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Epidemiological parameter review and comparative dynamics of influenza, respiratory syncytial virus, rhinovirus, human coronavirus, and adenovirus — Source link

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Distinguishing Viruses Responsible for Influenza-Like Illness

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Abstract

The many respiratory viruses that cause influenza-like illness (ILI) are reported and tracked as one entity, defined by the CDC as a group of symptoms that include a fever of 100 degrees Fahrenheit and a cough and/or a sore throat. In the United States alone, ILI impacts 9-49 million people every year. While tracking ILI as a single clinical syndrome is informative in many respects, the underlying viruses differ in their parameters and outbreak properties. Most existing models treat either a single respiratory virus or ILI as a whole. However, there is a need for models capable of comparing several individual ILI viruses. To address this need, here we present a flexible model and simulations of epidemics for influenza, RSV, rhinovirus, seasonal coronavirus, adenovirus, and SARS/MERS, parameterized by a systematic literature review and accompanied by a global sensitivity analysis. We find that for these biological causes of ILI, their parameter values, timing, prevalence, and proportional contributions differ substantially. These results demonstrate that distinguishing the viruses that cause influenza-like illness will be an important aspect of future work on ILI diagnostics, mitigation, modeling, and preparation for future unknown pandemics.

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1. Introduction

Emerging infectious diseases are a major threat to global health security, as exemplified by the recent COVID-19 pandemic. The ease of transmissibility makes respiratory pathogens especially suited for epidemic spread [1]. Viral respiratory infections account for a large burden of annual morbidity and mortality worldwide [2] and are the cause more than 400,000 hospitalizations in children less than 18 years old [3] in the United States every year, demonstrating the perpetual scale of the challenge.

Most of these viral infections are categorized as Influenza-like Illnesses (ILI), which are defined as cases of possible influenza, or other illnesses resulting in a set of symptoms that are indistinguishable from those attributed to influenza viruses [4]. The CDC characterizes ILI as infections presenting with a fever of 100°F, and a cough and/or a sore throat [5], although common symptoms attributed to ILI include fever, chills, malaise, dry cough, loss of appetite, body aches, and nausea, combinations of which manifest depending on various pathogen-specific, environment specific, and host-determined factors [6].

The number of people impacted by ILI in the USA and beyond is significant every single year, notwithstanding the COVID pandemic. ILINet, which consists of outpatient healthcare providers in all 50 states, Puerto Rico, the District of Columbia and the U.S. Virgin Islands, reports over 60 million patient visits during the 2018-19 season [7, 8]. Indeed, 8% of the US population is considered to be infected with symptomatic influenza-like illness every year [9].

Defining ILI as a syndromic cluster rather than a specific disease or diseases is informative for keeping track of syndromic case counts, as well as for important analysis and forecasting [10]. However, the cluster of symptoms known as ILI is caused by many underlying pathogens [11, 12], most commonly, influenza viruses, common cold viruses, such as rhinovirus, adenovirus, human

respiratory syncytial virus (RSV), parainfluenza virus (PIV), human metapneumovirus (hMPV) [13], and human coronaviruses (HCoV), a novel variant of which is responsible for the COVID-19 pandemic [14].

Despite the multifaceted biological etiology of ILI, diagnostic testing for specific viruses underlying ILI is relatively rare [5], and many of the diagnostic outcomes are based on syndromic evaluation at the point of care. There are no tailored discriminatory diagnostics for use at the point of care, to evaluate pathogens that impact 9-49 million people every year in the United States alone [5]. This creates a knowledge gap in which an emergent novel respiratory pathogen such as COVID-19 can go undetected [15]. An increased understanding of the biological dynamics of specific pathogens causing ILI is needed to prevent unnecessary suffering and death [16, 17, 18].

Although clinical studies have been conducted to assess the contribution of different viruses to ILI [19, 12, 20, 21, 22, 23], the reliance on syndromic diagnostics and the consequent impact on identification and of novel threats has not been assessed until recently [24]. Modeling studies that explore the mechanism of transmission and spread of ILI pathogens have also been conducted [25]. A recent study has shown that aggregrating the underlying ILI viruses separately rather than considering ILI as a single pathogen can improve ILI forecasts [24]. However, modeling studies using diagnostics measurements, and aimed at gaining insight into differing epidemic properties of the viruses underlying ILI, have been less abundant [26, 27].

To address the need for a flexible, abstract system that enables comparison of several ILI viruses in one paper, here we provide a deterministic model for five of the most common viral pathogens responsible for ILI. Our aim is to explore how pathogens with similar syndromes (and hence grouped together as ILI), can present with varied outbreak properties, thereby requiring varied interventions. We chose the pathogens on the basis of available literature, and the outcomes of a parallel clinical study conducted in Northern New Mexico - Influenza (A and B), Respiratory Syncytial Virus (RSV), rhinovirus, Human Coronavirus (HCoV), and Adenovirus. We parameterized the model by conducting a sys-

tematic literature review, and aligned the associated sensitivity analysis with the gap analysis performed in our clinical studies.

This study presents a shift in perspective that contributes a practical foundation for advancement of diagnostics, interventions and improved pandemic preparedness of anticipated and novel ILI pathogens, and for developing modeling strategies that can support biosurveillance architectures and pandemic preparedness.

2. Methods

2.1. Model Structure

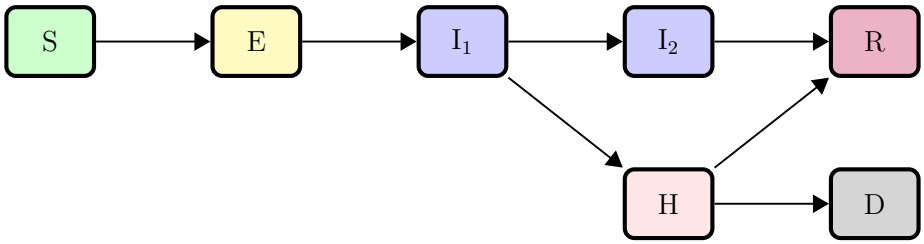

Figure 1: Transfer diagram for ILI virus transmission

Variable	Description
S	Number of susceptible individuals
E	Number of exposed (not infectious) individuals
I_1	Number of initially infectious individuals
I_2	Number of infected, non-hospitalized individuals
H	Number of hospitalized individuals
R	Number of recovered individuals
D	Number of deceased individuals

Table 1: Descriptions of state variables

Parameter	Description	Dimension
β	basic transmission rate	$individuals^{-1} \times time^{-1}$
c	reduction of transmission in hospital	dimensionless
γ_1	per capita rate of progress from exposed to infectious state	$time^{-1}$
γ_2	per capita rate of progress through initial infectious state	$time^{-1}$
γ_3	per capita rate of progress through hospitalized state	$time^{-1}$
γ_4	per capita rate of progress through non-hospitalized infectious state	$time^{-1}$
p_1	proportion of initially infectious population that becomes hospitalized	dimensionless
p_2	proportion of hospitalized population that die	dimensionless

Table 2: Parameter descriptions and dimensions

The equations governing this model of common upper respiratory virus dynamics are given by

$$\frac{dS}{dt} = -\beta S(I_1 + I_2 + cH) \tag{1a}$$
$$\frac{dE}{dt} = \beta S(I_1 + I_2 + cH) - \gamma_1 E \tag{1b}$$
$$\frac{dI_1}{dt} = \gamma_1 E - \gamma_2 I_1 \tag{1c}$$
$$\frac{dI_2}{dt} = \gamma_2(1 - p_1)I_1 - \gamma_4 I_2 \tag{1d}$$
$$\frac{dH}{dt} = \gamma_2 p_1 I_1 - \gamma_3 H \tag{1e}$$
$$\frac{dR}{dt} = \gamma_4 I_2 + \gamma_3(1 - p_2)H \tag{1f}$$
$$\frac{dD}{dt} = \gamma_3 p_2 H \tag{1g}$$

The total population is $N = S + E + I_1 + I_2 + H + R + D$.

To model five viruses that underly ILI during the course of one seasonal infection cycle, we developed a deterministic system of ordinary differential equations (Eq. 1). We then simulated daily infections of the five seasonal viruses after subtracting probable coinfections, and calculated the proportion of total daily infections contributed by each virus during the course of a hypothetical ILI season.

The model diagram (Fig. 1) illustrates the progression of ILI for 365 days in a human population of a hypothetical town containing 10,000 individuals. Five common seasonal ILI viruses, along with the historic outbreak coronaviruses SARS-CoV and MERS-Cov, are assumed to similar determininistic transmission structure.

The total population (N) consists of seven classes: susceptible (S), exposed but not infectious (E), first infectious class (I_1), second (non-hospitalized) infectious class (I_2), hospitalized (H), recovered (R), or deceased (D) (Table 1). Individuals are considered susceptible until they contact an infectious individual from (I_1), (I_2), or (H).

We modeled the progression of disease as follows: Given contact with an infectious individual, transmission takes place with some probability. After transmission has occurred, susceptible people move to the exposed class (E), where they spend a number of days equal to the period between infection and the onset of infectiousness (the latent period). In accordance with accepted literature, we assume that the latent period equals the incubation period, which is the period of time between exposure to the virus and the onset of symptoms.

After the latent period, individuals move to the first infectious class, (I_1). The duration of the first infectious period differs according to the underlying virus. Symptoms worsen for some proportion of individuals in the first infectious class, who then require hospitalization (H), where they remain infectious, with reduced transmission c. From the hospital, individuals either recover (R) or die (D). Individuals who remain sick, but do not require hospitalization for the duration of the second infectious period (I_2), typically do not suffer from serious manifestations of the disease, and we assume that they recover entirely. We assume that hospitalized individuals have 25% less contact with susceptible individuals than do infectious people outside the hospital, which results in 25% less transmission during hospitalization. We further assume that all recovered individuals (R) gain full immunity to the virus causing the illness.

We assume that the total infected population ($T = E + I_1 + I_2 + H$) and the total infectious population ($TI = I_1 + I_2 + H$) are homogeneously mixed. We assume that in the duration of a single year, demographics (natural birth or death) are negligible, and they are not modeled. We assume that the viruses act independently, although coinfection is not ruled out. Each epidemic begins with a single infected individual, and we calculate the transmission rate β for each virus is by solving for β in the expression for R_0 in Appendix B, using the mean R_0 values for each virus from the literature.

2.2. Model Parameterization

To parameterize the model, we reviewed the literature for epidemiological measurements of incubation period, infectious period, hospitalization period,

hospitalized proportion, case fatality proportion, and R_0 (cf. Table 2) for influenza A and B, RSV, rhinoviruses, coronaviruses, and adenoviruses. We included results from experimental and observational studies, as well as from systematic reviews. We also included estimates of R_0 from modeling studies, for even when symptomatically similar, many viral pathogens vary in their reproductive number. In the case of SARS, we included an estimate for the infectious period, since values were lacking in the literature [28]. We searched Google Scholar for each virus, using the name of the virus, a description of the parameter, and the type of study. For example, "influenza AND incubation period AND experimental" yielded a list of papers reporting the results of experimental studies to determine incubation period of influenza virus infections in humans. We then read the top 10 cited papers, examined the details of each study, and recorded the results (Table 3).

We iterated this process for each pathogen, until either no additional studies could be found, or the information garnered had already been incorporated in our assessment. We consulted modeling and review studies only when experimental and observational studies were not available for a given pathogen. We obtained from two to nine values for each parameter, with the exceptions of R_0 for Adenoviruses, and the hospitalization period for SARS and MERS, for which we found only one value each. We calculated the mean and standard deviation of each parameter (Table 3).

SARS-CoV-2, the virus that causes COVID-19, is a member of genus *Betacoronavirus*, along with SARS-CoV and MERS-CoV [29]. Our parameter review includes values for strains 229E, NL63, OC43, HKU1, SARS-CoV, and MERS-CoV, the six commonly circulating strains of Coronaviruses that existed prior to the advent of COVID-19. We generated a separate Coronavirus parameter table, focused on comparing the parameter values of the seasonal strains to those of the more recent SARS-CoV and MERS-CoV (Table 4). We collected means when possible; and when means were not available, we recorded medians.

2.3. Global Sensitivity Analysis

To prioritize the impact of parameters on model outputs for this nonlinear system, we carried out a global sensitivity analysis. We bounded the parameter space with the minimum and maximum parameters from the literature (Tables 3, 4, Appendix C.4). We simulated epidemics of five common upper respiratory viruses implicated in ILI: influenza, respiratory syncytial virus (RSV), Rhinovirus, seasonal human coronavirus (HCoV), and adenovirus, alongside outbreak strains of SARS-CoV and MERS-CoV, grouped together.

We assessed the impact of five model input variables of β (basic transmission rate), γ_1 (1/incubation period), γ_2 (1/onset to hospitalization), γ_3 (1/hospitalized period), and γ_4 (1/non-hospitalized period) on three response variables of total number of infections, magnitude of epidemic peak (peak height), and time to epidemic peak. We used Latin Hypercube Sampling (LHS) [30] to generate 10,000 sets of values from the total parameter space for each of the five parameters, for each of the viruses. We considered the parameter ranges for seasonal coronaviruses (HCoV) separately from SARS-CoV/MERS-CoV. We calculated β ranges by solving Equation B.4 for β and substituting the minimum and maximum values from the literature (Table D.5). In the case of adenovirus, we found only one R_0 value in the literature, and assumed minimum and maximum values of -20% and $+20\%$ from this single value. We solved the ODE system numerically for these sample input values using the default integration routine "ode" in R package deSolve, then constructed a dataframe of the marginal relations between the individual parameters and outputs. We generated sensitivity plots in R using Smoothed Conditional Means ("statsmooth") and trend lines using weighted least squares method Local Polynomial Regression Fitting in R ("loess") [31]. We assumed a uniform distribution on the parameters.

