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Complete Title: Weathering the pandemic: How the Caribbean Basin can use viral and environmental patterns to predict, prepare and respond to COVID-19.

Shortened Title: Predicting and managing COVID-19 outbreaks in the Caribbean

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Abstract

The 2020 coronavirus pandemic is developing at different paces throughout the world. Some areas, like the Caribbean Basin, have yet to see the virus strike at full force. When it does, there is reasonable evidence to suggest the consequent COVID-19 outbreaks will overwhelm healthcare systems and economies. This is particularly concerning in the Caribbean as pandemics can have disproportionately higher mortality impacts on lower and middle income countries. Preliminary observations from our team and others suggest that temperature and climatological factors could influence the spread of this novel coronavirus, making spatiotemporal predictions of its infectiousness possible. This review studies geographic and time-based distribution of known respiratory viruses in the Caribbean Basin in an attempt to foresee how the pandemic will develop in this region. This review is meant to aid in planning short- and long-term interventions to manage outbreaks at the international, national and sub-national levels in the region.

Text:

1. Introduction

On March 12, 2020, the World Health Organization (WHO) declared a pandemic of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, the pathogen responsible for the clinical disease known as COVID-19. Governments worldwide have been putting in place measures to limit the spread of the disease, but recent publications[1,2] suggest the pandemic could last up to 18 months. If so, it will be necessary to layer interventions. The reactive control measures employed so far have failed to control the crisis. Countries will have to choose paths of action going forth including a proactive, preventative approach to COVID-19 outbreaks.

Proactive planning is challenging when so little is known about SARS-CoV-2. Nevertheless, there is reason to believe the disease will have a predictable spatiotemporal spread based on environmental factors, particularly weather[3,4]**.** This knowledge can help countries and regions put measures in place at key points, as is done, for example, with Respiratory Syncytial Virus (RSV) for susceptible populations[5]. Influenza epidemics are likewise treated prophylactically with vaccines for the general population[6] plus social distancing interventions during seasonal peaks[7,8]. Similar interventions might work if this novel coronavirus does prove to be seasonal.

While understanding the geotemporal distribution of the pathogen could help citizens, institutions and governments in mitigation, preparation and response, it is important to note that spatiotemporal behavior of respiratory pathogens is not equally documented in all regions. This is particularly important in areas where SARS-CoV-2 has only recently been introduced, like the Caribbean Basin— the land areas bordering the Caribbean Sea. This region notoriously has high variability for data on the infectious patterns of respiratory viruses. An individual and community approach from the Caribbean nations, if implemented soon, could significantly curve the impact of COVID-19 epidemics in that area. This review puts forth several observations on why SARS-CoV-2 might exhibit a geotemporal pattern, what could be expected if the virus becomes endemic, and what actions might help manage the current crisis.

2. Virology of coronaviruses

Severe acute respiratory syndrome coronavirus 2, or SARS-CoV-2, is within the taxonomical family coronaviridae. This family of viruses has an envelope, a nucleocapsid, and a positive-sense, single-stranded RNA genome[9]. SARS-CoV-2 is classified into the genus Betacoronavirus, one of four genera within this family[10,11]. Genome sequencing analyses showed that SARS-CoV-2 is ~30k nucleotides in size, containing a single long open reading frame at the 5' terminal encoding viral replicase/transcriptase and several reading frames for structural proteins towards the 3' terminal, including envelope (E) protein, membrane (M) protein, nucleocapsid (N) protein, and spike (S) protein[11,12]. The surface-located trimeric S glycoprotein is the key determinant of viral host specificity, as it initiates infection by mediating receptor-recognition and membrane fusion [13,14,15]. Notably, the S gene of SARS-CoV-2 is highly divergent from other SARS-related coronaviruses, with less than 75% nucleotide sequence identity[11,16]. Despite significant differences in the S gene sequence, SARS-CoV-2 uses the same receptor as SARS-CoV: angiotensin-converting enzyme 2[11,17]. This suggests some similarities in manner of infection between the two species. Beyond the S protein, other virus and host proteins may contribute to subsequent membrane invagination and pathogenesis, but the molecules and mechanisms are unclear.

As the SARC-CoV-2 pandemic evolves, region-specific features may emerge. With confirmation of both direct and indirect transmission routes (via aerosol droplets and fomites, respectively), the central factor underlying viral transmission rate for SARS-CoV-2 is the viral viability while outside the human body[18,19, 20]. Different regions exhibit unique climate characteristics which are key to the virion decay rates of all respiratory viruses in droplets[21,22,23]. One possible explanation is that high temperature and humidity levels lead to inactivation of viral lipid membrane and consequently decrease the stability and transmission rate of virions[18,24]. While such observations and hypothesis may indicate that SARS-CoV-2 is expected to be better contained in the tropical regions compared to temperate zones, other determinants need to be considered. For example, in warm and humid climates, droplets evaporate less water and are more likely to settle on surfaces. Therefore, if SARS-CoV-2 is predominantly transmitted through touching contaminated surfaces, tropical regions may actually bear a higher risk of outbreak than temperate ones in moments of extreme humidity. This assumption is possible, since the indirect transmission route has been reported to be the important one for several respiratory viruses, including influenza[25,26,27,28]. However, the relationship of multiple SARS-CoV-2 transmission modes remains an open question. In addition, strain variations have the potential to change viral survival. Hence, surveillance of circulating SARS-CoV-2 in real-time should be intensively performed worldwide.

3. Geotemporal evolution of the 2020 coronavirus pandemic

A systematic review of the daily Situation Reports by WHO between 21 January 2020 and 4 April 2020[29] suggests that SARS-CoV-2 might express a seasonal pattern of infection. Data from national healthcare agencies and news hinted at latitudinal and/or climate-based relationships sub-nationally. Several observations have led to this hypothesis. Firstly, countries with the greatest epidemics all lie in the temperate zone of the Northern Hemisphere. As of 4 April

2020, there were 1,051,635 confirmed SARS-CoV-2 cases worldwide. The largest foci of infection were in China, Iran, Western Europe (particularly Italy and Spain) and the United States: these five countries account for ~60% of the infected. Secondly, the inter-tropical zone generally seemed less affected. The Caribbean Basin only started seeing cases on 2 March 2020, and did not report local transmission until a week later. The slow spread to the Caribbean could be attributed to distance from the pandemic's origin. However, despite geographical, ethnic and cultural proximity to China, the entire South-East Asian tropics and the Western Pacific Region (excluding China) had under 35,000 reported infected individuals combined, fewer cases than any one of the aforementioned large-foci countries. Thirdly, in some countries with large latitudinal spreads, a gradient of infection can be observed with outbreaks spreading faster the farther they are from the equator: this pattern was at the time of this writing observable in Brazil, Australia, and USA. Other research groups have made similar observations regarding the potential seasonality of SARS-CoV-2, though at present, many are pending peer-review[30,31]. It seems the uncontrolled outbreaks occur in the areas experiencing cold, dry winters while proximity to the tropics might correlate with a slower spread of infections.

