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ARTICLE

Associative evidence for the potential of humidification as a non-pharmaceutical intervention for influenza and SARS-CoV-2 transmission

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BACKGROUND: Both influenza and SARS-CoV-2 viruses show a strong seasonal spreading in temperate regions. Several studies indicated that changes in indoor humidity could be one of the key factors explaining this.
OBJECTIVE: The purpose of this study is to quantify the association between relevant epidemiological metrics and humidity in both influenza and SARS-CoV-2 epidemic periods.
METHODS: The atmospheric dew point temperature serves as a proxy for indoor relative humidity. This study considered the weekly mortality rate in the Netherlands between 1995 and 2019 to determine the correlation between the dew point and the spread of influenza. During influenza epidemic periods in the Netherlands, governmental restrictions were absent; therefore, there is no need to control this confounder. During the SARS-CoV-2 pandemic, governmental restrictions strongly varied over time. To control this effect, periods with a relatively constant governmental intervention level were selected to analyze the reproduction rate. We also examine SARS-CoV-2 deaths in the nursing home setting, where health policy and social factors were less variable. Viral transmissibility was measured by computing the ratio between the estimated daily number of infectious persons in the Netherlands and the lagged mortality figures in the nursing homes.
RESULTS: For both influenza and SARS-CoV-2, a significant correlation was found between the dew point temperature and the aforementioned epidemiological metrics. The findings are consistent with the anticipated mechanisms related to droplet evaporation, stability of virus in the indoor environment, and impairment of the natural defenses of the respiratory tract in dry air.
SIGNIFICANCE: This information is helpful to understand the seasonal pattern of respiratory viruses and motivate further study to what extent it is possible to alter the seasonal pattern by actively intervening in the adverse role of low humidity during fall and winter in temperate regions.
IMPACT: A solid understanding and quantification of the role of humidity on the transmission of respiratory viruses is imperative for epidemiological modeling and the installation of non-pharmaceutical interventions. The results of this study indicate that improving the indoor humidity by humidifiers could be a promising technology for reducing the spread of both influenza and SARS-CoV-2 during winter and fall in the temperate zone. The identification of this potential should be seen as a strong motivation to invest in further prospective testing of this non-pharmaceutical intervention.

Keywords: Influenza; SARS-CoV-2; COVID-19; Humidification; Dew point; Non-pharmaceutical intervention

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INTRODUCTION

During the current SARS-CoV-2 pandemic, many non-pharmaceutical interventions (NPIs), ranging from the reduction of contact intensity between hosts to interventions on the level of personal hygiene [1], are installed to reduce the viral transmission. Recently, ventilation of indoor spaces with fresh outdoor air and air cleaning are also recognized as important NPIs [2–5]. To identify the potential of other NPIs, it is helpful to study the effect of environmental factors on viral transmission. Several studies [6–8] indicated that the specific humidity is such a factor. In contrast to the well-controlled indoor temperature, indoor-specific humidity usually follows the seasonal variations of its outdoor counterpart. Specific humidity values outdoors and indoors are typically much lower in the winter than in summer, which causes indoor relative humidity (RH) values to also be much lower in winter since indoor temperatures are relatively constant year-round. It is technologically feasible to maintain both the indoor temperature and humidity at the desired level. The potential of

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humidity control as an NPI for influenza has been studied before [7, 9, 10], but for SARS-CoV-2 this NPI has hardly received attention [6]. Looking at the present development of the SARS-CoV-2 pandemic and possibly a revival of influenza, it is important to explore the potential of additional NPIs to support ongoing and upcoming pharmaceutical interventions.