3. Results

3.1. Model Simulation Results

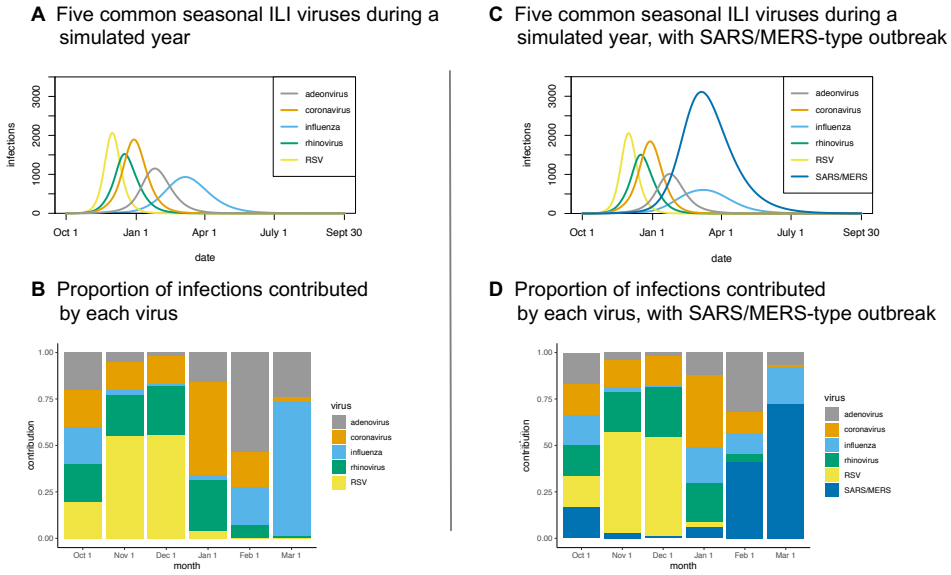

Figure 2: Seasonal and outbreak simulations. Panel 2A displays a numerical simulation of daily infections for five seasonal ILI viruses for one hypothetical year. The x-axis shows time in days; the y-axis shows number of infections. Each virus begins by infecting one individual, with 9,999 susceptible individuals. We assume no background immunity, vaccination, or mitigations; each virus acts independently; probable coinfections are subtracted. Inputted parameter values are the means from the literature (Table 3). Values for coronavirus are the means for the pre-SARS-CoV-2, endemic, seasonal coronaviruses OC43, 229E, HKU1, and NL63, considered as a group. Panel 2B displays six snapshots of the proportion contributed by each virus on the first day of each month of the hypothetical "flu" season. The x-axis shows the first day of each month; the y-axis shows the proportional contributions. Panels 2C and 2D are the analogous plots, with the inclusion of the outbreak coronaviruses SARS-CoV and MERS-CoV, considered as a group.

We find that when we numerically simulate seasonal epidemics for five common ILI viruses, setting all of their starting times at October 1st, the varied ranges of historic parameter values for each virus result in varied timing, prevalence, and contributions of these underlying biological causes of ILI (Figure 2). RSV peaks in December, followed by rhinovirus. Seasonal coronavirus peaks in January, adenovirus peaks in February, and influenza peaks in March. RSV has the greatest total cumulative infections and the highest peak (greatest maximum daily number of infections), while influenza has the least total cumulative infections and the lowest peak. The numerical simulation of SARS and MERS, not illustrated here as an epidemic curve because not considered seasonal, has the greatest overall number of cumulative infections.

We find that on the first day of any given month during the simulated ILI season, the composition of ILI attributable to the individual viruses varies considerably (see the stacked bar chart in (Figure 2)). On October 1st, each represents 20% of the total five infections, reflecting the initial condition that each epidemic begins with one infection. On November 1st and December 1st respectively, RSV constitutes 55% and 56% of total ILI infections. On January 1st, seasonal coronavirus contributes 50% of the total; on February 1st, adenovirus contributes 54%; on March 1st, influenza contributes 73%.

3.2. Model Parameterization Results

We find 104 studies that contained relevant parameter values (Table 3). According to our literature review, adenovirus exhibits the longest mean incubation period, seasonal coronavirus has the longest total mean infection period, and RSV has the highest mean R_0. Notably, out of the viruses studied, RSV incubation period values have the least standard deviation, while adenovirus values have the greatest standard deviation. Rhinovirus infectious period values have the least standard deviation, while SARS/MERS has the greatest. And finally, rhinovirus R_0 values have the least variation, while RSV R_0 values have the greatest variation.

We find that the seasonal and historical outbreak coronaviruses differ considerably in their defining epidemiological parameters. The incubation and hospitalization periods of SARS and MERS are almost double that of their seasonal counterparts, while their infectious period is more than double. The mean R_0 for the betacoronaviruses SARS and MERS is 3.81, while that of the seasonal coronavirus strains is 2.84 (Table 4).

Of the 104 studies, 10 provide values for the percentage of each of the five viruses in question identified among ILI patients. In these 10 studies, on average, at least one virus is identified in 62% of individuals with ILI symptoms. Out of these 62% (mean values), influenza is identified in a 21.3% of samples, RSV in 13.5% , rhinovirus in 22.6%, human coronavirus in 8.8%, and adenovirus in 8.1%. The presence or absence of co-infection is not taken into account in the percentages reported by these studies.

Virus	Range (Min to Max)	Mean	Standard Deviation	References
Incubation Period (days)				
Influenza	1-6.3	2.61	0.993	[32, 33, 34, 35, 36, 37, 38, 39, 40]
RSV	3-8	4.5	0.894	[39, 32, 41, 42, 43, 40]
Rhinovirus	0.42-5.5	2.36	1.10	[39, 44, 45, 46, 47, 48, 49, 32, 43, 40]
Human coronavirus	1.9-14.7	5.07	2.21	[39, 50, 43, 40, 51, 52, 53, 54]
Adenovirus	1-30	6.71	2.04	[55, 39, 56, 57, 58, 40, 59]
Infectious Period (days)				
Influenza	1-9	4.58	2.56	[33, 34, 37, 22, 60, 11]
RSV	1-21	7.72	1.94	[61, 62, 63, 11]
Rhinovirus	7-16	9.40	1.70	[11, 64, 65, 66, 67]
Human coronavirus	7-35	15.20	10.30	[11, 68, 69, 51, 54, 28]
Adenovirus	7-17	8.20	2.89	[55, 11, 70, 59]
Hospitalization Period (days)				
Influenza	3.5-11.3	6.36	3.27	[22, 71, 72, 11, 73]
RSV	2-17.5	5.24	2.32	[74, 75, 76, 11, 77, 73]
Rhinovirus	0.4-1.67	1.19	0.87	[11, 78, 79]
Human coronavirus	1.5-11	4.96	4.27	[11, 69, 80, 81]
Adenovirus	3.12-7	4.71	2.03	[11, 77, 82]
Hospitalization Proportion				
Influenza	0.000035-0.062	0.0037	0.0075	[83, 73, 84, 85, 11]
RSV	0.00034-0.29	0.021	0.0215	[86, 87, 83, 73, 88, 11, 62]
Rhinovirus	0.0093-0.024	0.0121	0.0108	[11, 89, 90]
Human coronavirus	0.00224-0.52	0.188	0.241	[11, 91, 92, 69]
Adenovirus	0.014-0.95	0.43	0.39	[12, 93, 11, 70]
Case Fatality Proportion				
Influenza	0.000106-0.0827	0.0312	0.0415	[94, 95, 96, 97, 98]
RSV	0.00031-0.165	0.0464	0.0627	[99, 74, 95, 100, 88, 101]
Rhinovirus	0-0.125	0.0451	0.0694	[64, 102, 103]
Human coronavirus	0-0.34	0.147	0.146	[104, 105, 91, 92, 101, 103]
Adenovirus	0.00075-0.166	0.103	0.0694	[12, 106, 107, 108, 109, 70]
R_0				
Influenza	1.06-3.4	1.68	0.871	[110, 111, 112, 113, 114, 115]
RSV	1.2-9.1	3.47	2.67	[62, 116, 117, 118, 119, 120, 121]
Rhinovirus	1.2-2.6	1.88	0.70	[120, 121, 122]
Human coronavirus	2.7-8	4.18	2.26	[123, 105, 124, 125, 101, 126, 127, 128]
Adenovirus	2.34 (one value)	2.34	NA	[26]

Table 3: ILI parameters from literature. Coronavirus refer to the six pre-SARS-CoV-2 strains.

Virus	Range (Min to Max)	Mean	Standard Deviation	References
Incubation Period (days)				
Seasonal coronaviruses	3.3-4.0	3.46	0.33	[39, 50, 43, 40, 51]
SARS and MERS	4.7-10	6.68	1.86	[52, 53, 54]
Infectious Period (days)				
Seasonal coronaviruses	10.1-13.46	11.29	1.53	[11, 68, 51]
SARS and MERS	23.5-35	28.5	4.81	[54, 28]
Hospitalization Period (days)				
Seasonal coronaviruses	2-4.9	3.68	1.22	[69, 80]
SARS and MERS	1.5-11	6.25	4.75	[11, 81]
Hospitalization Proportion				
Seasonal coronaviruses	0.0022-0.52	0.024	0.018	[11, 91, 92, 69]
SARS and MERS	0.00046	0.045	0.045	[129]
Case Fatality Proportion				
Seasonal coronaviruses	0-0.053	0.027	0.027	[91, 103]
SARS and MERS	0.06-0.34	0.18	0.10	[104, 105, 92, 101]
R_0				
Seasonal coronaviruses	2.2-3.7	2.84	0.57	[101, 130]
SARS and MERS	2.7-8	3.81	1.81	[123, 105, 124, 125, 126, 127, 128]

Table 4: This table distinguishes between endemic seasonal coronaviruses (229E, NL63, OC43, and HKU1) and historic sporadic outbreak coronaviruses (SARS-CoV and MERS-CoV).

3.3. Global Sensitivity Results

The global sensitivity analysis for our nonlinear system reveals several differences between the six viruses under consideration: influenza, RSV, rhinovirus, seasonal coronavirus, adenovirus, and SARS/MERS.

The impact of the basic transmission rate β on total cumulative infections is relatively tightly constrained for all six viruses (Appendix E). The trend line for influenza is slightly sigmoid, while the trend lines appear exponential for the other five, approaching 100% of the population asymptotically near their mean β values. For influenza and RSV, the Latin Hypercube Samples (LHS) for all five input variables have bimodal distributions for cumulative cases and time to peak. That is, for influenza and RSV, but not for the other four viruses, there are trivial numerical solutions for the system in which epidemics never take off, as well as nontrivial solutions, where they do take off. This is reflected in the disease-free equilibrium (Appendix A) and in the histograms (Appendix E).

The impact of β on peak height for the 10,000 LHS samples is not as constrained overall as for cumulative cases, although the variance is narrower than that of the other four input variables. The LHS sample distributions for output variable time to peak are bimodal for influenza and RSV, while they are unimodal for the other four viruses. Distributions for seasonal coronaviruses and historic outbreak coronaviruses (SARS/MERS) are unimodal (Appendix E).

An important difference between the seasonal and outbreak coronaviruses may be seen in Figure 3. Note that the y-axis for the outbreak coronaviruses represents approximately double the time period of the y-axis for seasonal coronaviruses. In both cases, the relationship of the transmission rate to the number of days to the epidemic peak is logarithmic and well constrained. In both cases, as the transmission rate increases, the time to peak shortens; conversely, as the transmission rate decreases, the time to peak is delayed. The other four input variables, representing speed of progression through the stages of disease, have unremarkable impacts on the output variables.

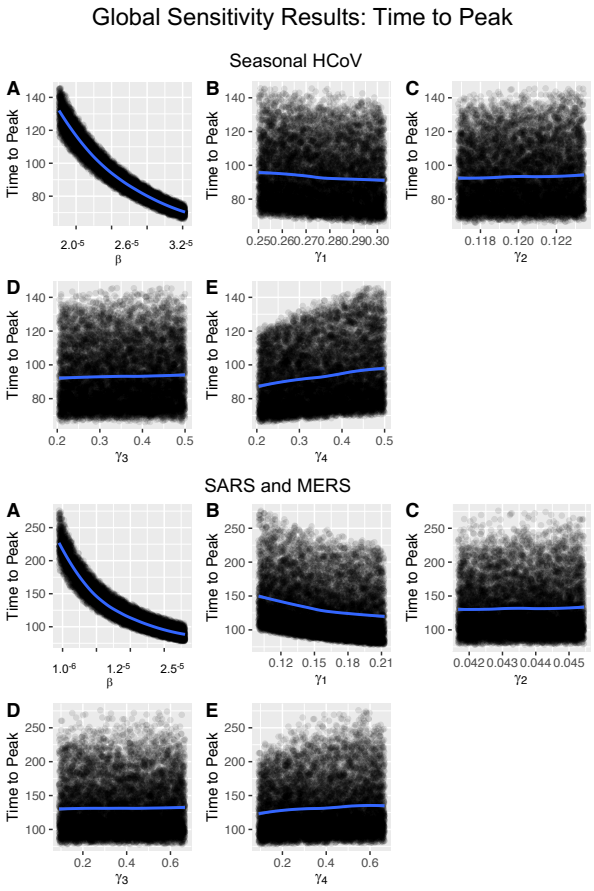

Figure 3: Global sensitivity analysis for seasonal coronaviruses (top) and historic outbreak coronaviruses SARS and MERS (bottom), showing the impact of five input variables on model output variable of time to epidemic peak. Note the different scale of the y axes on the β plots. Complete sensitivity results may be found in Appendix E.

4. Discussion

Although the five viruses considered here present clinically with similar symptoms, their parameters and epidemic characteristics differ, illustrating the vast potential not only for misdiagnosis and uninformed mitigation strategies, but for missing early signals of future novel emerging diseases. These results support those in Pei and Shaman's recent paper [24] that demonstate differing outbreak properties of individual viruses that contribute to ILI.

From our sensitivity analysis, it is apparent that virus transmission rates, and therefore also effective reproduction numbers, have much greater impact on the output variables than do the other four input variables, more biologically intrinsic to each virus, that represent speed of the phases of disease progression. From a mitigation perspective, the transmission rate is the variable we can impact with public health policies. For example, by implementing mask-wearing and physical distancing, we can reduce and delay epidemic peak(s) of outbreak respiratory viruses, reducing cases and deaths as well as the burden on the healthcare system.

Many of the studies that generated parameter values evaluated populations treated at clinics or admitted at hospitals. However, a significant proportion of illness and death may occur outside of hospitals and clinics (see Cohen et al. 2017). Our formula for R_0 is based on the traditional assumption of a naive population; however, our parameter review reports many values from clinical studies conducted on populations that have been exposed to the seasonal ILI viruses in circulation, and therefore have some level of background immunity. Thus, these values likely reflect the effective reproductive number (R_e) rather than R_0, with the exception of SARS-CoV and MERS-CoV, which were novel zoonoses when they appeared. Further, the studies reviewed herein have taken place over many decades, during which viral evolution may be presumed to have occurred.

In our simulations, we treat the viruses contributing to the clinical syndrome

of influenza-like illness as though they act independently, although a recent theoretical study has shown that even noninteracting pathogens are not necessarily mathematically independent [131]. A recent clinical study has shown rhinovirus can function to block subsequent infection by influenza [132]. Further studies are needed to assess the potential for both within-host and between-host viral interactions.