These observations are preliminary, dependent on testing and reporting, and could admittedly change as the pandemic evolves. However, their importance lies in them being compatible with spatiotemporal patterns previously described for respiratory viruses within and without the coronavirus family. If indeed SARS-CoV-2 behaves like other respiratory viruses, the Caribbean, tropical Africa, and many areas of the Southern Hemisphere can expect an uptick in COVID-19 cases come May 2020.

4. Geotemporal patterns of known respiratory viruses

Not all seasonal respiratory viruses experience the same spatiotemporal patterns. Nevertheless, assuming seasonality, the only way of predicting SARS-CoV-2 behavior in a given region is to extrapolate data from known pathogens. Most such studies are based on influenza, which has been extensively studied[32]. Identified factors that decrease respiratory viral transmission include high temperatures (30°C) and a relative humidity (RH) of 80%, while factors that increase it include cold and dry climates[33,34]. Limited evidence suggests SARS-CoV-2 is susceptible to similar factors: one non-peer-reviewed article observing patterns in China found that the severity of infectiousness, measured by effective reproductive number (*R*) decreased 0.0383 per increase in degree centigrade and decreased by 0.0224 per percentage-point increase in RH[31]. It seems favorable factors against SARS-CoV-2 infectiousness exist across the Caribbean Basin, where temperatures on average range from 20-27°C (April-May) to 23-32°C (June-July), and RH ranges 40-80% (April-July). An additional factor supporting the theory of slower spread to and within the Caribbean is observed with influenza, in which a latitudinal gradient has been shown to correlate with severity of infectiousness: the closer a location is to the equator, the lower the *R*[35,36,37].

A factor that does increase influenza transmission, however, is high precipitation levels in tropical zones. According to some observations[34], a precipitation threshold of at least 150 mm monthly is needed to elicit a peak in viral transmission; peaks are generally more common in the region's month of maximal precipitation. Nevertheless, there are within the Caribbean highly variable patterns of precipitation. To account for said variability, research often divides the Basin into climatological sub-regions. A 2012 study suggested that although overall amounts of precipitation in the Caribbean have been stable over the late twentieth and early twenty-first centuries, there were more heavy rain events overall[38]. This was particularly true for Cuba, Hispaniola and Jamaica, resulting in heavier precipitation events with longer dry periods in between. Puerto Rico now experiences similar meteorological changes[39]. The implication for respiratory viral transmission would be that peaks become more pronounced during the rainy season in the Greater Antilles.

Variabilities in climatological patterns make generalized recommendations for interventions in epidemics difficult, even for well-known viruses[40]. For example, the WHO divides the Caribbean Basin into just two influenza transmission zones, each with its own vaccine and separate recommendations regarding timing[41]. However, even geographically close, small countries can exhibit vastly different influenza patterns. In the Western Caribbean, reports show Guatemala has two high influenza peaks in March and July, Nicaragua has a primary peak in November and a smaller one in June, and Panama essentially has a single November peak with a mild uptick in July[42]. Among the islands, Puerto Rico historically has a peak in winter, but also shows a secondary peak in May[43]. Information in the South American Coast of the Caribbean is scarce, but needs might differ sub-nationally given how geographically diverse countries like Venezuela and Colombia are. Geographically diverse countries elsewhere have in fact documented sub-national variation in optimal timings of epidemic-prevention measures[44].

For the pandemic, preventive measures have mainly focused on social distancing— a method proven to delay or temporarily stretch out regional outbreaks so as to not overburden healthcare systems[7,8]. In the case of China, extreme state-enforced social distancing has substantially slowed the epidemic[29]. Multiple countries have followed suit and called for a complete lockdown, halting the economy. As the full blow of the epidemic has yet to reach the Caribbean Basin, it is possible to coordinate methods of social distancing while minimizing the impact to their societies. The same observations can be used to plan for future COVID-19 outbreaks, since the pandemic is expected to last several months, but proper prevention necessitates knowledge of local viral and meteorological trends, and coordination amongst and within nations.

Most of the above observations on spatiotemporal patterns and prevention come from influenza, eliciting reasonable concern that data cannot be extrapolated. However, other viruses unrelated to influenza do follow its trends under the right circumstances. RSV is an example of this, as it mimics patterns and transmission routes of influenza in temperate zones[37] and is similarly treated with time-specific prophylactic interventions[45].

Though less studied, trends are also found in coronaviruses, particularly in four endemic strains known to cause respiratory infections: 229-E, HKU1, NL63 and OC43. In Israel, 1,910 samples collected over a single season suggested human coronaviruses (HCoV) closely followed the seasonal patterns of RSV[46]. A 3-year-long Scotland-based study identified a coronavirus peak in the winter months, with a decrease or disappearance of the virus during the summer[47]. Recently, a pattern favoring cold, dry weather was also observed in Hong Kong in a 6-year-long study, though in this case coronaviruses were found year-round[48]. Interestingly, the Hong Kong study suggested the elderly (>80 y/o) were significantly more likely to acquire coronavirus than young children (<10 y/o), an intriguing finding considering that the COVID-19 epidemics have disproportionately affected the elderly. Though none looked into the causes of these trends, all three studies showed dominance or codominance of HCoV-OC43 among coronavirus strains.

Evidence from the 2003 Severe acute respiratory syndrome coronavirus (SARS-CoV) outbreak in Hong Kong suggested colder air surface temperature increased the daily incidence of SARS compared to warmer days[49]. Therefore, a relationship between temperature and infectiousness has been described for coronaviruses. Additionally, the seasonality of the Middle-Eastern Respiratory Syndrome coronavirus (MERS-CoV), which is disputed[50], seems to favor the summer months in the Arabian Peninsula, particularly June, their driest month[51]. This suggests that dryness is a driving factor for MERS-CoV infection, which matches the observed increased prevalence of COVID-19 in dry temperate seasons. Furthermore, MERS-CoV outbreaks have been documented to co-occur with or closely follow epidemic waves of influenza A in various Middle-

Eastern countries[52]. The observations from SARS-CoV and MERS-CoV would presumably pose a favorable decrease in SARS-CoV-2 transmission within the warm, humid Caribbean. Notably, HCoV-OC43, SARS-CoV, and MERS-CoV are all Betacoronaviruses, meaning they are phylogenetically close to SARS-CoV-2. Therefore, data from other coronaviruses and the similar portal of infection discussed above do support the idea that SARS-CoV-2 may follow the same patterns as influenza, and that timing interventions around influenza peaks in the Caribbean would be reasonable.

