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Landscape analysis of modelling activities around the world regarding the impact of SARS-CoV-2 on influenza activity

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Main findings

Our landscape analysis aimed to identify research modelling groups which have assessed the impact of SARS-CoV-2 on influenza activity, and could be approached to jointly develop models to predict influenza activity in the coming seasons based on different scenarios. We performed a scoping review and web search, and identified 7 research groups working on the interaction between influenza and SARS-CoV-2 or the impact of NPIs on influenza activity, and 4 additional studies that were slightly out of the scope of the review but used relevant modelling approaches. Of these, a research group at Princeton fits best with the FluCov aims and thus seems to be the most suitable candidate for further collaboration.

A second research group that was identified in the landscape analysis was the Bansal Lab (Disease ecology and network epidemiology research lab) at Georgetown University, who work on the impact of NPIs on infection spread and the interaction between COIVD-19 and influenza. Finally, there is a group at the Yale School of Public Health, that also works on future modelling of respiratory infections, especially Respiratory Syncytial Virus (RSV), and as such could also be an interesting partner.

Background

The emergence of the new SARS-CoV-2 virus and the accompanying prevention and control measures (e.g. non-pharmaceutical interventions (NPIs)) have had a major impact on the global circulation of other respiratory viruses, including influenza. The low levels of influenza activity observed since the start of the COVID-19 pandemic may have led to an increased proportion of susceptible subjects in the population and there is the strong potential for a resurgence of influenza cases in the coming season, especially with a scenario where NPIs are relaxed. Scenarios which consider the local context of NPIs and vaccination coverage rates (VCRs) of Influenza and COVID-19 are therefore required to support vaccine policy recommendations and ultimately best protect vulnerable populations.

FluCov

The aim of the FluCov project is to understand and communicate the impact of Covid-19 on: i) influenza activity and ii) prevention and control measures (e.g. vaccination) in the coming years. Starting in April 2021, the FluCov project collates data on SARS-CoV-2 and influenza activity, as well as prevention and control measures applied in 22 countries, to understand the impact of SARS-CoV-2 on influenza activity.

Landscape analysis

As part of the project, we performed a scoping review to prepare a landscape analysis of modelling activities worldwide regarding the impact of SARS-CoV-2 on influenza activity. The review aimed to identify studies and possible partners working on:

1. The impact of NPIs on the influenza activity and burden during the COVID-19 pandemic
2. The interaction between Influenza and SARS-CoV-2: virological competition aspects and impact of co-infections

Identified partners can be approached to jointly develop a modelling strategy to produce scenarios on the possible resurgence of influenza activity in the coming years (e.g. taking into account different parameters such as: a relaxation or continuation of non-pharmaceutical interventions, the evolution of the susceptibility to influenza), using the data collated within the FluCov project.

Research question

Here we report the main findings of the scoping review. The main research question of this scoping review was: *What potentially interesting modelling research groups that can be approached to collaborate on the development of models to predict influenza activity in the coming flu seasons based on different scenarios?*

Methods

Search strategy

Queries

To identify studies on the impact of NPIs on influenza activity, the search string (NPI OR non pharmaceutical interventions OR non pharmacological interventions) AND (influenza OR flu) was used, restricted to 2020 and 2021. The search was supplemented by screening the reference lists of included studies.

To identify studies on the interaction between influenza and SARS-CoV-2, a search in Pubmed was conducted on **10 June 2021** using the search string: ((COVID) OR (SARS-COV-2)) AND ((Influenza) OR (Flu)) AND (model*).

No geographical or language restrictions were applied, as long as an English abstract was available to decide on eligibility.

