The impact of heating, ventilation and air conditioning (HVAC) design features on the transmission of viruses, including the 2019 novel coronavirus (COVID-19): a systematic review of humidity

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Abstract

The aerosol route has been a pathway for transmission of many viruses. Similarly, recent evidence has determined aerosol transmission for SARS-CoV-2 to be significant. Consequently, public health officials and professionals have sought data regarding the role of Heating, Ventilation, and Air Conditioning (HVAC) features as a means to mitigate transmission of viruses, particularly coronaviruses. Using international standards, a systematic review was conducted to comprehensively identify and synthesize research examining the effect of humidity on transmission of coronaviruses and influenza. The results from 24 relevant studies showed that: increasing from mid (40-60%) to high (>60%) relative humidity (RH) for SARS-CoV-2 was associated with decreased virus survival; although SARS-CoV-2 results appear consistent, coronaviruses do not all behave the same; increasing from low (<40%) to mid RH for influenza was associated with decreased persistence, infectivity, viability, and survival, however effects of increased humidity from mid to high for influenza were not consistent; and medium, temperature, and exposure time were associated with inconsistency in results for both coronaviruses and influenza. Adapting HVAC humidity to mitigate virus transmission is a complex approach due to difficulties of humidity control; humidity is a feature to be considered in conjunction with other HVAC features.

Keywords: Heating, ventilation, air conditioning, HVAC, virus, transmission, coronavirus, COVID-19, systematic review, humidity
Practical Implications

While increasing relative humidity from mid (40-60%RH) to high (>60%RH) was associated with decreased SARS-CoV-2 survival, coronaviruses did not all behave the same way. As a result, blanket prescriptive humidity levels for coronavirus mitigation are difficult to ascertain. While influenza survival varied from mid to high RH, increased humidity from low (<40%RH) to mid (40-60%RH) RH was associated with decreased virus survival with maximum survival at low RH. When controlling humidity as an HVAC feature, practitioners should take into account virus type and temperature. Future research should also consider the impact of exposure time, temperature, and medium when designing experiments, while also working towards more standardized testing procedures.
Introduction

The World Health Organization (WHO) declared, in March 2020, a global pandemic due to Coronavirus Disease 2019 (COVID-19) which is caused by Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2)\(^1,2\). Throughout the world, public health authorities have sought evidence regarding virus transmission routes and corresponding public health measures to mitigate virus spread. Certain viruses can be transmitted via an aerosol route,\(^3\) facilitated by virus-laden aerosols, which are expelled by humans, that remain airborne for extended periods of time. Recent evidence suggests that, particularly in indoor environments with poor ventilation, SARS-CoV-2 can spread via airborne transmission.\(^4,5\) The American Society of Heating, Refrigerating, and Air-Conditioning Engineers (ASHRAE) released a statement in April 2021 declaring that “[a]irborne transmission of SARS-CoV-2 is significant and should be controlled. Changes to building operations, including the operation of heating, ventilating, and air-conditioning systems, can reduce airborne exposures”.\(^6\) As a result, determining the appropriate measures to help protect occupants of indoor spaces based on informed, interdisciplinary research is critical to managing and controlling the spread of infectious disease.\(^7\) Heating, ventilation, and air conditioning (HVAC) systems can be used to mitigate airborne transmission of viruses by diluting or removing the contaminated air where humans breathe from inside the building envelope.\(^7-10\) HVAC design features, particularly humidity, can influence transmission.

As part of their 2021 recommendations for minimizing infectious aerosol exposure, ASHRAE recommended “[maintaining] temperatures and humidity at set points,” potentially highlighting the role of humidity in transmission.\(^11\) Previous systematic reviews have also noted the impact of humidity on infectious agents.\(^4,12,13\) Derby et al\(^12\) reviewed the effect of low humidity (≤40% relative humidity [RH]) on virus viability and transmission and identified several studies, both
modelling and experimental, that found that humidity influenced virus transmission and virus survival.\cite{14-18} Some of these studies found that increasing humidity from low RH levels to approximately 50% RH was associated with decreased transmission.\cite{14,15,18} Other reviews have also highlighted the effect of temperature, exposure time, and air sampling techniques.\cite{4,12,13} While Derby et al focused on the impact of low humidity levels (<40% RH), they also grouped humidity levels to allow for comparisons across studies: low (20-30% RH), mid (~50% RH), and high (70-90% RH).\cite{12}

Coronaviruses have emerged as infectious agents of great concern for potential airborne transmission. Coronaviruses are lipid enveloped, single-stranded RNA (ssRNA) viruses.\cite{19} Seven human coronaviruses have been identified; however, SARS-CoV-2, Severe Acute Respiratory Syndrome coronavirus (SARS-CoV), and Middle East Respiratory Syndrome coronavirus (MERS-CoV) have received the most attention due to their pathogenicity and lethality.\cite{20} These coronaviruses had their first emergence in the last 18 years,\cite{20} with SARS-CoV in 2003, MERS-CoV in 2012, and SARS-CoV-2 in 2019. However, due to the potentially limited number of studies examining coronaviruses, studies examining the influence of humidity on influenza viruses may also provide useful information. As virus envelopes were found to be an important factor in virus transmission,\cite{12,13} Influenza (both A and B strains) was chosen for inclusion in the present review due to its structure as a lipid enveloped, ssRNA virus.\cite{14}

As mentioned, previous reviews have studied the role of humidity in virus transmission in some capacity.\cite{4,12,13} This systematic review builds on these previous reviews through an extensive and comprehensive search of the literature to identify and synthesize published research determining the impact of humidity in reducing virus transmission. While Derby et al focused on the role of low humidity,\cite{12} the present review seeks to provide a broader picture including all humidity levels.
As well, this review focuses on the enveloped, ssRNA coronaviruses and influenza viruses as opposed to viruses more generally. By doing so, the insight drawn from this review could help answer questions of the role of humidity in SARS-CoV-2 transmission mitigation in mechanically ventilated indoor environments. As well, a comprehensive synthesis of the existing scientific literature can identify gaps in current research, which can guide future research priorities.

**Methods**

As part of a larger research program to review the literature on HVAC design feature and airborne virus transmission, this systematic review was performed to identify and synthesize the scientific literature regarding the impact of humidity on virus transmission within the built environment. Results for other design features of interest (ventilation, ultraviolet radiation, and filtration) are reported separately. The systematic review is registered (CRD42020193968) and a protocol was developed a priori and made publicly available.\(^{21,22}\) Standards, as defined by the international Cochrane organization,\(^{23}\) for the conduct of systematic reviews were followed with modifications for questions related to etiology.\(^{24}\) Additionally, the review was reported according to relevant reporting standards.\(^{25}\)

**Search Strategy**

Using concepts related to virus, transmission, and HVAC, a research librarian (GMT) searched three electronic databases (Ovid MEDLINE, Compendex, Web of Science Core) from inception to June 2020 (see Appendix A for the Ovid MEDLINE search strategy). Prior to implementing the searches, two librarians peer-reviewed the strategies (TL, AH). An updated search was conducted in January 2021. Reference lists of all relevant papers and review articles were screened. Using Compendex and Web of Science, conference abstracts were identified and were not included, but
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literature was searched to identify if any relevant abstracts had been published as complete papers. Limits for language or year of publication were not placed on the search. However, only English-language studies were included due to the volume of available literature and resource constraints. References were managed in EndNote and duplicate records removed prior to screening.

Study Selection

Study selection occurred in two stages: title/abstract screening and full-text screening. In the first stage, two reviewers independently screened the titles and abstracts of all references identified by the searches of the electronic databases. Relevance of each record was classified as No, Yes, or Maybe. Conflicts between No and Yes/Maybe were resolved by one of the review team. Pilot testing was conducted with three sets of studies (n=199 each) to develop consistency among the review team. The review team met to discuss discrepancies and develop decision rules after each set of pilot screenings. In the second stage, two reviewers independently reviewed the full-text articles and applied the inclusion/exclusion criteria. Reviewers classified studies as Exclude or Include. Conflicts between Exclude or Include were resolved through consensus by the review team. One reviewer resolved conflicts when different exclusion reasons were given. Pilot tests with three sets of studies (n=30 each) were used for the second stage of screening. The review team met to resolve discrepancies after each pilot round. Covidence software was used to conduct screening.

Inclusion and Exclusion Criteria

Exclusion and inclusion criteria are listed in Appendix B. This systematic review was part of a larger effort to examine virus transmission and different HVAC design features. While all four design features were included in the search and screening process, only studies evaluating
humidity were synthesized here. In addition, literature examining both humidity and ultraviolet radiation was addressed in a separate systematic review on ultraviolet radiation. A variety of agents were included in the search with priority placed on studies of viruses or agents that simulated viruses. Other agents (e.g., fungi, bacteria) would be included if studies were not available specific to viruses. Studies using bacteriophages, which are viruses that infect bacterial cells, were included. Studies of the indoor built environment (e.g., office, public, residential buildings) which had mechanical ventilation were of particular interest. Primary research providing quantitative results of the association between humidity and virus transmission was included. Only English-language, peer-reviewed publications were included.

Risk of Bias Assessment

For experimental studies, the risk of bias was determined based on three key domains: selection bias, information bias and confounding. Reviewers assessed domains as high, low, or unclear risk of bias using signalling questions for the different study types that were included (e.g., animal studies, laboratory experiments, epidemiological studies) from guidance documents. Modelling studies were assessed using the following three key domains: definition, assumption, and validation. Definition considered model complexity and data sources, assumption considered the explanation and description of model assumptions, and validation considered model validation and sensitivity analysis. Reviewers assessed each domain as high, low, or unclear risk of bias based on signalling questions. Pilot tests were conducted among three review authors for risk of bias items, then two reviewers (DD, EK, or NF) applied the criteria to each relevant study independently and met to resolve discrepancies.
Data Extraction

General information about the study (authors, year of publication, country of corresponding author, year of publication, study design) and methods (setting, population [as applicable], intervention set-up, agent studied) was extracted. Details on humidity treatment parameters (where available) were extracted, including relative humidity (RH), absolute humidity (AH), medium, exposure time, and temperature, where applicable. The studies were grouped as aerosolized virus (Table 1), modelling (Table 2), animal (Table 3), and field studies (Table 4). Quantitative data were extracted, in addition to the results of any tests of statistical significance related to humidity. The primary outcome of interest was quantitative measures of the association between virus transmission and humidity. As such, data on actual transmission were extracted where available (i.e., infections), as well as information regarding virus survival, persistence, infectivity, viral load per hour, concentration, recovery, decay rate, death rate, and virus detection in air. In the animal and aerosolized virus tables, humidity was categorized as low (<40% RH), mid (40-60% RH), and high (>60% RH). Symbols were used to denote high virus survival (+), low virus survival (-) and mid virus survival (/) (i.e., between low and high). One reviewer extracted data and a second reviewer verified data for accuracy and completeness using a data extraction form spreadsheet to ensure consistency. The review team discussed discrepancies.