A limitation of our simulation results is that we have based them on mean historic parameter values, which does not take into account seasonal impacts on those parameters. Further, we have uniformly introduced the first infected individual for all viruses on October 1st of our hypothetical ILI season; however, in real world phenomena, these initial infections may happen at different times in different populations, and could happen in varied orders in different years.

The flexible deterministic model, numerical simulations, and sensitivity analysis included herein set the stage for future studies to investigate potential interactions of individual viruses that contribute to ILI. The parameterization study provides a meta-analysis of clinical studies during the past century that have provided the basic epidemiological parameters for modeling five of the common viruses contributing to the clinical syndrome of influenza-like illness. Along with previous work, the results presented herein indicate that in order to improve diagnosis, mitigation, and modeling of respiratory viruses, as well as to be prepared for the next pandemic, individual viruses contributing to influenza-like illness should be considered separately.

CREdiT authorship contribution statement

Julie A. Spencer: Conceptualization, Methodology, Formal analysis, Visualization, Writing - Original Draft, Writing - Review & Editing. **Deborah P. Shutt:** Conceptualization, Methodology. **Sarah K. Moser:** Investigation, Visualization. **Hannah Clegg:** Conceptualization, Investigation. **Helen J. Wearing:** Conceptualization, Methodology, Formal analysis, Supervision, Writing - Review & Editing. **Harshini Mukundan:** Conceptualization, Project administration, Funding acquisition, Supervision, Writing - Review &

Editing. **Carrie A. Manore:** Conceptualization, Methodology, Funding acquisition, Supervision, Writing - Review & Editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Disease-free Equilibrium

In the disease-free state, all infected classes are zero, that is, $E = I_1 = I_2 = H = 0$. Substituting and setting the derivatives equal to zero, it is evident that in the disease-free state, the other state variables R and D will continue to contain zero individuals, and that the Susceptible class S will remain equal to the total population N.

If we set any one of E, I_1, I_2, or H to zero, the other three state variables representing infected classes must also be zero. In this case, N=S=10000. Thus, where $x = (S, E, I_1, I_2, H, R, D)$ denotes solutions of the system, $x_{dfe} = (10000, 0, 0, 0, 0, 0, 0)$ represents the disease-free equilibrium for the system.

Appendix B. Derivation of Basic Reproductive Number

The basic reproductive number (R_0) is defined as the average number of secondary infections produced when one infected individual is introduced into a fully susceptible population. Four compartments, latently infected individuals (E), symptomatic and infected individuals (I_1), symptomatic and infected and non-hospitalized individuals (I_2), and hospitalized individuals (H), together characterize the total infected population for the ILI virus system. To calculate R_0 for this system, we derive the next generation matrix [133].

Method:

1. Derive the matrix for the transmission term describing everyone entering (E): the "F" matrix;

2. Derive the matrix for the transition terms describing everyone transitioning between infected classes (E, I_1, I_2, H): the "V" matrix;

3. Next Generation Matrix (NGM) $= (F)(V^{-1})$;

4. The largest dominant eigenvalue or spectral radius of the NGM $= R_0$ for the system.

The transmission term for the system is $\beta S(I_1 + I_2 + cH)$

$$\mathbf{F} = \begin{pmatrix} 0 & \beta S & \beta S & \beta S c \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \tag{B.1}$$

The transition terms for the system are $(-\gamma_1 E), (\gamma_1 E - \gamma_2 I_1), (\gamma_2(1-p_1)I_1 - \gamma_4 I_2), (\gamma_2 p_1 I_1 - \gamma_3 H)$.

$$\mathbf{V} = \begin{pmatrix} \gamma_1 & 0 & 0 & 0 \\ -\gamma_1 & \gamma_2 & 0 & 0 \\ 0 & -\gamma_2(1-p_1) & \gamma 4 & 0 \\ 0 & -\gamma_2 p_1 & 0 & \gamma 3 \end{pmatrix} \tag{B.2}$$

The next generation matrix is thus

$$\mathbf{FV^{-1}} = \begin{pmatrix} \beta S(\frac{1}{\gamma_2} - \frac{(p_1-1)}{\gamma_4} + \frac{cp_1}{\gamma_3}) & \beta S(\frac{1}{\gamma_2} - \frac{(p_1-1)}{\gamma_4} + \frac{cp_1}{\gamma_3}) & \frac{\beta S}{\gamma_4} & \frac{\beta Sc}{\gamma_3} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \tag{B.3}$$

The spectral radius, or the largest positive eigenvalue of the next generation matrix, is the basic reproductive number of the system at the disease-free equilibrium.

$$\mathbf{R_0} = \frac{\beta S(cp_1\gamma_2\gamma_4 - p_1\gamma_2\gamma_3 + \gamma_2\gamma_3 + \gamma_3\gamma_4)}{\gamma_2\gamma_3\gamma_4} \tag{B.4}$$

$$\mathbf{R_0} = \beta S\left(\frac{1}{\gamma_2} + \frac{cp_1}{\gamma_3} + \frac{(1-p_1)}{\gamma_4}\right) eq : R0_2 \tag{B.5}$$

This expression for the basic reproductive number (R_0) depends on the parameters $\beta, c, p_1, \gamma_2, \gamma_3$ and γ_4, and on the initial conditions of the state variables. Equation B.5 shows that R_0 for this system is a combination of the transmission

that takes place in the pre-symptomatic (I_1), symptomatic, (I_2), and hospitalized (H) compartments. This is the per-day transmission rate (β) multiplied by the time spent in each of these compartments.

Appendix C. Parameter Ranges

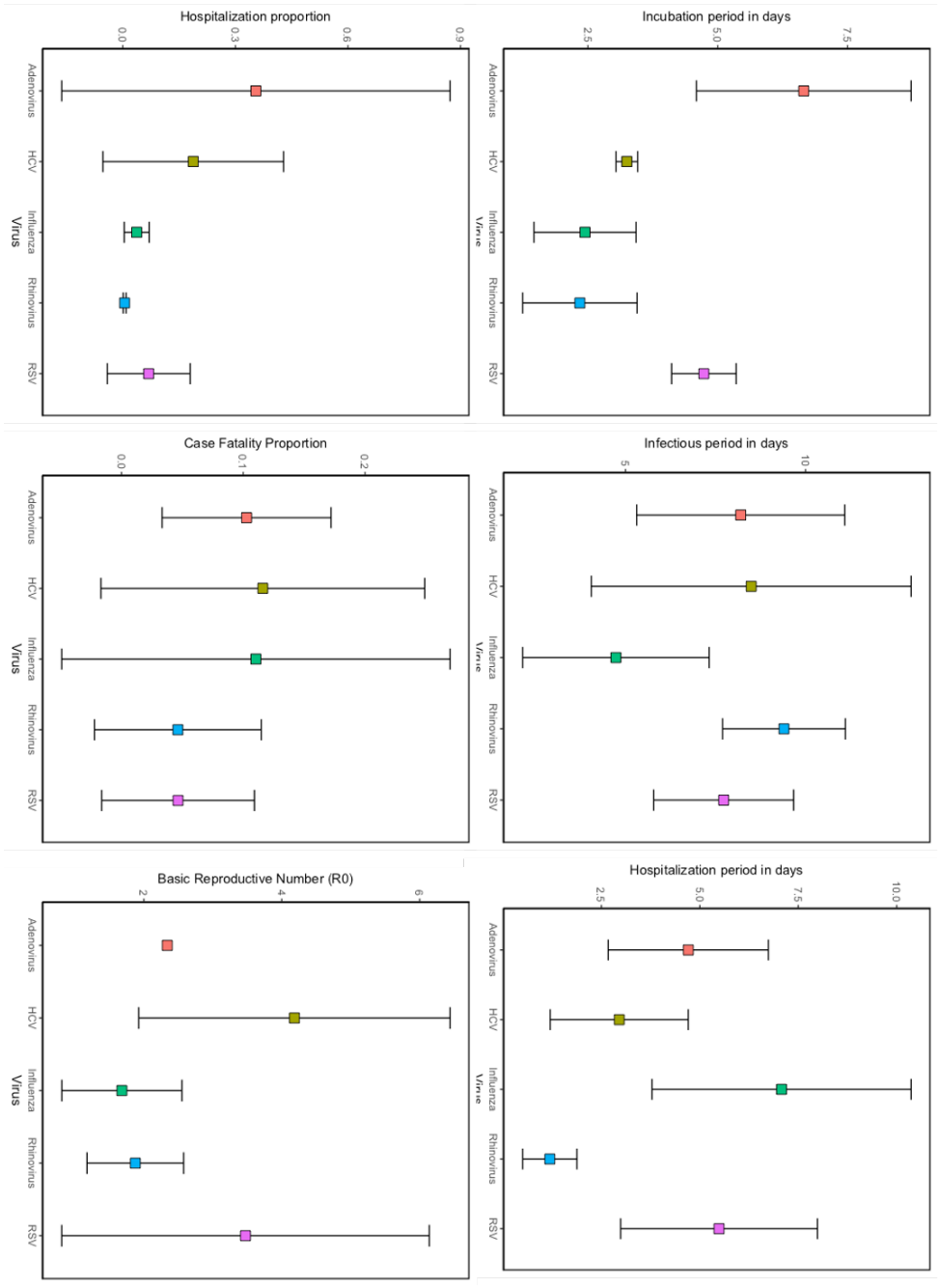

Figure C.4: Parameter ranges for five common ILI viruses from literature review

Appendix D. Transmission Rates

Virus	Min	Max	Mean
Influenza	9.69^{-6}	3.12^{-5}	1.54^{-5}
RSV	1.55^{-5}	1.18^{-4}	4.49^{-5}
Rhinovirus	1.81^{-5}	3.92^{-5}	2.83^{-5}
Seasonal HCoV	1.95^{-5}	3.28^{-5}	2.52^{-5}
Adenovirus	2.28^{-5}	3.42^{-5}	2.85^{-5}
SARS/MERS	9.47^{-6}	2.81^{-5}	1.34^{-5}

Table D.5: This table reports β (basic transmission rate) values calculated from solving Equation (6) for β, and substituting in the parameter values from the literature review (Tables 3 and 4).

Appendix F. References

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INFLUENZA parameters: incubation period, infectious period, hospitalization period, hospitalization proportion, case fatality, R0

parameter	type of study	study time	population	sample size	strain	definition of	method	notes	patient age	range	mean	citation
(Influenza A & B)												
incubation period												
	experimental	30 days	healthy adults	17	seasonal	inoculation to peak symptoms			adult	2-4 days, median 3.3	3 days	Zaas, A.K., Chen, M., Varkey, J., Veldman, T., Hero III, A.O., Lucas, J., Huang, Y., Turner, R., Gilbert, A., Lambkin-Williams, R. and Øien, N.C., 2009. Gene expression signatures diagnose influenza and other symptomatic respiratory viral infections in humans. Cell host & microbe, 6(3), pp.207-217.
	experimental	8 days	healthy males	16	FluA (H1N1)	inoculation to occurrence of symptoms			19-35	1-3 days	2 days	Fritz, R.S., Hayden, F.G., Calfee, D.P., Cass, L.M., Peng, A.W., Alvord, W.G., Strober, W. and Straus, S.E., 1999. Nasal cytokine and chemokine responses in experimental influenza A virus infection: results of a placebo-controlled trial of intravenous zanamivir treatment. The Journal of infectious diseases, 180(3), pp.586-593.
	experimental	49 days	male inmates	43	FluA (Hong Kong)	inoculation to onset			21-40	2-3 days	2.5 days	Couch, R.B., Gordon Douglas Jr, R., Fedson, D.S. and Kasel, J.A., 1971. Correlated studies of a recombinant influenza-virus vaccine. III. Protection against experimental influenza in man. Journal of Infectious Diseases, 124(5), pp.473-480.
	observational		admitted to hospital	8	seasonal	exposure to onset		exposed to diseased/dead chickens	5--15	3.7-6.3 days	5 days	Oner, A.F., Bay, A., Arslan, S., Akdeniz, H., Sahin, H.A., Cesur, Y., Epcacan, S., Yilmaz, N., Deger, I., Kizilyildiz, B. and Karsen, H., 2006. Avian influenza A (H5N1) infection in eastern Turkey in 2006. New England Journal of Medicine, 355(21), pp.2179-2185.
	observational		airline passengers	54	FluA(H5N1)	airline delay to onset				1-3 days	1.5 days	Moser, M.R., Bender, T.R., Margolis, H.S., Noble, G.R., Kendal, A.P. and Ritter, D.G., 1979. An outbreak of influenza aboard a commercial airliner. American journal of epidemiology, 110(1), pp.1-6.
	experimental	8 days	healthy adults	14	FluA(H1N1)	inoculation to onset			19-40	2-3 days	2.5 days	Kaiser, L., Briones, M.S. and Hayden, F.G., 1999. Performance of virus isolation and Directigen® Flu A to detect influenza A virus in experimental human infection. Journal of clinical virology, 14(3), pp.191-197.
	observational		asthmatic children	20	NA				43689	2-3 days	2.5 days	Kondo, S. and Abe, K., 1991. The effects of influenza virus infection on FEV1 in asthmatic children: the time-course study. Chest, 100(5), pp.1235-1238.
	systematic review					inoculation to onset of symptoms		range and central tendency	all	1-4 days	2 days	REVIEW: Lessler, J., Reich, N.G., Brookmeyer, R., Perl, T.M., Nelson, K.E. and Cummings, D.A., 2009. Incubation periods of acute respiratory viral infections: a systematic review. The Lancet infectious diseases, 9(5), pp.291-300.
	review	before 2004	literature							1-4 days	2.5	REVIEW: Wat, D., 2004. The common cold: a review of the literature. European Journal of Internal Medicine, 15(2), pp.79-88.
infectious period												
	experimental	8 days	healthy males		FluA(H1N1)		virus titer	mean viral shedding period 4.6 days	19-35	3.1-5.7 days	4.6 days	Fritz, R.S., Hayden, F.G., Calfee, D.P., Cass, L.M., Peng, A.W., Alvord, W.G., Strober, W. and Straus, S.E., 1999. Nasal cytokine and chemokine responses in experimental influenza A virus infection: results of a placebo-controlled trial of intravenous zanamivir treatment. The Journal of infectious diseases, 180(3), pp.586-593.
	experimental	49 days	male inmates		FluA (Hong Kong)				21-40	2-9 days	5.5 days	Couch, R.B., Gordon Douglas Jr, R., Fedson, D.S. and Kasel, J.A., 1971. Correlated studies of a recombinant influenza-virus vaccine. III. Protection against experimental influenza in man. Journal of Infectious Diseases, 124(5), pp.473-480.
	experimental								19-40	1-8 days	4.5 days	Kaiser, L., Briones, M.S. and Hayden, F.G., 1999. Performance of virus isolation and Directigen® Flu A to detect influenza A virus in experimental human infection. Journal of clinical virology, 14(3), pp.191-197.
		14 days	ferrets	8	FluA(H1N1)		culture + RT-PCR, titer			2 days	2 days	
	observational		index contacts	350	seasonal		culture + RT-PCR		all		2 days	Cowling, B.J., Fang, V.J., Riley, S., Peiris, J.M. and Leung, G.M., 2009. Estimation of the serial interval of influenza. Epidemiology (Cambridge, Mass.), 20(3), p.344.
	experimental	1 year	otherwise healthy ILI children		seasonal				6 months-10 yrs		8.9 days	Taylor, S., Lopez, P., Weckx, L., Borja-Tabora, C., Ulloa-Gutierrez, R., Lazcano-Ponce, E., Kerdpanich, A., Weber, M.A.R., de Los Santos, A.M., Tinoco, J.C. and Safadi, M.A.P., 2017. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. Journal of Infection, 74(1), pp.29-41.
	observational	1975-1995	healthy adults	59	seasonal	mean duration of illness			adult		6.8 days	Hall, C.B., Long, C.E. and Schnabel, K.C., 2001. Respiratory syncytial virus infections in previously healthy working adults. Clinical infectious diseases, 33(6), pp.792-796.
hospitalization period												
	observational	31 days (2016)	confirmed FluB outbreak in hospital			mean length of hosp. stay					11.3 days	Sansone, M., Wiman, Å., Karlberg, M.L., Brytting, M., Bohlin, L., Andersson, L.M., Westin, J. and Nordén, R., 2019. Molecular characterization of a nosocomial outbreak of influenza B virus in an acute care hospital setting. Journal of Hospital Infection, 101(1), pp.30-37.
	retrospective	19 years	respiratory disease patients						0-72 months		8 days	Kim, H.W., Brandt, C.D., Arrobio, J.O., Murphy, B., Chanock, R.M. and Parrott, R.H., 1979. Influenza A and B virus infection in infants and young children during the years 1957–1976. American Journal of Epidemiology, 109(4), pp.464-479.
	observational	2016-2017	ILI patients						all	4-6 days	5 days	Drăgănescu, A., Săndulescu, O., Florea, D., Vlaicu, O., Streinu-Cercel, A., Oţelea, D., Aramă, V., Luminos, M.L., Streinu-Cercel, A., Niţescu, M. and Ivanciuc, A., 2018. The influenza season 2016/17 in Bucharest, Romania–surveillance data and clinical characteristics of patients with influenza-like illness admitted to a tertiary infectious diseases hospital. Brazilian Journal of Infectious Diseases, 22(5), pp.377-386.
	experimental	1 year	otherwise healthy ILI children		seasonal				6 months-10 yrs		4 days	Taylor, S., Lopez, P., Weckx, L., Borja-Tabora, C., Ulloa-Gutierrez, R., Lazcano-Ponce, E., Kerdpanich, A., Weber, M.A.R., de Los Santos, A.M., Tinoco, J.C. and Safadi, M.A.P., 2017. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. Journal of Infection, 74(1), pp.29-41.