Causal evidence for the role of humidity on the transmission of respiratory viruses is mainly retrieved from laboratory experiments with various model animals: mice [11], guinea pigs [12], and ferrets [13] considering both animal-adapted viruses and human pathogenic viruses. Also, the transmission metrics differ per study: number of fatalities, presence of pulmonary lesions, frequency of seroconversion, and viral titer in nasal wash of exposed hosts. These differences in study design disallow a direct comparison between study results, but the general observation is that an RH in the range between 40 and 60%, at a (room) temperature of 20–23 °C, seems to reduce the transmission of the respiratory viruses considered. Several mechanisms have been identified that could explain the dependency on viral transmission of respiratory viruses on humidity and temperature [8, 14]. Firstly, the RH and temperature control the evaporation rate of droplets. Smaller droplets have a significantly lower terminal settling velocity and are also more susceptible to dispersion by indoor-air flows [15–18]. Hence, the residence time of respiratory droplets of infected hosts is prolonged in dry air. Secondly, the RH affects the stability of enveloped viruses in both air and on surfaces [19–21]. The latter could affect the possibility of the fomite infection route, although a recent systematic review study concludes this route is likely negligible in the transmission of SARS-CoV-2 [22]. A remaining plausible infection route from fomites is via "aerosolized fomites" [23], where active virions are resuspended from surfaces and inhaled by recipients [24]. The dependence of viral stability as a function of humidity is a complex relation. Several studies indicated that there is an optimal range in terms of RH at a fixed temperature that minimizes the viral survival time [21]. Thirdly, the effectiveness of the natural defenses of the respiratory tract depends on humidity. In particular, the clearance of the airways by mucociliary transport, the indispensable first line of defense of the human body, is hindered by inhaling dry air [25, 26]. This is attributed to a decreasing depth of the periciliary fluid layer, which squeezes the cilia, and increasing viscoelasticity of the mucuos layer on top of the epithelium cells that line the inner surfaces of the respiratory tract. It is also found that dry air can impair innate antiviral defense and tissue repair of the airways [27].

For ventilation purposes, indoor and outdoor air needs to be exchanged at a sufficient rate [28]. During this exchange the water vapor mass is conserved, such that the specific humidity (i.e., gram water vapor per kg air) between the indoor and outdoor environment is practically the same. In winter, however, indoor air is heated to room temperature. This means that the capacity of indoor air to hold water increases. The RH can be seen as the ratio between the actual water content of the air compared to its maximum holding capacity. Thus, as a consequence of heating, the indoor RH drops with respect to the outdoor RH, which is typically much larger than 40% for a country like the Netherlands (annual mean 80%, std 15%). While the intended warming effect is indeed physiologically beneficial, the drying effect is not. For quantitative analysis, it is fortunate that the indoor temperature is usually kept at a more or less constant level, so that the outdoor specific humidity becomes a reliable indicator for the physiologically important indoor RH. Humidification technology can be employed during cold periods in temperate regions to compensate the deficit of indoor water vapor. A study found that in the pre-school setting the application of humidity control strongly helps to reduce the transmission of influenza A [10]. More specially, they observed a significant reduction in the total number of influenza A virus-positive samples (air and fomite) and viral genome copies in the rooms with humidification compared to the control rooms. The number of influenza-like illness cases was also reduced by a factor of 2.3. Earlier studies on humidity control, in various settings, already pointed in a similar direction, but the statistical confidence was not fully satisfactory [7]. It should also be noted that the earlier studies were performed in a time when building isolation had less priority, such that natural ventilation rates with fresh outdoor air were presumably higher, thereby compensating, to some extent, the adverse effect of low indoor humidity [7]. A recent systematic review study on the effect of humidity control on dryness symptoms or upper respiratory infections in educational settings and workplaces concluded that, almost four decades later, the quality of the evidence is still too low to be confident of the overall findings of thirteen studies published between 1963 and 2018 [29]. Interventional studies are also supported by model studies, e.g., on the survival of influenza in a residential setting [9]. Controlled-chamber tests with diagnosed SARS-CoV-2 infected participants demonstrated that humidification results in a significant reduction of viral load in aerosols and an increased viral load on a surface [30]. The authors [30] concluded that, considering that aerosol-mediated transmission has a substantially higher risk compared to fomite-mediated transmission, humidification is important for building health and safety, next to ventilation and air filtration.

The association between meteorological variables and the prevalence of respiratory virus is well studied [31]. The prevalence of influenza is typically associated with a lower outdoor temperature. Since the temperature and dew point temperature strongly correlate, a dependency on outdoor temperature also implies an association with dew point and vice versa (confounders). As the dew point can be converted into a specific humidity via basic thermodynamic relations, this means that if there is an association with the outdoor temperature there is also an association with the specific humidity and thus the indoor RH (see above). A study [31] reported that the mean dew point temperature on days that influenza A and B were detected in their samples was 3.94 and 3.26 °C, respectively. In contrast, in days these viruses were not detected the mean dew point temperature was 6.93 and 6.52 °C. Interestingly, a dew point of 6.0 °C corresponds with an indoor RH of approximately 40%. Thus a similar threshold was observed in the animal experiments. Another study found that the onset of influenza in the United States was signaled by different specific humidity levels per state, and that this value is higher for states that have a higher annual average humidity [32]. The estimated prevalence of influenza in the Netherlands between 2015 and 2019 also shows a strong correlation with the specific humidity [33].