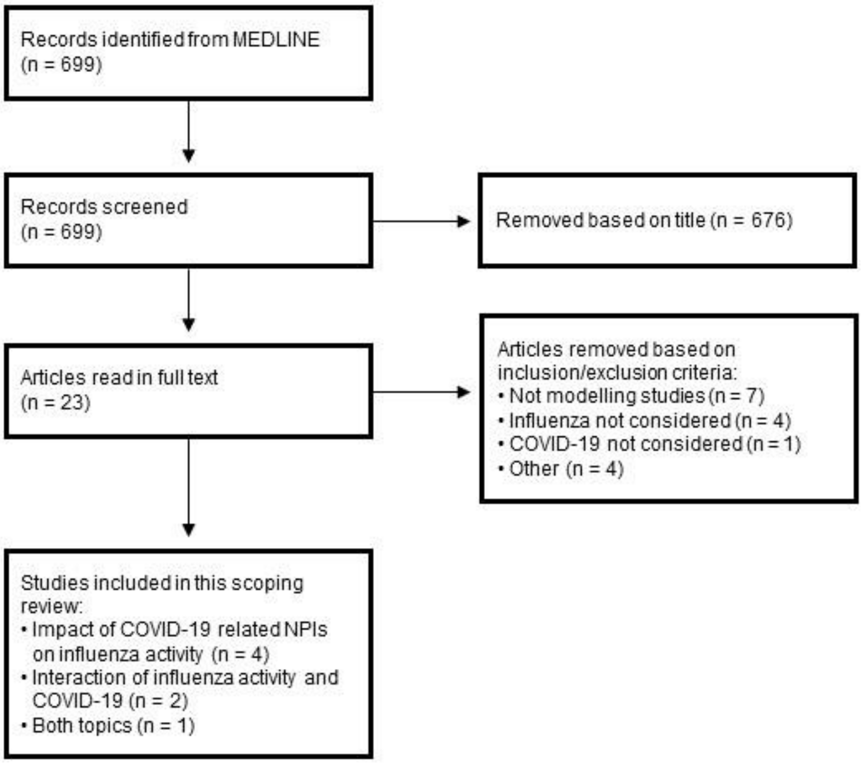
Databases
The literature search was conducted in PubMed.

Initial screening
All the articles were first screened based on their title and abstract, and those deemed as potentially eligible for inclusion were read in full copy. The literature search and article selection were conducted independently by two researchers (SW and MDR). In case of any disagreement, consensus was reached by discussion between both researchers.

Exclusion of papers
As the aim is to use the surveillance data that was collated within the FluCov project, studies on the impact of NPIs or the interaction between influenza and SARS-CoV-2 that were based on types of data that are different from the data collected within the project were excluded.

Web search
On top of the literature search, the websites of some research institutes and their modelling groups were consulted to see if any other modelling work related to both COVID-19 and influenza had been carried out.

Figure 1 Flow-chart of the literature search and article selection



Results

Query results
The first query resulted in **146** publications. The second query yielded **553** results published between 2020 and the search date. In total **699** publications were identified for initial screening.

After the initial screening, all original articles that evaluated the interaction between influenza and SARS-CoV-2 or the impact of NPIs were included in the scoping review. To be included, a paper had to report a modelling approach regarding the impact of COVID-19 prevention and control measures on the transmission of influenza or the seasonality of and correlation between SARS-CoV-2 and influenza viruses. This resulted in a total of **23** articles that were obtained and read in full text.

Excluded papers read in full text

Of the 23 selected publications, Gumel et al [2], De Visscher [15], Jung et al [19], and Ng and Gui [23] were excluded because these studies were solely about COVID-19 and not influenza. The paper of Burns and Gutfraind [11] was excluded as this was a preprint of Burns and Gutfraind [4]. Burns and Gutfraind [4] was deemed out of scope because it focused on a very small scale (schools) and a specific set of isolation policies in schools. A paper by Baker et al [5] on the implications of climatic and demographic change for seasonal influenza dynamics and evolution was excluded as it is not in direct line with the objectives of our review but was retained as background information.

Publications by Geng and Zhang [6], Yang et al [7], Oh et al [8], Zhang et al [9], and Stowe et al [18] were retrospective surveillance studies and as such did not contain the prospective modelling aspect required for FluCov. Perelson and Ke [14] and Pinky and Dobrovolny [20] were excluded as these publications focused on viral kinetics/dynamics modelling, which is not the type of modelling applicable to the FluCov data. Finally, a systematic review by Fricke et al [10] and a systematic review and meta-analysis of observational studies by Wang et al [16] were retained as background information (and for the identification of interesting additional publications from the reference lists).