	observational	2009-2011	children <5	17		median length of hospital stay			< 5	3-4 days	3.5 days	Broor, S., Dawood, F.S., Pandey, B.G., Saha, S., Gupta, V., Krishnan, A., Rai, S., Singh, P., Erdman, D. and Lal, R.B., 2014. Rates of respiratory virus-associated hospitalization in children aged< 5 years in rural northern India. Journal of Infection, 68(3), pp.281-289.
hospitalization proportion												
	observational	1 season	children			number hospitalized out of 1,000			< 5		0.0006	Iwane, M.K., Edwards, K.M., Szilagyi, P.G., Walker, F.J., Griffin, M.R., Weinberg, G.A., Coulen, C., Poehling, K.A., Shone, L.P., Balter, S. and Hall, C.B., 2004. Population-based surveillance for hospitalizations associated with respiratory syncytial virus, influenza virus, and parainfluenza viruses among young children. Pediatrics, 113(6), pp.1758-1764.
	observational	2009-2011	children <5 in India	245		numer hospitalized out of 10,000			< 5		0.0012	Broor, S., Dawood, F.S., Pandey, B.G., Saha, S., Gupta, V., Krishnan, A., Rai, S., Singh, P., Erdman, D. and Lal, R.B., 2014. Rates of respiratory virus-associated hospitalization in children aged< 5 years in rural northern India. Journal of Infection, 68(3), pp.281-289.
	retrospective, adjusted	2003-2013	all population			number hospitalized out of 100,000	PCR, culture, DFA, RIDT		all	0.00003-0.0018	0.00092	Millman, A. J., Read, C., Kirley, P., Aragon, D., Meek, J. I., Farley, M. M....Chaves, S. (2015). Improving Accuracy of Influenza-Associated Hospitalization Rate Estimates. Emerging Infectious Diseases, 21(9), 1595-1601. https://dx.doi.org/10.3201/eid
	observational	2004-2008	all population			number hospitalized out of 100,000			<6 months-≥75 yrs		0.00028	Ang, L.W., Lim, C., Lee, V.J.M., Ma, S., Tiong, W.W., Ooi, P.L., Lin, R.T.P., James, L. and Cutter, J., 2014 Influenza-associated hospitalizations, Singapore, 2004–2008 and 2010–2012. Emerging infectious diseases, 20(10), p.1652.
	observational	2010-2012	all population			number hospitalized out of 100,000			<6 months-≥75 yrs		0.0003	Ang, L.W., Lim, C., Lee, V.J.M., Ma, S., Tiong, W.W., Ooi, P.L., Lin, R.T.P., James, L. and Cutter, J., 2014 Influenza-associated hospitalizations, Singapore, 2004–2008 and 2010–2012. Emerging infectious diseases, 20(10), p.1652.
	observational	1 year	otherwise healthy ILI children	476	seasonal	number hospitalized out of 476			6 months-10 yrs		0.019	Taylor, S., Lopez, P., Weckx, L., Borja-Tabora, C., Ulloa-Gutierrez, R., Lazcano-Ponce, E., Kerdpanich, A., Weber, M.A.R., de Los Santos, A.M., Tinoco, J.C. and Safadi, M.A.P., 2017. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. Journal of Infection, 74(1), pp.29-41.
case fatality rate												
	observational	2009-2013	out of all respiratory	4378 annually		per person-year					0.00023	Cohen, C., Walaza, S., Treurnicht, F.K., McMorrow, M., Madhi, S.A., McAnerney, J.M. and Tempia, S., 2017. In-and out-of-hospital mortality associated with seasonal and pandemic influenza and respiratory syncytial virus in South Africa, 2009–2013. Clinical Infectious Diseases, 66(1), pp.95-103.
	retrospective	1979-2001	all registered deaths in Brazil	19 million	seasonal influenza	Brazil govt. data			all		0.003	Alonso, W.J., Viboud, C., Simonsen, L., Hirano, E.W., Daufenbach, L.Z. and Miller, M.A., 2007. Seasonality of influenza in Brazil: a traveling wave from the Amazon to the subtropics. American journal of epidemiology, 165(12), pp.1434-1442.
	retrospective	1997-2007	all U.S.		seasonal influenza				all		0.07	Quandelacy, T.M., Viboud, C., Charu, V., Lipsitch, M. and Goldstein, E., 2013. Age-and sex-related risk factors for influenza-associated mortality in the United States between 1997–2007. American journal of epidemiology, 179(2), pp.156-167.
	observational	2018	hospitalized ILI patients		seasonal influenza				all		0.0827	Mendez-Dominguez, N.I., Bobadilla-Rosado, L.O., Fajardo-Ruiz, L.S., Camara-Salazar, A. and Gomez-Carro, S., 2019. Influenza in Yucatan in 2018: Chronology, characteristics and outcomes of ambulatory and hospitalized patients. Brazilian Journal of Infectious Diseases, 23(5), pp.358-362.
	retrospective	1990-2008	New Zealand		seasonal influenza	deaths per 100,000 persons per year			all		0.000106	Kessaram, T., Stanley, J. and Baker, M.G., 2015. Estimating influenza-associated mortality in New Zealand from 1990 to 2008. Influenza and other respiratory viruses, 9(1), pp.14-19.
R0												
	from clinical data				Flu						1.73	Wallinga, J. and Lipsitch, M., 2006. How generation intervals shape the relationship between growth rates and reproductive numbers. Proceedings of the Royal Society B: Biological Sciences, 274(1609), pp.599-604.
	estimated				FluA(H1N1)					1.06-1.69	1.35	de Blasio, B.F., Iversen, B.G. and Tomba, G.S., 2012. Effect of vaccines and antivirals during the major 2009 A (H1N1) pandemic wave in Norway–and the influence of vaccination timing. PLoS One, 7(1), p.e30018.
	estimated				FluA(H1N1)						3.4	Sonthichai, C., Iamsirithaworn, S., Cummings, D.A.T., Shokekird, P., Niramitsantipong, A., Khumket, S., Chittaganpitch, M. and Lessler, J., 2011. Effectiveness of non-pharmaceutical interventions in controlling an influenza A outbreak in a school, Thailand, November 2007. Outbreak, surveillance and investigation reports, 4(2), pp.6-11.
	estimated	1972-1997	USA, France, Australia		seasonal	Rp = transmissibility at beginning of epidemic in partially immune population					1.3	Chowell, G.M.A.M., Miller, M.A. and Viboud, C., 2008. Seasonal influenza in the United States, France, and Australia: transmission and prospects for control. Epidemiology & Infection, 136(6), pp.852-864.
	estimated	1996-2006	Brazil		seasonal						1.03	Chowell, G., Viboud, C., Simonsen, L., Miller, M. and Alonso, W.J., 2010. The reproduction number of seasonal influenza epidemics in Brazil, 1996–2006. Proceedings of the Royal Society B: Biological Sciences, 277(1689), pp.1857-1866.
	estimated (review)			24 studies	seasonal						1.28	Biggerstaff, M., Cauchemez, S., Reed, C., Gambhir, M. and Finelli, L., 2014. Estimates of the reproduction number for seasonal, pandemic, and zoonotic influenza: a systematic review of the literature. BMC infectious diseases, 14(1), p.480.

RSV parameters: incubation period, infectious period, hospitalization period, hospitalization rate, case fatality rate, R0