5. Conclusion

This pandemic has already overwhelmed many health systems, but regions that are currently less affected, including the Caribbean Basin, could prepare for the next several months by observing the spatiotemporal behavior of the pathogen's spread. If SARS-CoV-2 interacts with climate and weather as theorized above, it is likely that areas in the Greater Caribbean with Air Surface Temperatures (AST) >25°C and RH>70% might be considered areas of relatively decreased environmental risk (Figure 1)[53]. These two variables combined may have the potential of reducing the incidence of COVID-19 for at least parts of the Region. For example, based off recent patterns of heat and precipitation, it would be reasonable for Puerto Rico to expect a higher rate of infection in May-June with a sharp decrease for June-July-August. This follows the trend of influenza over the last 5 years, which in turn follows trends in temperature and precipitation[54,55,56] (Figure 2). There is also a seasonal trend for all acute respiratory illnesses to decrease during the warmer months, which will minimize confounding of COVID-

19 with other respiratory syndromes. Currently, Puerto Rico is under an astringent 4-week lockdown; it is unclear when and to what extent restrictions will be lifted. Based on the afore-mentioned trends, some restrictions would need to remain through July to limit outbreaks. Temperature forecasts for the rest of the Caribbean are consistent for the upcoming months: AST is expected to be "warmer than usual" through August[57] (Figure 3). Presumably this will soften the overall impact of COVID-19 outbreaks. Precipitation forecasts are more variable[58] (Figure 4).

These forecasts may allow Caribbean jurisdictions to plan for better, smarter public health interventions such as controlling and limiting massive activities, promoting outreach and educational materials, establishing coherent and coordinated lockdowns, promoting voluntary social distancing, increasing production of medical supplies and disinfectants, or closing public gathering spaces to limit the reach of outbreaks. International collaboration is also of essence: a cooperative, transparent system of epidemic vigilance is needed. Outbreaks near borders can have far-reaching implications, especially when illegal immigration is considered. A health crisis has already developed along the United States-Mexico border with immigrants primarily from Central America[59,60,61,62]. Now their packed transport and living conditions increase the chances of transmission for SARS-CoV-2 and other pathogens, posing a health risk to their community and beyond.

As the epidemics have yet to reach the proportions seen in the temperate zones of the Northern Hemisphere, preparation can still be done and requires addressing other potential health hazards. The Caribbean Basin will enter the rainy season in a few weeks, with a 58% chance of a major hurricane impacting it[63]. The Caribbean Public Health Agency has already put forth[64] that heavy showers are expected in May, with likely floods for the Greater Antilles and Guianas, and short-term droughts in other areas. The rains will increase the incidence of endemic vector-borne diseases including Dengue[65,66,67], Zika[68], and Chikungunya[69]. Consequently, jurisdictions should prepare for potential impacts in food production, water availability, and wildfires, in addition to preparing for epidemics.

Aeroallergens and pollutants are another category of health-related seasonal factors with clinical implications in the upcoming months. Saharan dust incursions into the Caribbean typically increase in May and can cause respiratory symptoms[70],[71],[72]. Sub-nationally, factors like PM10 or mold levels affect air quality and have documented impacts on respiratory health[73], though regional tracing of these variables is very limited. As for the indoor environment, now more than ever it is important to address the presence of aeroallergens in homes, as these too are linked to respiratory health[74]. Clinical familiarity with spatiotemporal patterns of aeroallergens and pollutants is therefore advised.

The assumption that these seasonal forecasts will predict COVID-19 outbreaks is by any stretch preliminary-- it would take years to gather enough data to precise how the virus spreads. Additionally, many variables beyond weather can impact SARS-CoV-2 transmissibility: socioeconomic factors, care-seeking behaviors, population density, etc. Intrinsic pathogen factors like mutation rates add another layer of complexity as patterns become a moving target rather than a static picture. Nonetheless, the above approach presuming seasonality makes scientific sense, is consistent with the data available, and is in line with recommendations for several other pathogens. Its use could have a substantial impact in management of this pandemic.

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Figure 1. Based on temperature, relative humidity, and the impact of each on the transmission of known viruses, a forecast can be produced regarding areas where SARS-CoV-2 infectivity will be relatively high or low. Environmental conditions favoring higher infectivity are represented towards the red side of the spectrum and those favoring lower infectivity toward the purple end on the right side. Note that the Northern Caribbean favors the latter while most of the continental United States does not. Source: Climate Explorer. CRUv4 vapor pressure in blocks of two months averaged 2000-2018, based on station reports summarize to monthly averages. Interpretation in personal communication with Professor Mark Jury, PhD, from the University of Puerto Rico. Available at: https://climexp.knmi.nl/start.cgi. Accessed 22 March 2020