Data Synthesis

Meta-analysis was not possible due to heterogeneity across studies in terms of study design, humidity levels tested, outcomes assessed, and results reported. Evidence tables were developed to describe the studies and their results. A narrative synthesis of results was conducted by study grouping (aerosolized virus, modelling, animal, and field studies).
Results

The searches yielded 12,177 unique citations. 2,428 were identified as potentially relevant based on title/abstract screening and 568 met the inclusion criteria (Figure 1). 124 studies were relevant to humidity with 65 relevant to viruses more broadly. Of those 65, 24 were specific to lipid enveloped, ssRNA viruses: coronavirus (n=6) and influenza (n=18). Two relevant studies\textsuperscript{33,34} were related and are considered as one in the analyses that follow, therefore, 23 studies were synthesized. Studies were published between 1943 and 2020 (median year 2013). The majority of studies (n=10) were laboratory experiments, with six experimental animal studies, one field observational study, and six modelling studies. Details of individual studies are provided in Tables 1, 2, 3, and 4, and risk of bias assessments are provided in Tables 5 and 6. Table 7 shows a visual representation of the relative change (↑ increase, ↓ decrease, - no change) in virus infectivity between low (<40%), mid (40%-60%), and high (>60%) RH. Studies were funded by national research funding organizations (n=15) and public foundations (n=2), with three studies reporting no external funding and three studies not reporting funding sources.

Aerosolized Viruses

Coronaviruses. Five experimental studies examined coronaviruses using SARS-CoV-2 (BetaCoV/USA/WA1/2020),\textsuperscript{35} SARS-CoV-2 England-2,\textsuperscript{36} MERS-CoV isolate HCoV-EMC/2012,\textsuperscript{37,38} and hCoV-229E\textsuperscript{39} (Table 1). These studies were conducted by aerosolizing the virus into a rotating drum\textsuperscript{35,36,38,39} or environmental chamber.\textsuperscript{37}

Two studies examined SARS-CoV-2 and showed different results. Smither et al found that increased RH from mid (40-60%) to high (≥60%) was associated with increased survival in both artificial saliva (AS) and tissue culture medium (TCM), although survival in TCM was less at
higher RH than in AS at the same RH.\textsuperscript{36} Schuit et al found that humidity alone did not significantly affect virus survival.\textsuperscript{35} Discrepancy in results could be due to differences in the studies’ experimental set-up and test procedures, e.g., exposure time up to 60\textsuperscript{35} vs 90\textsuperscript{36} minutes.

Two studies analyzed the effect humidity on MERS viruses, including MERS-CoV\textsuperscript{37} and MERS-CoV isolate HCoV-EMC/2012.\textsuperscript{38} Van Doremalen et al found increased RH from mid to high RH was associated with decreased virus survival (i.e., the highest survival was at mid RH levels), noting a significant effect of humidity on virus survival.\textsuperscript{37} Van Doremalen et al did not test at low (≤40\%) RH levels. Pyankov et al found that increasing RH was associated with increasing virus survival when coupled with decreasing temperature; these results were statistically significant during the 30- and 60-minute exposure times.\textsuperscript{38} Mid RH levels were not tested.

Ijaz et al examined a full spectrum of RH ranges and found that increasing humidity from low to mid RH was associated with increased virus survival for hCoV-229E, with the highest survival for coronavirus at mid RH.\textsuperscript{39} As well, increased humidity from mid RH to high RH was associated with decreased hCoV-229E survival.

Aerosolized coronaviruses were not consistent as to minimum and maximum survival versus humidity. Two studies found that high humidity was associated with minimum virus survival for MERS-CoV\textsuperscript{37} and hCoV-229E at 20±1°C\textsuperscript{39} (70\%RH and 80±5\%RH, respectively). Two studies found low humidity was associated with minimum survival for MERS-CoV\textsuperscript{38} and hCoV-229E at 6±1°C\textsuperscript{39} (24\%RH/38°C and 30±5\%RH, respectively). One study found that mid humidity levels (40-60\%RH) were associated with minimum virus survival.\textsuperscript{36} Two studies found that mid humidity was associated with maximum virus survival (50±5\%RH and 40\%RH)\textsuperscript{37,39} and two studies found that high humidity was associated with maximum virus survival (79\%RH/25°C and 68-
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88%RH). Schuit et al did not find a significant effect of humidity so minimum and maximum survival could not be determined.

Influenza. Six studies analyzed the effect of humidity on influenza viruses (Table 1). Influenza strains investigated include Influenza A PR8, Influenza A WSNH strain, H1N1, and the Influenza A/Mexico/4018/2019 (H1N1). Settings included a 4 m³ room, rotating drums, a Wells refluxing atomizer or stirred settling chamber, and environmental chamber.

Three studies found that increased humidity from low to mid RH associated with decreased virus survival and infectivity. Harper found increasing humidity from low to mid RH was associated with decreased viability at 7-8°C at exposure times of 0, 0.1, 4, 6, and 23 hours, 20.5-24 °C and exposure times of 0.1, 0.5, 1, 4, 6, and 23 hours, and at 32°C with exposure times of 0.1, 0.5, 1, 4, and 6 hours. Harper found that increasing humidity from low to mid RH was associated with similar viability at 7-8°C with exposure times of 0.5 and 1 hour, at 20.5-24 °C with an exposure of 0 hours, and at 32°C with exposure times of 0 and 23 hours. When increasing humidity from low to mid RH, Kormuth et al found no significant effect of humidity on infectivity; Van Doremalen et al did not test low RH levels.

For increased humidity from mid to high RH, two studies found decreased survival and significantly decreased infectivity. Harper found increased humidity from mid to high was associated with decreased viability at 7-8°C and an exposure time of 23 hours. One study found that increased humidity from mid to high was associated with increased survival. Harper found increased viability when increasing humidity from mid to high RH at 7-8°C and an exposure time of 0 and 0.1 hours. Two studies found no significant effect when increasing humidity from mid
to high RH.\textsuperscript{37,41} As well, Harper found similar viability when increasing humidity from mid to high RH at 20.5-24°C and 32°C at all exposure times and at 0.5, 1, 4, and 6 hours for 7-8°C.

Unlike coronaviruses, many of the influenza studies presented consistent results for minimum and maximum survival versus humidity level. Most consistently, four of the six aerosol influenza studies found that low humidity was associated with maximum survival (~15%RH and <40%RH, respectively),\textsuperscript{18,40} viability (<40%RH),\textsuperscript{33,34} and infectivity (23%RH).\textsuperscript{16} For minimum survival, Hemmes et al found that high humidity was associated with minimum survival (~90%RH)\textsuperscript{18} and that high humidity was associated minimum viability at 7-8°C (>60%RH).\textsuperscript{33,34} Both Noti et al and Harper at 20.5-24°C and 32°C found that both mid and high RH was associated with minimum virus survival and infectivity as there was little to no difference in survival and infectivity at the two RH ranges (43-73%RH and >40%RH, respectively).\textsuperscript{16,33,34} Schaffer et al found that mid humidity was associated with maximum survival (40-60%RH).\textsuperscript{40} Two studies found that humidity was not associated with any significant difference in infectivity\textsuperscript{41} and viability,\textsuperscript{37} as such, minimum and maximum survival could not be determined.

\textit{Modelling Studies}

\textbf{Coronaviruses.} One modelling study\textsuperscript{42} examined the effect of humidity on SARS-CoV-2 in terms of viral survival load per hour to determine optimal temperature/RH pairs for virus inactivation (Table 2). Spena et al\textsuperscript{42} used experimental data from Pyankov et al\textsuperscript{38} and Van Doremalen et al\textsuperscript{37} for MERS-CoV, MERS isolate HCoV-EMC, SARS-CoV-1, and SARS-CoV-2 in the development of the model. Spena et al\textsuperscript{42} noted that specific enthalpy is a better predictor of ideal virus control than humidity; their study indicates a target value of 55kJ/kg is optimal. Unfortunately, this target results in high absolute humidity values well above typical set points for mechanical systems. To achieve 55kJ/kg specific enthalpy, HVAC settings require an indoor RH of approximately 93% at
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20°C, decreasing almost linearly to 60% RH at 25°C (Fig. 5). Spena et al. indicate a triangular subsector on the psychrometric chart within the ASHRAE recommended quadrangular comfort zone which is both optimal for virus control and comfort. Their findings indicate an important trade-off exists between controlling virus activity and typical building indoor air design parameters.

Influenza. Five modelling studies examined the effect of influenza (Table 2). Three of the five studies used animal transmission data from Lowen et al. and one study included data from Harper for aerosolized viruses. Model types included a heuristic model, a mathematical model using mathematical exponential decay, a Gaussian breath plume model, an Auto-Regressive Conditional Heteroskedasticity model, and a model for the size and dynamics of Influenza A.

