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The relationship between cyclonic weather regimes and seasonal influenza over the Eastern Mediterranean

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HIGHLIGHTS

• The occurrence of Cyprus Lows and Influenza are significantly correlated over Israel, the Palestinian Authority and Jordan.
• The occurrence of Cyprus Lows precedes the onset/maximum of Influenza incidence by 1-2 weeks and follows their timing.
• This relationship can be used to develop tools to estimate the compatibility of the environment for Influenza occurrence.

GRAPHICAL ABSTRACT

ABSTRACT

The prediction of the occurrence of infectious diseases is of crucial importance for public health, as clearly seen in the ongoing COVID-19 pandemic. Here, we analyze the relationship between the occurrence of a winter low-pressure weather regime - Cyprus Lows - and the seasonal Influenza in the Eastern Mediterranean. We find that the weekly occurrence of Cyprus Lows is significantly correlated with clinical seasonal Influenza in Israel in recent years (R = 0.91; p < .05). This result remains robust when considering a complementary analysis based on Google Trends data for Israel, the Palestinian Authority and Jordan. The weekly occurrence of Cyprus Lows precedes the onset and maximum of Influenza occurrence by about one to two weeks (R = 0.88; p < .05 for the maximum occurrence), and closely follows their timing in eight out of ten years (2008–2017). Since weather regimes such as Cyprus Lows are more robustly predicted in weather and climate models than individual climate variables, we conclude that the weather regime approach can be used to develop tools for estimating the compatibility of the transmission environment for Influenza occurrence in a warming world. Furthermore, this approach may be applied to other regions and climate sensitive diseases. This study is a new cross-border inter-disciplinary regional collaboration for appropriate adaptation to climate change in the Eastern Mediterranean.

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1. Introduction

The World Health Organization (WHO) has estimated that in 2012 approximately 12.6 million deaths (23% of all deaths worldwide) were attributed to changeable environmental factors, of which many could be potentially influenced by ongoing climate change (WHO, 2016). In addition, the Lancet Commission on Health and Climate Change determined that “Climate change could be the greatest public health threat of the 21st century” (Watts et al., 2015, 2017, 2018). There is clear evidence that climate change in the last 50 years has affected human health, partly by altering the epidemiology of climate sensitive diseases (e.g., Patz et al., 2005; Mirsaeidi et al., 2016). Specifically, climate change leads to alterations in the mean, variability, seasonality and/or extremes in one or more climatic variables such as temperature, precipitation, humidity, aerosols etc. These changes influence the dispersal of pathogens, the transmission environment and the host’s resilience (Vittecoq et al., 2017). Health effects related to climate change tend to emerge as seasonal and geographical alterations in the spread of disease (Wu et al., 2016; Dennis and Fisher, 2018; Hoogeveen, 2020).

Seasonal Influenza is a serious threat to public health, causing morbidity, mortality and absence from work and school (Osthus et al., 2017). According to data released by the Centers for Disease Control and Prevention of the United States, seasonal Influenza led to deaths (~80,000) and hospitalizations (~900,000) of more people in the United States in 2017–2018 than any Flu outbreak in decades (https://www.cdc.gov/flul/about/burden/2017-2018.htm). The European Centre for Disease Control estimated that illness associated with seasonal Influenza was responsible for 30% of the burden of infectious diseases in the case of Influenza (Weisheimer and Palmer, 2014). However, model forecasts are generally more robust in predicting weather regimes occurrences and timing (Weisheimer and Palmer, 2014; Grams et al., 2017). A weather regime can be considered as a capsule containing much of the information on the transmission environment, including the synergistic relations between individual climatic variables like temperature, precipitation, humidity and wind (Lamb, 1950, 1972; Stein and Alpert, 1993; Alpert and Sholokhman, 2011; Santos et al., 2016). Moreover, a weather regime approach also has the advantage of retaining the physical relationship between the individual climatic variables.