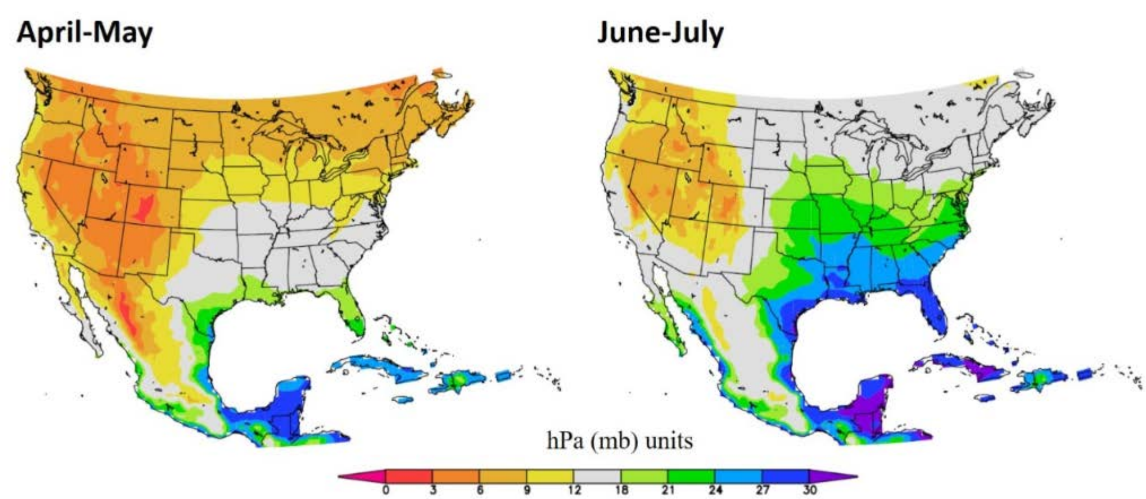


Figure 2. Caption : Caption : The upper panels exhibit Influenza-Like-Illness (ILI), confirmed influenza cases and air surface temperature (°C) per month in Puerto Rico (Period 2015-2017). The lower panels show Influenza-Likeliness-Illness (ILI), confirmed influenza cases and monthly precipitation (mm) (Period 2015-2017). The incidence declines in the warmer months, except for the uptick of influenza in May-June which seems to be driven by precipitation. Health Data Source: Centers for Disease Control (CDC). National, regional and state level outpatient illnesses and viral surveillance and Puerto Rico Department of Health. Available at: https://gis.cdc.gov/grasp/fluview/fluportaldashboard.html. Accessed 23 March 2020. Climate Data Source: Daymet Software Version 3.0; Daymet Data Version 3.0. (Daily Surface Weather and Climatological Summaries Available at: https://daymet.ornl.gov/ Accessed on March 30, 2020. For extraction and analysis of climate data: Thornton et al. 1997; 201

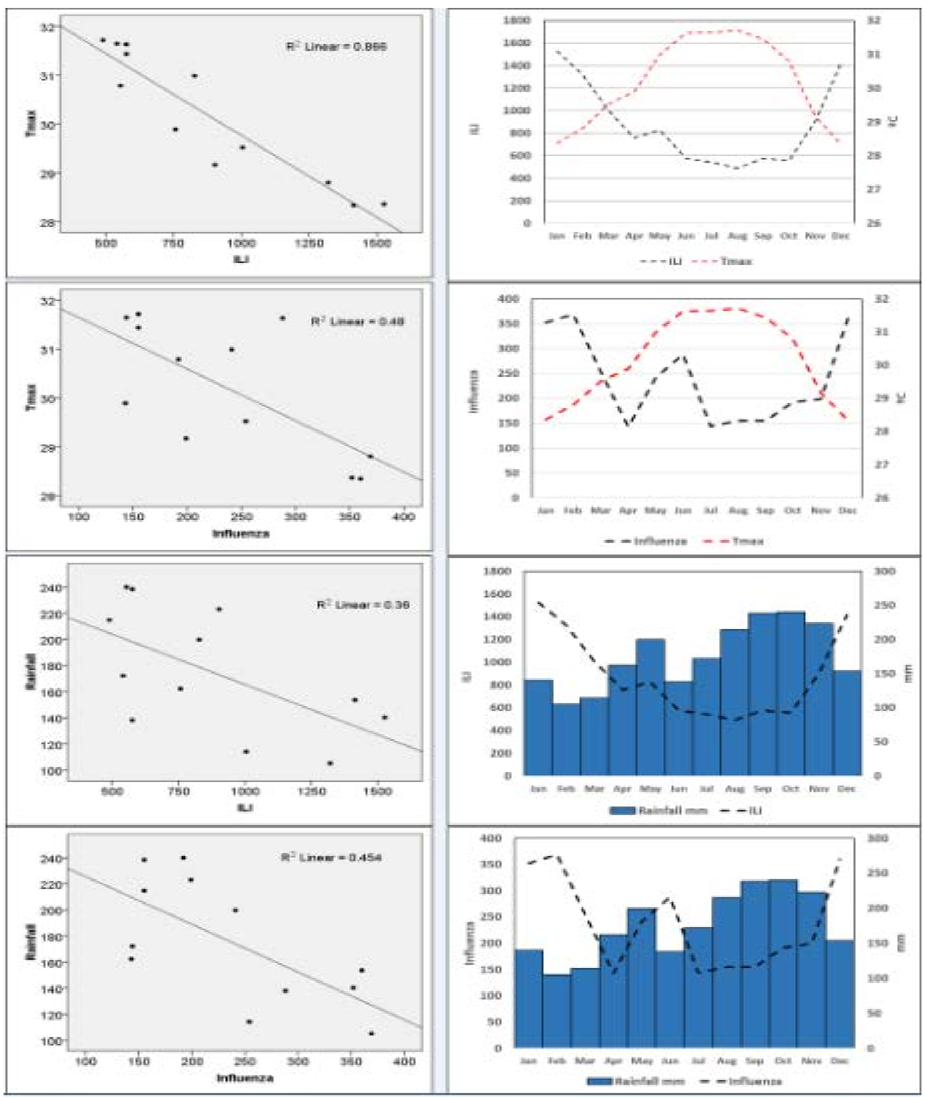


Figure 3. Temperatures will be much warmer than usual in land masses West of Hispaniola, especially Cuba and Belize, and along the coasts of Venezuela and Suriname. They will be mildly warmer than usual in the rest of the Guianas, Hispaniola, Puerto Rico and the Lesser Antilles. Source: Caribbean Regional Climate Center, World Meteorological Association. Temperature Outlook for March-April-May 2020. Available at: http://rcc.cimh.edu.bb/temperature-outlook-march-april-may-2020/. Accessed 22 March 2020.

