Acta Biomed 2022; Vol. 93, N. 4: e2022212 DOI: 10.23750/abm.v93i4.12645

Evaluation of the combined effect of mobility and seasonality on the COVID-19 pandemic: a Lombardy-based study

Yuri Matteo Falzone[1], Luca Bosco[1], Giacomo Sferruzza[1], Tommaso Russo[1], Marco Vabanesi[1], Signorelli Carlo[5], Massimo Filippi[1,2,3,4,5]

[1]Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy; [2]Neurorehabilitation Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy; [3]Neurophysiology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy; [4]Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy; [5]Vita-Salute San Raffaele University, Milan, Italy

Abstract. Restrictions to human mobility had a significant role in limiting SARS-CoV-2 spread. It has been suggested that seasonality might affect viral transmissibility. Our study retrospectively investigates the combined effect that seasonal environmental factors and human mobility played on transmissibility of SARS-CoV-2 in Lombardy, Italy, in 2020; Environmental data were collected from accredited open-source web services. Aggregated mobility data for different points of interests were collected from Google Community Reports. The Reproduction number (R_t), based on the weekly counts of confirmed symptomatic COVID-19, non-imported cases, was used as a proxy for SARS-CoV-2 transmissibility. Assuming a non-linear correlation between selected variables, we used a Generalized Additive Model (GAM) to investigate with univariate and multivariate analyses the association between seasonal environmental factors (UV-index, temperature, humidity, and atmospheric pressure), location-specific mobility indices, and R_t; UV-index was the most effective environmental variable in predicting R_t. An optimal two-week lag-effect between changes in explanatory variables and R_t was selected. The association between R_t variations and individually taken mobility indices differed: Grocery & Pharmacy, Transit Station and Workplaces displayed the best performances in predicting R_t when individually added to the multivariate model together with UV-index, accounting for 85.0%, 85.5% and 82.6% of R_t variance, respectively. According to our results, both seasonality and social interaction policies played a significant role in curbing the pandemic. Non-linear models including UV-index and location-specific mobility indices can predict a considerable amount of SARS-CoV-2 transmissibility in Lombardy during 2020, emphasizing the importance of social distancing policies to keep viral transmissibility under control, especially during colder months. (www.actabiomedica.it)

Key words: SARS-CoV-2, UV, environmental factors, transmissibility, GAM analysis

Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causative agent of coronavirus disease 2019 (COVID-19), emerged in Wuhan (China) in December 2019. COVID-19 rapidly spread worldwide, reaching the epidemiological criteria to be declared a pandemic by the World Health Organization (WHO) in March 2020 (1).

During 2020, the COVID-19 pandemic had a striking impact not only on healthcare systems, but also on social politics and welfares. Lombardy (Italy), one of the most populated regions in Europe, was among the first ones suffering the whirlwind effects of the pandemic in the Western world, with a burden of infections that overwhelmed the healthcare systems capacities (2). To contain the pandemic, governments worldwide applied different non-pharmaceutical interventions in order to reduce SARS-CoV-2 transmissibility. In Lombardy, strict restrictions to mobility and social interaction were imposed, with aggregate mobility data displaying a relevant drop during spring (3). Several studies have already established the crucial role that social distancing policies, restrictions to individuals mobility patterns, and non-pharmaceutical interventions as a whole have played in slowing the spreading of the virus (4–6).

During late spring 2020, many countries in the Northern hemisphere loosened these restrictions, due to a sustained reduction in viral transmissibility and a lower pressure on healthcare systems. This led some authors to question the eventuality of a "second wave" of the pandemic, during autumn (7). Direct, droplet-mediated, human-to-human transmission has been recognized as the main viral route of transmission. However, consistent evidence of susceptibility of SARS-CoV-2 to environmental factors, such as temperature, humidity, and simulated sunlight, has emerged from experimental data, proposing similarities with other viruses with a lipidic envelope (8,9). SARS-CoV-2 has proven itself highly resilient in saliva and other body fluids on surfaces outside the human body, making the putative role of environmental factors on its persistence potentially crucial in the transmission of the disease (10).

Some studies have already investigated the role of environmental factors such as temperature, humidity, and UV-index on SARS-CoV-2 virulence at different latitudes, achieving mixed and nonconclusive results. (11–15) Most of these works have, however, some major limitations: 1) data analyzed were mostly derived from the first "pandemic wave", an early phase in which epidemic growth was unbalanced by low immunity, so that even strong environmental drivers were unlikely to affect transmissibility; 2) the reduction in social interactions determined by government-imposed non-pharmaceutical interventions worldwide has been rarely weighted alongside environmental drivers, therefore acting as a possible strong confounding factor; 3) testing and reporting of cases around the globe, and sometimes even inside the same country, has varied significantly, so that country-specific limitations of data quality may support inconsistent inferences on evidences about the role of climatic factors (15). Now that the era of SARS-CoV-2 vaccines has begun, uncertainty about the duration of natural and vaccine-induced immunity prompts new efforts in clarifying viral transmission dynamics. Indeed, the aim of the current study is to retrospectively investigate the effects of seasonal environmental factors and social interaction data on transmissibility of SARS-CoV-2 in Lombardy, during 2020.

Methods

Data sources

In this retrospective study, we assessed data at regional level for Lombardy (Italy) during the period from May 18, 2020 to December 13, 2020. Epidemiological data, including number of new confirmed cases and estimates of the reproduction number (R_t), were collected from the national deputed entity, *Istituto Superiore di Sanità* (ISS). R_t estimate is based on the weekly counts of confirmed symptomatic COVID-19, non-imported cases, referring to when symptoms developed. R_t represents the average number of secondary cases that would arise at a given time from a primary infected case if the conditions remained stable after that time.(16) Due to its calculation method, R_t relates to a subgroup of cases and to a rolling time window of around one week, which accounts for the reporting delay between symptom onset and case notification. (17) Since daily transmissibility may be influenced by particular events or random daily variation, ISS reports the average R_t value of the previous week (seven days, corresponding to one generation time) (17).