Weather regime classifications have been traditionally based on manual, compositing and machine learning techniques (Yarnal et al., 2001). However, these classifications cannot be immediately applicable to all regions. This has stimulated the development of a semi-objective synoptic classification targeted specifically at the south-eastern part of the Eastern Mediterranean region (Alpert et al., 2004a). The semi-objective synoptic classification describes well the local weather and has many implications (Alpert et al., 2004a, 2004b; Saaroni et al., 2010a, 2010b; Hochman et al., 2018a, 2018b, 2019a, 2019b, 2020; Faranda et al., 2017). For example, Hochman et al. (2018b) have provided evidence that by the end of the 21st century, the duration of the summer is projected to extend by 49% (+ –60 days), while the winter is expected to be shortened by 56% (−– 60 days) under the “business as usual” greenhouse gas scenario (RCP8.5). The authors (Hochman et al., 2018b) concluded that these alterations may lead to substantial changes in the timing of seasonal health hazards including seasonal influenza.

High-quality climatic and infectious disease information is sparse in some regions of the world, e.g., in several of the Eastern Mediterranean countries. In this respect, Google Trends is a freely accessible tool that may provide insights into population behavior and health related phenomena through the words people search in Google search engines. Nulti et al. (2014) reviewed the potential usage and limitations of Google Trends in healthcare research, and suggested a documentation procedure to improve reproducibility of the results. Recent studies have further concluded that social media data can aid in the surveillance of infectious diseases (Huang and Wang, 2018) such as Influenza (Santillana et al., 2015) and the Zika viruses (Adebayo et al., 2017). However, Lazer et al. (2014) have argued that the use of big data analysis, such as Google Flu Trends (GFT), should only be used as complementary information, rather than being used as a substitute to traditional clinical data collection and analysis.

For this study, we set a cross-border inter-disciplinary regional collaboration, composed of climatologists, epidemiologists and public health professionals from the Palestinian Authority, Israel and Germany (Hochman et al., 2020c). The purpose of this study is to investigate the potential link between weather regime occurrences and climate sensitive infectious diseases, and discuss in how far this relationship can help to inform decisions in the health sector. As a case study, the weekly occurrences of an Eastern Mediterranean weather regime - Cyprus Lows - together with precipitation, temperature and humidity, are related to seasonal influenza in Israel, the Palestinian Authority and Jordan.

2. Materials and methods

Climatic data were acquired from the National Centre for Environmental Prediction/National Centre for Atmospheric Research (NCEP/NCAR) reanalysis archive (Kalnay et al., 1996). We used daily values for 2004–2017 on a 2.5° × 2.5° horizontal grid spacing. The semi-
objective synoptic classification algorithm (Alpert et al., 2004a) was applied to NCEP/NCAR reanalysis variables including 1000 hPa Geopotential height, air temperature and horizontal wind components U and V at 25 grid points (27.5°N-37.5°N, 30°E-40°E, Fig. 1) over the Eastern Mediterranean. Five main groups of weather regimes (based on the original 19 weather regimes), were defined: The Persian Trough, dominant in summer; the Red Sea Trough, peaking in the autumn; the Sharav Low, often occurring in spring; the High-pressure systems appearing throughout the year; and Cyprus Lows, prevailing in winter. Cyprus Lows are mid-latitude low-pressure systems that tend to develop over the Eastern Mediterranean (Fig. 1). They are associated with cool air transport over the region, typically originating from Eastern Europe, over the warmer Mediterranean Sea where it becomes moist and unstable (Alpert et al., 1990). This air is transported towards Israel, the Palestinian Authority and Jordan, leading to wet conditions and low temperatures (Fig. 1). We further use average temperature at 2 m, accumulated precipitation, average specific humidity and average relative humidity over the same region in order to compare these individual climatic variables with our weather regime approach.

Epidemiological data were acquired from different open data sources for 2004–2017. These included the Israel Center for Disease Control (ICDC) weekly reports of positive specimens for Influenza out of total specimens collected by sentinel network at the Israeli Ministry of Health (hereafter Flu+) and the rate of weekly visits to “Maccabi Healthcare Services” clinics due to Influenza-Like-Illness (hereafter ILI, https://www.health.gov.il/English/MinistryUnits/ICDC/Infectious_diseases/Flu/Pages/FWR.aspx). In addition, we extract the Relative Search Volume (RSV) for the term “Influenza” by week. For Israel we used the Influenza term in Hebrew (תעפש). For the Palestinian Authority and Jordan, we used the Influenza term in Arabic (ل综合性). The Google Trends database was accessed on February 1st 2019 for Hebrew and on March 11th 2019 for Arabic (https://trends.google.co.il). We assume that these are the most widely searched terms in the three countries when considering Influenza occurrence. It is worth noting here that Google Trends data is analyzed as complementary information to the clinical Influenza data bases as recommended by Lazer et al. (2014), especially as clinical Influenza data is not available for the Palestinian Authority and Jordan. Moreover, the information we use in this study is based on raw RSV data rather than the GFT analysis (see Section 1).