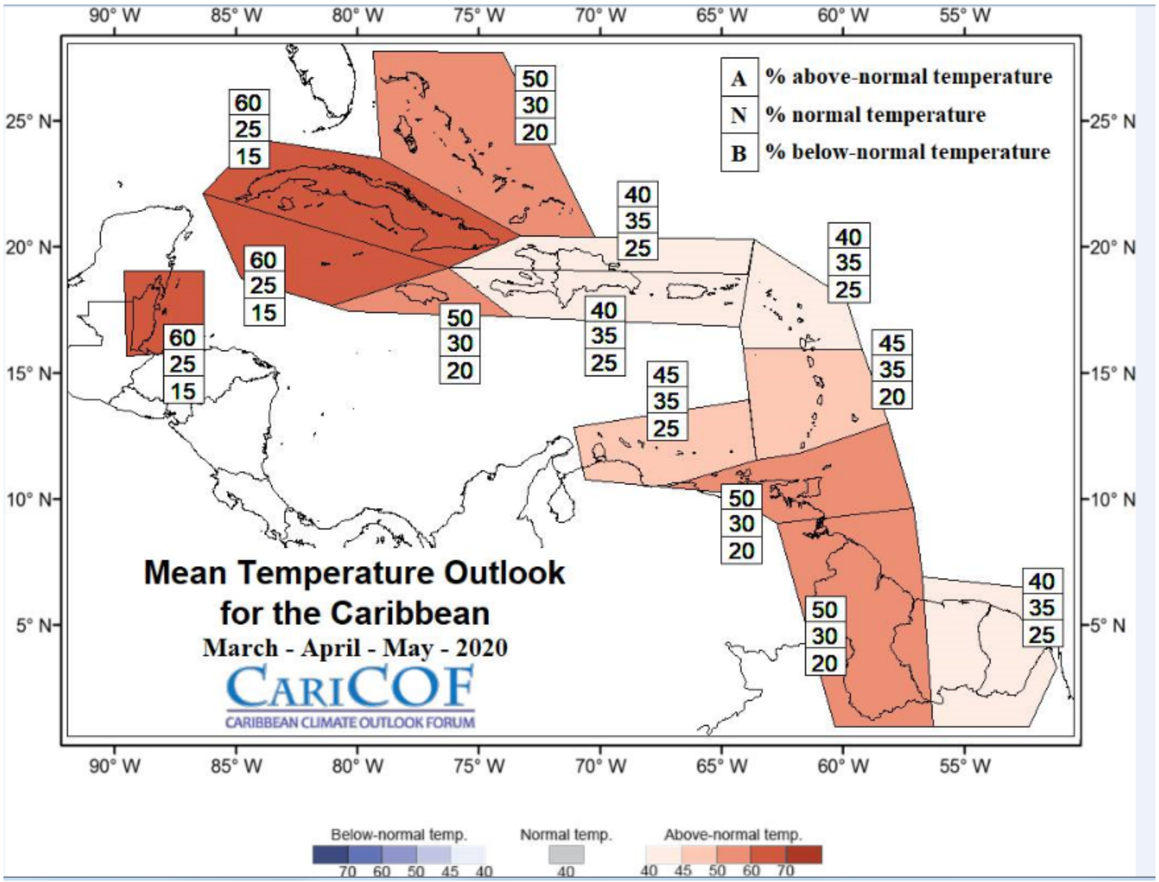
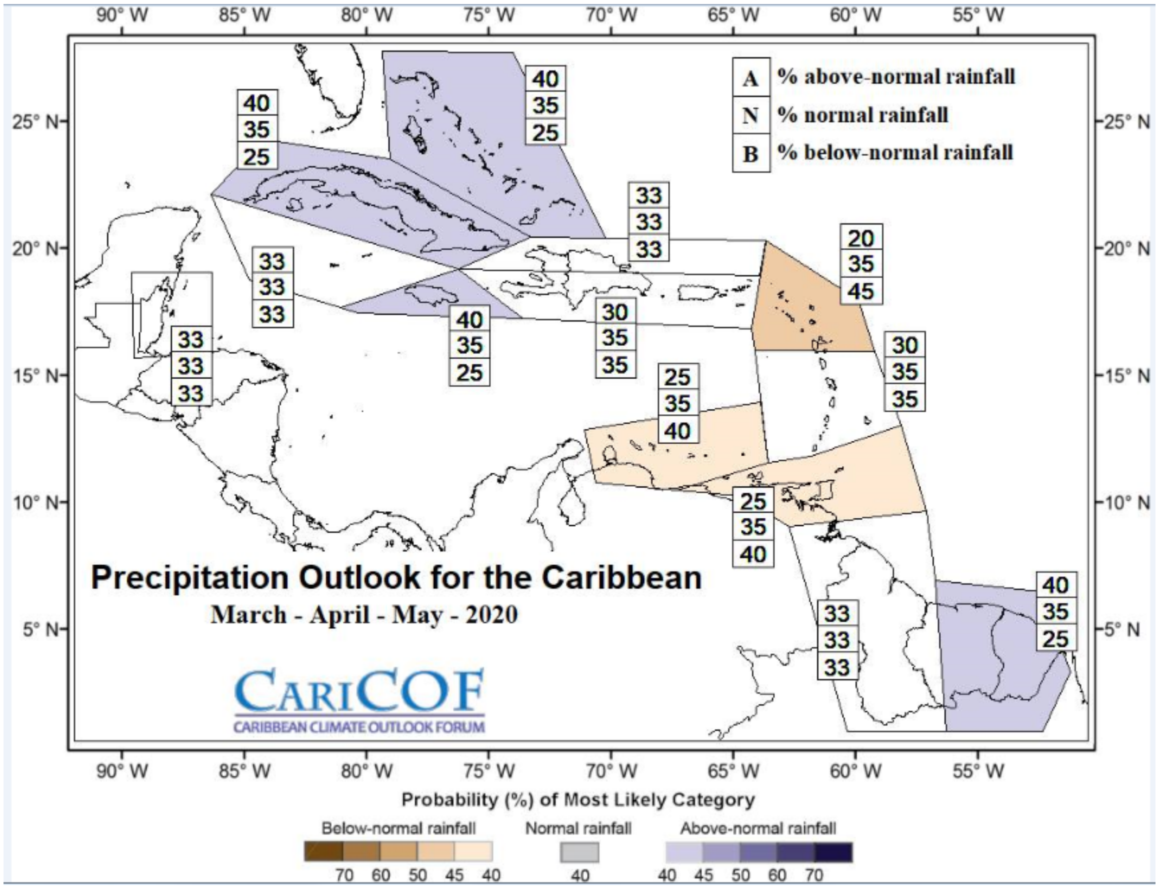


Figure 4. Precipitation will mildly increase in the insular portion of the Caribbean North-West and the eastern Guianas. The coasts of Venezuela, with its associated islands, and the Leeward Islands are expected to have mildly decreased levels of precipitation. Source: Caribbean Regional Climate Center, World Meteorological Association. Temperature Outlook for March-April-May 2020. Available at: https://rcc.cimh.edu.bb/precipitation-outlook-march-april-may-2020/. Accessed 22 March 2020



References:

1 Ferguson NM, Laydon D, Nedjati-Gilani G, Imai N, Ainslie K, Baguelin M, Bhatia S, Boonyasiri A, Cucunubá Z, Cuomo-Dannenburg G, Dighe A. Impact of non-pharmaceutical interventions (NPIs) to reduce COVID-19 mortality and healthcare demand. *Imperial College COVID-19 Response Team.* 16 March

2020. https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-fellowships/Imperial-College-COVID19-NPI-modelling-16-03-2020.pdf. Accessed: March 16, 2020.