Mean daily values for UV-index, provided in a time series format, were collected from the Tropospheric Emission Monitoring Internet Service (TEMIS) archive, hosted by the Royal Netherlands Meteorological Institute (KNMI, http://www.temis.nl/uvradiation/UVarchive.html) as part of a project of the European Space Agency (ESA). TEMIS provides validated near-real time satellite-based UV-index and UV dose timeseries for different UV locations around the globe (18). Ispra (45.8° N, 8.6° E, Lombardy, Italy) cloud-free erythemal UV-index time series was adopted for this study.

Average temperature at 2 meters above ground surface, average atmospheric pressure at ground surface, and average of relative humidity at 2 meters height were collected from the NASA Prediction Of Worldwide Energy Resources (POWER) Data Access Viewer (DAV, http://power.larc.nasa.gov). The parameters in POWER Release-8 are provided on a global grid with a spatial resolution of 0.5° latitude by 0.5° longitude.

Aggregate and anonymized mobility data fluctuations were collected from Google Community Mobility Reports (https://www.google.com/covid19/mobility/). These datasets describe relative variation in individual mobility dynamics, affecting selected categories of Points Of Interest (POIs), when compared to "baseline-days", which represent normal values for a specific day of the week, averaged from the five-week period (Jan 3 – Feb 6, 2020). Changes are calculated using the same kind of aggregated and anonymized data used to show popular times for places in Google Maps. Google Community Mobility Reports locations are grouped within six categories: *Residential*, *Retail & Recreation*, *Grocery & Pharmacy*, *Parks*, *Transit Stations*, *Workplaces,* and *Residential Areas.* Specific POIs for each mobility index are listed in Supplementary Table 1. Country- and region-wise data for each parameter are available on a daily basis (since Feb 15, 2020).

Data selection and processing

In accordance with R_t calculation method, we aggregated daily environmental and mobility daily values on a weekly basis (Monday to Sunday) to account for the 30 weeks from May 18 to December 13, 2020.

Among mobility parameters provided by Google Community Mobility Reports, five were considered relevant to our analysis (*Transit Stations*, *Retail & Recreation*, *Workplaces*, *Grocery & Pharmacies*, *Parks*) as being specifically affected by the national government mobility restriction measures. *Residential* mobility was excluded, as positive variations in this index are actually indicative of decreased mobility, suggesting instead increased activities in locations around the home environment.

Table 1. Lag effect analysis of influences on R_t. Each variable was evaluated at different lag times to explore potential plausible biological association with R_t. Numbers in boxes denote Akaike's information criterion (AIC) for that model. Lowest values mean a better fitting model. Models fitting best for positive week lags (1 week, 2 weeks) mean that explanatory variables preceded homologous Rt fluctuations. * Represents the best fitting model for the selected variable.

	0 week	**1-week lag**	**2-week lag**
UV-index	-8.15	-9.23	-16.12*
Temperature	-3.90*	-0.54	0.37
Relative Humidity	-3.25*	-0.69	0.03
Atmospheric Pressure	0.85	-0.85	-1.07*
Retail & Recreation	-0.02	-0.58	-0.69*
Grocery & Pharmacy	-4.40	-16.75	-18.87*
Workplaces	-3.63	-15.46*	-12.01
Transit Stations	-1.02	-3.11	-8.71*
Parks	-8.09*	-3.67	2.04

Data analysis

Assuming a non-linear relation between the selected data, we used a Generalized Additive Model (GAM) to investigate with univariate and multivariate analyses the association between seasonality, mobility indices and R_t. Shapiro-Wilk test was performed in order to assess R_t values deviation from normal distribution. R_t frequency distribution is shown in Supplementary Figure 1. It has been demonstrated that R_t follows a negative binomial probability distribution, converging to the Poisson distribution for large value of the parameter *k* of the discrete probability distribution (19). For this reason, logarithm link function was selected for predictive GAM. The model applied to investigate a univariate association between variables and the R_t is described as follows:

$$\log(R_{ti+lag}) = \alpha + f(x_i, k = 8) + \delta \times \log(R_{ti-1}) \qquad (1)$$

where α is the intercept, f denotes the smoother function, based on the penalized smoothing splines, x_i denotes the i^{th}-week predictive variable, including environmental variables (temperature, UV-index, humidity, and atmospheric pressure) and mobility indexes. *K* represents the number of delimiting knots of predictor variable in the GAM model. The term $(\delta \times \log(Rt_{i-1}))$ was used to correct the autocorrelation