parameter	type of study	study time	population	sample size	strain	definition of parameter	notes	patient age	range	mean	citation
incubation period											
	systematic review			review article			range and central tendency		3-7 days	5 days	REVIEW: Lessler, J., Reich, N.G., Brookmeyer, R., Perl, T.M., Nelson, K.E. and Cummings, D.A., 2009. Incubation periods of acute respiratory viral infections: a systematic review. The Lancet infectious diseases, 9(5), pp.291-300.
	experimental	30 days	healthy adults	20	RSV	inoculation to peak symptoms		adult	4-7 days, median 5.9	5.5 days	Zaas, A.K., Chen, M., Varkey, J., Veldman, T., Hero III, A.O., Lucas, J., Huang, Y., Turner, R., Gilbert, A., Lambkin-Williams, R. and Øien, N.C., 2009. Gene expression signatures diagnose influenza and other symptomatic respiratory viral infections in humans. Cell host & microbe, 6(3), pp.207-217.
	experimental	10 days	adult males	41	RSV			adult	3-7 days	4 days	Johnson KM, Chanock RM, Rifkind D, Dravetz HM, Knight V. 1961. Respiratory syncytial virus infection in adult volunteers. J.A.M.A. 176:663-677, 1961.
	experimental	10 days	healthy adults	22	RSV	inoculation to presence of virus	** 3-8 days is length of time virus was present after inoculation	21-50 yrs	3-8 days	3 days	Pringle, C.R., Filipiuk, A.H., Robinson, B.S., Watt, P.J., Higgins, P. and Tyrrell, D.A.J., 1993. Immunogenicity and pathogenicity of a triple temperature-sensitive modified respiratory syncytial virus in adult volunteers. Vaccine, 11(4), pp.473-478.
	experimental	5 days	adults	36	RSV	inoculation to peak symptoms		adult	4-5 days	5 days	Tyrell, D.A.J., Cohen, S. and Schilarb, J.E., 1993. Signs and symptoms in common colds. Epidemiology & Infection, 111(1), pp.143-156.
	review	before 2004	literature	NA					4-5 days	4.5 days	REVIEW: Wat, D., 2004. The common cold: a review of the literature. European Journal of Internal Medicine, 15(2), pp.79-88.
infectious period											
	observational	1975-1995	healthy adults	211	NA	mean duration of illness		adult		9.5 days	Hall, C.B., Long, C.E. and Schnabel, K.C., 2001. Respiratory syncytial virus infections in previously healthy working adults. Clinical infectious diseases, 33(6), pp.792-796.
	observational	<= 1976	hospitalized infants RSV	23		duration of RSV viral shedding		infants	1- 21 days	6.7 days	Weber, A., Weber, M. and Milligan, P., 2001. Modeling epidemics caused by respiratory syncytial virus (RSV). Mathematical biosciences, 172(2), pp.95-113.
	NA (source: CDC)	NA	NA			mean duration of contagious period		all	3-8 days	5.5 days	CDC, "RSV Transmission," https://www.cdc.gov/rsv/about/transmission.html
	experimental	1 year	otherwise healthy ILI children	235		mean duration of ILI episode		6 months-10 yrs		9.2 days	Taylor, S., Lopez, P., Weckx, L., Borja-Tabora, C., Ulloa-Gutierrez, R., Lazcano-Ponce, E., Kerdpanich, A., Weber, M.A.R., de Los Santos, A.M., Tinoco, J.C. and Safadi, M.A.P., 2017. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. Journal of Infection, 74(1), pp.29-41.
hospitalization											
	observational	1993-1995	children <= 4	10767	NA	number of days from admittance to discharge		<= 4 yrs		4.9 days	Howard, T.S., Hoffman, L.H., Stang, P.E. and Simoes, E.A., 2000. Respiratory syncytial virus pneumonia in the hospital setting: length of stay, charges, and mortality. The Journal of pediatrics, 137(2), pp.227-232.
	observational	2001-2003	hosp. respiratory	413		median duration of hospital stay in days		all	6-17.5 days	9.5 days	Morrow, B.M., Hatherill, M., Smuts, H.E., Yeats, J., Pitcher, R. and Argent, A.C., 2006. Clinical course of hospitalised children infected with human metapneumovirus and respiratory syncytial virus. Journal of paediatrics and child health, 42(4), pp.174-178.
	observational	1980-1996	hosp. bronchiolitis	1648281		median length of hospital stay		< 5 yrs	2-5 days	3 days	Shay, D.K., Holman, R.C., Newman, R.D., Liu, L.L., Stout, J.W. and Anderson, L.J., 1999. Bronchiolitis-associated hospitalizations among US children, 1980-1996. Jama, 282(15), pp.1440-1446.
	observational	1 year	otherwise healthy ILI children	235		median duration of hospitalization		6 months-10 yrs		6 days	Taylor, S., Lopez, P., Weckx, L., Borja-Tabora, C., Ulloa-Gutierrez, R., Lazcano-Ponce, E., Kerdpanich, A., Weber, M.A.R., de Los Santos, A.M., Tinoco, J.C. and Safadi, M.A.P., 2017. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. Journal of Infection, 74(1), pp.29-41.
	observational	2003-2006	children in Hong Kong hospitalized for acute respiratory infection			mean duration of hospitalization		< 18 years		4.04 days	Chiu, S.S., Chan, K.H., Chen, H., Young, B.W., Lim, W., Wong, W.H.S. and Peiris, J.M., 2010. Virologically confirmed population-based burden of hospitalization caused by respiratory syncytial virus, adenovirus, and parainfluenza viruses in children in Hong Kong. The Pediatric infectious disease journal, 29(12), pp.1088-1092.
	observational	2009-2011	children < 5	50	NA	median length of hospital stay		< 5	3-5 days	4 days	Broor, S., Dawood, F.S., Pandey, B.G., Saha, S., Gupta, V., Krishnan, A., Rai, S., Singh, P., Erdman, D. and Lal, R.B., 2014. Rates of respiratory virus-associated hospitalization in children aged< 5 years in rural northern India. Journal of Infection, 68(3), pp.281-289.
hospitalization											
	observational	2011-2012	adults with cardiopulmonary disease or congestive heart failure	445	NA	proportion hospitalized during study	*excluded from plot. study pop has advanced pulmonary disease or congestive heart failure.	>50		0.29	Falsey, A.R., Walsh, E.E., Esser, M.T., Shoemaker, K., Yu, L. and Griffin, M.P., 2019. Respiratory syncytial virus–associated illness in adults with advanced chronic obstructive pulmonary disease and/or congestive heart failure. Journal of medical virology, 91(1), pp.65-71.
	observational	1996-2000	3 HMO databases			proportion hospitalized per season		all		0.062	Mullooly, J.P., Bridges, C.B., Thompson, W.W., Chen, J., Weintraub, E., Jackson, L.A., Black, S., Shay, D.K. and Vaccine Safety Datalink Adult Working Group, 2007. Influenza-and RSV-associated hospitalizations among adults. Vaccine, 25(5), pp.846-855.
	observational	2000-2001	children ARI	592	NA	proportion hospitalized during study		< 5		0.0035	Iwane, M.K., Edwards, K.M., Szilagyi, P.G., Walker, F.J., Griffin, M.R., Weinberg, G.A., Coulen, C., Poehling, K.A., Shone, L.P., Balter, S. and Hall, C.B., 2004. Population-based surveillance for hospitalizations associated with respiratory syncytial virus, influenza virus, and parainfluenza viruses among young children. Pediatrics, 113(6), pp.1758-1764.
	observational	2009-2011	children < 5	245	NA	proportion hospitalized during study		< 5		0.0035	Broor, S., Dawood, F.S., Pandey, B.G., Saha, S., Gupta, V., Krishnan, A., Rai, S., Singh, P., Erdman, D. and Lal, R.B., 2014. Rates of respiratory virus-associated hospitalization in children aged< 5 years in rural northern India. Journal of Infection, 68(3), pp.281-289.
	observational	1989-2000	children < 2	4618	NA	proportion hospitalized per year during study		< 2		0.02	Avendano, L.F., Palomino, M.A. and Larranaga, C., 2003. Surveillance for respiratory syncytial virus in infants hospitalized for acute lower respiratory infection in Chile (1989 to 2000). Journal of clinical microbiology, 41(10), pp.4879-4882.

	observational	1 year	otherwise healthy ILI children	235		number hospitalized out of 235		6 months-10 yrs		0.021	Taylor, S., Lopez, P., Weckx, L., Borja-Tabora, C., Ulloa-Gutierrez, R., Lazcano-Ponce, E., Kerdpanich, A., Weber, M.A.R., de Los Santos, A.M., Tinoco, J.C. and Faridi, N., 2017. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. Journal of Infection, 74(1), pp.29-41.
	observational	<= 1976	hospitalized infants RSV	23		hospitalization proportion		infants		0.016	Weber, A., Weber, M. and Milligan, P., 2001. Modeling epidemics caused by respiratory syncytial virus (RSV). Mathematical biosciences, 172(2), pp.95-113.
case fatality rate											
	review	1966-2009	children	36 studies				<= 18 yrs		0.165	REVIEW: Welliver Sr, R.C., Checchia, P.A., Bauman, J.H., Fernandes, A.W., Mahadevia, P.J. and Hall, C.B., 2010. Fatality rates in published reports of RSV hospitalizations among high-risk and otherwise healthy children. Current medical research and opinion, 26(9), pp.2175-2181.
	observational	1993-1995	hospitalized children	10767		nationally weighted # deaths/# cases			0.004 - 0.0075	0.0575	Howard, T.S., Hoffman, L.H., Stang, P.E. and Simoes, E.A., 2000. Respiratory syncytial virus pneumonia in the hospital setting: length of stay, charges, and mortality. The Journal of pediatrics, 137(2), pp.227-232.
	observational	2009-2013	all respiratory illness	4378 annually		deaths per person-year		all		0.00031	Cohen, C., Walaza, S., Treurnicht, F.K., McMorrow, M., Madhi, S.A., McAnerney, J.M. and Tempia, S., 2017. In and out-of-hospital mortality associated with seasonal and pandemic influenza and respiratory syncytial virus in South Africa, 2009–2013. Clinical Infectious Diseases, 66(1), pp.95-103.
	observational	2001-2003	hosp. respiratory	413		deaths during study		< 5 yrs		0.0015	Morrow, B.M., Hatherill, M., Smuts, H.E., Yeats, J., Pitcher, R. and Argent, A.C., 2006. Clinical course of hospitalised children infected with human metapneumovirus and respiratory syncytial virus. Journal of paediatrics and child health, 42(4), pp.174-178.
	observational	2000	hosp. acute bronchiolotis	636		deaths during study		< 1 yr		0.007	Tsolia, M.N., Kafetzis, D., Danelatou, K., Astra, H., Kallergi, K., Spyridis, P. and Karpathios, T.E., 2003. Epidemiology of respiratory syncytial virus bronchiolitis in hospitalized infants in Greece. European journal of epidemiology, 18(1), pp.55-61.
	observational	1989-2000	hosp. children < 2	4618		"fatality rate"		< 2 yrs		0.001	Avendano, L.F., Palomino, M.A. and Larranaga, C., 2003. Surveillance for respiratory syncytial virus in infants hospitalized for acute lower respiratory infection in Chile (1989 to 2000). Journal of clinical microbiology, 41(10), pp.4879-4882.
	review	before 2013				"mortality"			.08-.1	0.09	Lee, N., Qureshi, S.T., Other viral pneumonias. Crit Care Clin 29 (2013) 1045–1068
R0											
	estimated								1.2-2.1	1.65	Weber, A., Weber, M. and Milligan, P., 2001. Modeling epidemics caused by respiratory syncytial virus (RSV). Mathematical biosciences, 172(2), pp.95-113.
	estimated									3	Reis J., Shaman, J., 2016. RetrospectiveParameterEstimationand Forecastof RespiratorySyncytialVirusin the UnitedStates.PLoSComputBiol 12(10):e1005133.doi:10.1371/journal.pcbi.1005133
	estimated	2003-2009							2.26-8.9	4.6	Velasco-Hernández, J.X., Núñez-López, M., Comas-García, A., Cherpitel, D.E.N. and Ocampo, M.C., 2015. Superinfection between influenza and RSV alternating patterns in San Luis potosí state, México. PloS one, 10(3), p.e0115674.
	estimated								1.2-2.1	1.65	Duvvuri, V.R., Granados, A., Rosenfeld, P., Bahl, J., Eshaghi, A. and Gubbay, J.B., 2015. Genetic diversity and evolutionary insights of respiratory syncytial virus A ON1 genotype: global and local transmission dynamics. Scientific reports, 5, p.14268.
	estimated	1989-2009							8.9-9.1	9	Pitzer, V.E., Viboud, C., Alonso, W.J., Wilcox, T., Metcalf, C.J., Steiner, C.A., Haynes, A.K. and Grenfell, B.T., 2015. Environmental drivers of the spatiotemporal dynamics of respiratory syncytial virus in the United States. PLoS pathogens, 11(1), p.e1004591.
	estimated	2018				R0 at peak timing				2.82	Reis, J. and Shaman, J., 2018. Simulation of four respiratory viruses and inference of epidemiological parameters. Infectious Disease Modelling, 3, pp.23-34.
	estimated	2012-2017				average R0				1.6	Levy, N., Iv, M. and Yom-Tov, E., 2018. Modeling influenza-like illnesses through composite compartmental models. Physica A: Statistical Mechanics and its Applications, 494, pp.288-293.

ADENOVIRUS parameters: incubation period, infectious period, hospitalization period, reduction of transmission in hospital, hospitalization rate, case fatality rate, R0
NOTE: adenovirus in the elderly produces keratoconjunctivitis, not a respiratory infection

parameter	type of study	study time	population	sample size	strain	definition of	notes	patient age	range	mean	citation
incubation period		2001-2002		102			* excluded from	elderly (noso)	1-30 days	15.5 days	Sendra-Gutiérrez, J.M., Martín-Rios, D., Casas, I., Sáez, P., Tovar, A. and Moreno, C., 2004. AN OUTBREAK OF
	systematic review			review			range and central tendency	all	4-8 days	6 days	Lessler, J., Reich, N.G., Brookmeyer, R., Perl, T.M., Nelson, K.E. and Cummings, D.A., 2009. Incubation periods of acute respiratory viral infections: a systematic review. The Lancet infectious diseases, 9(5), pp.291-300.
	anecdotal re adenovirus	July to Sept 1996		736	observational	no definition, no citation		federal service training academy	6-9 days	7.5 days	Feikin, D.R., Mooney, J.F., Talkington, D.F., Thacker, W.L., Code, J.E., Schwartz, L.A., Erdman, D.D., Butler, J.C. and Cetron, M.S., 1999. An outbreak of acute respiratory disease caused by Mycoplasma pneumoniae and adenovirus at a federal service training academy: new implications from an old scenario. Clinical infectious diseases, pp.1545-1550.
	experimental	1945	adult males	5	ARD	inoculation to onset of symptoms	ARD assumed to be adenovirus	adult	5-6 days	5.5 days	Commission on Acute Respiratory Diseases, 1947. Experimental transmission of minor respiratory illness to human volunteers by filter-passing agents. I. Demonstration of two types of illness characterized by long and short incubation periods and different clinical features. Journal of Clinical Investigation, 26(5), pp.957-973.
	textbook chapter	NA		NA		no definition			4-12 days	8 days	Berger, S., 2010. Infectious Diseases of Bhutan 2010 edition. * O'Reilly Media, Inc.".
	reference chapter	NA		NA		no definition			2-4 days	3 days	Tanz, R.R. "Sore Throat", Kliegman, R.M., Lye, P.S., Bordini, B.J., Toth, H. and Basel, D., 2017. Nelson Pediatric Symptom-Based Diagnosis E-Book. Elsevier Health Sciences.
	review	before 2004	literature						4-14 days	9 days	REVIEW: Wat, D., 2004. The common cold: a review of the literature. European Journal of Internal Medicine, 15(2), pp.79-88.
	textbook chapter	NA					in textbook		2-14 days	8 days	Robinson, C., & Echavarria, M. (2007). Adenoviruses. In P. R. Murray, E. J. Baron, J. Jorgensen, M. Pfaller & M. L. Landry (Eds.), Manual of Clinical Microbiology (9th ed., pp. 1589) ASM Press.
infectious period											
	observational	2001-2002		102				elderly (noso)	17 days max	9 days	Sendra-Gutiérrez, J.M., Martín-Rios, D., Casas, I., Sáez, P., Tovar, A. and Moreno, C., 2004. AN OUTBREAK OF ADENOVIRUS TYPE 8. Euro Surveill, 9(3), pp.27-30.
	observational	1 year	otherwise healthy ILI children	141	seasonal	mean duration of ILI episode		6 months-10 years		9.2 days	Taylor, S., Lopez, P., Weckx, L., Borja-Tabora, C., Ulloa-Gutierrez, R., Lazcano-Ponce, E., Kerdpanich, A., Weber, M.A.R., de Los Santos, A.M., Tinoco, J.C. and Safadi, M.A.P., 2017. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. Journal of Infection, 74(1), pp.29-41.
	observational		children positive for adenovirus	74						10.6 days	Hong, J.Y., Lee, H.J., Piedra, P.A., Choi, E.H., Park, K.H., Koh, Y.Y. and Kim, W.S., 2001. Lower respiratory tract infections due to adenovirus in hospitalized Korean children: epidemiology, clinical features, and prognosis. Clinical infectious diseases, 32(10), pp.1423-1429.
	textbook chapter	NA	adults			viral shedding period after recovery			up to 1 week	4 days	Robinson, C., & Echavarria, M. (2007). Adenoviruses. In P. R. Murray, E. J. Baron, J. Jorgensen, M. Pfaller & M. L. Landry (Eds.), Manual of Clinical Microbiology (9th ed., pp. 1589) ASM Press.
	textbook chapter	NA	children			viral shedding period following illness	* excluded from plot		3-6 weeks	31.5 days	Robinson, C., & Echavarria, M. (2007). Adenoviruses. In P. R. Murray, E. J. Baron, J. Jorgensen, M. Pfaller & M. L. Landry (Eds.), Manual of Clinical Microbiology (9th ed., pp. 1589) ASM Press.
hospitalization period											
	observational	1 year	otherwise healthy ILI children	141	seasonal	median duration of hospitalization		6 months-10 years		4 days	Taylor, S., Lopez, P., Weckx, L., Borja-Tabora, C., Ulloa-Gutierrez, R., Lazcano-Ponce, E., Kerdpanich, A., Weber, M.A.R., de Los Santos, A.M., Tinoco, J.C. and Safadi, M.A.P., 2017. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. Journal of Infection, 74(1), pp.29-41.
	observational	2003-2006	children in Hong Kong hospitalized for acute respiratory infection			mean duration of hospitalization		< 18 years		3.12 days	Chiu, S.S., Chan, K.H., Chen, H., Young, B.W., Lim, W., Wong, W.H.S. and Peiris, J.M., 2010. Virologically confirmed population-based burden of hospitalization caused by respiratory syncytial virus, adenovirus, and parainfluenza viruses in children in Hong Kong. The Pediatric infectious disease journal, 29(12), pp.1088-1092.
	observational	2 years	immunocompetent children hospitalized due to adenovirus	78		mean duration of hospitalization		17 ± 10 months		7 days	Peled, N., Nakar, C., Huberman, H., Scherf, E., Samra, Z., Finkelstein, Y., Hoffer, V. and Garty, B.Z., 2004. Adenovirus infection in hospitalized immunocompetent children. Clinical pediatrics, 43(3), pp.223-229.
hospitalization rate											
								< 18		0.418	Galindo-Fraga, A., Ortiz-Hernández, A.A., Ramírez-Venegas, A., Vázquez, R.V., Moreno-Espinosa, S., Llamosas-Gallardo, B., Pérez-Patrigeon, S., Salinger, M., Freimanis, L., Huang, C.Y. and Gu, W., 2013. Clinical characteristics and outcomes of influenza and other influenza-like illnesses in Mexico City. International Journal of Infectious Diseases, 17(7), pp.e510-e517.
								18-59		0.667	Galindo-Fraga, A., Ortiz-Hernández, A.A., Ramírez-Venegas, A., Vázquez, R.V., Moreno-Espinosa, S., Llamosas-Gallardo, B., Pérez-Patrigeon, S., Salinger, M., Freimanis, L., Huang, C.Y. and Gu, W., 2013. Clinical characteristics and outcomes of influenza and other influenza-like illnesses in Mexico City. International Journal of Infectious Diseases, 17(7), pp.e510-e517.
	observational	1957	military recruits			percent hospitalized due to adenovirus in 1 yr				0.1	Hilleman, M.R., Gauld, R.L., BUTLER, R., Stallones, R.A., Hedberg, C.L., Warfield, M.S. and Anderson, S.A., 1957. Appraisal of occurrence of adenovirus-caused respiratory illness in military populations. American journal of hygiene, 66(1), pp.29-41.
	observational	1 year	otherwise healthy ILI children	141	seasonal	percent hospitalized		6 months-10 years		0.014	Taylor, S., Lopez, P., Weckx, L., Borja-Tabora, C., Ulloa-Gutierrez, R., Lazcano-Ponce, E., Kerdpanich, A., Weber, M.A.R., de Los Santos, A.M., Tinoco, J.C. and Safadi, M.A.P., 2017. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. Journal of Infection, 74(1), pp.29-41.
	observational	1990-1998	children w/ lower respiratory tract infection			percent of study patients hospitalized				0.95	Hong, J.Y., Lee, H.J., Piedra, P.A., Choi, E.H., Park, K.H., Koh, Y.Y. and Kim, W.S., 2001. Lower respiratory tract infections due to adenovirus in hospitalized Korean children: epidemiology, clinical features, and prognosis. Clinical infectious diseases, 32(10), pp.1423-1429.
case fatality rate											
	observational							18-59		0.067	Galindo-Fraga, A., Ortiz-Hernández, A.A., Ramírez-Venegas, A., Vázquez, R.V., Moreno-Espinosa, S., Llamosas-Gallardo, B., Pérez-Patrigeon, S., Salinger, M., Freimanis, L., Huang, C.Y. and Gu, W., 2013. Clinical characteristics and outcomes of influenza and other influenza-like illnesses in Mexico City. International Journal of Infectious Diseases, 17(7), pp.e510-e517.
	observational		adenovirus infected children				excluded from plot: nosocomial	young children		0.67	Wesley, A.G., Pather, M. and Tait, D., 1993. Nosocomial adenovirus infection in a paediatric respiratory unit. Journal of Hospital Infection, 25(3), pp.183-190.
	observational		pediatric chronic care residents					children		0.16	Gerber, S.I., Erdman, D.D., Pur, S.L., Diaz, P.S., Segreti, J., Kajon, A.E., Belkengren, R.P. and Jones, R.C., 2001. Outbreak of adenovirus genome type 7d2 infection in a pediatric chronic-care facility and tertiary-care hospital. Clinical infectious diseases, 32(5), pp.694-700.