Included papers

Of the **7** remaining publications, **4** addressed the impact of COVID-19 related NPIs on influenza activity and **2** addressed the interaction of influenza activity and the COVID-19 pandemic. **1** study by Zipfel and Bansal [12] involved both topics. An overview of the main aspects of these publications is given in Table 1.

Papers per topic

Included papers will now be presented for each main topic (impact of NPIs and interaction between influenza and SARS-CoV-2).

Impact of NPIs on influenza activity

Modelling studies in this area focused on different aspects. Wang et al [3] focused on the effect of COVID-19 prevention and control measures on the transmission of common respiratory viruses in a pediatric population, Zipfel and Bansal [12] and Li et al [21] on the infection spread, You [13] on influenza-related outcomes, and Baker et al [22] on RSV and seasonal influenza circulation.

Methods/models

To model the impact of COVID-19 related NPIs on influenza activity, Wang et al [3] applied interrupted time series analysis to compare differences in the detection rates of four selected respiratory viruses and polynomial curve fitting to predict the absolute number of respiratory virus detections and detection rates. The remaining studies all used a transmission model approach; Zipfel and Bansal [12] used a spatiotemporal regression model and a mechanistic metapopulation model to respectively assess deviations in the current influenza season, to compare multiple hypothesized drivers of a decrease in influenza, and transmission reduction scaled with COVID-19 risk perception. You [13] designed a Monte Carlo simulation model to estimate clinical outcomes such as clinic visits, hospitalization, deaths, medical costs, the number of influenza cases, and DALYs over several seasons. Li et al [21] developed a mathematical model on the effect of influenza vaccination and public health interventions on COVID-19 spread during the influenza season by extending the SEIR (Susceptible-Exposed-Infectious-Recovered) model with social distancing measures and cross-infections. Baker et al [22] modelled the impact of COVID-19 NPIs on RSV and seasonal influenza circulation using epidemiological SIR(S) (Susceptible-Infectious-Recovered-(Susceptible)) models and regression models.

Used data

To model the impact of COVID-19 related NPIs on influenza activity, the following data was used. Wang et al [3] used demographic and admission information combined with throat swab samples for respiratory virus detection. Zipfel and Bansal [12] used weekly influenza case data (ILI vs all-cause visits to physician), while You [13] used influenza associated hospital admission and death rates by age-group for influenza seasons 2019 and 2020. Li et al [21] used cumulative numbers of confirmed, death, cured, and suspected COVID-19 cases from January-March 2020, and finally Baker et al [22] used laboratory surveillance data from 2020.

Interaction between influenza and SARS-CoV-2

Regarding the main focus of the modelling studies, Tang et al [1] focused on understanding the seasonality of and correlation between SARS-CoV-2 and influenza viruses. Zipfel and Bansal [12] analyzed the behavioral and ecological interaction between influenza and COVID-19, and the expected effect of this interaction on the influenza season burden. Nielsen et al [17] presented estimates of excess mortality attributable to several pathogens simultaneously (e.g. COVID-19 and influenza) while correcting for seasonality and excess temperatures.

Methods/models

Several methods were applied to model the interaction between influenza and SARS-CoV-2. Tang et al [1] used time series decomposition and correlation to analyze seasonal patterns. Zipfel and Bansal [12] used intervention analysis to assess deviations in the current influenza season, spatiotemporal regression models to compare drivers of the decrease in influenza, and a mechanistic metapopulation model incorporating transmission reduction and COVID-19 risk perception. Finally, Nielsen et a [17] applied a statistical Attributable Mortality Model (ATTMOMO), which is an extension of the EuroMOMO FluMOMO model that estimates influenza-related mortality.

Used data

To study the interaction between influenza and SARS-CoV-2, Tang et al [1] used weekly percentage positive rates of 4 common human coronaviruses, seasonal factors, Zipfel and Bansal [12] used weekly influenza case data (ILI vs all-cause visits to physician), and Nielsen et al [17] used primary care symptom surveillance (e.g. ILI), secondary care severe symptom surveillance (e.g. ICD-10 codes), percentage positive tests, mortality rates, and total population count.