For SARS-CoV-2, the statistical confidence of studies that appeared early in the pandemic is limited. However, these studies involve data from many countries and consistently found a declining trend of positive test cases with temperature, absolute humidity, specific humidity, or dew point [34]. A detailed spatial-temporal study toward lagged meteorological impacts on the SARS-CoV-2 incidence figures for longer times and 200 different counties in the United States convincingly showed that both a lower temperature and lower outdoor RH result in a significantly increased risk factor [35]. For the Netherlands, it was observed that the number of hospitalization of SARS-CoV-2 cases in an early stage of the pandemic had a significant negative correlation with the specific humidity [33].

The objective of this work is to improve the associative evidence basis for humidity as a potential NPI to reduce the transmission of both influenza and the SARS-CoV-2 viruses in a temperate country like the Netherlands. As both SARS-CoV-2 and influenza are enveloped viruses, it can be expected that the transmission characteristics are comparable. The hypothesis is that indoor RH plays an important role in the transmission of both viruses. As the indoor humidity is controlled by the outdoor specific humidity and

equivalently the dew point temperature, a negative correlation is expected between the transmission metrics and the dew point. It should be anticipated that both viruses become endemic and develop seasonality. This could cause an ongoing pressure on the health care system in coming years. For this reason, we combine in this study influenza and SARS-CoV-2 data. A complicating factor to quantify the role of an environmental factor on viral transmission, like humidity, is the time-variation of many socio-economic factors and the installation of governmental interventions. In this study, we control for this effect by selecting periods where interventions are either absent on a national level (two decades with influenza periods) or the level of intervention varies only weakly and by focusing on infections in a specific setting where policy and social factors are less variable. This retrospective study can contribute to assess the potential of humidity control as an NPI for both influenza and SARS-CoV-2 in temperate regions and motivate further prospective studies to this NPI.

METHODS

Influenza-associated mortality data

The National Institute for Public Health and the Environment (RIVM) [36] and Statistics Netherlands (CBS) [37] produce, in collaboration with other institutes, yearly surveillance of influenza and other respiratory viruses in the Netherlands. These reports include several metrics such as the estimated incidence figures, detailed analysis of specimens from patients, and the overall mortality numbers in the epidemic weeks. The relation between the estimated influenza incidence figures and environmental factors is already studied in detail [33]. Therefore, these data are not included again in our analysis.

Via the Dutch municipal system, the presumed cause of death is centrally reported to Statistics Netherlands (CBS). The yearly number of cases where influenza was reported as the primary cause of death is not in-line with the cumulative excess mortality observed during the influenza epidemic weeks. This indicates that influenza likely acts as a hidden health factor or causes displaced mortality in certain risk groups, but is not recognized as a primary cause of death. Therefore, we assume that the total mortality in influenza periods, minus a multi-year averaged baseline mortality, provides a more complete metric to assess the health impact of influenza. Another advantage of using overall mortality data is that for many years, 1995–2021, data per week are available. Compared to the estimated number of influenza cases, the mortality data do not involve a possible test-bias.

SARS-CoV-2 reproduction number

The National Institute for Public Health and the Environment (RIVM) maintains a detailed database of all COVID-19 data in the Netherlands. From this source, we obtain the reproduction number $R(t)$, which is the most direct metric for the transmissibility of SARS-CoV-2. In the early stage of the pandemic, $R(t)$ was estimated by the number of hospitalizations. Since June 12, 2020, $R(t)$ is computed from the daily number of positive tests. In most cases, the day of first symptoms was known. The time between the first day of symptoms of a new case and the first day of symptoms of the person who infected them was approximately 4 days on average. RIVM provides both the estimated $R(t)$ as well as the corresponding 95% confidence interval [36].

SARS-CoV-2 number of infectious persons

By combining serological data and hospital admissions RIVM computed the number of infectious persons for each day $N(t)$. The serological survey started with 3200 persons in April 2020 and increased to a total of 7700 participants. Each participant is asked to fill in a questionnaire and send a blood sample to RIVM at regular intervals. These blood samples were tested for the presence of SARS-CoV-2 antibodies. Based on this information the ratio between hospital admissions and the number of infected persons is determined. The daily reported number of hospital admissions can then be converted into an estimate of the number of infectious persons.