	observational	1995-1996	hospitalized infants					< 2 years		0.166	Larrañaga, C., Martínez, J., Palomino, A., Peña, M. and Carrión, F., 2007. Molecular characterization of hospital-acquired adenovirus infantile respiratory infection in Chile using species-specific PCR assays. Journal of clinical virology, 39(3), pp.175-181.
	observational	2013-2018	adult patients w/ acute respiratory infection in Korean military hospitals					adults		0.00075	Ko, J.H., Woo, H.T., Oh, H.S., Moon, S.M., Choi, J.Y., Lim, J.U., Kim, D., Byun, J., Kwon, S.H., Kang, D. and Heo, J.Y., 2019. Ongoing outbreak of human adenovirus-associated acute respiratory illness in the Republic of Korea military, 2013 to 2018. Korean J Intern Med, 34(5), pp.1171-1171.
	observational	1990-1998	children positive for adenovirus	74						0.12	Hong, J.Y., Lee, H.J., Piedra, P.A., Choi, E.H., Park, K.H., Koh, Y.Y. and Kim, W.S., 2001. Lower respiratory tract infections due to adenovirus in hospitalized Korean children: epidemiology, clinical features, and prognosis. Clinical infectious diseases, 32(10), pp.1423-1429.
R0											
	estimated	2018	simulated			R0 at peak timing				2.34	Reis, J. and Shaman, J., 2018. Simulation of four respiratory viruses and inference of epidemiological parameters. Infectious Disease Modelling, 3, pp.23-34.

HUMAN CORONAVIRUS parameters: incubation period, infectious period, onset of symptoms to hospitalization, hospitalization period, hospitalization proportion, case fatality, R0

parameter	type of study	study time	population	sample size	strain	definition of parameter	notes	patient age	value range	mean	citation
incubation period	review	pre-2009	literature		SARS	incubation period		all	3.6-4.4 days	4 days	Lessler, J., Reich, N.G., Brookmeyer, R., Perl, T.M., Nelson, K.E. and Cummings, D.A., 2009. Incubation periods of acute respiratory viral infections: a systematic review. The Lancet infectious diseases, 9(5), pp.291-300.
	experimental	1967	adults	26	229E culture	inoculation to onset		18-50	2-4 days	3.3 days	Bradburne, A.F., Bynoe, M.L. and Tyrrell, D.A., 1967. Effects of a" new" human respiratory virus in volunteers. British medical journal, 3(5568), p.767.
	experimental	June 1986-July 1989	adults	34	229E culture	inoculation to peak symptoms		adult	3-4 days	3.5 days	Tyrell, D.A.J., Cohen, S. and Schilarb, J.E., 1993. Signs and symptoms in common colds. Epidemiology & Infection, 111(1), pp.143-156.
	review	before 2004	literature			incubation period		all	2-4 days	3 days	Wat, D., 2004. The common cold: a review of the literature. European Journal of Internal Medicine, 15(2), pp.79-88.
	observational	winter 2018	Olympic athletes & staff	112	229E,OC43,NL63	incubation period		adult		3.5 days	Valtonen, M., Waris, M., Vuorinen, T., Erola, E., Hakanen, A.J., Mjosund, K., Grönroos, W., Heinonen, O.J. and Ruuskanen, O., 2019. Common cold in Team Finland during 2018 Winter Olympic Games (PyeongChang): epidemiology, diagnosis including molecular point-of-care testing (POCT) and treatment. British journal of sports medicine, 53(17), pp.1093-1098.
	observational	April 1-May 23, 1013	hospitalized	23	MERS	incubation period		all	1.9-14.7 days	5.2 days	Assiri, A., Al-Tawfiq, J.A., Al-Rabeeah, A.A., Al-Rabiah, F.A., Al-Hajjar, S., Al-Barrak, A., Flemban, H., Al-Nassir, W.N., Balkhy, H.H., Al-Hakeem, R.F. and Makhdoom, H.Q., 2013. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. The Lancet infectious diseases, 13(9), pp.752-761.
	retrospective	2015	confirmed cased (Korea)	36	MERS	incubation period	patients who died	all	5.2-7.9 days	6.4 days	Virlogeux, V., Park, M., Wu, J.T. and Cowling, B.J., 2016. Association between severity of MERS-CoV infection and incubation period. Emerging infectious diseases, 22(3), p.526.
	retrospective	2015	confirmed cases (Korea)	134	MERS	incubation period	patients who survived	all	6.3-7.8 days	7.1 days	Virlogeux, V., Park, M., Wu, J.T. and Cowling, B.J., 2016. Association between severity of MERS-CoV infection and incubation period. Emerging infectious diseases, 22(3), p.526.
	review	pre-May 2003	consensus document		SARS	incubation period		all		10 days	World Health Organization, 2003. Consensus document on the epidemiology of severe acute respiratory syndrome (SARS) (No. WHO/CDS/CSR/GAR/2003.11). World Health Organization.
	review	2003-2004	literature		SARS	incubation period		all	4.0-5.3 days	4.7 days	Anderson, R.M., Fraser, C., Ghani, A.C., Donnelly, C.A., Riley, S., Ferguson, N.M., Leung, G.M., Lam, T.H. and Hedley, A.J., 2004. Epidemiology, transmission dynamics and control of SARS: the 2002–2003 epidemic. Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences, 359(1447), pp.1091-1105.
infectious period											
	observational	1 year	otherwise healthy ILI children	103		mean duration of ILI episode		6 months-10 years		10.1 days	Taylor, S., Lopez, P., Weckx, L., Borja-Tabora, C., Ulloa-Gutierrez, R., Lazcano-Ponce, E., Kerdpanich, A., Weber, M.A.R., de Los Santos, A.M., Tinoco, J.C. and Safadi, M.A.P., 2017. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. Journal of Infection, 74(1), pp.29-41.
	observational		neonates w/ NL63		229E,OC43,NL63	duration of illness			1-4 weeks	13.46 days	Kaiser, L., Regamey, N., Roiha, H., Deffernez, C. and Frey, U., 2005. Human coronavirus NL63 associated with lower respiratory tract symptoms in early life. The Pediatric infectious disease journal, 24(11), pp.1015-1017.
	observational	Aug 2001-Aug 2002	children hospitalized w/ HcoV-NL63		NL63	mean duration of fever		≤18 years	1-5 days	2.6 days	Chiu, S.S., Hung Chan, K., Wing Chu, K., Kwan, S.W., Guan, Y., Man Poon, L.L. and Peiris, J.S.M., 2005. Human coronavirus NL63 infection and other coronavirus infections in children hospitalized with acute respiratory disease in Hong Kong, China. Clinical infectious diseases, 40(12), pp.1721-1729.
	observational	winter 2018	Olympic athletes & staff	112	229E,OC43,NL6	duration of illness		adults	2-25 days	10.33 days	Valtonen, M., Waris, M., Vuorinen, T., Erola, E., Hakanen, A.J., Mjosund, K., Grönroos, W., Heinonen, O.J. and Ruuskanen, O., 2019. Common cold in Team Finland during 2018 Winter Olympic Games (PyeongChang): epidemiology, diagnosis including molecular point-of-care testing (POCT) and treatment. British journal of sports medicine, 53(17), pp.1093-1098.
	review	2003-2004	literature		SARS	infectiousness	from Fig. 5		27-35 days	31 days	Anderson, R.M., Fraser, C., Ghani, A.C., Donnelly, C.A., Riley, S., Ferguson, N.M., Leung, G.M., Lam, T.H. and Hedley, A.J., 2004. Epidemiology, transmission dynamics and control of SARS: the 2002–2003 epidemic. Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences, 359(1447), pp.1091-1105.
	estimated	2002-2003	literature/model		SARS	mean infectious period				23.5 days	Chowell, G., Castillo-Chavez, C., Fenimore, P.W., Kribs-Zaleta, C.M., Arriola, L. and Hyman, J.M., 2004. Model parameters and outbreak control for SARS. Emerging Infectious Diseases, 10(7), p.1258.
onset to											
	observational	April 1-May 23, 2013	confirmed MERS-CoV	23	MERS	onset of symptoms to ICU admission		all	1-10 days	5 days	Assiri, A., Al-Tawfiq, J.A., Al-Rabeeah, A.A., Al-Rabiah, F.A., Al-Hajjar, S., Al-Barrak, A., Flemban, H., Al-Nassir, W.N., Balkhy, H.H., Al-Hakeem, R.F. and Makhdoom, H.Q., 2013. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. The Lancet infectious diseases, 13(9), pp.752-761.
	review	pre-2017	literature	NA	MERS	onset of symptoms to hospitalization		all		4 days	Fehr, A.R., Channappanavar, R. and Perlman, S., 2017. Middle East respiratory syndrome: emergence of a pathogenic human coronavirus. Annual review of medicine, 68, pp.387-399.
	observational	2013	confirmed MERS-CoV	17	MERS	onset of symptoms to hospitalization		all		3 days	Al-Tawfiq, J.A., Hinedi, K., Ghandour, J., Khairalla, H., Musleh, S., Ujayli, A. and Memish, Z.A., 2014. Middle East respiratory syndrome coronavirus: a case-control study of hospitalized patients. Clinical Infectious Diseases, 59(2), pp.160-165.
	retrospective	2002-2003	1st 205 probable cases	205	SARS	onset of symptoms to isolation	median	all	2-6 days	4 days	Lipsitch, M., Cohen, T., Cooper, B., Robins, J.M., Ma, S., James, L., Gopalakrishna, G., Chew, S.K., Tan, C.C., Samore, M.H. and Fisman, D., 2003. Transmission dynamics and control of severe acute respiratory syndrome. Science, 300(5627), pp.1966-1970
	observational	2014	hospitalized confirmed	9	MERS	onset to hospitalization		all	0-8 days	3 days	Corman, V.M., Albarrak, A.M., Omrani, A.S., Albarrak, M.M., Farah, M.E., Almasri, M., Muth, D., Sieberg, A., Meyer, B., Assiri, A.M. and Binger, T., 2016. Viral shedding and antibody response in 37 patients with Middle East respiratory syndrome coronavirus infection. Clinical Infectious Diseases, 62(4), pp.477-483.
hospitalization period											
	observational	1 year	otherwise healthy ILI children	103		median duration of hospitalization		6 months-10 years		1.5 days	Taylor, S., Lopez, P., Weckx, L., Borja-Tabora, C., Ulloa-Gutierrez, R., Lazcano-Ponce, E., Kerdpanich, A., Weber, M.A.R., de Los Santos, A.M., Tinoco, J.C. and Safadi, M.A.P., 2017. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. Journal of Infection, 74(1), pp.29-41.
	observational	Aug 2001-Aug 2002	children w/ HcoV-NL63		NL-63	mean duration of hospitalization		≤18 years		2.46 days	Chiu, S.S., Hung Chan, K., Wing Chu, K., Kwan, S.W., Guan, Y., Man Poon, L.L. and Peiris, J.S.M., 2005. Human coronavirus NL63 infection and other coronavirus infections in children hospitalized with acute respiratory disease in Hong Kong, China. Clinical infectious diseases, 40(12), pp.1721-1729.