[2] Department of Health and Human Services, United States Government. U.S. Government COVID-19 Response Plan, PanCAP Adapted. Available at: https://int.nyt.com/data/documenthelper/6819-covid-19-response-plan/d367f758bec47cad361f/optimized/full.pdf#page=1. Accessed March 17, 2020.

[3] Metcalf CJE, Walter KS, Wesolowski A, Buckee CO, Shevliakova E, Tatem AJ, et al. Identifying climate drivers of infectious disease dynamics: recent advances and challenges ahead. *Proc R Soc B*. 2017;284(1860):20170901. pmid:28814655

[4] Martinez ME. The calendar of epidemics: Seasonal cycles of infectious diseases. *PLoS Pathog*. 2018;14(11):e1007327. Pmid:30408114

[5] Committee on Infectious Diseases. Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. *Pediatrics*. 2014 Aug 1;134(2):e620-38.

[6] Centers for Disease Control and Prevention (CDC). Prevention and control of seasonal influenza with vaccines. Recommendations of the Advisory Committee on Immunization Practices--United States, 2013-2014. *MMWR. Recommendations and reports: Morbidity and mortality weekly report.* 2013 Sep 20;62(RR-07):1.

[7] Wheeler CC, Erhart LM, Jehn ML. Effect of school closure on the incidence of influenza among school-age children in Arizona. *Public health reports*. 2010 Nov;125(6):851-9.

[8] Earn DJ, He D, Loeb MB, Fonseca K, Lee BE, Dushoff J. Effects of school closure on incidence of pandemic influenza in Alberta, Canada. *Ann intern med*. 2012 Feb 7;156(3):173-81

[9] Perlman S, Netland J. Coronaviruses post-SARS: update on replication and pathogenesis. *Nat Rev Microbiol*. 2009 Jun;7(6):439-50.

[10] Chan JF, To KK, Tse H, Jin DY, Yuen KY. Interspecies transmission and emergence of novel viruses: lessons from bats and birds. *Trends Microbiol.* 2013 Oct 1;21(10):544-55.

[11] Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, Si HR, Zhu Y, Li B, Huang CL, Chen HD. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020 Feb 3:1-4.

[12] Chan JF, Kok KH, Zhu Z, Chu H, To KK, Yuan S, Yuen KY. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerg Microbes Infect*. 2020 Jan 1;9(1):221-36.

[13] Li F. Structure, function, and evolution of coronavirus spike proteins. *Annu Rev Virol*. 2016 Sep 29;3:237-61.

[14] Lu G, Wang Q, Gao GF. Bat-to-human: spike features determining 'host jump'of coronaviruses SARS-CoV, MERS-CoV, and beyond. *Trends Microbiol*. 2015 Aug 1;23(8):468-78.

[15] Hulswit RJ, de Haan CA, Bosch BJ. Coronavirus spike protein and tropism changes. *Adv virus res*. 2016 Jan 1 (Vol. 96, pp. 29-57).

[16] Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, Wang W, Song H, Huang B, Zhu N, Bi Y. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet*. 2020 Feb 22;395(10224):565-74.

[17] Li WH, Moore MJ, Vasilieva N, Sui JH, Wong SK, et al. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. *Nature*. 2003;426:450–54.

[18] Moriyama M, Hugentobler WJ, Iwasaki A. Seasonality of Respiratory Viral Infections. *Annu Rev Virol*. 2020 Mar 20; DOI: 10.1146/annurev-virology-012420-022445 Accessed 21 Mar 2020

[19] Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, Xing F, Liu J, Yip CC, Poon RW, Tsoi HW. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet*. 2020 Feb 15;395(10223):514-23.

[20] Peng X, Xu X, Li Y, Cheng L, Zhou X, Ren B. Transmission routes of 2019-nCoV and controls in dental practice. *Int J Oral Sci*. 2020 Mar 3;12(1):1-6.

[21] Lowen AC, Mubareka S, Steel J, Palese P. Influenza virus transmission is dependent on relative humidity and temperature. *PLOS Pathog*.2007; 3:1470–76

[22] Yang W, Marr LC. Dynamics of airborne influenza A viruses indoors and dependence on humidity. *PloS one*. 2011;6(6).

[23] Irwin CK, Yoon KJ, Wang C, Hoff SJ, Zimmerman JJ, Denagamage T, O'Connor AM. Using the systematic review methodology to evaluate factors that influence the persistence of influenza virus in environmental matrices. *Appl Environ Microbiol*. 2011 Feb 1;77(3):1049-60.

[24] De Jong JC, Trouwborst T, Winkler KC. Mechanisms of inactivation of viruses and macromolecules in air. *Airborne Transmission and Airborne Infection*. 1973:124-30.

[25] Boone SA, Gerba, CP Significance of fomites in the spread of respiratory and enteric viral disease. *Appl Environ Microbiol*. 2007; 73: 1687–1696

[26] Brankston G, Gitterman L, Hirji Z, Lemieux C, and Gardam M. Transmission of influenza A in human beings. *Lancet Infect Dis*. 2007; 7: 257–265

[27] Spicknall IH, Koopman JS, Nicas M, Pujol JM, Li S, Eisenberg JN. Informing optimal environmental influenza interventions: how the host, agent, and environment alter dominant routes of transmission. *PLoS Comput Biol*. 2010; 6: e1000969

[28] Otter JA, Donskey C, Yezli S, Douthwaite S, Goldenberg SD, Weber DJ. Transmission of SARS and MERS coronaviruses and influenza virus in healthcare settings: the possible role of dry surface contamination. *J Hosp Infect*. 2016 Mar 1;92(3):235-50.

[29] World Health Organization. Coronavirus disease (COVID-2019) situation reports. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/. Accessed January 21, 2020 through March 21, 2020.

[30] Sajadi MM, Habibzadeh P, Vintzileos A, Shokouhi S, Miralles-Wilhelm F, Amoroso A. Temperature and latitude analysis to predict potential spread and seasonality for COVID-19. Available at SSRN 3550308. 2020 Mar 5.