Three studies found that increased humidity from low to mid RH was associated with decreased virus transmission, viability, and concentration. Two studies found that increased humidity from mid to high RH was associated with decreased virus transmission and virus concentration. One study found that increased humidity from mid to high RH was associated with increased viability. Koep et al found that increased AH from 2.67 mb to 9.45 mb AH was associated with decreased virus survival and that increased RH from 40% to 60% RH was associated with decreased survival. Halloran et al found humidity from 20% to 80% RH was associated with similar transmission probability. Additionally, Halloran et al found that decreasing temperature from 20°C to 5°C was associated with increased transmission probability, while increasing temperature from 20°C to 30°C was associated with decreased transmission probability.
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*Animal Studies*

**Influenza.** Six animal studies examining the effect of humidity on viruses used influenza (see Table 3).\textsuperscript{14,15,47-50} Three studies came from the same research group.\textsuperscript{14,15,50} Strains used were Influenza A (PR8),\textsuperscript{47,48} Influenza A/Panama/2007/99 (Pan/99; H3N2),\textsuperscript{14} Influenza A/Panama/2007/1999 (H3N2) (Pan/99),\textsuperscript{14,49,50} Influenza A/Netherlands/602/2009 (H1N1) (NL/09),\textsuperscript{15,50} and Influenza A/Indiana/8/2011 (H3N2v).\textsuperscript{49}

Five studies found that increased humidity from low to mid RH was associated with decreased virus persistence,\textsuperscript{47} infectivity,\textsuperscript{48} and transmission.\textsuperscript{14,15,49}

Two studies found that increased humidity from mid to high RH was associated with decreased virus persistence at 5°C, 20°C, and 27-29°C.\textsuperscript{14,47} However, three other studies found that increased humidity from mid to high RH was associated with increased infectivity at 22.2-23.8°C\textsuperscript{48} and transmission at 20°C (65%RH) and 23°C.\textsuperscript{14,49} Steel et al found that increased humidity from low to high RH (mid not tested) was associated with decreased transmission at 20°C and 30°C.\textsuperscript{50}

Like that of aerosolized influenza studies, six studies found that low humidity was associated with maximum virus survival (23-43%RH,\textsuperscript{47} 23%RH,\textsuperscript{48} 20%RH,\textsuperscript{14} 20%RH,\textsuperscript{15} 20%RH,\textsuperscript{50} and 30%RH,\textsuperscript{49} respectively). Three studies found that high humidity (89%RH,\textsuperscript{47} 80%RH,\textsuperscript{14} and 80%RH\textsuperscript{50}) was associated with minimum virus survival and two studies found mid humidity levels were associated with minimum virus survival (45-60%RH\textsuperscript{48} and 50%RH,\textsuperscript{49} respectively).

*Field Studies*

**Influenza.** One study found no significant effect of absolute and relative humidity on Influenza A and B detection in different settings on a university campus in Hong Kong (Table 4).\textsuperscript{51}

*Risk of Bias*
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All animal and field experimental studies had low risk of bias for the three domains (Table 5): selection bias, information bias and confounding. Seven of the aerosolized virus experimental studies had low risk of bias for all three domains (Table 5). For the remaining aerosolized virus experimental studies, one had unclear information bias due to lack of clarity regarding exposure time and one had unclear information bias and high selection bias because the test and tracer material were not identical. One was assessed with high risk of bias due to confounding for our comparison of interest because both humidity and temperature were changed, where 79% RH and 25°C was compared with 24% RH and 38°C. The six modelling studies had low risk of bias for all three domains (Table 6): definition, assumption, and validation.

Discussion

This systematic review focussed on the HVAC design feature of humidity and its effect on transmission of coronavirus and influenza, both enveloped, ssRNA viruses. Several important findings were revealed. First, increased humidity from mid to high RH for SARS-CoV-2 was associated with decreased virus survival. Second, although SARS-CoV-2 results appear consistent, coronaviruses do not all behave the same and consistent minimum/maximum survival versus humidity level could not be determined. Third, increased humidity from low to mid RH for influenza was associated with decreased persistence, infectivity, viability, and survival; however, increased RH from mid to high for influenza did not show consistent results. Fourth, low humidity was associated with maximum influenza survival; however, the humidity level for minimum survival was not consistent. Fifth, even though both were enveloped, ssRNA viruses, coronaviruses and influenza did not behave the same. For example, SARS-CoV-2 data found that increased humidity from low to mid or mid to high was associated with either no effect or increased survival, while influenza data, using H1N1 as an example, found that increased
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humidity from mid to high was associated with either no effect\textsuperscript{16,37,41} or decreased transmission\textsuperscript{50}. Sixth, similar to results reported in previous reviews\textsuperscript{12,13} of humidity and viruses, medium, temperature, and exposure time contributed to inconsistency in results for both coronaviruses and influenza.

The relationship between airborne virus transmission and relative humidity is decidedly complex. Ijaz et al propose that airborne survival of vertebrate viruses under various environmental conditions cannot be predicted based on viral structure and composition\textsuperscript{39}. According to Lowen et al, there is likely more than one mechanism by which relative humidity affects virus transmission\textsuperscript{15}. Not only does relative humidity affect viral particles, it can also have an impact on the host. Lowen et al suggest that low relative humidity can damage nasal epithelia and reduce mucociliary clearance\textsuperscript{15}. This would render the host more susceptible to respiratory virus infections.

Temperature and suspending medium are oftentimes entangled with the effects of relative humidity\textsuperscript{33,34,39,50}. However, Hemmes et al asserted that relative humidity has a larger effect on the survival of aerosolized viruses compared to temperature\textsuperscript{18}. Salt and protein concentrations in the suspending medium can have a marked effect on the aerosol stability of a virus\textsuperscript{37}. Lester found that decreasing the salt concentration of influenza A virus-lung suspension eliminated the deleterious effect of increasing the relative humidity to 50%\textsuperscript{48}. Kormuth et al found that human bronchial epithelial extracellular material (HBE ECM) protected aerosolized influenza virus from relative humidity dependent decay\textsuperscript{41}. They go on to state that protein is most likely protecting the virus from decay but other elements of HBE ECM should not be ruled out.

Relative humidity also affects the settling of virus-containing respiratory droplets. High relative humidity is linked with increased settling\textsuperscript{14,17,41}, thereby preventing the formation of droplet
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However, Yang and Marr’s analysis revealed that relative humidity plays a larger role in virus inactivation than removal through settling.\(^{17}\)

It is understood that increasing humidification is not feasible in all types of facilities due to existing design limitations.\(^{16,46}\) Noti et al suggest that high risk, low humidity areas should be identified during the design and construction phase and appropriate consideration should be given to designs that minimize infection risk.\(^{16}\) Spena et al identified a region on the psychrometric chart that satisfies ASHRAE Standard 55’s comfort zone requirements while also providing optimal humidity conditions to decrease SARS-CoV-2 survival.\(^{42}\) In general, Spena et al suggest increasing humidification of supply air in the winter season and decreasing dehumidification of supply air in the summer season.\(^{42}\)

Implications for Research

Based on the included studies, several key implications for research were found, such as the influence of medium, temperature, and exposure time; the need for statistical analysis to better understand and interpret results; and the need for standardized testing procedures. For example, for SARS-CoV-2, increased RH from low to high was associated with an increase or no change in infectivity, where the difference was attributed to differences in exposure time and/or suspending medium. Interestingly, increased RH from low to high was associated with an increase in infectivity for MERS-CoV, where one study decreased the temperature while increasing the RH. While this is one example, the complexity of other factors can be seen through the review content.

While one study\(^{36}\) directly compared mediums, it was not the only study to comment on the perceived influence of medium on the results. Smither et al\(^{36}\) compared Artificial Saliva (AS) and tissue culture medium (TCM), finding that there were fewer particles observed in AS than in TCM,
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perhaps contributing to the amount of viable virus present. While the difference in medium has implications for research, practitioners may want to consider the results from AS as they are more applicable to real-world transmission or virus survival scenarios. Additionally, using human bronchial epithelial extracellular material (HBE ECM), Kormuth et al found no significant effect of humidity on viruses. Kormuth et al suggested that a lack of results could be due to “protection conferred by supplementation of the viruses with HBE ECM”. This theory was further tested using Phi6 both with and without HBE ECM. Additionally, Kormuth et al questioned “how well the media composition represented that of actual aerosols and droplets expelled by an infected host”. As such, researchers should be aware of the influence of medium when testing humidity while also considering their research goals (e.g., choosing a medium such as AS to simulate real-world scenarios).

Five studies used multiple temperatures when examining the influence of humidity on viruses. The relationship between temperature and humidity is complex. For example, Ijaz et al found that “the fluidity of the lipid-containing envelope is stabilized at low temperature, thus protecting the virion; however, further studies are needed to explain these phenomena”. As well, the Lowen group found that humidity and temperature as a combined approach could have an impact on virus survival, suggesting that “[i]nfluenza virus transmission indoors could potentially be curtailed by simply maintaining room air at warm temperatures (20°C) and either intermediate (50%) or high (80%) RHs”. Additionally, Harper found that high temperatures were associated with the lowest survival at all levels of humidity, finding the influence of humidity “negligible”. As a result, researchers should consider the influence of temperature in addition to the influence of humidity.
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Exposure time was also found to be a factor when testing the effect of humidity. Schuit et al questioned whether insufficient exposure time explained the inability to detect a RH relationship for SARS-CoV-2 that was similar to hCoV-229E. Smither et al found that, in conjunction with the effect of medium, increased exposure time resulted in two patterns of virus survival. For SARS-CoV-2 in AS, increased exposure time was associated with increased differences between virus survival between mid and high RH. In TCM, increased exposure time was associated with decreased differences between survival at mid and high RH. Similarly, Harper found that aerosols were able to remain viable for a considerable amount of time “in favourable conditions”. However, Harper also noted that favourable conditions vary by virus.