All data were standardized to the 0–1 range in order to correlate and compare different data sources with different numerical values. Moreover, the seasonal cycle was computed and Taylor diagrams were portrayed (Taylor, 2001). A Taylor diagram can provide a concise statistical summary of how well the different data sources match each other in terms of their correlation, their root-mean-square difference and the
ratio of their variances. We further use a stepwise linear regression model to evaluate the weather regime and different meteorological variables relationship to the seasonal cycle of Influenza. The model was trained for 2008–2017 and validated on the 2004–2007 period. The student t-test is used to check for statistical significance of the correlation coefficients at the 5% significance level. Finally, we investigate the ability of the weather regime approach in depicting the onset and maximum occurrence of the Influenza season. The onset (maximum) is defined as the first week of the season with above zero (one) normalized incidence rates or weekly occurrence of Cyprus Lows. It should be noted that all datasets are Open Access for reproducibility and transparency and the modeling framework was validated as recommended by Walters et al. (2018).

3. Results

Data from the ICDC weekly reports of positive specimens for Influenza at the Israeli Ministry of Health (Flu+) and the rate of weekly visits to “Maccabi Healthcare Services” clinics due to Influenza-Like-Illness (ILI) are used to characterize the occurrence of seasonal Influenza in Israel for 2008–2017. These variables are positively related with the weekly occurrence of the Cyprus Lows, precipitation and relative humidity, and negatively related with temperature and specific humidity (Fig. 2a, b; Table S1). The weekly occurrence of Cyprus Lows has the highest correlation with weekly occurrence of Flu+ ($R = 0.91; p < 0.05$), while accumulated precipitation ($R = 0.6$), mean temperature ($R = −0.87$), specific humidity ($R = −0.83$) and relative humidity ($R = 0.81$) are also skillful. This strong link is found for both clinical Influenza occurrence data sources, i.e., Flu+ and ILI in Israel ($R = 0.84$ for Cyprus Lows). The weekly occurrence of Cyprus Lows depicts the average onset of Influenza occurrence at week 39 and the maximum occurrence at week 6 (Fig. 3). This reveals a preceding lag of 2 weeks for the onset and 1 week for the maximum occurrence. Again, this is true for the clinical weekly Influenza occurrence.

Additionally, the weekly Relative Search Volume (RSV) for the Influenza term in Google Trends were gathered separately for the three regions, i.e., Israel, Palestinian Authority and Jordan (details in Section 2). While the results are largely similar to the clinical Influenza data, Precipitation (Pr), Relative Humidity (RH) and Temperature (T2m) show the strongest correlation in all three regions when considering Google Trends data (Figs. 2, 4; Table S1). The reason may be that the individual variables have a strong impact on human behavior, which the Google Trends tool was designed to detect (Nuti et al., 2014). In terms of seasonality, Google Trends estimates the onset of Influenza at week 35 and the maximum occurrence at week 2 (Fig. 5). In this case, the Influenza onset and maximum precede all the climatic variables, with closer relation to weekly precipitation amounts (cf. Figs. 3 and 5). The observed seasonal occurrence of Influenza in all three regions using Google Trends is very similar (Fig. 5). The large similarity between the three countries suggests that indeed the regional environmental factors may play an important role. When analyzing the individual years in terms of ILI and Flu+ relationship to Cyprus Low occurrence, some year-to-year variability is identified (Fig. S1). For example, differences in the seasonality of Influenza between years with a relatively low occurrence of Cyprus Lows (e.g., 2013) compared to years with a higher occurrence (e.g., 2009). Still, the tight relationship between Cyprus Lows and Influenza is retained.