	observational	2001-2003	children w/ HcoV-NL hospitalized for acute respiratory tract infections	12		mean duration of hospitalization		≤3 years		4.9 days	Boivin, G., Baz, M., Côté, S., Gilca, R., Deffrasnes, C., Leblanc, É., Bergeron, M.G., Déry, P. and De Serres, G., 2005. Infections by human coronavirus NL in hospitalized children. The Pediatric infectious disease journal, 24(12), pp.1045-1048.
	observational	2014	hospitalized confirmed	37	MERS	average time of hospitalization		all		11 days	Corman, V.M., Albarrak, A.M., Omrani, A.S., Albarrak, M.M., Farah, M.E., Almasri, M., Muth, D., Sieberg, A., Meyer, B., Assiri, A.M. and Binger, T., 2016. Viral shedding and antibody response in 37 patients with Middle East respiratory syndrome coronavirus infection. Clinical Infectious Diseases, 62(4), pp.477-483.
hospitalization											
	observational	1 year	otherwise healthy ILI children	103	seasonal	percent hospitalized		6 months-10 years		0.019	Taylor, S., Lopez, P., Weckx, L., Borja-Tabora, C., Ulloa-Gutierrez, R., Lazcano-Ponce, E., Kerdpanich, A., Weber, M.A.R., de Los Santos, A.M., Tinoco, J.C. and Safadi, M.A.P., 2017. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. Journal of Infection, 74(1), pp.29-41.
	observational	Jan-Mar 2002	HcoV-NL63 positive patients	19	NL63	percent hospitalized		1 month-100 years		0.21	Bastien, N., Anderson, K., Hart, L., Caeseele, P.V., Brandt, K., Milley, D., Hatchette III, T., Weiss, E.C. and Li, Y., 2005. Human coronavirus NL63 infection in Canada. The Journal of infectious diseases, 191(4), pp.503-506.
	observational		coronavirus positive patients w/ clinical respiratory infection	48		percent hospitalized		all		0.52	Reina, J., López-Causapé, C., Rojo-Molinero, E. and Rubio, R., 2014. Clinico-epidemiological characteristics of acute respiratory infections by coronavirus OC43, NL63 and 229E. Revista Clínica Española (English Edition), 214(9), pp.499-504.
	observational	Aug 2001-Aug 2002	children w/ HcoV-NL63		NL63	percent hospitalized		≤18 years		0.0022	Chiu, S.S., Hung Chan, K., Wing Chu, K., Kwan, S.W., Guan, Y., Man Poon, L.L. and Peiris, J.S.M., 2005. Human coronavirus NL63 infection and other coronavirus infections in children hospitalized with acute respiratory disease in Hong Kong, China. Clinical infectious diseases, 40(12), pp.1721-1729.
case fatality											
	review		confirmed MERS-coV cases		MERS	case fatality rate		all		0.33	Ramadan, N. and Shaib, H. (2019) 'Middle East respiratory syndrome coronavirus (MERS-CoV): A review', Germs, 9(1), pp. 35-42.
	retrospective	2015	MERS-CoV South Korea	186	MERS	case fatality rate				0.19	Chang, H.J., 2017. Estimation of basic reproduction number of the Middle East respiratory syndrome coronavirus (MERS-CoV) during the outbreak in South Korea, 2015. Biomedical engineering online, 16(1), p.79
	observational	Jan-Mar 2002	HcoV-NL63 positive children	19	NL63	case fatality rate				0.053	Bastien, N., Anderson, K., Hart, L., Caeseele, P.V., Brandt, K., Milley, D., Hatchette III, T., Weiss, E.C. and Li, Y., 2005. Human coronavirus NL63 infection in Canada. The Journal of infectious diseases, 191(4), pp.503-506.
	observational		coronavirus positive patients w/ clinical respiratory infection	48		case fatality rate		all		0	Reina, J., López-Causapé, C., Rojo-Molinero, E. and Rubio, R., 2014. Clinico-epidemiological characteristics of acute respiratory infections by coronavirus OC43, NL63 and 229E. Revista Clínica Española (English Edition), 214(9), pp.499-504.
	review		MERS-CoV		MERS	case fatality rate			6–16%	0.11	Lee, N., Qureshi, S.T., Other viral pneumonias. Crit Care Clin 29 (2013) 1045–1068
	observational	1995-2000	HcoV positive elderly patients w/ underlying conditions	5		case fatality rate		> 65 years		0	Falsey, A.R., Walsh, E.E. and Hayden, F.G., 2002. Rhinovirus and coronavirus infection-associated hospitalizations among older adults. The Journal of infectious diseases, 185(9), pp.1338-1341.
	retrospective	2002-2019	confirmed cases	2494	MERS	case fatality rate		all		0.344	WHO, "MERS Situation Update, November 2019," accessed on January 30, 2020. http://applications.emro.who.int/docs/EMRPUB-CSR-241-2019-EN.pdf?ua=1&ua=1&ua=1
R0											
	estimated		MERS-CoV Saudi Arabia		MERS	R0				4.5	Majumder, M.S., Rivers, C., Lofgren, E. and Fisman, D., 2014. Estimation of MERS-coronavirus reproductive number and case fatality rate for the spring 2014 Saudi Arabia outbreak: insights from publicly available data. PLoS currents, 6.
	estimated	2015	MERS-CoV South Korea	186	MERS	R0				8	Chang, H.J., 2017. Estimation of basic reproduction number of the Middle East respiratory syndrome coronavirus (MERS-CoV) during the outbreak in South Korea, 2015. Biomedical engineering online, 16(1), p.79
	estimated		SARS-CoV Hong Kong		SARS	R0				2.7	Leung, G.M., Chung, P.H., Tsang, T., Lim, W., Chan, S.K., Chau, P., Donnelly, C.A., Ghani, A.C., Fraser, C., Riley, S. and Ferguson, N.M., 2004. SARS-CoV antibody prevalence in all Hong Kong patient contacts. Emerging infectious diseases, 10(9), p.1653.
	estimated	2015	MERS-CoV South Korea		MERS	R0			0.1351 or 5.3973	2.77	Kim, Y., Lee, S., Chu, C., Choe, S., Hong, S. and Shin, Y., 2016. The characteristics of Middle Eastern respiratory syndrome coronavirus transmission dynamics in South Korea. Osong public health and research perspectives, 7(1), pp.49-55.
	estimated		hCoV			R0			2.2-3.7	2.95	Lee, N., Qureshi, S.T., Other viral pneumonias. Crit Care Clin 29 (2013) 1045–1068
	estimated	2002-2003	SARS-Singapore/Hong Kong	205	SARS	R0			2.2-3.6	3	Lipsitch, M., Cohen, T., Cooper, B., Robins, J.M., Ma, S., James, L., Gopalakrishna, G., Chew, S.K., Tan, C.C., Samore, M.H. and Fisman, D., 2003. Transmission dynamics and control of severe acute respiratory syndrome. Science, 300(5627), pp.1966-1970
	review	2002-2003	SARS (literature)		SARS	R0				3	Bauch, C.T., Lloyd-Smith, J.O., Coffee, M.P. and Galvani, A.P., 2005. Dynamically modeling SARS and other newly emerging respiratory illnesses: past, present, and future. Epidemiology, pp.791-801.
	retrospective/estimated	2002-2003	SARS	1512	SARS	R0				2.7	Riley, S., Fraser, C., Donnelly, C.A., Ghani, A.C., Abu-Raddad, L.J., Hedley, A.J., Leung, G.M., Ho, L.M., Lam, T.H., Thach, T.Q. and Chau, P., 2003. Transmission dynamics of the etiological agent of SARS in Hong Kong: impact of public health interventions. Science, 300(5627), pp.1961-1966.

RHINOVIRUS parameters: incubation period, infectious period, hospitalization period, hospitalization proportion, case fatality, R0

parameter	type of study	study time	population	sample size	strain	definition of parameter	notes	patient age range	value range	mean	citation
incubation period											
	systematic review	before 2009	literature	8 exp/obs studies			range and central tendency		2-4 days	2 days	REVIEW: Lessler, J., Reich, N.G., Brookmeyer, R., Perl, T.M., Nelson, K.E. and Cummings, D.A., 2009. Incubation periods of acute respiratory viral infections: a systematic review. The Lancet infectious diseases, 9(5), pp.291-300.
	review	before 2011	literature		citation network						REVIEW: Reich NG, Perl TM, Cummings DAT, Lessler J, 2011. Visualizing clinical evidence: citation networks for the incubation periods of respiratory viral infections. PLoS One 6(4), 1-6.
	experimental	30 days	male prisoners	13	RV type 15	inoculation to appearance of symptoms		adult	2-4 days	3 days	Douglas, RG, Rossen, RD, Butler, WT, Couch, RB, 1967. Rhinovirus neutralizing antibody in tears, parotid saliva, nasal secretions and serum. The Journal of Immunology, 99(2), 297-303.
	experimental	30 days	asthmatic subjects	10	RV type 16 +allergen	inoculation to appearance of symptoms		18 to 55	1-5.5 days	2.5 days	Avila, PC, Abisheganaden, JA, Wong, H, Liu, J, Yagi, S, Schnurr, DS, Kishiyama, JL, Boushey, HA, 2009. Effects of allergic inflammation of the nasal mucosa on the severity of rhinovirus 16 cold. Journal of Allergy and Clinical Immunology, 105(5), 923-931.
	experimental	30 days	asthmatic subjects	10	RV type 16	inoculation to appearance of symptoms		18 to 55	1-1 days	1 days	Avila et al (above).
	experimental	5 days	healthy adults	21	RV type 23	inoculation to appearance of symptoms		18 to 45	2-2 days	2 days	Drake CL, Roehrs TA, Royer H, Koshorek G, Turner RB, Roth T, 2000. Effects of an experimentally induced rhinovirus cold on sleep, performance, and daytime alertness. Physiology and Behavior: 71(1-2), 75-81.
	experimental	5 days	healthy adults	27	T-39 and HH	inoculation to peak symptoms		adult	2-3 days	2.5 days	Naclerio RM, Proud D, Lichtenstein LM, Kagey-Sobotka A, Hendley JO., Sorrentino J, Gwaltney JM. 1987. Kinins are generated during experimental rhinovirus colds. Th Journal of Infectious Diseases: 157(1), 133-142.
	experimental	5 days	healthy adults	18	T-39	inoculation to appearance of symptoms	earliest possible sore/scratchy throat	adult	0.42-0.67 days	0.55 days	Harris JM, Gwaltney JM, 1996. Incubation periods of experimental rhinovirus infection and illness. Clinical Infectious Diseases: 23, 1287-90.
	experimental	30 days	healthy adults	20	HRV	inoculation to peak symptoms		adult	2-4 days	3 days	Zaas, A.K., Chen, M., Varkey, J., Veldman, T., Hero III, A.O., Lucas, J., Huang, Y., Turner, R., Gilbert, A., Lambkin-Williams, R. and Øien, N.C., 2009. Gene expression signatures diagnose influenza and other symptomatic respiratory viral infections in humans. Cell host & microbe, 6(3), pp.207-217.
	experimental	5 days	adults	193	RV9 and RV14	inoculation to peak symptoms		adult	2-3 days	2.5 days	Tyrell, D.A.J., Cohen, S. and Schlarb, J.E., 1993. Signs and symptoms in common colds. Epidemiology & Infection, 111(1), pp.143-156.
	review	before 2004	literature						2-7 days	4.5 days	REVIEW: Wat, D., 2004. The common cold: a review of the literature. European Journal of Internal Medicine, 15(2), pp.79-88.
infectious period											
	observational	1 year	otherwise healthy ILI children	986		mean duration of ILI episode		6 months-10 days		9.6 days	Taylor, S., Lopez, P., Weckx, L., Borja-Tabora, C., Ulloa-Gutierrez, R., Lazcano-Ponce, E., Kerdpanich, A., Weber, M.A.R., de Los Santos, A.M., Tinoco, J.C. and Safadi, M.A.P., 2017. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. Journal of Infection, 74(1), pp.29-41.
	observational	winters 1992-3 and 1993-4	elderly patients w/ single rhinovirus infection	96		median duration of illness	*excluded from plot	elderly		16 days	Nicholson, K.G., Kent, J., Hammersley, V. and Cancio, E., 1996. Risk factors for lower respiratory complications of rhinovirus infections in elderly people living in the community: prospective cohort study. Bmj, 313(7065), pp.1119-1123.
	observational	Sept-Oct 1994	HSV culture-positive adults			median duration of cold episode		adult		11 days	Arruda, E., Pitkäranta, A.N.N.E., Witek, T.J., Doyle, C.A. and Hayden, F.G., 1997. Frequency and natural history of rhinovirus infections in adults during autumn. Journal of clinical microbiology, 35(11), pp.2864-2868.
	experimental		healthy adult males	32	inoculation w/ NIH 1734	viral shedding period		adult		10 days	Douglas Jr, R.G., Cate, T.R., Gerone, P.J. and Couch, R.B., 1966. Quantitative rhinovirus shedding patterns in volunteers. American Review of Respiratory Disease, 94(2), pp.159-167.
	textbook chapter					average length of symptoms		all		7 days	Landry, Marie Louise. *Rhinoviruses* . In P. R. Murray, E. J. Baron, J. Jorgensen, M. Pfaller & M. L. Landry (Eds.), Manual of Clinical Microbiology (9th ed., pp. 1405) ASM Press.
hospitalization period											
	observational	1 year	otherwise healthy ILI children	986		median duration of hospitalization		6 months-10 years		1.5 days	Taylor, S., Lopez, P., Weckx, L., Borja-Tabora, C., Ulloa-Gutierrez, R., Lazcano-Ponce, E., Kerdpanich, A., Weber, M.A.R., de Los Santos, A.M., Tinoco, J.C. and Safadi, M.A.P., 2017. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. Journal of Infection, 74(1), pp.29-41.
	retrospective	Jan 2014-Apr 2015	hospitalized children	198		diff. btw. length of hospital stay for HRV positive vs. no respiratory virus		children		0.4 days	Tam, P.Y.I., Zhang, L. and Cohen, Z., 2018. Clinical characteristics and outcomes of human rhinovirus positivity in hospitalized children. Annals of thoracic medicine, 13(4), p.230.
	observational	2003-2005	RSV positive children hospitalized for acute respiratory illness	332		median length of stay		< 5 years		1.67 days	Iwane, M.K., Prill, M.M., Lu, X., Miller, E.K., Edwards, K.M., Hall, C.B., Griffin, M.R., Staat, M.A., Anderson, L.J., Williams, J.V. and Weinberg, G.A., 2011. Human rhinovirus species associated with hospitalizations for acute respiratory illness in young US children. Journal of Infectious Diseases, 204(11), pp.1702-1710.
hospitalization proportion											
	observational	1 year	otherwise healthy ILI children	986		percent hospitalized		6 months-10 years		0.024	Taylor, S., Lopez, P., Weckx, L., Borja-Tabora, C., Ulloa-Gutierrez, R., Lazcano-Ponce, E., Kerdpanich, A., Weber, M.A.R., de Los Santos, A.M., Tinoco, J.C. and Safadi, M.A.P., 2017. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. Journal of Infection, 74(1), pp.29-41.
	observational	2008-2010	US adults seen in hospital, ED, or outpatient clinic			rhinovirus associated hospitalization per year		adult		0.003	Miller, E.K., Linder, J., Kraft, D., Johnson, M., Lu, P., Saville, B.R., Williams, J.V., Griffin, M.R. and Talbot, H.K., 2016. Hospitalizations and outpatient visits for rhinovirus-associated acute respiratory illness in adults. Journal of Allergy and Clinical Immunology, 137(3), pp.734-743.
	observational	1998-2001	ILI infants			percent hospitalized out of infants with HRV		infant		0.0093	Lee, W.M., Lemanske Jr, R.F., Evans, M.D., Vang, F., Pappas, T., Gangnon, R., Jackson, D.J. and Gern, J.E., 2012. Human rhinovirus species and season of infection determine illness severity. American journal of respiratory and critical care medicine, 186(9), pp.886-891.
case fatality proportion											
	observational		elderly patients w/ single RSV infection	96		percent of patients who died		elderly		0.0104	Nicholson, K.G., Kent, J., Hammersley, V. and Cancio, E., 1996. Risk factors for lower respiratory complications of rhinovirus infections in elderly people living in the community: prospective cohort study. Bmj, 313(7065), pp.1119-1123.
	observational	2012	elderly patients w/ RSV-associated respiratory infection	32		percent of patients who died		elderly		0.125	Fica, A., Dabanch, J., Andrade, W., Bustos, P., Carvajal, I., Ceroni, C., Triantafilo, V., Castro, M. and Fasce, R., 2015. Clinical relevance of rhinovirus infections among adult hospitalized patients. Brazilian Journal of Infectious Diseases, 19(2), pp.118-124.
	observational	1995-2000	RSV positive elderly patients w/ underlying conditions	4		percent of patients who died		> 65 years		0	Falsey, A.R., Walsh, E.E. and Hayden, F.G., 2002. Rhinovirus and coronavirus infection-associated hospitalizations among older adults. The Journal of infectious diseases, 185(9), pp.1338-1341.
R0											
	estimated	2018	simulated			R0 at peak timing				2.6	Reis, J. and Shaman, J., 2018. Simulation of four respiratory viruses and inference of epidemiological parameters. Infectious Disease Modelling, 3, pp.23-34.
	estimated	2012-2017	simulated			average R0 value				1.2	Levy, N., Iv, M. and Yom-Tov, E., 2018. Modeling influenza-like illnesses through composite compartmental models. Physica A: Statistical Mechanics and its Applications, 494, pp.288-293.
	estimated from non-invasive observation		wild chimpanzees			average R0				1.83	Scully, E.J., Basnet, S., Wrangham, R.W., Muller, M.N., Otali, E., Hyeroba, D., Grindle, K.A., Pappas, T.E., Thompson, M.E., Machanda, Z. and Watters, K.E., 2018. Lethal respiratory disease associated with human rhinovirus C in wild chimpanzees, Uganda, 2013. Emerging infectious diseases, 24(2), p.267.