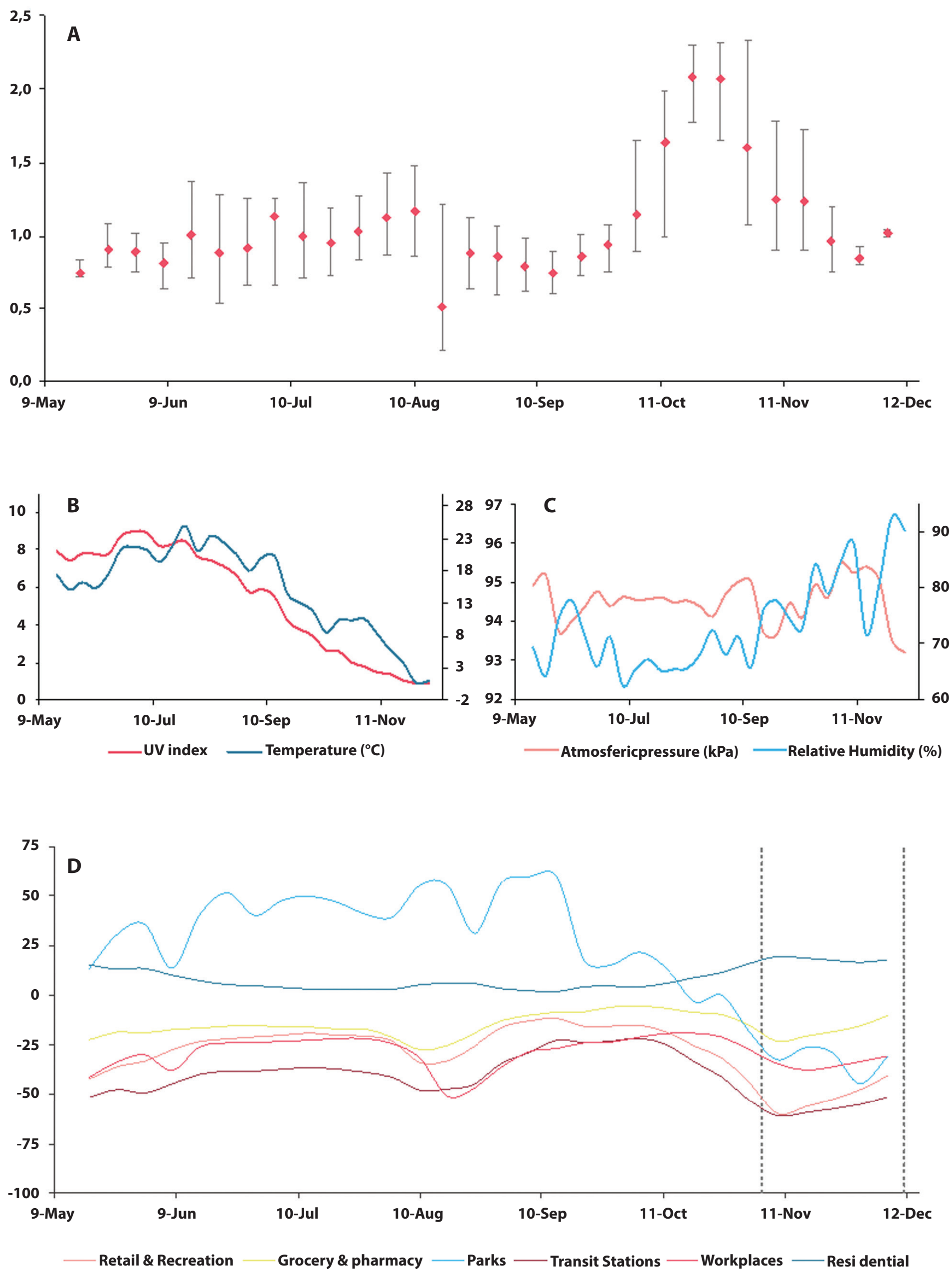


Figure 1. Observed trends in R_t and explanatory variables

of R_t time series, as shown by the autocorrelation function (ACF) (Supplementary Figure 2). Different lag-effects were evaluated for each variable to explore potential plausible biological association with R_t. Akaike's information criterion (AIC) was used to compare different models.

Multivariate analysis of influences on R_t

Due to the high collinearity among mobility indices (Supplementary Table 2), the impact of each selected index was evaluated individually to avoid the risk of type I error due to concurvity in GAM. Each mobility

Table 2. Univariate analysis of influences on R_t: Each model is evaluated at the pre-determined 2-week lag. UV-index and Grocery & Pharmacy based models display the best performances in predicting R_t variations. Parks and Retail & Recreation based models result as statistically non-significant. Edf; effective degrees of freedom; Ref.df: reference degrees of freedom; Dev exp: percent of deviance explained; AdjR2: adjusted R-squared; AIC: Akaike's information criterion.

	Edf	Ref.df	F-value	*p*-value	Dev.exp	AdjR2	AIC
UV-index	4.76	5.58	4.21	0.010	75.7	0.69	-13.40
Retail & Recreation	1.00	1.00	1.28	0.270	47.3	0.43	-0.69
Grocery & Pharmacy	4.46	5.25	6.39	0.001	79.5	0.74	-18.87
Workplaces	2.98	3.61	5.21	0.005	71.0	0.67	-12.01
Transit Stations	6.28	6.81	3.18	0.029	74.2	0.65	-8.71
Parks	1.00	1.00	0.04	0.850	44.7	0.40	2.04

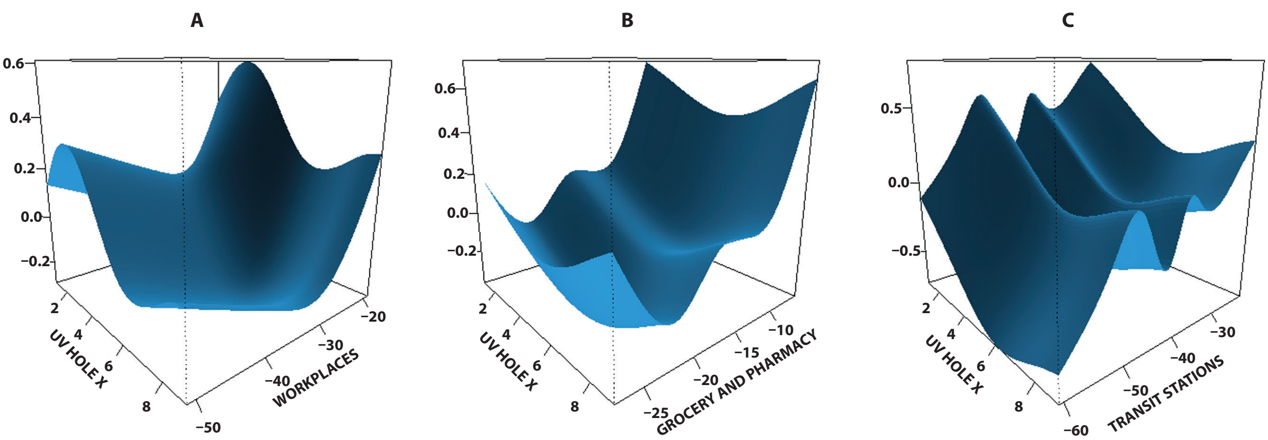


Figure 2. Three-dimensional effect graph of interacting influencing factors on the variation of $\log(R_t)$

index was individually added to GAM together with UV-index, considering a preselected two-week lag, in order to explore the potential role of each mobility index in predicting R_t, adjusted for a seasonal variation. The model used to investigate the multivariate association between UV-index, mobility, and R_t is described as follows:

$$\log(Rt_i+_2) = \alpha + f_1(M_i, k = 8) + f_2(UV_i, k = 8) + \delta \times \log(Rt_i+_1) \quad (2)$$

where M represents the i^{th}-week mobility index and UV the i^{th}-week average of UV-index. AIC score minimization was used to evaluate the impact of each mobility index in predicting R_t, keeping into account seasonality.

