e Influenza. Vaccinando contro l'influenza, inoltre, si riducono le complicanze da influenza nei soggetti a rischio e gli accessi al pronto soccorso.

Grazie per l'attenzione