Other research implications arising from this review are the need for reporting of statistical analyses and standard procedures for testing. Only four of the 18 experimental studies included statistical analysis in their presentation of results. Two of the four studies found significant results; while two studies found nonsignificant results which the authors attributed to study design issues. An unfortunate limitation of this review is that studies with statistical analyses were presented alongside studies that did not conduct or report statistical analyses in order to allow for a full understanding of the available humidity/virus literature. While attempts were made to ensure clarity when reporting results, differences between survival were reported without supporting statistical analysis from the original documentation and as such, could potentially influence overall findings. Additionally, these findings are further complicated by inconsistencies in testing procedures across the included studies. For example, Schuit et al attributed their nonsignificant results to short exposure times and Kormuth et al suggested that medium choice may have affected study outcomes. Additionally, as Derby et al previously noted, not all of the studies tested a full spectrum of RH levels. Two experimental studies did not test low (<40%RH)
humidity$^{36,37}$ and two experimental studies$^{38,50}$ did not test mid (40-60\%RH) humidity. As a result, it can be difficult to make comparisons even among similar viruses.

**Implications for Practice**

In their January 2021 Core Recommendations for Reducing Airborne Infectious Aerosol Exposure ASHRAE recommended “[maintaining] temperatures and humidity at set points”.$^{11}$ Spena et al considered the ASHRAE comfort zone for domestic and office-like environments in their model of SARS-CoV-2.$^{42}$ They found that SARS-CoV-2 infectivity would be effectively suppressed for only a portion of the temperature and RH in the ASHRAE comfort zone. This indicated target zone is of high humidity and would be challenging in buildings where mould/mildew control is important, or in older buildings in cold climates where condensation can be a problem. Cold regions would require very significant humidification efforts when outdoor make-up air has very low absolute humidity at inlet. As this modelling study by Spena et al was released early in the SARS-CoV-2 pandemic timeline, the model includes data for Phi6, HCoV-EMC (MERS), SARS-CoV, and one SARS-CoV-2 study to provide inputs for SARS-CoV-2 modelling.$^{42}$ While the enthalpy was not calculated within the scope of this review, the results of Schuit et al$^{35}$ and Smither et al$^{36}$ potentially do not support the findings of Spena et al.$^{42}$ Schuit et al did not find a significant effect of humidity, possibly due to short exposure times.$^{35}$ However, Smither et al found that high humidity was associated with maximum survival at 19-22°C,$^{36}$ whereas the modelling by Spena et al suggests that mid to high RH is associated with increased inactivation or decreased survival.$^{42}$ As such, it would be interesting to see how the results of Spena et al change with new research.

**Conclusion**
This systematic review identified 24 studies examining the role of humidity as an HVAC intervention and its effect on transmission of the lipid enveloped, ssRNA influenza and coronaviruses. Similar to previous reviews,\textsuperscript{12,13} it was found that while humidity can have an effect on viruses, aerosol medium, temperature, and exposure time can also influence the role of humidity. While SARS-CoV-2 results appear to be consistent as increased humidity from mid to high RH was associated with decreased virus survival, not all coronaviruses behave the same way. Additionally, increasing humidity from low to mid RH for influenza was associated with decreased survival; however, increasing RH from mid to high for influenza was not consistent. When examining humidity as a HVAC intervention, medium, temperature, and exposure time should be considered. As well, due to inconsistencies across viruses, while recommended levels for specific viruses could potentially be determined, generalized approaches to humidity cannot be made.
References

1. World Health Organization (WHO). WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020. Accessed April 4, 2021.

2. World Health Organization (WHO). Naming the coronavirus disease (COVID-19) and the virus that causes it. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-19)-and-the-virus-that-causes-it. Accessed April 15, 2021.

3. Leung NHL. Transmissibility and transmission of respiratory viruses. Nat Rev Microbiol. 2021. doi: 10.1038/s41579-021-00535-6

4. Noorimotlagh Z, Jaafarzadeh N, Martinez SS, Mirzaee SA. A systematic review of possible airborne transmission of the COVID-19 virus (SARS-CoV-2) in the indoor air environment. Environ Res. 2021;193:110612. doi: 10.1016/j.envres.2020.110612

5. Rahimi NR, Fouladi-Fard R, Aali R, Shahryari A, Rezaali M, Ghafouri Y, Ghalhari MR, Asaadi-Ghalhari M, Farzinnia B, Gea OC, Fiore M. Bidirectional association between COVID-19 and the environment: a systematic review. Environ Res. 2021;194:110692. doi: 10.1016/j.envres.2020.110692

6. ASHRAE. ASHRAE epidemic task force releases updated airborne transmission guidance. 5 April 2021. American Society of Heating, Refrigerating, and Air-Conditioning Engineers (ASHRAE). https://www.ashrae.org/about/news/2021/ashrae-epidemic-task-force-releases-updated-airborne-transmission-guidance. Accessed April 22, 2021.

7. Luongo JC, Fennelly KP, Keen JA, Zhai ZJ, Jones BW, Miller SL. Role of mechanical ventilation in the airborne transmission of infectious agents in buildings. Indoor Air. 2016;26:666-678. doi:10.1111/ina.12267

8. Li Y, Leung GM, Tang JW, Yang X, Chao CYH, Lin JZ, Lu JW, Nielsen PV, Niu J, Qian H, Sleigh AC, Su H-JJ, Sundell J, Wong TW, Yuen PL. Role of ventilation in airborne transmission of infectious agents in the built environment – a multidisciplinary systematic review. Indoor Air. 2007;17:2-18. doi:10.1111/j.1600-0668.2006.00445.x

9. Bing-Yuan, Zhang Y-H, Leung NHL, Cowling BJ, Yang Z-F. Role of viral bioaerosols in nosocomial infections and measures for prevention and control. J Aerosol Sci. 2018;117:200-211. doi:10.1016/j.jaerosci.2017.11.011

10. Tang JW, Marr LC, Li Y, Dancer SJ. Covid-19 has redefined airborne transmission. BMJ. 2021;373:n913. doi: https://doi.org/10.1136/bmj.n913

11. ASHRAE. Core Recommendations for Reducing Airborne Infectious Aerosol Exposure. 6 January 2021. American Society of Heating, Refrigerating, and Air-Conditioning Engineers (ASHRAE). https://www.ashrae.org/file%20library/technical%20resources/covid-19/core-recommendations-for-reducing-airborne-infectious-aerosol-exposure.pdf Accessed April 16, 2021.

12. Derby MM, Hamekhasi M, Eckels S, et al. Update of the scientific evidence for specifying lower limit relative humidity levels for comfort, health, and indoor environmental quality in occupied spaces (RP-1630). Sci Technol Built Environ. 2017;23:30-45. doi: 10.1080/23744731.2016.1206430

13. Da Silva PS, Nascimento MSJ, Soares RRG, Sousa SIV, Mesquita JR. Airborne spread of infectious SARS-CoV-2: Moving forward using lessons from SARS-CoV and MERS-CoV. Sci Total Environ. 2020;764:142802. doi: 10.1016/j.scitotenv.2020.142802
Humidity and virus transmission

14. Lowen, AC, Mubareka S, Steel J, Palese P. Influenza virus transmission is dependent on relative humidity and temperature. *PLOS Pathog.* 2007;3(10):1470-1476. doi: 10.1371/journal.ppat.0030151

15. Lowen AC, Steel J. Roles of humidity and temperature in shaping influenza seasonality. *J Virol.* 2014;88(14):692-7695. doi: 10.1128/JVI.03544-13.

16. Noti JD, Blachere FM, McMillen CM, et al. High humidity leads to loss of infectious influenza virus from simulated coughs. *PLOS one.* 2013;8(2):e57485. doi: 10.1371/journal.pone.0057485.

17. Yang W, Marr LC. Dynamics of airborne influenza A viruses indoors and dependence on humidity. *PloS one.* 2011;6(6):e21481. doi: 10.1371/journal.pone.0021481

18. Hemmes JH, Winkler KC, Kool SM. Virus survival as a seasonal factor in influenza and poliomyelitis. *Nature.* 1960;188:430-431. doi: 10.1007/BF02538737

19. Cavanagh D, Britton P. Coronaviruses: General features. *Encyclopedia of Virology.* 2008:549-554. doi: 10.1016/B978-012374410-4.00370-8

20. Zhu Z, Lian X, Su X, Wu W, Marraro GA, Zeng Y. From SARS and MERS to COVID-19: a brief summary and comparison of severe acute respiratory infections caused by three highly pathogenic human coronaviruses. *Resp Res.* 2020;21(1). doi:10.1186/s12931-020-01479-w

21. Thornton GM, Fleck BA, Zhong L, Hartling L. The impact of heating, ventilation and air conditioning (HVAC) design features on the transmission of viruses, including the 2019 novel coronavirus (COVID-19): protocol for a systematic review and environmental scan. Open Science Framework. 2020. https://doi.org/10.17605/OSF.IO/Y62V7

22. Thornton G, Zhong L, Fleck B, Hartling L. The impact of heating, ventilation and air conditioning (HVAC) design features on the transmission of viruses, including the 2019 novel coronavirus (COVID-19): a systematic review. PROSPERO. 08 July 2020. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020193968 Accessed July 8, 2020

23. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA. Cochrane handbook for systematic reviews of interventions version 6.0. Updated July 2019. Cochrane. Available from www.training.cochrane.org/handbook.

24. Moola S, Munn Z, Sears K, et al. Conducting systematic reviews of association (etiology): The Joanna Briggs Institute’s approach. Int J Evid Based Healthc. 2015;13(3):163-169. doi: 10.1097/XEB.0000000000000064

25. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ. 2009;339:b2535. doi:10.1136/bmj.b2535

26. Kowalski, WJ. *Ultraviolet germicidal irradiation handbook: UVGI for air and surface disinfection.* Heidelberg: Springer-Verlag; 2009.

27. Williams-Nguyen J, Bueno I, Sargeant JM, Nault AJ, Singer RS. What is the evidence that point sources of anthropogenic effluent increase antibiotic resistance in the environment? Protocol for a systematic review. *Anim Health Res Rev.* 2016;17(1):9-15. doi: 10.1017/S1466252316000037

28. Office of Health Assessment and Translation (OHAT), Division of the National Toxicology Program, National Institute of Environment Health Sciences. Handbook for conducting a literature-based health assessment using OHAT approach for systematic review and evidence integration. National Toxicology Program, US Department of Health and Human
**Humidity and virus transmission**

Services, 4 March 2019.
https://ntp.niehs.nih.gov/ntp/ohat/pubs/handbookmarch2019_508.pdf Accessed November 28, 2020.

29. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.2. Updated February 2021. Cochrane. Available from www.training.cochrane.org/handbook

30. Samuel GO, Hoffmann S, Wright RA, et al. Guidance on assessing the methodological and reporting quality of toxicologically relevant studies: A scoping review. Environ Int. 2016;92-93:630-646. doi:10.1016/j.envint.2016.03.010

31. Mateus ALP, Otete HE, Beck CR, Dolan GP, Nguyen-Van-Tam JS. Effectiveness of travel restrictions in the rapid containment of human influenza: a systematic review. Bull World Health Organ. 2014;92(12):868-880D. doi:10.2471/BLT.14.135590

32. Organisation for Economic Co-operation and Development (OECD). Guidance Document on the Validation of (Quantitative) Structure-Activity Relationship [(Q)SAR] Models. OECD Series on Testing and Assessment No. 69, OECD Publishing, 3 September 2014. doi: 10.1787/9789264085442-en. Accessed January 4, 2021.

33. Harper GJ. Airborne micro-organisms: survival tests with four viruses. *J Infect Dis*. 1961;59:479-486. doi: 10.1017/S0022172400039176

34. Harper GJ. The influence of the environment on the survival of airborne virus particles in the laboratory. 1963;13:64-71. doi: 10.1007/bf01243824

35. Schuit, M, Ratnesar-Shumate S, Yolitz J, et al. Airborne SARS-CoV-2 is Rapidly Inactivated by Simulated Sunlight. *J Infect Dis*. 2020;222(4):564-571. doi: 10.1093/infdis/jiaa334.

36. Smither SJ, Eastaugh LS, Findlay JS, Lever MS. Experimental aerosol survival of SARS-CoV-2 in artificial saliva and tissue culture media at medium and high humidity. *Emerg Microbes Infect*. 2020;9(1):1415-1417. doi: 10.1080/22221751.2020.1777906.

37. van Doremalen N, Bushmaker T, Munster VJ. Stability of Middle East respiratory syndrome coronavirus (MERS-CoV) under different environmental conditions. *Euro Surveill*. 2013;18(38):pii=20590.

38. Pyankov OV, Bodnev SA, Pyankova OG, Agranovski IE. Survival of aerosolized coronavirus in the ambient air. *J Aerosol Sci*. 2018;115: 158-163. doi: 10.1016/j.jaerosci.2017.09.009.

39. Ijaz MK, Brunner AH, Sattar SA, Nair RC, Johnson-Lussenburg CM. Survival characteristics of airborne human coronavirus 229E. *J Gen Virol*. 1985;66:2743-2748. doi: 10.1099/0022-1317-66-12-2743.

40. Schaffer FL, Soergel ME, Straube DC. Survival of airborne influenza virus: effects of propagating host, relative humidity, and composition of spray fluids. *Arch Virol*. 1976;51(4):263-273. doi: 10.1007/BF01317930

41. Kormuth KA, Lin K, Prussin AJ, et al. Influenza virus infectivity is retained in aerosols and droplets independent of relative humidity. *J Infect Dis*. 2018;218(5):739-747. doi: 10.1093/infdis/jiy221.

42. Spena A, Palombi L, Corcione M, Caresta M, Spena, VA. On the optimal indoor air conditions for SARS-CoV-2 inactivation: An enthalpy-based approach. *Int J Environ Res Public Health*. 2020;17(17):6083. doi: 0.3390/ijerph17176083.
43. Zuk T, Rakowski F, Radomski JP. A model of influenza virus spread as a function of temperature and humidity. *Comput Biol Chem.* 2009;33(2):176-180. doi: 10.1016/j.compbiolchem.2008.12.001.

44. Posada JA, Redrow J, Celik I. A mathematical model for predicting the viability of airborne viruses. *J Virol Methods.* 2010;164:88-95. doi: 10.1016/j.jviromet.2009.12.004.

45. Halloran SK, Wexler AS, Ristenpart WD. A comprehensive breath plume model for disease transmission via expiratory aerosols. *PloS one.* 2012;7(5):e37088. doi: 10.1371/journal.pone.0037088.

46. Koep TH, Enders FT, Pierret C, et al. Predictors of indoor absolute humidity and estimated effects on influenza virus survival in grade schools. *BMC Infect. Dis.* 2013;13:71. doi: 10.1186/1471-2334-13-71.

47. Loosli CG, Lemon HM, Robertson OH, Appel E. Experimental air-borne influenza infection. I. Influence of humidity on survival of virus in air. *Proc Soc Exp Biol Med.* 1943;53(2):205-206. doi: 10.3181/00379727-53-14251P.

48. Lester W. The influence of relative humidity on the infectivity of air-borne influenza A virus, PR8 strain. *J Infect Dis.* 1948;88(3):361-368. doi: 10.1084/jem.88.3.361.

49. Gustin KM, Belser JA, Veguilla V, et al. Environmental conditions affect exhalation of H3N2 seasonal and variant influenza viruses and respiratory droplet transmission in ferrets. *PloS one.* 2015;10(5):e0125874. doi: 10.1371/journal.pone.0125874.

50. Steel J, Palese P, Lowen AC. Transmission of a 2009 pandemic influenza virus shows a sensitivity to temperature and humidity similar to that of an H3N2 seasonal strain. *J Virol.* 2011;85(3):1400-1402. doi:10.1128/JVI.02186-10.

51. Xie CY, Lau EHY, Yoshida T, et al. Detection of influenza and other respiratory viruses in air sampled from a university campus: A longitudinal study. *Clin Infect Dis.* 2020;70(5):850-858. doi: 10.1093/cid/ciz296.

52. Blanchere FM, Cao G, Lindsley WG, Noti JD, Beezhold DH. Enhanced detection of infectious airborne influenza virus. *J Virol Methods.* 2011;176:120-124. doi: 10.1016/j.jviromet.2011.05.030.
### Table 1. Aerosolized virus