All statistical analyses in the study were performed with R statistical package (R Foundation for Statistical Computing, Vienna, Austria), version 4.0.3.

Results

A 30-week period was included in the analysis. A total of 358 818 new confirmed cases were reported in the study period in Lombardy, accounting for the 3.56% of the total population and for the 80.87% of all confirmed cases since the first documented case in Lombardy, in February 20, 2020. R_t ranged from 0.52 [95% C.I.: 0.22–1.21] to 1.17 [0.86–1.48] for the entirety of summer; it steeply increased during the transition to autumn and reached its peak at 2.09 [1.77–2.30] in the third week of October 2020 (Figure 1a). Mean weekly UV-index and temperatures ranged from 0.87 to 9.02 and from 0.70 °C to 25.04 °C, respectively. UV-index reached its peak in the last week of June, four weeks before the highest weekly temperature recorded value (Figure 1b). Humidity and atmospheric pressure trends are displayed in Figure 1c.

All mobility indices included in the analysis show a reduction when compared to baseline, except for *Parks*. In particular, *Retail & Recreation* and *Transit Station* ranged from -11.86% to -59.86% and from -21.57% to -60.71% respectively, with the downward peak reached in the second week of November. *Workplace* and *Grocery & Pharmacy* ranged from -18.86% to -51.14% and from -5.86% to -27.57% respectively, with the downward peak reached on the second week of August, concurrently with holiday season. *Parks* ranged from +60.14% in the second week of September (the fact that baseline mobility was calculated in the month of January accounts for this result), to -44.57% in the last week of October. After the loosening of mobility restrictions, following the end of the first pandemic wave, mobility curves kept a relatively stable profile during summer, except for a downward shift during holiday weeks in August. Mobility indices dropped again in October, as a consequence of governmental social-distancing policies instituted for the second pandemic wave (Figure 1d). Using UV-index and mobility indices, we evaluated how seasonal factors and social distancing measures influenced the COVID-19 transmissibility, fitting a GAM model.

(A) Sampling of R_t values (95% C.I.) and trend during the 30 weeks of our observation period. (B) UV-index (left axis) and temperature (°C, right axis) trends. (C) Atmospheric pressure (kPa, left axis) and humidity (%, right axis) trends. (D) Mobility indices trends in percent variation from baseline, considered individually. The red area between dashed vertical lines represents the introduction of "red zones" by the national government, defined by stay-at-home orders and strict restrictions to mobility implemented on regional basis.

Lag-effect analysis

The effect of environmental and mobility indices variation on R_t was not straightforward, as shown in Table 1. A GAM model including UV-index and atmospheric pressure displayed the best predictive effect on R_t considering a lag-effect of two weeks, whereas temperature and humidity had the best predictive performance with a biologically unconvincing zero-week lag. Temperature and UV-index both displayed a definite seasonal variation and a strong correlation between each other, considering a four-week lag for temperature (Pearson coefficient 0.97) (Figure 1b).

The lag-effect of mobility indices variation differed. GAM models assessing *Retail & Recreation, Grocery & Pharmacy* and *Transit Stations* performed the best considering a lag-effect of two weeks, while *Workplaces* shows optimal performance with a one-week lag. *Parks* was the only mobility index to display the best performance considering an unconvincing zero-week lag.

Considering the AIC value (Table 1) and the predictable yearly dynamics of the UV-index, making it the fittest proxy for seasonality, the two-week UV-index lag was adopted for the main analysis, reflecting both the biological time needed for an external factor to influence transmissibility and for incubation time, as already shown by previous studies (4,5).

Univariate analysis of influences on R_t

The regression model with cubic splines was used to analyze the influences of each individual explanatory variable on R_t and corresponding fitting degree of the model. According to our results, both seasonality and social distancing have a role in curbing the pandemic curve. The regression model used to analyze the influence of each individual mobility index on R_t highlights a significant association with both UV-index and some mobility trends; all estimates and significance levels are listed in Table 2. In particular, the GAM including UV-index as single predictor variable explains 75.7% of R_t deviance in Lombardy (adjusted R^2 = 0.69; AIC = -13.40). Concerning mobility indices, the highest explained deviance is 79.5% for the *Grocery & Pharmacy* (adjusted R^2 = 0.74; AIC = -18.87). The lowest level of association was detected for *Retail & Recreation* and *Parks*, with a deviance explained of 47.3% (adjusted R^2 = 0.43; AIC = -0.69) and 44.7% (adjusted R^2 = 0.40; AIC = 2.04), respectively; for these parameters, the *p-value* of the smoother resulted not significant.

Multivariate analysis of influences on Rt

Multivariate GAM models of R_t incorporating time-series correction, UV-index, and mobility indices taken individually, considering a predetermined lag-effect of two weeks, were applied. All estimates and significance levels are listed in Table 3.

In the aforementioned multivariate setting, *Grocery & Pharmacy* displayed the best correlation with the response variable, with 85.0% deviance explained

Table 3. Multivariate analysis of influences on R_t: Each model is evaluated at the pre-determined +2-week lag, and consists of mobility indices individually added to the model together with UV-index. Grocery & Pharmacy, Transit Stations and Workplaces based models confirms themselves to be the most impactful predictors of Rt variations, when weighted for seasonality. Edf; effective degrees of freedom; Ref df: reference degrees of freedom; Dev.exp: percent of deviance explained; AdjR2: adjusted R-squared; AIC: Akaike's information criterion.