Identified research institutes/modelling groups

Based on literature review

In total, **7** publications used transmission models to mimic the interaction of influenza activity and the COVID-19 pandemic. Our literature review identified **4** additional research groups that applied SIR-based models, namely Burns and Gutfraind [4], De Visscher [15], and Jung et al [19], or simulation/projection models (Zhang et al [9]). However, these were not included in our review as they were not explicitly in scope (e.g. Zhang et al [9], De Visscher [15], and Jung et al [19] only focused on COVID-19 and the study of Burns and Gutfraind [4] was based in a limited setting (school)).

Table 1. Overview included publications

	Title	First author	Publ. year	Study area	Main topic	Methods/ models	Used data
[1]	Finding the Correlation between COVID-19 and Influenza Obscured by Seasonal Patterns: A Mathematical Modelling Study	Tang, L.	2021	USA	Seasonality and interaction between SARS-CoV-2 and influenza	Time series decomposition and correlation	Percentage positive rates of 4 common human corona viruses; seasonal factors
[3]	Time Distributions of Common Respiratory Pathogens Under the Spread of SARS-CoV-2 Among Children in Xiamen, China	Wang, J.	2021	China	COVID-19 prevention measures and transmission of common respiratory viruses	Interrupted time series analysis; polynomial curve fitting	Demographic and admission information; throat swab samples
[12]	Assessing the interactions between COVID-19 and influenza in the United States	Zipfel, C.	2020	USA	Impact NPIs on infection spread, characterize potential interaction between COVID-19 and other respiratory infections (taking influenza as case study)	Spatiotemporal regression model; mechanistic metapopulation model	Influenza case data
[13]	Impact of COVID-19 infection control measures on influenza-related outcomes in Hong Kong	You, J.H.	2020	Hongkong	Impact of NPIs on influenza-related outcomes	Monte Carlo simulation model	Influenza associated hospital admission and death rates
[17]	Estimates of mortality attributable to COVID-19: a statistical model for monitoring COVID-19 and seasonal influenza, Denmark, spring 2020	Nielsen, J.	2021	Denmark	Mortality estimation models for COVID-19 and influenza	Statistical Attributable Mortality Model (ATTMOMO)	Excess mortality estimates
[21]	Modeling the impact of mass influenza vaccination and public health interventions on COVID-19 epidemics with limited detection capability	Li, Q.	2020	China	Development of a mathematical model on the effect of influenza vaccination and PHI on the spread of COVID-19 during the influenza season	Extended SEIR model	Confirmed, death, cured, suspected COVID-19 cases
[22]	The impact of COVID-19 nonpharmaceutical interventions on the future dynamics of endemic infections	Baker, R.E.	2020	USA	Modeling the impact of SARS-CoV-2 NPIs on RSV and seasonal influenza circulation	Epidemiological SIR(S) models; regression models	Historic and recent RSV case data, influenza case data, population and birth data, humidity data

Table 2 lists the research groups that could be of interest for FluCov, including any related projects or papers found through their websites or an internet search. A detailed overview (e.g. research questions, applied methods, developed models, data specifications, main results) of the 11 corresponding publications can be found here.