COMPOSITION OF ILI literature review

NOTE: 55-74% (average 62%) of patients with ILI who were sampled had viruses detected (Sentilhes, Taylor, Galindo-Fraga, Nandi, Varghese, Mahony, Graat, van Gageldonk-Lafeber, Van Beek, Van Asten)

Citation	year(s) of study	Sample Size	Positive samples	age range	population	influenza A/B	adenovirus	HcoV	rhinovirus*	RSV	coinfection	% of ILI patients with detected viruses
Sentilhes, A.C., Choumlivong, K., Celhay, O., Sisouk, T., Phonekeo, D., Vongphrachanh, P., Brey, P. and Buchy, P., 2013. Respiratory virus infections in hospitalized children and adults in Lao PDR. Influenza and other respiratory viruses, 7(6), pp.1070-1078.	8/2009-10/2010	292	% of 162 positive. 140 single virus detected; 22 coinfections detected	all, med 2.2	hospitalized for acute lower respiratory infection	13.00%	6.00%	4.00%	35.00%	26.00%	8.00%	55.00%
and Klimov, A., 2012. Multisite virological influenza surveillance in India: 2004–2008. Influenza and other respiratory viruses, 6(3), pp.196-203.	9/2004-12/2008	13928	only influenza	all, med 14.66	ILI and SARI	4.43%	NA	NA	NA	NA	NA	
Laguna-Torres, V.A., Gómez, J., Ocaña, V., Aguilar, P., Saldarriaga, T., Chavez, E., Perez, J., Zamalloa, H., Forshey, B., Paz, I. and Gomez, E., 2009. Influenza-like illness sentinel surveillance in Peru. PloS one, 4(7), p.e6118.	6/2006-5/2008	% of 6835 ILI	2688 positive	all, med 13	ILI only	34.80%	1.80%	NA	0.50%	0.60%	0.90%	
A., 2016. Epidemiology and etiology of influenza-like-illness in households in Vietnam; it's not all about the kids!. Journal of Clinical Virology, 82, pp.126-132.	2008-2013	945	% of 271 positive	all	ILI	17.00%	NA	8.00%	28.00%	3.00%	NA-all single	62.30%
Taylor, S., Lopez, P., Weckx, L., Borja-Tabora, C., Ulloa-Gutierrez, R., Lazcano-Ponce, E., Kerdpanich, A., Weber, M.A.R., de Los Santos, A.M., Tinoco, J.C. and Safadi, M.A.P., 2017. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. Journal of Infection, 74(1), pp.29-41.	2/2010-8/2011	6266	% of 3717 ILI. 2958 pos.	6 mo- 10 yrs	children w/ ILI	15.80%	9.80%	5.60%	41.50%	9.70%	not clear	
Dia, N., Sarr, F.D., Thiam, D., Sarr, T.F., Espié, E., OmarBa, I., Coly, M., Niang, M. and Richard, V., 2014. Influenza-like illnesses in Senegal: not only focus on influenza viruses. PLoS One, 9(3), p.e93227.	2012-2013	1038 pos. patients	% of 1678 viruses	all	ILI patients	19.00%	22.00%	2.00%	19.00%	9.00%	not clear	
Freymuth, F., Vabret, A., Rozenberg, F., Dina, J., Petitjean, J., Gouarin, S., Legrand, L., Corbet, S., Brouard, J. and Lebon, P., 2005. Replication of respiratory viruses, particularly influenza virus, rhinovirus, and coronavirus in HuH7 hepatocarcinoma cell line. Journal of medical virology, 77(2), pp.295-301.	1999-2002	5258 total	1797	<18	hosp. children	18.30%	6.50%	1.90%	15.10%	44.00%	not clear	
Louie, J.K., Hacker, J.K., Gonzales, R., Mark, J., Maselli, J.H., Yagi, S. and Drew, W.L., 2005. Characterization of viral agents causing acute respiratory infection in a San Francisco University Medical Center Clinic during the influenza season. Clinical Infectious Diseases, 41(6), pp.822-828.	Jan -Mar 2002	266 diag. acute resp infection	103 positive	>=18	ARI diagnosis	52.40%	23.30%	1.90%	23.30%	11.60%		
Fowlkes, A., Giorgi, A., Erdman, D., Temte, J., Goodin, K., Di Lonardo, S., Sun, Y., Martin, K., Feist, M., Linz, R. and Boulton, R., 2013. Viruses associated with acute respiratory infections and influenza-like illness among outpatients from the Influenza Incidence Surveillance Project, 2010–2011. The Journal of infectious diseases, 209(11), pp.1715-1725.	8/2010-7/2011	4212	2443	all	ARI & ILI	21.20%	5.70%	7.30%	21.10%	6.20%	not clear	
Galindo-Fraga, A., Ortiz-Hernández, A.A., Ramírez-Venegas, A., Vázquez, R.V., Moreno-Espinosa, S., Llamosas-Gallardo, B., Pérez-Patrigeon, S., Salinger, M., Freimanis, L., Huang, C.Y. and Gu, W., 2013. Clinical characteristics and outcomes of influenza and other influenza-like illnesses in Mexico City. International Journal of Infectious Diseases, 17(7), pp.e510-e517.	same	913	821 viruses in 678 subjects	ALL	ILI	24.00%	9.00%	14.40%	25.30%	10.30%	11.90%	64.00%
Nandi, T., Khanna, M., Pati, D.R., Kumar, B. and Singh, V., 2018. Epidemiological surveillance and comparative analysis of patients with influenza like illness and other respiratory viruses. International Journal of Infectious Diseases, 73, p.203.		100	% of 100 patients	all	ILI	36.78%	NA	2.83%	5.66%	NA		68.85%
Varghese, B.M., Dent, E., Chilver, M., Cameron, S. and Stocks, N.P., 2018. Epidemiology of viral respiratory infections in Australian working-age adults (20–64 years): 2010–2013. Epidemiology & Infection, 146(5), pp.619-626.	2010-2013	3201	1789 positive	20-64		NA	1.30%	NA	18.60%	3.10%	not clear	55.80%
Mahony, J.B., Petrich, A. and Smieja, M., 2011. Molecular diagnosis of respiratory virus infections. Critical reviews in clinical laboratory sciences, 48(5-6), pp.217-249.						NA	NA	NA		54.42%		
BOLLAERTS, K., Antoine, J., Van Casteren, V., Ducoffre, G., HENS, N. and Quolin, S., 2013. Contribution of respiratory pathogens to influenza-like illness consultations. Epidemiology & Infection, 141(10), pp.2196-2204.	2004-2008	??		all		NA	NA	NA		NA		
Graat, J.M., Schouten, E.G., Heijnen, M.L.A., Kok, F.J., Pallast, E.G., de Greeff, S.C. and Dorigo-Zetsma, J.W., 2003. A prospective, community-based study on virologic assessment among elderly people with and without symptoms of acute respiratory infection. Journal of clinical epidemiology, 56(12), pp.1218-1223.	Oct 98-Oct 99	652	107 episodes in 97 subjects	>=60 yrs	ILI	7.00%	0.00%	17.00%	32.00%	0.00%		58.00%
Buecher, C., Mardy, S., Wang, W., Duong, V., Vong, S., Naughtin, M., Vabret, A., Freymuth, F., Deubel, V. and Buchy, P., 2010. Use of a multiplex PCR/RT-PCR approach to assess the viral causes of influenza-like illnesses in Cambodia during three consecutive dry seasons. Journal of medical virology, 82(10), pp.1762-1772.	2005-2007	234	83	all	ILI	NA	3.60%	21.70%	43.40%	7.20%	yes	
van Gageldonk-Lafeber, A.B., Heijnen, M.L.A., Bartelds, A.I., Peters, M.F., van der Plas, S.M. and Wilbrink, B., 2005. A case-control study of acute respiratory tract infection in general practice patients in The Netherlands. Clinical Infectious Diseases, 41(4), pp.490-497.	2000-2003	645	156	all	ARTI incl ILI	NA	NA	7.00%	24.00%	NA	3.00%	58.00%
van Beek, J., Veenhoven, R.H., Bruin, J.P., Van Boxtel, R.A., de Lange, M.M., Meijer, A., Sanders, E.A., Rots, N.Y. and Luytjes, W., 2017. Influenza-like illness incidence is not reduced by influenza vaccination in a cohort of older adults, despite effectively reducing laboratory-confirmed influenza virus infections. The Journal of infectious diseases, 216(4), pp.415-424.	2011/12	1992	141	60-89	ILI	18.90%	NA	18.20%	8.40%	4.90%		64.90%
van Beek, J., Veenhoven, R.H., Bruin, J.P., Van Boxtel, R.A., de Lange, M.M., Meijer, A., Sanders, E.A., Rots, N.Y. and Luytjes, W., 2017. Influenza-like illness incidence is not reduced by influenza vaccination in a cohort of older adults, despite effectively reducing laboratory-confirmed influenza virus infections. The Journal of infectious diseases, 216(4), pp.415-424.	2012/13	2368	260	60-89	ILI	34.20%	NA	11.30%	21.10%	6.50%		73.80%
van Asten, L., van den Wijngaard, C., van Pelt, W., van de Kassteele, J., Meijer, A., van der Hoek, W., Kretzschmar, M. and Koopmans, M., 2012. Mortality attributable to 9 common infections: significant effect of influenza A, respiratory syncytial virus, influenza B, norovirus, and parainfluenza in elderly persons. The Journal of infectious diseases, 206(5), pp.628-639.	2000-2001	592	361	< 5	hosp ARI children	3.00%			20.00%			61.00%
Iwane, M.K., Edwards, K.M., Szilagyi, P.G., Walker, F.J., Griffin, M.R., Weinberg, G.A., Coulen, C., Poehling, K.A., Shone, L.P., Balter, S. and Hall, C.B., 2004. Population-based surveillance for hospitalizations associated with respiratory syncytial virus, influenza virus, and parainfluenza viruses among young children. Pediatrics, 113(6), pp.1758-1764.												

*Rhinovirus included other enteroviruses in many studies.