SARS-CoV-2 mortality in nursing home care

The number of deceased persons $D(t)$ within the population of nursing homes residents is registered on the day of death. RIVM only incorporates persons above 70 years in the statistics.

Meteorological data

Meteorological data are obtained from the Royal Netherlands Meteorological Institute (KNMI) [38]. This institute maintains multiple observational stations and maintains a database that contains several decades of data. The specific humidity is not directly available but can be computed from the temperature and the RH or by the dew point. In this study, the dew point $Td(t)$ was selected as the relevant metric for humidity. The regional variations in $Td(t)$ are small in the Netherlands because of the limited elevation differences and modest country size. The distance to the coastline results in some variation. To obtain a representative value for the Netherlands observational data from five stations have been averaged: De Bilt (Central), Eindhoven (South), Rotterdam (West), Hoogeveen (North), and Twente (East). The meteorological data is averaged in a time window of four days in accordance with the computation of $R(t)$ by RIVM.

Governmental intervention data

To quantify the level of governmental intervention we use the Containment & Health index (C&H), which is a parameter within the Oxford Coronavirus Government Response Tracker [39]. This index is a combination of a wide range of indicators such as closures of specific settings, mobility restrictions, economic measures and health indicators related to testing policy, the extent of contact tracing, requirements to wear face coverings, and policies around vaccine rollout. The C&H index does not measure the level that the public complies with an intervention. Also, the effectiveness of each intervention is difficult to assess and the risk of confounding is high, as many interventions are installed simultaneously [1]. Therefore, we apply the C&H index not as an absolute indicator, but in a relative sense to identify rapid interventions (lockdowns), gradual trends with the installation or release of interventions and to find periods where the intervention level is less variable and the impact of environmental factors was presumably stronger.

Statistical analysis

Since meteorological differences within the Netherlands are relatively small, it is assumed that there is no need to correct for spatial differences and it suffices to apply a temporal analysis of both influenza and SARS-CoV-2 epidemic periods.

The weekly excess mortality was computed by subtracting a 10-year moving average from the weekly total mortality figures in the period 1995–2019. The maximum weekly excess mortality per influenza endemic period was retrieved manually. An averaging window was centered around each maximum to obtain the mean curve of the excess mortality during an influenza period in the Netherlands. The level of association and time delay was determined by bivariate analyses between week averaged dew point temperature and the weekly excess mortality figures for different time lags.

For SARS-CoV-2, the reproduction number $R(t)$ was compared with the dew point temperature $Td(t)$ averaged over one reproduction period (4 days). It was assumed that in periods with a relatively constant C&H index, environmental factors have a more significant impact on the variability of the reproduction number and thus the transmission of SARS-CoV-2. The level of association was quantified via bivariate analyses between $R(t)$ and $Td(t)$.

In nursing home care, the policy was consistently focused on maximum protection of susceptible residents and also social-behavioral factors are less variable compared to other settings like schools, recreational and work locations. For this reason, it was assumed that the expression of environmental factors on SARS-CoV-2 transmission is stronger in the nursing home care setting compared to the national metrics. The strategy was to quantify the translation from the estimated number of infectious persons in the Netherlands, $N(t)$, to the number of nursing home deaths per day $D(t)$. A delay time of 12 days was assumed, based on the reproduction time (~4 days) and the median time between the day of first symptoms and the moment of death (~8 days). The association was quantified by a univariate analysis of both $N(t–12)$, $D(t)$, and $Td(t–12)$ over selected periods.

Reporting summary

Further information on research design is available in the Nature Research Reporting Summary linked to this article.