[31] Wang J, Tang K, Feng K, Lv W. High Temperature and High Humidity Reduce the Transmission of COVID-19. Available at SSRN 3551767. 2020 Mar 9.

[32] Azziz Baumgartner E, Dao CN, Nasreen S, Bhuiyan MU, Mah-E-Muneer S, Mamun AA, Sharker MY, Zaman RU, Cheng PY, Klimov AI, Widdowson MA. Seasonality, timing, and climate drivers of influenza activity worldwide. *J Infect Dis*. 2012 Sep 15;206(6):838-46.

[33] Lowen AC, Steel J, Mubareka S, Palese P. High temperature (30 C) blocks aerosol but not contact transmission of influenza virus. *J Virol*. 2008 Jun 1;82(11):5650-2.

[34] Tamerius JD, Shaman J, Alonso WJ, Bloom-Feshbach K, Uejio CK, Comrie A, Viboud C. Environmental predictors of seasonal influenza epidemics across temperate and tropical climates. *PLoS Pathog*. 2013 Mar;9(3).

[35] Chowell G, Towers S, Viboud C, Fuentes R, Sotomayor V, Simonsen L, et al. The influence of climatic conditions on the transmission dynamics of the 2009 A/H1N1 influenza pandemic in Chile. *BMC Infect Dis*. 2012;12:298.

[36] Chowell G, Viboud C, Simonsen L, Miller M, Alonso WJ. The reproduction number of seasonal influenza epidemics in Brazil, 1996–2006. *Proc R Soc B Biol Sci*. 2010;277(1689):1857–66.

[37] Bloom-Feshbach K, Alonso WJ, Charu V, Tamerius J, Simonsen L, Miller MA, Viboud C. Latitudinal variations in seasonal activity of influenza and respiratory syncytial virus (RSV): a global comparative review. *PLoS one*. 2013;8(2).

[38] Stephenson TS, Vincent LA, Allen T, Van Meerbeeck CJ, McLean N, Peterson TC, Taylor MA, Aaron-Morrison AP, Auguste T, Bernard D, Boekhoudt JR. Changes in extreme temperature and precipitation in the Caribbean region, 1961–2010. *Int J Climatol*. 2014 Jul;34(9):2957-71.

[39] Gould WA, Díaz EL, Álvarez-Berríos NL, Aponte-González F, Archibald W, Bowden JH, Carrubba L, Crespo W, Fain SJ, González G, Goulbourne A, Harmsen E, Holupchinski E, Khalyani AH, Kossin J, Leinberger AJ, Marrero-Santiago VI, Martínez-Sánchez O, McGinley K, Méndez-Lázaro P, Morell J, Oyola MM, Parés-Ramos IK, Pulwarty R, Sweet WV, Terando A, and Torres-González S. 2018: US Caribbean. In: *Impacts, risks, and adaptation in the United States: Fourth national climate assessment, volume II*. US Global Change Research Program. 2018. pp. 809–871. doi: 10.7930/NCA4.2018.CH20**.**

[40] Hirve S, Newman LP, Paget J, Azziz-Baumgartner E, Fitzner J, Bhat N, Vandemaele K, Zhang W. Influenza seasonality in the tropics and subtropics–when to vaccinate?. *PloS one*. 2016;11(4).

[41] World Health Organization. Influenza Updates. Available at: https://www.who.int/influenza/surveillance_monitoring/updates/en/. Accessed: 12 March 2020

[42] Caini S, Alonso WJ, Balmaseda A, Bruno A, Bustos P, Castillo L, De Lozano C, De Mora D, Fasce RA, De Almeida WA, Kusznierz GF.

Characteristics of seasonal influenza A and B in Latin America: Influenza surveillance data from ten countries. *PloS one*. 2017;12(3).

[43] Department of Health, Government of Puerto Rico. Vigilancia de influenza de Puerto Rico: Informe semanal. Available at: http://www.salud.gov.pr/Estadisticas-Registros-y-Publicaciones/Estadisticas%20Influenza/Informe%20Influenza%20Semana%209%202020.pdf. Accessed: 16 March 2020.

[44] Koul PA, Broor S, Saha S, Barnes J, Smith C, Shaw M, Chadha M, Lal RB. Differences in influenza seasonality by latitude, northern India. *Emerg Infect Dis*. 2014 Oct;20(10):1723.

[45] Brady MT, Byington CL, Davies HD, Edwards KM, Jackson MA, Maldonado YA, Murray DL, Orenstein WA, Rathore MH, Sawyer MH, Schutze GE. Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. *Pediatrics*. 2014 Aug 1;134(2)

[46] Friedman N, Alter H, Hindiyeh M, Mendelson E, Shemer Avni Y, Mandelboim M. Human coronavirus infections in Israel: epidemiology, clinical symptoms and summer seasonality of HCoV-HKU1. *Viruses*. 2018 Oct;10(10):515.

[47] Gaunt ER, Hardie A, Claas EC, Simmonds P, Templeton KE. Epidemiology and clinical presentations of the four human coronaviruses 229E, HKU1, NL63, and OC43 detected over 3 years using a novel multiplex real-time PCR method. *J Clin Microbiol*. 2010 Aug 1;48(8):2940-7.

[48] Yip CC, Lam CS, Luk HK, Wong EY, Lee RA, So LY, Chan KH, Cheng VC, Yuen KY, Woo PC, Lau SK. A six-year descriptive epidemiological study of human coronavirus infections in hospitalized patients in Hong Kong. *Virol Sin*. 2016 Feb 1;31(1):41-8.

[49] Lin K, Fong DY, Zhu B, Karlberg J. Environmental factors on the SARS epidemic: air temperature, passage of time and multiplicative effect of hospital infection. *Epidemiol Infect*. 2006 Apr;134(2):223-30.

[50] Al-Tawfiq JA, Memish ZA. Lack of seasonal variation of Middle East respiratory syndrome coronavirus (MERS-CoV). 2018. Available at: https://scholarworks.iupui.edu/bitstream/handle/1805/17636/Al-Tawfiq_2018_lack.pdf?sequence=1. Accessed 23 March 2020.

[51] Nassar MS, Bakhrebah MA, Meo SA, Alsuabeyl MS, Zaher WA. Global seasonal occurrence of middle east respiratory syndrome coronavirus (MERS-CoV) infection. *Eur Rev Med Pharmacol Sci*. 2018 Jun 1;22(12):3913-8.