Table 2. Research institutes identified from literature

	Researchers	Institute/Department	Related projects/papers
[1]	Liwei Tang, Min Liu, Bingyu Ren, Zhijun He, Yongsui Li, Jianfeng Chen, Jing Tian	College of Life Sciences and Oceanography, Shenzen University, Shenzen, China	None
[3]	Jinhui Wang, Tiantian Xiao, Feifan Xiao, Shaoxian Hong, Shunqin Wang, Jiancheng Lin, Yong Li, Xiaochuan Wang, Kai Yan, Deyi Zhuang	Xiamen Key Laboratory of Neonatal Diseases, Xiamen Children's Hospital (Children's Hospital of Fudan University Xiamen Branch), Xiamen, China	None
[4]	Adam A.C. Burns, Alexander Gutfraind	Division of Epidemiology and Biostatistics, School of Public Health, University of Illinois at Chicago, Chicago, IL, USA	None
[9]	Kevin Zhang, Avika Misra, Patrick J. Kim, Seyed M. Moghadas, Joanne M. Langley, Marek Smieja	Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada	Papers: - "Simulated Identification of Silent COVID-19 Infections Among Children and Estimated Future Infection Rates With Vaccination" - Projecting the impact of a two-dose COVID-19 vaccination campaign in Ontario, Canada
[12]	Casey M. Zipfel, Shweta Bansal	Department of Biology, Georgetown University, Washington DC, USA - Bansal Lab (Disease ecology and network epidemiology research lab)	Paper: - "The missing season: The impacts of the COVID-19 pandemic on influenza"
[13]	Joyce H.S. You	School of Pharmacy, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China	None
[15]	A. De Visscher	Department of Chemical and Materials Engineering, Gina Cody School of Engineering and Computer Science, Concordia University, Montreal, QC, Canada	None
[17]	Jens Nielsen, Naja Hulvej Rod, Lasse S Vestergaard, Theis Lange	Infectious Disease Epidemiology and Prevention, Statens Serum Institut, Denmark; Section of Epidemiology, Department of Public Health, University of Copenhagen, Denmark	None
[19]	Se Young Jung, Hyeontae Jo, Hwijae Son, Hyung Ju Hwang	Department of Mathematics, Pohang University of Science and Technology	None
[21]	Qian Li, Biao Tang, Nicola Luigi Bragazzi, Yanni Xiao, Jianhong Wu	Laboratory for Industrial and Applied Mathematics, Department of Mathematics and Statistics, York University, Toronto, Ontario, Canada	Wu is chairholder of NSERC Sanofi–York Industrial Research Chair in Vaccine Mathematics, Modelling and Manufacturing (IRC)
[22]	Rachel E. Baker, Sang Woo Park, Wenchang Yang, Gabriel A. Vecchi, C. Jessica E. Metcalf, Bryan T. Grenfell	Princeton Environmental Institute/Department of Ecology and Evolutionary Biology, Princeton University, Princeton, NJ, USA	Paper: - "Implications of climatic and demographic change for seasonal influenza dynamics and evolution"

Based on online search/network

The following research groups wereadditionally identified based on a web search (note: the Universities of Sydney and Auckland did not appear to have websites).

- **LSHTM** (https://cmmid.github.io/topics/covid19/): only been involved in an opinion piece on the potential of seasonal influenza vaccine and the PPV23 vaccine during the pandemic.
- **Imperial College** (https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/covid-19-publications/): none
- **University of Michigan** (https://midas.umich.edu/fighting-covid-19-with-data-science-research/): none
- **Hong Kong University** (https://fightcovid19.hku.hk/category/research/): No transmission model but this paper assesses the reduced transmissibility of influenza as a consequence of NPIs: *Cowling, B. J. et al. Impact assessment of non-pharmaceutical interventions against coronavirus disease 2019 and influenza in Hong Kong: an observational study. Lancet Public Heal. 5, e279–e288 (2020).*
- **Institut Pasteur**: none
- **Yale School of Public Health** (Daniel Weinberger): future modelling for RSV in the US (not influenza)

Conclusion

In summary, this scoping review identified 7 research groups working on the interaction between influenza and SARS-CoV-2 and influenza or the impact of NPIs on influenza activity, and 4 additional studies that were out of scope but that used some interesting modelling approaches. Of these, the research of Baker et al [22] from Princeton fits best with the FluCov aims and thus seems the most suitable candidate for further collaboration. A second potentially interesting research group is the Bansal lab (Disease ecology and network epidemiology research lab) from Georgetown University, who worked on the impact of NPIs on infection spread and the interaction between COIVD-19 and influenza (Zipfel & Bansal, [12]). Based on the internet search, Daniel Weinberger and his team at the Yale School of Public Health, was also found to work on future modelling of respiratory infections (especially RSV) and as such could be an interesting party to approach.

Limitations

Due to time constraints, we limited our literature search to PubMed and did not include other databases such as Embase. Another limitation is that the literature review includes references up until **10 June 2021** and new papers may have appeared in the meantime (note: we have done regular checks regarding this point but have not found any major new publications, however this was done in a non-fully systematic manner).

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The study

In June 2021 a scoping review was conducted in PubMed to identify modelling groups working on SARS-CoV-2 and influenza activity. Eleven potentially interesting research groups were identified that can be approached for collaboration with the FluCov project.

Learn more

You can find this publication and more information on the FluCov project on our project page: www.nivel.nl/en/flucov

About this publication

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