RESULTS

Influenza

Figure 1 shows the number of deceased persons per week from the years 1995 to 2019. The maxima in the winter months can

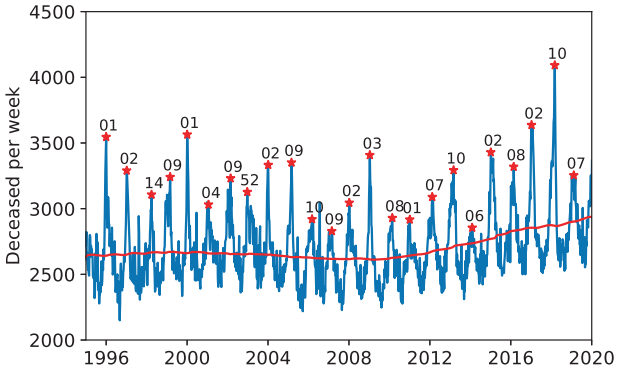

Fig. 1 Number of deceased persons per week as reported by Statistics Netherlands (CBS). The red line represents a moving average of 10 years around each week. The stars depict mortality maxima in influenza epidemic periods and the corresponding week number is given.

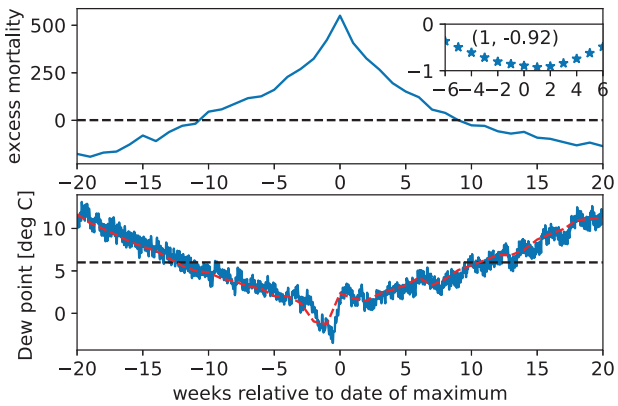

Fig. 2 Excess mortality per week and the dew point per hour (solid line) and week (dashed). Both variables are averaged over windows centered around the maximum mortality in the influenza epidemic periods in the years 1995–2019 depicted by the star symbol in Fig. 1. The inset axes show the Pearson correlation for different time lags (weeks).

typically be associated with influenza events (depicted by stars). These peaks appeared between week 52 and week 14. The highest maximum corresponds to the influenza event of 2017–2018, which was also accompanied by a high number of hospital admissions at that time. Other maxima outside this period are associated with extreme temperatures in the summer months and are not considered in this work.

Figure 2 shows the average signature of the influenza events between 1995 and 2019, as shown in Fig. 1, in terms of the excess mortality rate and the dew point temperature. These curves show a very strong resemblance. The minimum value of the Pearson correlation (pr) is −0.92 for a lag time of 1 week. This implies that the minimum in the dew point appeared before the maximum in the excess mortality. The dew point reference line of 6.0 °C corresponds with a relative indoor humidity of approximately 40% at an indoor temperature of 20 °C. Positive excess mortality starts 1 or 2 weeks later after the dew point has passed this reference line. These observations strongly suggest that the dew point (indoor humidity) affects the transmission of influenza, at least in an associative sense.

SARS-CoV-2

Figure 3 shows $R(t)$, $Td(t)$ and C&H index during the SARS-CoV-2 epidemic period in the Netherlands, and provides additional information on the status of the vaccination program and

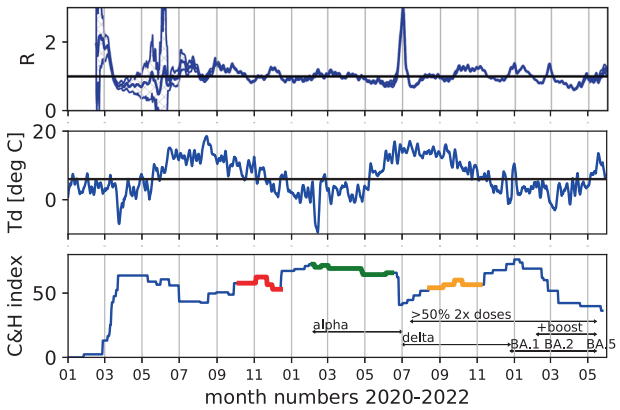

Fig. 3 Reproduction number (R), dew point temperature (Td), and C&H index during the SARS-CoV-2 pandemic (month numbers in 2020–2022). The red, green, and yellow sections in C&H index graph indicate the periods that are further analyzed in Fig. 4. This graph indicates the periods that more than 50% of the Dutch population has received at least two vaccine doses and a booster, and the periods that the different SARS-CoV-2 (Original, Alpha, Delta, Omicrons) were found in more than 50% of pathogen surveillance results.

dominance of the Original, Alpha, Delta, and Omicron variants. SARS-CoV-2 appeared in February 2020 in the Netherlands and the first hospital case was reported in February 27. The Dutch government defined several measures with rapidly increasing strength between February 27, 2020, and March 25, 2020, which is visible in the C&H index that increased from 0 to 60. This first intervention seems successful given the decline of $R(t)$ between March 25 and May 1, 2020. The uncertainty in the computation of $R(t)$ during the first months is relatively high. After June 12, 2020, the uncertainty in $R(t)$ is smaller due to a change in the methodology to compute $R(t)$, which was based on hospital admission before this date and data from the test centers afterward.