	Edf	Ref df	F-Value	*p*-Value	Dev.exp	AdjR2	AIC
UV-index	4.76	5.58	4.21	0.007	75.7	0.69	-13.40
Retail & Recreation	1.00	1.00	1.10	0.310	76.0	0.69	-12.60
Grocery & Pharmacy	4.37	5.15	6.66	0.001	85.0	0.79	-23.75
Workplaces	2.64	3.19	4.08	0.019	82.6	0.76	-19.88
Transit Stations	6.46	6.80	4.00	0.010	85.5	0.78	-20.19
Parks	1.00	1.00	1.65	0.210	77.4	0.70	-13.84

(adjusted R^2 = 0.79; AIC = -23.75). A reduction in the AIC score was also recorded for *Workplaces* (adjusted R^2 = 0.76; AIC = -19.88) and *Transit Station* (adjusted R^2 = 0.78; AIC = -20.19).

GAM multivariate results are shown in (Figure 2a, 2b, 2c) as the smoother components plot for UV-index and each mobility index taken individually. Our model displays a steep downward curb in R_t curve when *Workplaces* and *Grocery & Pharmacy* shift in the -20% to -30% and -5 to -15% interval, respectively, net of seasonality. *Transit Station* mobility index has a more complex association pattern, reflecting the degrees of freedom for the smoothing spline (= 6.46). However, a trend towards R_t reduction in the -20% to -60% interval is still observable. All of the displayed models show a net effect of mobility indices in curbing R_t, despite seasonality. Our models contain only one mobility index per each, preventing us from evaluating the overall effect of UV-index on R_t, controlling for mobility.

A negative association between *Workplaces* (Fig.2A), *Grocery & Pharmacy* (Fig.2B), and *Transit Stations* (Fig. 2C) reduction and R_t (vertical axis)

Discussion

To the best of our knowledge, this is the first study to investigate the combined interplay of environmental and social interaction factors in SARS-CoV-2 transmissibility. In fact, one of the uncertainties regarding future reopening is the possibility for the pandemic to keep a near-stable seasonal profile, flattening in summer and exacerbating during the cold season, similarly to what has been observed in several mid-latitude regions during 2020 (20). The results inferred by our data might be helpful in evaluating the timing and stringency of future interventions.

Multiple factors may drive seasonal trends in respiratory viral infections, including change in social dynamics and intrinsic susceptibility of viruses to weather and environmental factors (21). Indeed, using publicly available empirical data, collected for one of the most hardly hit regions in Europe(2) we explored multiple variables as possible contributors to a seasonal trend in SARS-CoV-2 transmissibility, namely mobility indices, solar UV radiation, temperature, atmospheric pressure, and humidity, assessing their effect with different time lags, in order to find the best fitting framework for our model. As already established by previous works, the biological effect carried out by external factors on case growth is not immediate (4,5,22). Among selected environmental variables, UV-index displayed the strongest and the most plausible biological temporal correlation with R_t, making it the fittest to explain a putative environmental susceptibility of SARS-CoV-2.

According to our model, solar UV radiation, rather than temperature, might represent the key environmental factor contributing to SARS-CoV-2 transmissibility, accounting for 75.7% of R_t deviance at the univariate analysis, holding a non-linear effect. The germicidal role of solar UV radiation (mainly UV-A and UV-B wavelengths) has already been explored, and recent experimental data suggests that solar UV exposure of a mid-latitude site during summer may lead to SARS-CoV-2 inactivation in the span of minutes (23,24). Solar UV exposure also plays a known and crucial role in the synthesis of vitamin D, which has a modulating effect on the immune response (25). At the same time, epidemiological data exist supporting a negative association between COVID-19 transmissibility, severity, and UV radiation (14,26,27).

On the other hand, social distancing policies have been implemented in many countries as the main countermeasure to the pandemic flood, and their association with SARS-CoV-2 transmissibility has been already established in several studies, using different proxies for the estimate (4,5,28). In our study, we decided to consider mobility data *per se*, instead of focusing on the deployment of the policies that drove the drop in aggregate mobility values. The effect of specific restrictive interventions, evaluated by previous studies, was not assessed in the present study. Our model confirms that mobility plays a fundamental role in SARS-CoV-2 transmissibility, independently from environmental factors. Google Community Mobility Reports provide open-source data and have already proved to be useful in predicting COVID-19 case incidence (29).

According to our analysis, *Grocery & Pharmacy*, *Transit Station* and *Workplaces* predicted a considerable amount of R_t variance, when taken individually, and maintain their significance when coupled with UV-index in a multivariate analysis. Conversely, *Parks* showed little-to-no effect on viral transmissibility. Surprisingly enough, *Retail & Recreation* did not show a significant role in transmissibility either. This counterintuitive result, despite a similar graphical pattern between *Retail & Recreation* and the aforementioned significant indices, may be due to an intrinsic feature of our dataset. In fact, similar relative changes in two indices may imply great differences in the absolute number of people actually involved, depending on the selected index. A small relative variation toward heavily frequented POIs may have a more meaningful impact on R_t when compared to a bigger relative variation of less frequented POIs. This result is particularly meaningful in the light of the heavily implemented governmental bans on social events, restaurants closures, and restriction to leisure activities in general.

Our model showed a strong correlation between social distancing policies (proxied by mobility patterns), seasonal environmental factors (proxied by UV-index), and fluctuation of SARS-CoV-2 transmissibility. This correlation was even stronger when mobility indices and UV-index were both included in the model, accounting for up to 85.5% of R_t variance, thus suggesting their key role in transmissibility.