| First author Year Country | Experimental design | Outcome | Virus | Effect of Humidity | Medium | Exposure Times | Temperature | Result | Association |
|---------------------------|---------------------|---------|-------|--------------------|--------|----------------|-------------|--------|-------------|
| **Coronaviruses**         |                     |         |       |                    |        |                |             |        |             |
| Ijaz 1985<sup>39</sup>    | Coronavirus 229E was aerosolized into a rotating drum | Humidity vs recovery | hCoV-229E | Low | High | Tryptose Phosphate Broth | 20 ± 1 °C | Increased RH from 30 ± 5% to 50 ± 5% associated with increased recovery (hCoV-229E half life from 26.76 ± 6.21 h to 67.33 ± 8.24 h) Increased RH from 50 ± 5% to 80 ± 5% associated with decreased recovery (hCoV-229E half life from 67.33 ± 8.24 h to 3.34 ± 0.16 h) | Increased RH from low to mid levels associated with increased recovery Increased RH from mid to high levels associated with decreased recovery Minimum recovery was associated with high RH (80 ± 5% RH) at 20 ± 1 °C Minimum recovery was associated with low RH (30 ± 5% RH) at 6 ± 1 °C Maximum recovery was associated with mid RH (50 ± 5% RH) at 6 ± 1 °C and 20 ± 1 °C |
| Van Doremalen 2013<sup>37</sup> | MERS-CoV was aerosolized in an environmental chamber | Humidity vs viability | MERS (MERS-CoV isolate HCoV-EMC/2012) | Low | Mid | Dulbecco’s Modified Eagle Medium | Continuous sampling during aerosolization | Increased RH from 30 ± 5% to 50 ± 5% associated with increased recovery (MERS-CoV isolate HCoV-EMC half life from 34.46 ± 3.21 h to 102.53 ± 9.38 h) Increased RH from 50 ± 5% to 80 ± 5% associated with decreased recovery (MERS-CoV half life from 102.53 ± 9.38 h to 86.01 ± 5.28 h) | Increased RH from mid to high levels associated with decreased viability Low RH was not reported Minimum viability associated with high RH (70%RH) Maximum viability associated with mid RH (40%RH) |
| Pyankov 2018<sup>38</sup> | MERS (MERS-CoV isolate HCoV-EMC/2012) was aerosolized into a rotating drum | Humidity vs virus survival | MERS (MERS-CoV isolate HCoV-EMC/2012) | Low | Mid | Dulbecco’s Modified Eagle Medium supplemented with 2% fetal calf serum | 79% RH and 25 °C vs 24% RH and 38 °C | Increasing RH from 24% (38 °C) to 79% (25 °C) associated with increased virus survival | Increasing RH from low (24% RH/38°C) to high (79% RH/25°C) levels associated with increased virus survival Mid RH levels not reported |
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| Study | Region | Virus Strain | Humidity vs | Virus Survival | RH Range | Increased RH from 40-60% to 68-88% Associated With | Increased RH from Mid to High Levels Associated With | Low Levels Not Reported | Minimum Survival Associated With Low RH (24%/38 °C) | Maximum Survival Associated With 79% (79%/25 °C) |
|-------|--------|--------------|-------------|----------------|----------|-------------------------------------------------|----------------------------------------------------|-------------------------|-----------------------------------------------|-----------------------------------------------|
| Smither 2020<sup>15</sup> England-2 | United Kingdom | SARS-CoV-2 England-2 | Humidity vs virus survival | SARS-CoV-2 England-2 | NR - + | Tissue Culture Medium (TCM) | Increased RH from 40-60% to 68-88% associated with increased survival of SARS-CoV-2 England-2 | Increased RH from mid to high levels associated with increased survival in TCM at all sample times | Low levels not reported | Minimum survival associated with mid RH (40-60%RH) Maximum survival associated with high RH (68-88%RH) |
| | | | | | | | Increased RH from 40-60% to 68-88% associated with little change in survival of SARS-CoV-2 England-2 at 0 minutes. | Increased RH from mid to high levels associated with little change in AS | | 0 minutes: Increased RH from mid to high levels associated with little change in AS | |
| | | | | | | | Increased RH from 40-60% to 68-88% associated with increased survival at 15 minutes | Increased RH from mid to high levels associated with increased survival in AS | | 15, 30, and 90 minutes: Increased RH from mid to high levels associated with increased survival in AS | |
| | | | | | | | Increased RH from 40-60% to 68-88% associated with slightly increased survival of SARS-CoV-2 England-2 at 30 minutes | Increased RH from mid to high levels associated with little change in AS | | 60 minutes: Increased RH from mid to high levels associated with little change in AS | |
| | | | | | | | increased RH from 40-60% to 68-88% associated with relatively no difference in survival at 60 minutes | Minimum survival associated with mid RH (40-60%RH) Maximum survival associated with high RH (68-88%RH) | | | |
| | | | | | | | Increased RH from 40-60% to 68-88% associated with increased survival at 90 minutes | | | | |
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| Schuit 2020<sup>23</sup> USA | SARS-CoV-2 (BetaCoV/USA/WA1/2020) was aerosolized into a rotating drum | Humidity vs decay rate | SARS-CoV-2 (BetaCoV/USA/WA1/2020) | * | * | * | Simulated saliva or fresh culture medium | 30 sec, every 5 min up to 1 hr | 20 °C | Increased RH did not significantly affect decay rate of deSARS-CoV-2 (Covid 19) for samples taken up to 60 minutes. “While a similar effect was not observed for SARS-CoV-2 in the present study, it is possible that the shorter test durations used in the present study precluded detection of this effect of relative humidity. It is possible that additional tests of longer duration without simulated sunlight would allow a better assessment of the effect of relative humidity on SARS-CoV-2 in aerosols” (p.568) | Increased RH had no significant effect on decay rate | RH % for minimum and maximum decay not determined |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Hemmes 1960<sup>18</sup> Netherlands | Influenza A was aerosolized in a 4 m<sup>3</sup> test room | Humidity vs death rate and virus survival | Influenza A virus (PR<sub>8</sub>) | + | / | - | allantoic fluid and 2% Difco peptone | “adequate” intervals of time | 20°C | Increased RH from ~15% to ~90% associated with an increased death rate of influenza virus and a sharp transition between 40-60% RH and another sharp transition at 80% RH | Increased RH from low to mid levels associated with increased death rate (decreased survival) Increased RH from mid to high levels associated with increased death rate (decreased survival) minimum survival associated with high RH (~90%RH) Maximum survival associated with low RH (~15%RH) |
| Harper 1961, 1963<sup>33,34</sup> England | Influenza A was generated into a rotating drum | Humidity vs viability | Influenza A | + | / | - | Allantoic fluid | 0, 0.1, 0.5, 1, 4, 6, 23 hrs. | 7-8°C | Low to mid RH (& low to high RH): Increased RH from low to mid levels associated with decreased viability at 0, 0.1, 4, 6, 23 h; Increased RH from low to mid levels associated with similar viability at 0.5, 1 h Mid to high RH: Increased RH from mid to high levels associated with increased viability at 0, 0.1 h; Increased RH from mid to high levels associated with similar viability at 0.5, 1, 4, 6 h; | Low to mid RH (& low to high RH) 0, 0.1, 4, 6, 23 h: Increased RH from low to mid levels associated with decreased viability 0.5, 1 h: Increased RH from low to mid levels associated with similar viability Mid to high RH 0, 0.1 h: |
| Temperature | RH Levels | Viability变化 |
|------------|----------|----------------|
| 20.5-24 °C | Low to mid RH (& low to high RH): Increased RH from low to mid levels associated with similar viability at 0 h; Increased RH from low to mid levels associated with decreased viability at 0.1, 0.5, 1, 4, 6, 23 h; Increased RH from mid to high levels associated with similar viability (see Harper 1963) |  |
|             | Mid to high RH: Increased RH from mid to high levels associated with similar viability (see Harper 1963) |  |
|             | Minimum viability associated with mid and high RH |  |
|             | Maximum viability associated with low RH |  |
| 32°C        | Low to mid RH (& low to high RH): Increased RH from low to mid levels associated with decreased viability at 0.1, 0.5, 1, 4, 6 h; Increased RH from mid to high levels associated with decreased viability at 0.1, 0.5, 1, 4, 6, 23 h; Increased RH from low to mid levels associated with similar viability at 0 h; Increased RH from mid to high levels associated with similar viability (see Harper 1963) |  |
|             | Minimum viability associated with mid and high RH |  |
|             | Maximum viability associated with low RH |  |
### Humidity and Virus Transmission

| Study          | Virus Type       | Experimental Setup                                                                 | Environmental Conditions | Outcome | Notes |
|----------------|------------------|------------------------------------------------------------------------------------|--------------------------|---------|-------|
| Schaffer 1976 | Influenza A (WSN, strain) | Aerosolized in a Wells refluxing atomizer (stirred settling chamber) | Increased RH from mid to high levels associated with increased viability | Increased RH from low to mid levels associated with decreased survival; increased RH from mid to high levels associated with relatively higher survival than at mid RH. | Increased RH from low to mid levels associated with similar viability at 0, 23 h. Mid to high RH: Increased RH from mid to high levels associated with similar viability. Minimum viability associated with mid and high RH. Maximum viability associated with low RH. |
| Noti 2013     | Aerosolized Influenza A (H1N1) | Coughed into a simulated examination room chamber using two manikins | Increased RH from 23% to 43% associated with decreased % infectivity (77.2% to 14.6%); Increased RH from 43% to 73% associated with similar % infectivity (14.6% to ~17%; Figure 3) | Increased RH from 23% to 43% associated with decreased % infectivity (77.2% to 14.6%); Increased RH from 43% to 73% associated with similar % infectivity (14.6% to ~17%; Figure 3) | Increased RH from low to mid levels associated with significantly decreased infectivity. Increased RH from mid to high levels associated with similar infectivity. Minimum infectivity associated with mid and high RH (43-73%RH). Maximum infectivity associated with low RH (<40%RH). |
# Humidity and virus transmission

| Source           | Virus Type    | Methodology                        | Humidity vs | Influenza A                      | Humidity vs | Influenza A | Media                      | Temperature | Notes                                                                 |
|------------------|---------------|------------------------------------|-------------|---------------------------------|-------------|-------------|---------------------------|-------------|----------------------------------------------------------------------|
| Van Doremalen    | Influenza A   | Aerosolized in an environmental    | from 40% to 70% | Increased RH from 40% to 70% had no significant effect on viability | from 40% to 70% | Increased RH from mid to high levels had no significant effect on viability | Dulbecco’s Modified Eagle Medium | 20°C        | Low RH was not reported. RH % for minimum and maximum viability not determined (not statistically significant) |
| 2013 USA         | (A/Mexico/4018/2019 (H1N1)) | chamber                                      | NR          | Increased RH from low to mid levels and increased RH from mid to high levels associated with no significant effect | Increased RH from mid to high levels had no significant effect on viability | Human Bronchial Epithelial Extracellular Material (HBE ECM) | Continuous sampling during aerosolization | 25 ± 1°C     | RH % for minimum and maximum decay not determined (not statistically significant) |
| Kormuth          | Influenza A   | Aerosolized into a rotating drum    | from 40% to 70% | RH had no significant effect on infectivity of H1N1 in HBE ECM | from 40% to 70% | Increased RH from mid to high levels had no significant effect on viability | Human Bronchial Epithelial Extracellular Material (HBE ECM) | 35 min, 1 hr   | Low RH was not reported. RH % for minimum and maximum viability not determined (not statistically significant) |
| 2018 USA         | (H1N1)        |                                     | Increased RH from low to mid levels and increased RH from mid to high levels associated with no significant effect |                   | Increased RH from mid to high levels had no significant effect on viability |                       | 25 ± 1°C     | RH % for minimum and maximum decay not determined (not statistically significant) |

NR = Not Recorded; ND = Not Detected
+ denotes the effect of the relative humidity range was least detrimental, - denotes effect of relative humidity range was most detrimental, / denotes the effect was moderate in comparison to other, * denotes humidity was found to have no effect
RH categories. Low: <40% RH, Medium 40%-60% RH, High >60% RH
### Table 2. Modelling Studies

| First author Year | Study Design | Virus | Humidity level tested | Outcomes | Association |
|-------------------|-------------|-------|-----------------------|----------|-------------|
| Spena 2020<sup>42</sup> Italy | Experimental data from literature was used to develop a model to determine the influence of humidity on SARS-CoV-2 viral survival load | SARS-CoV-2 | ASHRAE comfort zone “for domestic and office-like environments” (p.4) [four corners on psychrometric chart] 1. 80%RH; 20 °C 2. 50%RH; 26 °C 3. 30%RH; 20 °C 4. 20%RH; 27 °C | Viral Survival Load at 1-hour vs specific enthalpy “…optimal pairs of temperature and relative humidity values for coronavirus viral load inactivation, wherein SARS-CoV-2 infectivity actually appears to be nearly suppressed.” (p.9) | Optimal pairs [three corners on psychrometric chart] 1. 80%RH; 20 °C 2. 50%RH; 26 °C 3. 45%RH; 26°C | High and mid RH optimal pairs associated with coronavirus inactivation |
| Zuk 2009<sup>43</sup> Poland | A heuristic model of Influenza A transmission was developed using experimental results of Lowen et al. (2007) to determine transmission as a function of temperature and relative humidity | Influenza A | 20%, 35%, 50%, 65%, and 80% | gamma vs RH, transmission vs RH | At 5 °C Increased RH from 35% to 80% associated with lower transmission rates Increased RH from low to mid associated with decreased transmission Increased RH from mid to high associated with decreased transmission |
| Posada 2010<sup>44</sup> USA | A mathematical model using mathematical exponential decay was used to predict the viability of Influenza A using data from Schaffer et al. (1976) as a function of humidity | Influenza A | 20%-80% | Viability vs RH | Increased RH from low to mid levels associated with decreased viability Increased RH from mid to high levels associated with increased viability |
| Yang 2011<sup>17</sup> USA | The size distribution and dynamics of Influenza A viruses emitted from a cough in typical residential and public settings was modeled | Influenza A | 10% - 90% | IAV inactivation rate, concentration, distribution, and removal efficiency vs. RH and two different ACH. IAV size distribution and removal efficiency at fixed RH and two different ACH | Increased RH from 10% to 50% associated with decreased virus concentration; increased RH from 50% to 90% associated with decreased virus concentration |
| Study        | Methodology                                                                 | Virus | Range   | Measurement                        | Results                                                                                                                                 |
|--------------|------------------------------------------------------------------------------|-------|---------|------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|
| Halloran 2012 | A Gaussian breath plume model for expiratory aerosols was used to determine the effect of relative humidity on transmission of Influenza virus using conditions similar to those used by Lowen et al. (2007) | Influenza | 0% - 100% | Virus Transmission vs. Ventilation/RH | Increased RH from low to mid levels associated with decreased virus concentration  
Increased RH from mid to high levels associated with decreased virus concentration  
For RH from 0% to 80% RH, similar probability for RH from 20% to 80%  
For RH <80% RH, probability decreased at >95% RH at 20°C and 30°C for pulmonary;  
Probability decreased at >85% RH at 5°C for pulmonary;  
Probability increased at >95% RH at 5°C, 20°C and 30°C for nasopharyngeal-tracheobronchial  
Decreasing temperature from 20 to 5°C associated with increased probability  
Increasing temperature from 20 to 30°C associated with decreased probability |
| Koep 2013     | Using field measurements from two Minnesota grade schools and five published animal studies, a Auto-Regressive Conditional Heteroskedasticity model was used to determine the effect of humidity in the reduction of influenza virus survival | Influenza | 2.64 - 9.45 mb AH | Influenza survival vs. AH | Increased AH from 2.67 mb to 9.45 mb AH associated with decreased influenza virus survival (75% to 45% survival)  
Increased RH from 40% to 60% associated with decreased influenza survival (~47% (Figure 4) to 34% survival (p.4)) |
### Table 3. Experimental Animal Studies