In the summer of 2020, $R(t)$ was mainly larger than 1.0. At the same time the intervention level was released somewhat compared to the first intervention period in March, C&H index <50, while the dew point temperature (4 days averaged) was larger than 12.0 °C for the entire summer. After the summer of 2020, the Dutch government responded with a new set of interventions, and the C&H index increased from 45 in July 2020 to 69 at the end of December 2020. The intervention level remained relatively high until mid-June 2021. In this period $R(t)$ remained close to 1.0 but cumulatively this resulted in a high number of infections and ongoing pressure on the health system.

The release of C&H index in June 2021 in combination with the arrival of the more contagious Delta strain of the SARS-CoV-2 virus in the Netherlands resulted in a strong increase of $R(t)$. In the summer of 2021, $R(t)$ decreased again, but in the remainder of 2021 and 2022, many interventions were re-installed, the Omicron strain appeared and a booster vaccine dose was administrated.

Figure 4 shows a more detailed analysis of selected periods, marked in Fig. 3, with a given dominant SARS-CoV-2 strain, a relatively constant C&H index, no large changes in the degree of vaccination, and a limited uncertainty in the computation of $R(t)$. The Pearson correlation coefficient of $Td(t)$ and $R(t)$ is less than −0.8 ($p < 1e{-}4$) for the selected periods. In the period that the Omicron variants appeared there were large changes in C&H and vaccination status (booster). The Omicron variants resulted in less hospitalization, and were received as very contagious but mild variants. Therefore, it is questionable if the remaining measures, contained in the C&H index, are actually followed up in practice. For these reasons, we excluded an analysis of the Omicron period

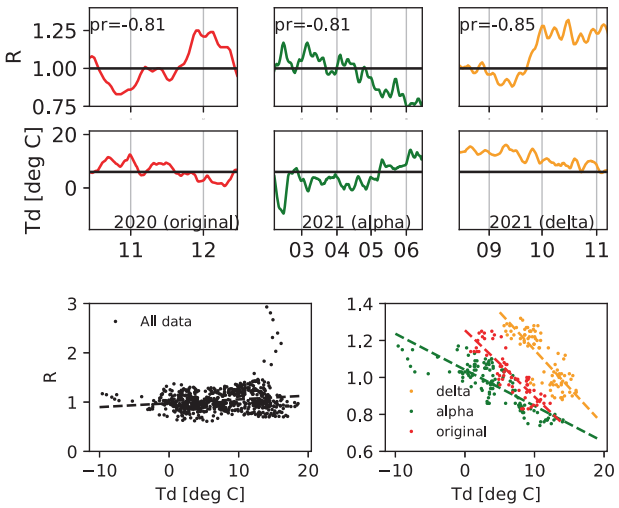

Fig. 4 Reproduction number (*R*) and dew point temperature (*Td*) versus time (months) of selected periods indicated in Fig. 3, and a combined scatter plot of *R* versus *Td*. Red corresponds with the Original variant, green with the Alpha variant, and yellow with Delta. The black points in the scatter plot correspond with all data points. Dashed lines in the corresponding colors are based on a least-square linear regression.

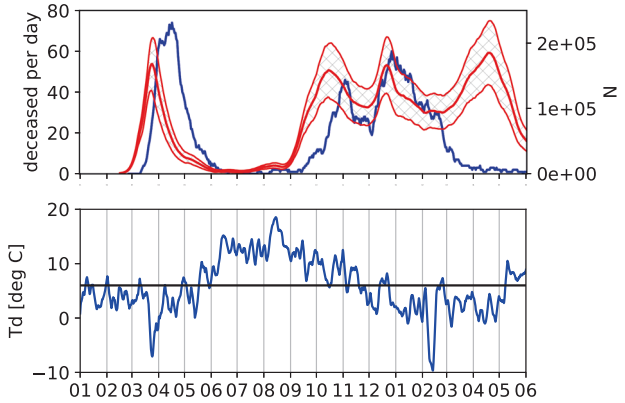

Fig. 5 Deceased persons per day in nursing homes (blue line), daily number of infectious persons *N*(*t*) (red line), and the dew point temperature. From January 2020 to June 2021.

as we expect strong confounding with changes in policy, social factors, vaccine and infection-induced immunity, and changes in the characteristics of the virus (Omicron subvariants BA.1/2/5).