Fig. 2. Taylor diagrams for meteorological variables per week vs. seasonal Influenza data bases in Israel for 2008–2017 period. CL: number of Cyprus Lows; Pr: Cumulative Precipitation; −T2m: minus Average Temperature; −SH: minus Average Specific Humidity; RH: Average Relative Humidity. a) Flu+: percent of positive Influenza specimens in Israeli Ministry of Health b) ILI: Influenza incidence rate at Maccabi Healthcare Services clinics c) Google Trends Influenza: Relative Search Volume for the Influenza term by week (תራות in Hebrew – Google Trends accessed 1.2.2019).
Next, we quantify the relationship between the meteorological variables and seasonal Influenza occurrence in Israel. As a first choice, a stepwise multiple linear regression model is adopted for the relation between the predictors, i.e., Cyprus Lows and four individual meteorological variables (temperature, precipitation, specific humidity and relative humidity) and the predictand (Flu+) for 2008–2017. It is found that the number of Cyprus Lows per week can explain 82% of the variance with a root mean square difference of 0.14. Adding the other meteorological variables only marginally contributes to a higher explained variance (Table S2). Thus, the simple linear regression model between the weekly occurrence of Cyprus Lows and Flu+ developed for 2008–2017 is used to validate the occurrence of Influenza for 2004–2007. A significant correlation ($R = 0.78$) between modeled and observed Influenza occurrence is identified using the student t-test at the 5% significance level (Fig. 6). Furthermore, a close inspection of Fig. 6 suggests that the seasonal variability of Cyprus Lows closely follows the seasonal variability of Influenza occurrence, especially close to maximum occurrence of Influenza. In addition, we tested other potential regression models for predicting Flu+ from the weekly occurrence of Cyprus Lows. Only marginal improvement is shown for increasing order of polynomial or Sine non-linear models (Table S2).

Fig. 7 displays the relationship between the onset and maximum of the weekly occurrence of Cyprus Lows and Flu+ for 2008–2017. Considerable variability is shown in the onset (Fig. 7a) and maximum (Fig. 7b) of Influenza, which the Cyprus Lows weekly occurrence closely follows in eight out of ten years. The correlation between the onset of Cyprus Lows and Flu+ is 0.49 (Fig. 7a), while the correlation for the maximum occurrence is 0.88 (Fig. 7b). Again, the variability of the onset (maximum) of Cyprus Lows follows the variability of Flu+ onset (maximum).

The above analysis demonstrates the relationship between Cyprus Lows weekly occurrence and the weekly occurrence of Influenza.

4. Discussion and conclusions

In this study, we analyze the relationship between weather regimes and seasonal Influenza over the Eastern Mediterranean for the period 2004–2017. We find that Cyprus Low weekly occurrence has the highest significant correlation ($R = 0.91; p < .05$) with weekly clinical Influenza data over Israel with respect to individual climate variables such as precipitation, temperature, specific humidity and relative humidity. However, the individual climate variables show the highest correlations with Influenza when performing a complementary analysis for the Palestinian Authority, Jordan and Israel using Google Trends data. The weekly occurrence of Cyprus Lows precedes the onset and peak of Influenza occurrence with a lag of about 1 to 2 weeks, and a correlation for maximum occurrence of $R = 0.88 (p < .05)$. The evolution of both curves matches in eight out of ten years. This is an important finding, since the Influenza virus has ~3 days incubation period, and ~3 additional days until a patient visits a clinic and a few more days for positive virus identification.

The role of weather in the spread of Influenza is not yet fully understood. Thus, it is not possible to explicitly determine the biological mechanism relating Cyprus Lows and Influenza occurrence. However, the environmental setting given by the typical cold weather associated with the Cyprus Low may affect directly or indirectly Influenza through the host and/or the pathogen, i.e., the epidemiological triangle (e.g., Fuhmann, 2010). For example, the host susceptibility to infection during Cyprus Low days may increase due to seasonal hormonal
changes, which may be related to a reduction in exposure to sun light. For example, some studies suggest that low levels of Vitamin D may weaken the immune response (Cannell et al., 2006), while high levels may reduce the risk of both Influenza and COVID-19 infections and death (Grant et al., 2020; Merzon et al., 2020). Furthermore, rapid changes in weather, which may influence both the host susceptibility and the pathogen survival, can also increase the risk of an Influenza epidemic (Liu et al., 2020). Indeed, the winter season in the Eastern Mediterranean is typically associated with rapid changes in weather governed by transitions from Cyprus Lows to high-pressure systems (Alpert et al., 2004b). The strongest variability in weather regime transitions is especially evident in early winter (Faranda et al., 2017), which also corresponds to the onset of the Influenza season. In addition, the ability of the Influenza virus to cause infection is higher when the air is sufficiently cold (Polozov et al., 2008). Finally, studies have provided evidence that fluctuations in the duration of social contacts may relate to weather conditions (e.g., Smieszek, 2009; Willem et al., 2012). Indeed, indoor social contacts during Cyprus Low days may be more frequent and longer lasting.