| First author | Year | Country | Experimental Summary | Outcome | Virus | Effect at each RH* | Temperature | Data | Association |
|--------------|------|---------|----------------------|---------|-------|-------------------|-------------|------|-------------|
| Loosli       | 1943 | USA     | Groups of 10 mice were placed in a room with aerosolized influenza for 20+ minutes at varying RHs (17-90%) | Humidity vs virus persistence (determined by infections in exposed mice) | Influenza A (PR8) | + / - | 27-29 °C | Increased RH from 23% to 48% to 89% associated with decreased persistence of Influenza over time | Increased RH from low to mid levels associated with decreased persistence at 27-29 °C |
|              |      |         |                      |         |       |                   |             |      |              |
|              |      |         |                      |         |       |                   |             |      |              |
| Lester       | 1948 | USA     | Naive mice in groups of 10 were placed in wire cages divided into compartments in a room and exposed to aerosolized Influenza A | Humidity vs infectivity (determined by fatalities) | Influenza A (PR8) | + - + | 72-75 °F (22.2-23.8 °C) | Increased RH from 23% to 60% RH associated with decreased fatalities (100% to 22.5%); Increased RH from 60% to 80% associated with increased fatalities (22.5% to 100%) | Increased RH from low to mid levels associated with decreased infectivity (decreased fatalities) at 22.2-23.8 °C |
|              |      |         |                      |         |       |                   |             |      |              |
|              |      |         |                      |         |       |                   |             |      |              |
| Lowen        | 2007 | USA     | Inoculated and naive guinea pigs were housed in adjacent cages inside an environmental chamber | Humidity vs transmission | Influenza A [Influenza A/Panama/2007/99 (Pan/99; H3N2)] | + / - | 20 °C | Increased RH from 20% to 50% associated with decreased transmission (100%, 75% to 25%,25%); Increased RH from 50% to 80% associated with decreased transmission (25%, 25% to 0%, 0%) | Increased RH from low to mid levels associated with decreased transmission at 5°C and 20°C |
|              |      |         |                      |         |       |                   |             |      |              |
|              |      |         |                      |         |       |                   |             |      |              |

* RH: Relative Humidity
## Humidity and virus transmission

| Study | Methodology | Temperature | Humidity Change | Transmission Change | Notes |
|-------|-------------|-------------|-----------------|---------------------|-------|
| Steel 2011<sup>50</sup> USA | Inoculated and naive guinea pigs were housed in adjacent cages inside an environmental chamber | 5 °C | + / - | Increased RH from 35% to 50% associated with a little change in influenza transmission (100%, 100% to 100%, 75%); Increased RH from 50% to 80% associated with decreased transmission (100%, 75% to 50%, 50%) | Minimum viability associated with high RH (80%RH) Maximum viability associated with low RH (20%RH) |
| Steel 2011<sup>50</sup> USA | Influenza A/Panama/2007/1999 (H3N2) (Pan/99) | 20 °C | + NR - | Increased RH from 20% to 80% associated with decreased transmission (100%, 100%, 75% to 25%, 0%, 0%) | Increased RH from low to high associated with decreased transmission 20°C and 30°C Mid RH not reported Minimum viability associated with high RH (80%RH) Maximum viability associated with low RH (20%RH) |
| Steel 2011<sup>50</sup> USA | Influenza A/Panama/2007/1999 (H3N2) and A/Netherlands/602/2009 (H1N1) (NL/09) | 30 °C | + NR - | Increased RH from 20% to 80% associated with decreased transmission (25%, 0% to 0%, 0%) | |
| Steel 2011<sup>50</sup> USA | Influenza A/Panama/2007/1999 (H3N2) and A/Netherlands/602/2009 (H1N1) (NL/09) | 20 °C | + NR - | Increased RH from 20% to 80% associated with decreased transmission (100% to 0%) | |
| Steel 2011<sup>50</sup> USA | Influenza A/Panama/2007/1999 (H3N2) and A/Netherlands/602/2009 (H1N1) (NL/09) | 30 °C | + NR - | Increased RH from 20% to 80% associated with decreased transmission (25% to 0%) | |
| Steel 2011<sup>50</sup> USA | Influenza A/Panama/2007/1999 (H3N2) and A/Netherlands/602/2009 (H1N1) (NL/09) | 23 °C | + NR NR | Previously unpublished data: 100% transmission at 5 °C and 20% RH Increased RH from 20% to 50% associated with a little change in influenza transmission (100% to 100%, 75%) where 50% RH data is from Lowen et al (2007) | Increased RH from low to mid associated with decreased transmission at 5°C Mid RH data from Lowen et al (2007) Maximum viability associated with low RH (20%RH) |
| Lowen 2014<sup>43</sup> USA | Inoculated and naive guinea pigs were housed in adjacent cages inside an environmental chamber | 5 °C | + NR NR | Increased RH from 35% to 50% associated with a little change in influenza transmission (100%, 100% to 100%, 75%); Increased RH from 50% to 80% associated with decreased transmission (100%, 75% to 50%, 50%) | |
| Lowen 2014<sup>43</sup> USA | Influenza A/Panama/2007/1999 (H3N2) and A/Netherlands/602/2009 (H1N1) | 20 °C | + NR - | Increased RH from 20% to 80% associated with decreased transmission (100%, 75% to 25%, 0%, 0%) | |
| Lowen 2014<sup>43</sup> USA | Influenza A/Panama/2007/1999 (H3N2) and A/Netherlands/602/2009 (H1N1) | 30 °C | + NR - | Increased RH from 20% to 80% associated with decreased transmission (25% to 0%) | |
| Lowen 2014<sup>43</sup> USA | Influenza A/Panama/2007/1999 (H3N2) and A/Netherlands/602/2009 (H1N1) | 23 °C | + NR NR | Increased RH from 30% to 50% associated with decreased influenza transmission (2/3 to 1/3); Increased RH from 50% to 70% associated with increased transmission (1/3 to 2/3) | Increased RH from low to mid associated with decreased transmission at 23°C Increased RH from mid to high associated with associated with increased transmission at 23°C |
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| Influenza A/Indiana/8/2011 (H3N2v) | + | - | / | 23 °C | Increased RH from 30% to 50% associated with decreased influenza transmission (3/3 to 0/3); Increased RH from 50% to 70% associated with increased influenza transmission (0/3 to 2/3) | Minimum viability associated with mid RH (50%RH) | Maximum viability associated with low RH (30%) |
|-----------------------------------|---|---|---|------|---------------------------------------------------------------------------------|------------------------------------------------|------------------------------------------------|

* + denotes the effect of the relative humidity range was least detrimental, - denotes effect of relative humidity range was most detrimental, / denotes the effect was moderate in comparison to other RH categories. Low: <40% RH, Medium 40%-60% RH, High >60% RH

NR = not reported
### Table 4. Field Studies

| First author Year Country | Setting/Population | Study Type | Humidity level tested | Investigated Parameter | Result |
|---------------------------|-------------------|------------|-----------------------|------------------------|--------|
| Xie 2020<sup>31</sup> China | University campus in Hong Kong. Locations include canteens, lecture halls, shuttle buses, and the University Health Service | Observational | 4.2−22.9 g/m<sup>3</sup> | 27.1%–98.3% | Effect of absolute humidity and relative humidity on Influenza A and B detection in air. AH did not have a statistically significant association with influenza detection; RH included in univariate analysis (P value= 0.752) but not multivariate analysis. |
### Table 5. Risk of Bias for Experimental Studies

| Study            | Selection Bias | Information Bias | Confounding* |
|------------------|----------------|------------------|--------------|
| **Human/Field Studies** |                |                  |              |
| Xie (2020)       | Low            | Low              | Low          |
| **Animal Studies** |                |                  |              |
| Loosli (1943)    | Low            | Low              | Low          |
| Lester (1948)    | Low            | Low              | Low          |
| Lowen (2007)     | Low            | Low              | Low          |
| Steel (2011)     | Low            | Low              | Low          |
| Lowen (2014)     | Low            | Low              | Low          |
| Gustin (2015)    | Low            | Low              | Low          |
| **Aerosolized Studies** |            |                  |              |
| Ijaz (1985)      | Low            | Low              | Low          |
| Van Doremalen (2013) | Low         | Low              | Low          |
| Pyankov (2018)   | Low            | Low              | High         |
| Smith (2020)     | Low            | Low              | Low          |
| Schuit (2020)    | Low            | Low              | Low          |
| Hemmes (1960)    | Low            | Unclear          | Low          |
| Harper (1961)    | High           | Unclear          | Low          |
| Schaffer (1976)  | Low            | Low              | Low          |
| Noti (2013)      | Low            | Low              | Low          |
| Kormuth (2018)   | Low            | Low              | Low          |

* Confounding assessed for our comparison of interest.