[52] He D, Chiu AP, Lin Q, Cowling BJ. Differences in the seasonality of MERS-CoV and influenza in the Middle East. *Int J Infect Dis*. 2015 Nov;40:15.

[53] Climate Explorer. CRUv4 vapor pressure in blocks of two months averaged 2000-2018, based on station reports summarize to monthly averages. Interpretation in personal communication with Professor Mark Jury, PhD, from the University of Puerto Rico. Available at: https://climexp.knmi.nl/start.cgi. Accessed 22 March 2020.

[54] Centers for Disease Control (CDC). National, regional and state level outpatient illnesses and viral surveillance. Available at: https://gis.cdc.gov/grasp/fluview/fluportaldashboard.html. Accessed 23 March 2020.

[55] Thornton PE, Thornton MM, Mayer BW, Wei Y, Devarakonda R, Vose RS, and Cook RB. 2018. Daymet: Daily Surface Weather Data on a 1-km Grid for North America, Version 3. ORNL DAAC, Oak Ridge, Tennessee, USA. https://doi.org/10.3334/ORNLDAAC/1328

[56] Thornton PE, Running SW, White MA. 1997. Generating surfaces of daily meteorological variables over large regions of complex terrain. Journal of Hydrology 190: 214 - 251. https://doi.org/10.1016/S0022-1694(96)03128-9

[57] Caribbean Regional Climate Center, World Meteorological Association. Temperature Outlook for March-April-May 2020. Available at: http://rcc.cimh.edu.bb/temperature-outlook-march-april-may-2020/. Accessed 22 March 2020.

[58] Caribbean Regional Climate Center, World Meteorological Association. Temperature Outlook for March-April-May 2020. Available at: https://rcc.cimh.edu.bb/precipitation-outlook-march-april-may-2020/. Accessed 22 March 2020

[59] MacLean SA, Agyeman PO, Walther J, Singer EK, Baranowski KA, Katz CL. Characterization of the mental health of immigrant children separated from their mothers at the US–Mexico border. *Psychiatry Res*. 2019 Sep 4:112555.

[60] Weigel MM, Armijos RX. Food insecurity, Cardiometabolic health, and health care in US-Mexico border immigrant adults: An exploratory study. *J. Immigr. Minor. Health*. 2019 Oct 1;21(5):1085-94.

[61] Koleski J, Aldulaimi S, Moran E. From Dehydration to Fractures: Medical Issues Faced by People Crossing the United States: Mexico Border. *J. Immigr. Minor. Health*. 2019 Oct 1;21(5):1181-4.

[62] Rodriguez-Lainz A, DeSisto C, Waterman S, Wiedemann MS, Moore CW, Williams WW, Moser K. Influenza vaccination coverage among US-Mexico land border crossers: 2009 H1N1 pandemic and 2011–2012 influenza season. *Travel Med Infect Dis*. 2019 Jan 1;27:99-103.

[63] Klotzbach PJ, Bell MM, Jones J. Extended range forecast of Atlantic seasonal hurricane activity and landfall strike probability for 2020. Department of Atmospheric Science, Colorado State University. 2 April 2020.

[64] Caribbean Public Health Organization and Pan-American Health Organization. *Caribbean Health Climatic Bulletin*. 2020 March;1(4):1-3. Available at: **https://rcc.cimh.edu.bb/files/2020/03/Caribbean-Health-Climatic-Bulletin-Vol4-Issue1-March-2020.pdf**. Accessed: 20 March 2020.

[65] Laureano-Rosario AE, Duncan AP, Mendez-Lazaro PA, Garcia-Rejon JE, Gomez-Carro S, Farfan-Ale J, Savic DA, Muller-Karger FE. Application of artificial neural networks for dengue fever outbreak predictions in the northwest coast of Yucatan, Mexico and San Juan, Puerto Rico. *Trop Med Infect Dis*. 2018 Mar;3(1):5.

[66] Méndez-Lázaro P, Muller-Karger FE, Otis D, McCarthy M, Peña-Orellana M. Assessing Climate Change effects on dengue incidence in San Juan, Puerto Rico. *Int J Environ Res Public Health*. 2014;11(9), 9409-9428; doi:10.3390/ijerph110909409

[67] Guzman, Alfonso, and Raul E. Istúriz. "Update on the global spread of dengue." *Int J Antimicrob Agents.* 36 (2010): S40-S42.

[68] Pan American Health Organization. Countries and territories with autochthonous transmission of Zika virus in the Americas reported in 2015-2017. Washington DC: PAHO/WHO. Available at: https://www.paho.org/hq/index.php?option=com_content&view=article&id=11603:countries-and-territories-with-autochthonous-transmission-of-zika-virus-in-the-americas-reported-in-2015-2017&Itemid=41696&lang=en. Accessed: 22 March 2020

[69] Stapleford KA, Moratorio G, Henningsson R, Chen R, Matheus S, Enfissi A, Weissglas-Volkov D, Isakov O, Blanc H, Mounce BC, Dupont-Rouzeyrol M. Whole-genome sequencing analysis from the chikungunya virus Caribbean outbreak reveals novel evolutionary genomic elements. *PLoS Neglect Trop D*. 2016 Jan;10(1).

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[70] Akpinar-Elci M, Martin FE, Behr JG, and Diaz R. Saharan dust, climate variability, and asthma in Grenada, the Caribbean, *Int J Biometeorol*. 2015;59, 1667-1671.

[71] Matthew J, Bekele I and Pinto Pereira LM. Clinical features of a paediatric asthma population in Trinidad. *Clin Respir J*. 2013;7: 189–196.

[72] Prospero JM and Mayol-Bracero OL. Understanding the transport and impact of African dust on the Caribbean basin. *Bull Am Meteorol Soc*, 2013;94.9:1329-1337. DOI: 10.1175/BAMS-D-12-00142.1, 2013.

[73] Lewis LM, Mirabelli MC, Beavers SF, Kennedy CM, Shriber J, Stearns D, Morales González JJ, Santiago MS, Félix IM, Ruiz-Serrano K, Dirlikov E. Characterizing environmental asthma triggers and healthcare use patterns in Puerto Rico. *J Asthma*. 2019 Jun 5:1-2.

[74] Vesper S, Choi H, Perzanowski MS, Acosta LM, Divjan A, Bolaños-Rosero B, Rivera-Mariani F, Chew GL. Mold populations and dust mite allergen concentrations in house dust samples from across Puerto Rico. *Int J Environ Health Res*. 2016 Mar 3;26(2):198-207.