Figure 5 shows the number of deceased persons in nursing homes $D(t)$ and the estimated number of infectious persons $N(t)$. It is seen that $D(t)$ followed $N(t)$ with some delay as expected. The remarkable observation is that the translation from $N(t)$ to $D(t)$ seems quite different in the first and third waves compared to the second wave, where the translation seems much slower. The fourth wave $N(t)$ is not visible in $D(t)$ anymore. This could be attributed to the progressing state of the vaccination program that started with the administration of vaccines in the nursing home care setting in January 18, 2021.

Table 1 shows that in periods with dry air ($Td < 6.0$ °C) the mean ratio $N(t–12)/D(t)$ is between two to three thousand while in the periods with a higher humidity this ratio is significantly higher, around four to five thousand. Figure 6 shows a scatter plot of $D(t)$ versus $N(t–12)$ for dry and humid air conditions. The slopes of the regression lines visualize the difference in the mean ratio of $N(t–12)/D(t)$, as reported in Table 1.

DISCUSSION

These observations extend the associative evidence basis for the role of humidity on both the transmission of influenza and SARS-CoV-2. Hence, it seems in line with mechanistic considerations in the literature on droplet residence time, virus stability, and natural physiological defense, which are all negatively affected by low humidity. This supports the use of humidification as an NPI for the spread of both viruses during dry-air periods in temperate regions.

The observed association between the dew point and excess mortality in influenza periods between 1995 and 2019 is consistent with a previously reported association between the specific humidity and the estimated prevalence of influenza in the Netherlands [33]. It is also consistent with other international studies on the meteorological determinants of the seasonality of influenza [31].

The correlation between the reproduction number of SARS-CoV-2 and the dew points are also consistent with a spatial-temporal analysis of hospital admission figures during the first wave of the pandemic in the Netherlands [33]. This result is also consistent with other international studies on the role of meteorological factors in the early development of the SARS-CoV-2 pandemic [34, 35]. The relatively large number of nursing home deaths compared to the number of infectious persons in the Netherlands in dry air versus humid air is also consistent with the hypothesis that transmissibility of SARS-CoV-2 in dry air is higher. It is also imaginable that airways are more vulnerable in dry air, especially for the older age groups, and that more serious symptoms develop, which could result in a higher fatality rate. From the present data, it was not possible to test this hypothesis.

In this work, three methods were applied to control for the effect of government policy changes to allow for a study to the effect of a single environmental factor on the transmission of respiratory viruses: influenza periods 1995–2019 where interventions on a national level were absent, selection of a relatively constant intervention level in SARS-CoV-2 periods and by examining a specific setting with a focus on health care. This does not completely rule out the effect of changes in the interventions, for example, less mobility restrictions versus vaccine rollout to the next age group, or the presence of changes in individual hygiene [40] and societal change.

Other environmental factors could have interfered with the analysis. In particular, the temperature strongly correlates with the dew point (pr = 0.87, $p < 1e–4$). A lower temperature, in combination with other meteorological variables, typically results in less ventilation rates in indoor spaces in winter versus summer months. This results in more rebreathing of exhaled breath of a possible infector that shares the same indoor space, and gives a significant increase to the risk of infection by long-range airborne transmission in the winter months [2]. Based on pre-pandemic measurements of CO2 concentrations in UK classrooms, the estimated number of secondary infections from a single infector entering a classroom, during a pre/asymptomatic period of 5 days, varies between 0.53 (0.35–0.70) in January and 0.28 (0.12–0.42) in July [2]. This calculation indicates that the reduction of ventilation is an important factor to take into account, but it probably cannot completely explain the observed variations in the population-based reproduction number. Thereby nothing that ventilation rates in most indoor spaces were likely higher in the period since autumn 2020 than in the pre-pandemic years and the number of persons sharing indoor spaces during a workday was less than the number of students in UK classrooms ($N = 33$). It was also concluded, by the same authors, that other factors like changing humidity should be taken into account to explain the seasonality of respiratory infections [2].