Our study has several limitations. First, due to the weekly calculation of R_t estimate, the examined period of 30 weeks might imply low sampled data, affecting the model predictive value at the extremes of our curves, as shown by the large confidence intervals (Supplementary Figure 3). Moreover, due to the cyclical nature of some of the selected variables, an eight-month period may have limited our observable range for these factors. However, considering UV-index, due to an observation period roughly covering the time span between both solstices, a broad estimate of its whole seasonal half-cycle is expected to be included in our analysis. Second, we performed our analysis on a relatively small scale, so that further studies are needed to evaluate its generalization on a national or global scale. However, small-scale analysis has the advantage to limit data heterogeneity. In fact, nation-scale data averages may hide parameter variations occurring locally; conversely, an extreme variation in a spatially distinct smaller subsection can disproportionately sway a larger region's mean value. Third, the chosen mobility dataset has intrinsic limitations: it does not stratify for different demographics, missing a possible heterogeneity in viral susceptibility among different populations; it does not contain all POIs, in particular schools may be the great absentee from our dataset, being often debated as a source of infection spread; it does not consider inter-regional travels. However, due to the capillary diffusion of Google Maps and Location Services among general population, Google Community Mobility Reports may represent the most meaningful and all-encompassing mobility data aggregator available to date; therefore, we expect our assumption based on this open-source service to hold robustly. Fourth, R_t has intrinsic limitations that must be acknowledged (30). However, since relatively few data are needed for its calculation and due to its general reliability, R_t is universally considered a reliable index for the measurement of transmissibility in epidemics and was therefore adopted as our main response variable.

In conclusion, our results emphasize the importance of social distancing policies to keep viral transmissibility under control, especially during colder months. According to our analysis, smart-working policies, online grocery shopping, and avoidance of public transport overcrowding may be the most valuable measures to apply to contain case growth. UV-index displayed the best predictive value for SARS-CoV-2 transmissibility among the investigated environmental factors. With the coming of summer, which may mitigate future case growth, relaxations on mobility restriction, especially now that a new vaccine era has begun, may be considered. Further studies are needed to confirm our results on a more extended time and geographical scale.

Acknoledgements: We acknowledge Istituto Superiore di Sanità (ISS), the Emission Monitoring Internet Service (TEMIS) archive, NASA Prediction Of Worldwide Energy Resources (POWER) Data Access Viewer and Google Community Mobility Reports for their publicly available and detailed data which were used to inform our analysis.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

References

1. WHO. Rolling updates on coronavirus disease (COVID-19). https://www. who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen.
2. Remuzzi A, Remuzzi G. COVID-19 and Italy: what next?. The Lancet 2020;395(10231):1225–8.
3. Google - COVID-19 Community Mobility Reports. https://www.google.com/covid19/mobility/
4. Badr HS, Du H, Marshall M, Dong E, Squire MM, Gardner LM. Association between mobility patterns and COVID-19 transmission in the USA: a mathematical modelling study. The Lancet Infectious Diseases 2020;20(11):1247–54.
5. Li Y, Campbell H, Kulkarni D, H, et al. The temporal association of introducing and lifting non-pharmaceutical interventions with the time-varying reproduction number (R) of SARS-CoV-2: a modelling study across 131 countries. The Lancet Infect Dis 2021; 21(2):193-202
6. Rader B, Scarpino SV, Nande A, et al. Crowding and the shape of COVID-19 epidemics. Nat Med 2020;26(12):1829–34.
7. Cacciapaglia G, Cot C, Sannino F. Second wave COVID-19 pandemics in Europe: a temporal playbook. Sci Rep 2020;10(1):15514.
8. Yap TF, Liu Z, Shveda RA, Preston DJ. A predictive model of the temperature-dependent inactivation of coronaviruses. Appl Phys Lett 2020;117(6):060601.
9. 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):564–71.
10. Goh GK-M, Dunker AK, Foster JA, Uversky VN. Shell disorder analysis predicts greater resilience of the SARS-CoV-2 (COVID-19) outside the body and in body fluids. Microb Pathog 2020;144:104177.
11. Bashir MF, Ma B, Bilal, et al. Correlation between climate indicators and COVID-19 pandemic in New York, USA. Sci Total Environ 2020;728:138835.
12. Ma Y, Zhao Y, Liu J, et al. Effects of temperature variation and humidity on the death of COVID-19 in Wuhan, China. Sci Total Environ 2020;724:138226.
13. Tosepu R, Gunawan J, Effendy DS, et al. Correlation between weather and Covid-19 pandemic in Jakarta, Indonesia. Sci Total Environ 2020;725:138436.
14. Isaia G, Diémoz H, Maluta F, et al. Does solar ultraviolet radiation play a role in COVID-19 infection and deaths? An environmental ecological study in Italy. Sci Total Environ 2020; 757:143757.
15. Carlson CJ, Gomez ACR, Bansal S, Ryan SJ. Misconceptions about weather and seasonality must not misguide COVID-19 response. Nat Commun 2020;11(1):4312.
16. Cori A, Ferguson NM, Fraser C, Cauchemez S. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. Am J Epidemiol 2013;178(9):1505–12.
17. Guzzetta G, Merler S. Stime della trasmissibilità di SARS-CoV-2 in Italia 2020. https://www.epicentro.iss.it/coronavirus/open-data/rt.pdf
18. Zempila M-M, van Geffen JHGM, Taylor M, et al. TEMIS UV product validation using NILU-UV ground-based measurements in Thessaloniki, Greece. Atmos Chem Phys 2017;17(11):7157–74.
19. The Royal Society. Reproduction number (R) and growth rate (r) of the COVID-19 epidemic in the UK: methods of estimation, data sources, causes of heterogeneity, and use as a guide in policy formulation. https://royalsociety.org/-/media/policy/projects/set-c/set-covid-19-R-estimates.pdf?la=en-GB&hash=FDFFC11968E5D247D8FF64193 0680BD6
20. The Johns Hopkins Coronavirus Resource Center (CRC). https://coronavirus.jhu.edu/map.html.
21. Mallapaty S. Why COVID outbreaks look set to worsen this winter. Nature 2020;586(7831):653–653.
22. Carleton T, Cornetet J, Huybers P, Meng KC, Proctor J. Global evidence for ultraviolet radiation decreasing COVID-19 growth rates. Proc Natl Acad Sci USA 2021;118(1):e2012370118.
23. Herman J, Biegel B, Huang L. Inactivation times from 290 to 315 nm UVB in sunlight for SARS coronaviruses CoV and CoV-2 using OMI satellite data for the sunlit Earth. Air Qual Atmos Health 2020; 1-17.