### Table 6. Risk of Bias for Modelling Studies

| Study            | Definition | Assumption | Validation |
|------------------|------------|------------|------------|
| Zuk (2009)       | Low        | Low        | Low        |
| Halloran (2012)  | Low        | Low        | Low        |
| Yang (2011)      | Low        | Low        | Low        |
| Posada (2010)    | Low        | Low        | Low        |
| Koep (2013)      | Low        | Low        | Low        |
| Spena (2020)     | Low        | Low        | Low        |
Table 7: Virus infectivity relative change between low RH (<40%RH), mid RH (40%-60%RH), high RH (>60%RH)

| Study | Virus | Low to mid RH | Mid to high RH | Low to high RH |
|-------|-------|---------------|----------------|---------------|
| **Temperature ~ 20°C** | | | | |
| **Coronavirus** | | | | |
| Aerosolized | | | | |
| Ijaz 1985\textsuperscript{39} | hCoV-229E | ↑ | ↓ | |
| van Doremalen 2013\textsuperscript{17} | MERS-CoV | | | |
| Pyankov 2018\textsuperscript{38} | MERS-CoV | | | (38 C to 25 C) |
| Smither 2020\textsuperscript{36} | SARS-CoV-2 in Tissue Culture Medium | | | |
| Smither 2020\textsuperscript{36} | SARS-CoV-2 in Artificial Saliva | | | 15, 30, 90 min |
| Schuit 2020\textsuperscript{15} | SARS-CoV-2 | | | |
| **Influenza** | | | | |
| Aerosolized | | | | |
| Hemmes 1960\textsuperscript{18} | Influenza A (PR8) | | | |
| Harper 1961/1963\textsuperscript{33,34} | Influenza A | 0,1,0,5,1,4,6,23 h | 0 h | |
| Schaffer 1976\textsuperscript{40} | Influenza A (WSN\textsubscript{A}) | | | |
| Noti 2013\textsuperscript{16} | Influenza A (H1N1) | | | |
| van Doremalen 2013\textsuperscript{37} | Influenza A (H1N1) | | | |
| Kormuth 2018\textsuperscript{41} | Influenza A (H1N1) | | | |
| **Animal** | | | | |
| Loosli 1943\textsuperscript{37} | Influenza A (PR8) | | | |
| Lester 1948\textsuperscript{48} | Influenza A (PR8) | | | |
| Lowen 2007\textsuperscript{14} | Influenza A (H3N2) | | | 65%RH |
| | | | | 80%RH |
| Steel 2011\textsuperscript{50} | Influenza A (H3N2) | | | |
| Steel 2011\textsuperscript{50} | Influenza A (H1N1) | | | |
| Gustin 2015\textsuperscript{49} | Influenza A (H3N2) | | | |
| Gustin 2015\textsuperscript{49} | Influenza A (H3N2\textsubscript{v}) | | | |
| **Temperature ~5°C** | | | | |
| **Coronavirus** | | | | |
| Ijaz 1985\textsuperscript{39} | hCoV-229E | | | |
| **Influenza** | | | | |
| Aerosolized | | | | |
| Harper 1961/1963\textsuperscript{33,34} | Influenza A | 0,0,1,4,6,23 h | 0,0,1 h | 0,5,1,4,6, h |
| Lowen 2007\textsuperscript{14} 2014\textsuperscript{15} | Influenza A (H3N2) | | | 23 h |
| **Temperature ~30°C** | | | | |
| **Influenza** | | | | |
| Aerosolized | | | | |
| Harper 1961/1963\textsuperscript{33,34} | Influenza A | 0,1,0,5,1,4,6 h | | |
| Animal | | | | |
| Steel 2011\textsuperscript{50} | Influenza A (H3N2) | | | |
| Steel 2011\textsuperscript{50} | Influenza A (H1N1) | | | |
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Figure 1. Flow of studies through the selection process (note: search was conducted for all HVAC design features but only studies of relative humidity and coronavirus or influenza are included in this manuscript)
Appendix A: Search Strategy for Ovid MEDLINE

Database: Ovid MEDLINE(R) ALL 1946 to Present
Search Strategy:

| # | Searches                                                                 |
|---|--------------------------------------------------------------------------|
| 1 | exp Aerosols/                                                             |
| 2 | Air Microbiology/                                                         |
| 3 | exp Viruses/                                                              |
| 4 | (aerosol or aerosols or bioaerosol or bioaerosols).mp.                    |
| 5 | droplet nuclei.mp.                                                       |
| 6 | infectio*.mp.                                                            |
| 7 | (pathogen or pathogens).mp.                                              |
| 8 | (virus or viruses or viral or virome).mp.                                |
| 9 | or/1-8 [MeSH + Keywords – Virus concept]                                  |
| 10| Air Conditioning/                                                         |
| 11| Air Filters/ or Filtration/                                               |
| 12| Humidity/                                                                |
| 13| Ventilation/                                                             |
| 14| Ultraviolet Rays/                                                        |
| 15| air condition*.mp.                                                       |
| 16| (air change rate or air change rates or air changes per hour or air exchange rate or air exchange rates or air exchanges per hour).mp. |
| 17| (airflow or air flow).mp.                                                |
| 18| built environment.mp.                                                    |
| 19| computational fluid dynamics.mp.                                         |
| 20| ((distance adj6 index) or long distances).mp.                            |
| 21| HVAC.mp.                                                                 |
| 22| (filter or filters or filtration).mp.                                    |
| 23| humidity.mp.                                                             |
| 24| (ultraviolet or UV).mp.                                                  |
| 25| ventilat*.mp.                                                            |
| 26| or/10-25 [MeSH + Keywords – HVAC concept]                                |
| 27| Air Pollution, Indoor/                                                   |
| 28| exp Disease Transmission, Infectious/                                    |
| 29| (indoor adj1 (air quality or environment*)).mp.                          |
| 30| transmission.mp.                                                         |
| 31| or/27-30 [MeSH + Keywords – Transmission concept]                        |
| 32| 9 and 26 and 31                                                          |
| 33| remove duplicates from 32                                                |

MeSH = Medical Subject Headings
### Appendix B. Inclusion and exclusion criteria for systematic review

| Item       | Inclusion criteria                                                                 | Exclusion criteria                                                                 |
|------------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| **Agent**  | ![Inclusion criteria for Agent](#)                                                  | **Exclusion criteria**                                                               |
|            | • Viruses                                                                          | **We planned a staged process: if we identified studies specific to viruses for each HVAC design feature, we would not include other pathogens**; however, for design features where we did not find studies specific to viruses, we would expand to other pathogens. |
|            | • Aerosols                                                                         |                                                                                      |
|            | • Bioaerosols                                                                       |                                                                                      |
|            | • Droplet nuclei                                                                    |                                                                                      |
|            | • Other pathogens (e.g., bacteria, fungi)                                           |                                                                                      |
| **HVAC**   | ![Inclusion criteria for HVAC](#)                                                  | **Examination HVAC / mechanical / or other ventilation mechanisms overall, but not by specific design features.** |
|            | • Ventilation (ventilation rate, air changes per hour (ACH), air exchange, airflow pattern, pressurization) |                                                                                      |
|            | • Filtration (air filtration, filter type, MERV rating, filter age and/or use, pressure drop, holding capacity, replacement, change frequency) |                                                                                      |
|            | • Ultraviolet germicidal irradiation (UVGI; power, dose, uniformity of dose, flow rate, bioaerosol inactivation efficiency, location) |                                                                                      |
|            | • Humidity or relative humidity                                                     |                                                                                      |
| **Setting**| ![Inclusion criteria for Setting](#)                                               | **Outdoor settings**                                                                 |
|            | • Office buildings                                                                  | **Indoor settings with natural ventilation**                                          |
|            | • Public buildings (e.g., schools, day cares)                                       |                                                                                      |
|            | • Residential buildings                                                             |                                                                                      |
|            | • Hospitals and other healthcare facilities (e.g., clinics)                         |                                                                                      |
|            | • Transport vehicles (e.g., aircraft) or hubs (e.g., airports)                      |                                                                                      |
| **Outcomes**| ![Inclusion criteria for Outcomes](#)                                              | **Qualitative data**                                                                 |
|            | • Quantitative data evaluating the correlation or association between virus transmission and above HVAC features |                                                                                      |
| **Study design** | ![Inclusion criteria for Study design](#)                                          | **Review articles**                                                                 |
|            | • Primary research, including:                                                      | **Commentaries, opinion pieces**                                                     |
|            | • Epidemiological studies                                                           | **Qualitative studies**                                                              |
|            | • Observational studies (e.g., cohort, case-control, cross-sectional)              |                                                                                      |
|            | • Experimental studies (including human or animal)                                  |                                                                                      |
|            | • Modelling studies, including CFD                                                  |                                                                                      |
| **Language**| ![Inclusion criteria for Language](#)                                               | **Unpublished, not peer-reviewed**                                                   |
|            | • English                                                                          |                                                                                      |
| **Year**   | ![Inclusion criteria for Year](#)                                                  |                                                                                      |
|            | • No restrictions                                                                  |                                                                                      |
| **Publication status** | ![Inclusion criteria for Publication status](#)                                |                                                                                      |
|            | • Published, peer-reviewed                                                         |                                                                                      |

*CFD = computational fluid dynamics; HVAC = heating, ventilation, and air conditioning; MERV = minimum efficiency reporting value; UVGI = ultraviolet germicidal irradiation*