Lower temperatures are also associated with longer indoor residence time, which is typically 21–22 h per day [40]. Two

Table 1. Comparison of the number of infectious persons in the Netherlands and deceased persons in nursing homes in different periods of time.

Start	End	Mean $N(t-12)$	Mean $D(t)$	Ratio of means	Mean Td [°C]
March 1, 2020	May 31, 2020	59.1×10^3	30.7	1.93×10^3	3.4
June 1, 2020	August 31, 2020	7.14×10^3	1.55	4.60×10^3	12.9
September 1, 2020	November 30, 2020	98.4×10^3	20.1	4.90×10^3	9.1
December 1, 2020	February 28, 2021	117×10^3	38.4	3.05×10^3	2.2

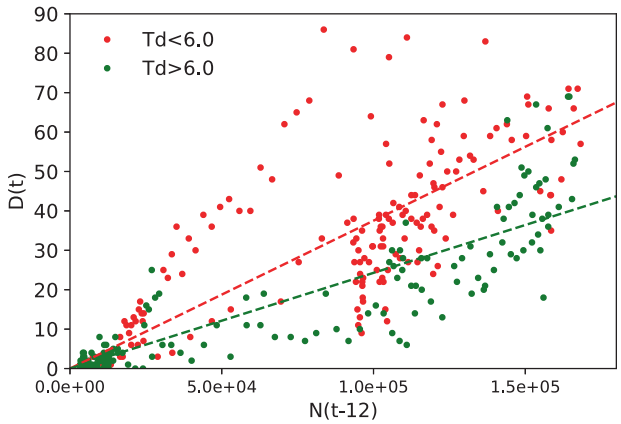

Fig. 6 Number of deaths per day in the nursing home setting $D(t)$ versus the estimated number of infectious persons in the Netherlands shifted by 12 days $N(t-12)$. Data separation for dry-air transmission periods with an averaged dew point: $Td < 6$ °C (red), and humid-air transmission periods: $Td > 6$ °C (green). Dashed lines represent the corresponding least-square regression fit, with an estimated slope (95% confidence interval) in the range (22.4–26.0 1e–5) for humid-air periods and (34.0–40.7 1e–5) for dry-air periods.

studies found that people spend 1–2 h longer indoors (+7%) during cold weather and about 0.5 h (+2%) longer during rainy days [41, 42]. The effect of extended indoor residence time by weather effects seems limited, but the contact patterns can significantly change. A study in Flanders, a neighboring region of the Netherlands, found that on cold days the number of contacts at schools and the number of contacts with a duration of more than 1 h was significantly larger on cold working days, while the number of contacts not related to work or school, such as leisure, transport, and private contacts, was markedly lower on cold working days [40]. This yields a mixed picture, and the net effect of changing social patterns as a function of meteorological variables on secondary viral transmission at the population level is uncertain. Moreover, during the SARS-CoV-2 pandemic, there were contact restrictions in many settings and periods, which further obscures the quantification of this effect. Also claims appeared on the effect of solar insolation on daily new SARS-CoV-2 cases [43] and conflicting claims on the effect of pollen concentrations in the atmosphere [44, 45]. These environmental variables also correlate with the dew point and temperature. Therefore, the results presented here should be regarded as purely associative.

Nonetheless, based on the observed correlations and known physical mechanisms, it is recommended to conduct more prospective studies on the potential of humidity control as an NPI for SARS-CoV-2. Ideally, with a well-controlled methodology as applied for influenza in a previous study [10].

CONCLUSION

The present analysis indicates that there is a strong negative association between humidity and the transmission of both SARS-CoV-2 and influenza. As such, the statistical results are in line with known mechanistic explanations for the adverse role of low humidity. In all, this indicates that there is a potential for active humidification as an NPI to reduce the spread of these viruses. A prospective analysis is required to provide further evidence for the suitability per social setting.

DATA AVAILABILITY

All data sources used in the work are publicly available [36–38]. Upon request, the corresponding authors can assist to retrieve data.

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AUTHOR CONTRIBUTIONS

GHK initiated the study, collected the data, and performed the statistical analysis. All authors contributed to the study design, interpreted the results, and contributed critically to the writing of the manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

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