The present results suggest that the weather regime approach can be used to develop a tool for estimating the compatibility of the Influenza transmission environment in a changing climate. This is particularly important, since weather and climate model forecasts are generally more robust in predicting weather regimes occurrences and timing than individual climatic variables, especially at regions distant from the El-Niño (e.g., Weisheimer and Palmer, 2014; Grams et al., 2017). This can be achieved by applying the methodology to sub-seasonal, seasonal, annual, decadal and even multi-decadal scales using climate model predictions / projections (Marotzke et al., 2016; Vitart and Robertson, 2018). We envisage that this novel approach could be applied to other regions (Soebiyanto et al., 2015; Chun et al., 2019) and infectious illnesses, such as vector-borne diseases and infectious gastroenteritis or even the SARS-CoV-2 and its associated disease COVID-19. Unfortunately, climatology tools and data are under-utilized in public health (Fuhrmann, 2010; Hochman et al., 2020c). This study exemplifies the potential for inter-disciplinary collaboration.

The present results and methodology can potentially be helpful for public health in practical terms, i.e., better understanding of the correlation between weather regimes and Influenza may improve vaccination policy and medical resources allocation. For example, health systems may roughly estimate the timing of seasonal Influenza surge and improve the timing of seasonal vaccination campaigns for the general population.

![Fig. 4. Same as Fig. 2c but for Google Trends Influenza in: a) Jordan and b) Palestinian Authority. (Influenza in Arabic “انفلونزا” – Google Trends accessed 11.3.2019).](image)

![Fig. 5. Annual cycle of seasonal Influenza and Cyprus Lows (CL) per week vs. Google Trends Influenza: Relative Search Volume rates for Influenza in the Palestinian Authority, Jordan and Israel. The annual cycle is computed for 2008–2017.](image)

### Table 1

| Predictors                  | R²   | RMSD |
|-----------------------------|------|------|
| Cyprus Lows                 | 0.82 | 0.14 |
| Temperature                 | 0.76 | 0.16 |
| Precipitation               | 0.36 | 0.26 |
| Relative humidity           | 0.66 | 0.19 |
| Specific humidity           | 0.68 | 0.19 |
| All predictors together     | 0.89 | 0.11 |
and actual illness patterns may help countries with limited monitoring of diseases to plan timely health promotion, including seasonal vaccination and campaigns for preventive measures, as well as plan allocation of medical resources. However, this type of information should not replace investments in traditional data gathering and analysis, but rather serve as a complement to it (Lazer et al., 2014). As a caveat, we note that seasonal Influenza occurrence, as most other infectious diseases, may be influenced by: vaccination effectiveness, public awareness, biological and socio-economic factors etc., which are not easily quantified and measured (Caini et al., 2018). We further note that laboratory confirmed Influenza cases may also suffer from inaccuracies. In fact, a recent review article that tested the quality of different laboratory tests for viral respiratory infections, including Influenza found that the pooled sensitivity of the different tests was 90.9% (95% confidence interval of 88.7%–93.1%) and specificity of 96.1% (95% confidence interval of 94.2%–97.9%; Vos et al., 2019). In addition, laboratory tests are indeed just the tip of the iceberg with respect to the actual incidence rates of Influenza or any other infectious disease.

Climatic changes and associated health risks know no borders. The challenges climate change pose to society and especially to public health, can be properly met only with regional collaborations as clearly revealed in the COVID-19 pandemic (Otu et al., 2020). This manuscript was prepared as part of a Jordanian, Palestinian, Israeli and German collaboration towards the establishment of a Regional Climate Change Adaptation Center (RCCAC). The collaborators are committed to this important regional trans-national cooperation, which will benefit the people of this vulnerable part of the world.

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CRediT authorship contribution statement

All authors have contributed to conceptual development of the study. AH performed the majority of the analysis and drafted the manuscript. AH was also partly supported by the Arava Institute for Environmental Studies as part of a project funded by the European Union.

Declarations of competing interest

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

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Data availability

The paper and/or the Supplementary Materials contain or provide instructions to access all the data needed to evaluate the conclusions drawn in the paper. Additional data is available from the corresponding author upon request.
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