24. Ratnesar-Shumate S, Williams G, Green B, et al. Simulated Sunlight Rapidly Inactivates SARS-CoV-2 on Surfaces. J Infect Dis 2020;222(2):214–22.
25. Prietl B, Treiber G, Pieber T, Amrein K. Vitamin D and Immune Function. Nutrients 2013;5(7):2502–21.
26. Sehra ST, Salciccioli JD, Wiebe DJ, Fundin S, Baker JF. Maximum Daily Temperature, Precipitation, Ultraviolet Light, and Rates of Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 in the United States. Clin Infect Dis 2020; 71(9):2482-2487
27. Cacho PM, Hernández JL, López-Hoyos M, Martínez-Taboada VM. Can climatic factors explain the differences in COVID-19 incidence and severity across the Spanish regions?: An ecological study. Environ Health 2020;19(1):106.
28. Kraemer MUG, Yang C-H, Gutierrez B, et al. The effect of human mobility and control measures on the COVID-19 epidemic in China. Science 2020;368(6490):493–7.
29. Sulyok M, Walker M. Community movement and COVID-19: a global study using Google's Community Mobility Reports. Epidemiol Infect 2020;148:e284.
30. Adam D. A guide to R — the pandemic's misunderstood metric. Nature 2020;583(7816):346–8.

Correspondence:
Received: 6 December, 2021
Accepted: 10 December, 2021
Full first name Dr. Yuri Matteo Falzone MD
Department of Neurology
San Raffaele Scientific Institute and University
Via Olgettina, 60, 20132, Milan, Italy
telephone number: +39 02 26432813
E-mail: falzone.yuri@hsr.it

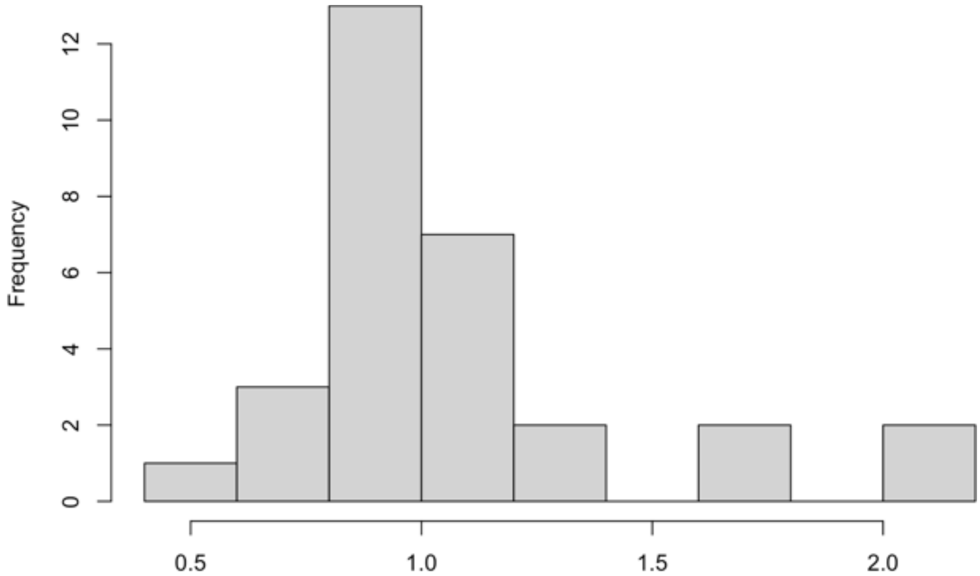
MATTIOLI 1885 | ACTA BIOMEDICA | Official Journal of the Society of Medicine and Natural Sciences of Parma and Centre on health systems' organization, quality and sustainability, Parma, Italy

Acta Biomed 2022; Vol. 93, N. 4: e2022212 - DOI: 10.23750/abm.v93i4.12645

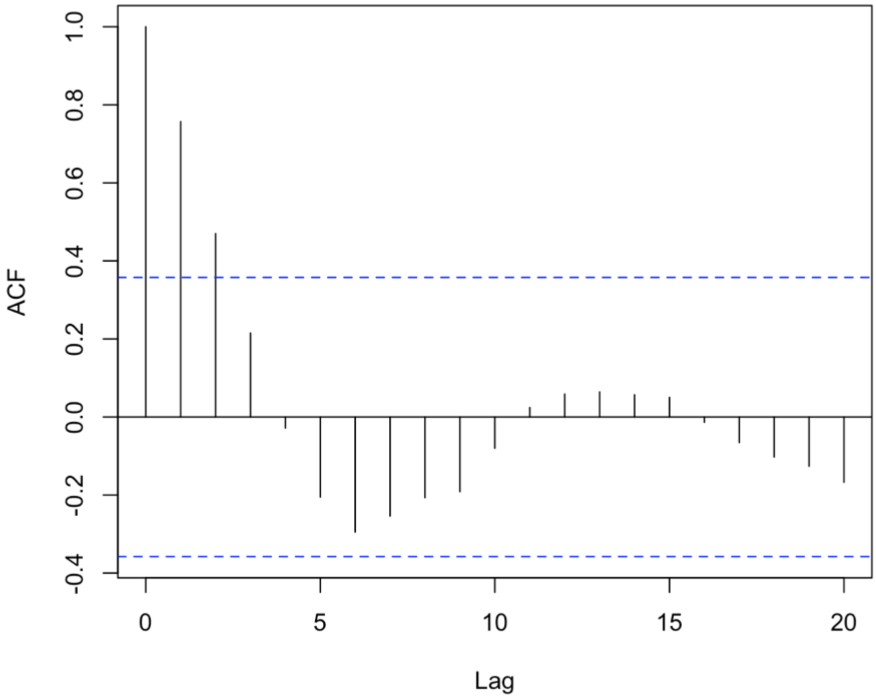
SUPPLEMENTARY FILES

Mobility index	**included Points Of Interest (POIs)**
Retail & Recreation	Restaurants, cafes, shopping centers, theme parks, museums, libraries, and movie theaters·
Grocery & Pharmacy	Grocery markets, food warehouses, farmers markets, specialty food shops, drug stores, and pharmacies·
Parks	National parks, public beaches, marinas, dog parks, plazas, and public gardens·
Transit Stations	Public transport hubs such as subway, bus, and train stations
Workplaces	Places of work
Residential Areas	Places of residence

Supplementary Table 1: Google mobility indices and corresponding Points Of Interests (POIs). Insights are based on data from users who have opted-in to Location History for their Google Account.



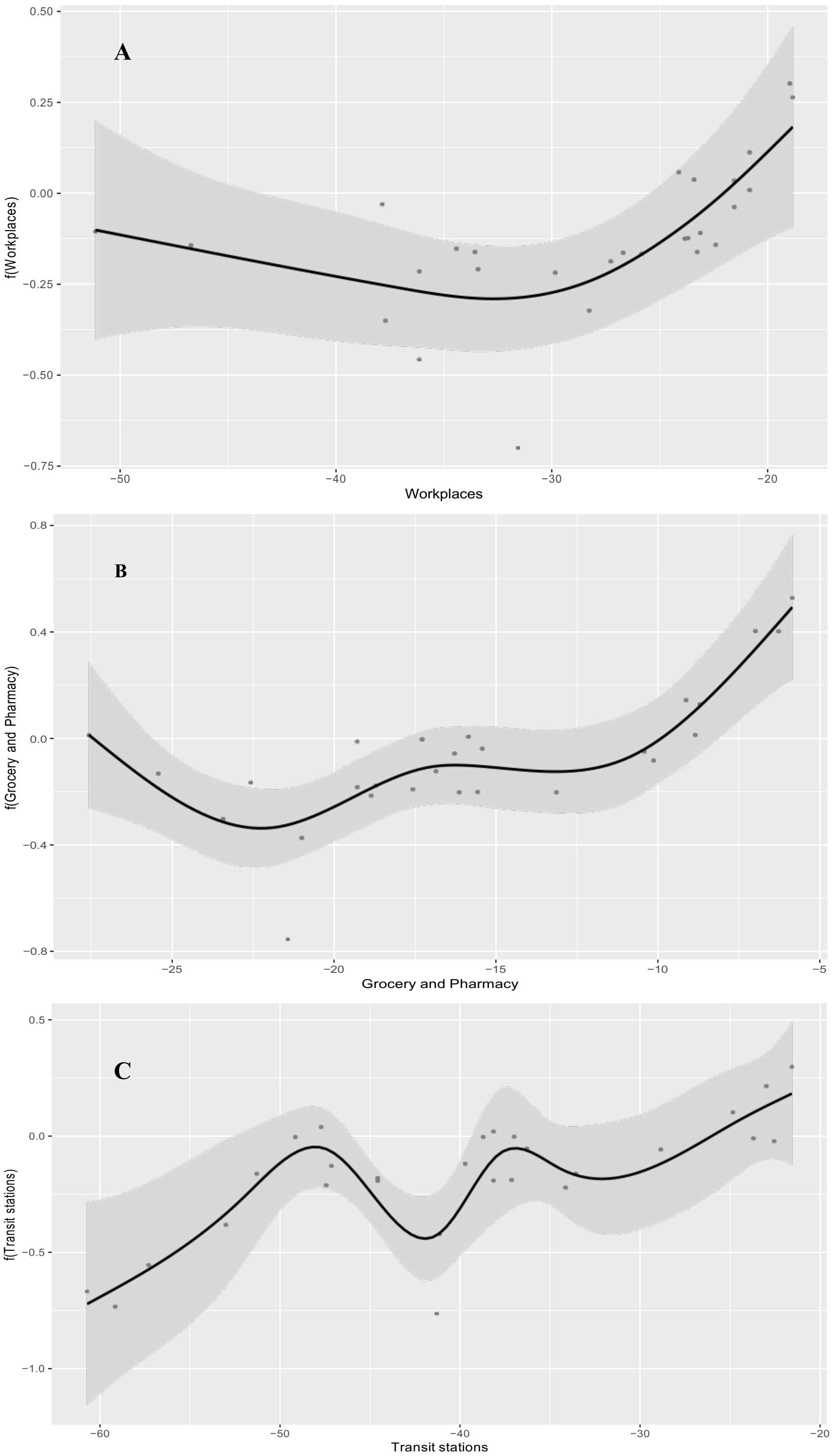
Supplementary figure 1: Histogram of Lombardy R_t frequency distribution. Available samplings display a non-normal, positively skewed distribution of R_t frequency.



Supplementary figure 2: Autocorrelation of R_t time series. Vertical lines represent autocorrelation at different time lags (weeks). Dashed lines represent level of significance at 95%. Autocorrelation function (ACF) displayed a significant correlation in R_t time series.

	UV-index	Retail & Recreation	Grocery & Pharmacy	Workplaces	Transit Stations	Parks
UV-index	1·00	0·51*	-0·35	0·61	0·21	0·84*
Retail & Recreation	··	1·00	0·55*	0·63*	0·92*	0·76*
Grocery & Pharmacy	··	··	1·00	0·76*	0·74*	-0·06
Workplaces	··	··	··	1·00	0·71	0·16
Transit Stations	··	··	··	··	1·00	0·54*
Parks	··	··	··	··	··	1·00

Supplementary Table 2: Comparison of R (Pearson correlation coefficient) among the explanatory variables. Asterisk (*) indicates significant correlation at the probability level of 0·01.



Supplementary figure 3: Smoothing component plots for log(R_t) associated with mobility indices, accounting for UV-index. The smooth terms for *Workplaces* (A), *Grocery & Pharmacy* (B), and *Transit stations* (C) show an effect of mobility indices reduction in curbing R_t, irrespective of environmental seasonality. Y-axis is the partial effect of the variable and shadow section is the standard-error confidence intervals. An apparent R_t increase is observable for extreme levels of reduction of *Workplaces* and *Grocery & Pharmacy* mobility indices. Left parts of the smoothing components plots were built by the model fitting on a small number of observations, limiting the predictive value of the models in these sections, as shown by the enlargement of confidence intervals.