Race and Sex Differences in Vital Signs Associated with COVID-19 and Flu Diagnoses in Mississippi

Brigitte E. Martin[1] · Michael R. Garrett[1,2,3]

Abstract

Early detection of viral infections, such as COVID-19 and flu, have potential to reduce risk of morbidity, mortality, and disease transmission through earlier intervention strategies. For example, detecting changes in vital signs have the potential to more rapidly diagnose respiratory virus diseases. The objective of this study was to utilize the University of Mississippi Medical Center's extensive clinical database (EPIC) to investigate associations between temperature, pulse rate, blood pressure (BP), and respiration rate in COVID-19 and flu diagnosed patients. Data from 1,363 COVID-19 (March 3, 2020, to February 27, 2021) and 507 flu (October 1, 2017, to September 30, 2018) diagnosed patients with reported demographic dimensions (age, first race, and sex) and office visit dimensions (BMI, diastolic BP, pulse rate, respiration rate, systolic BP, and temperature) was obtained, including day of diagnosis and additional encounter visits 60 days before and after first unique diagnosis. Patients with COVID-19 or flu were disproportionately obese, with 93% of COVID-19 and 79% of flu patients with BMI ≥ 30. Most striking, Black women 50–64 years of age disproportionately carried the burden of disease. At the time of diagnosis, temperature was significantly increased for all patients, yet pulse rate was only significantly increased for flu diagnosis, and BP was not significantly different in either. Our findings show the need for more complete demographic and office visit dimension data from patients during epidemic and pandemic events and support further studies needed to understand association between vital signs and predicting respiratory disease.

Keywords COVID-19 · Flu · Mississippi · Pulse rate · Temperature · Racial disparities

Introduction

Racial and ethnic disparities are clearly evident in certain types of infections common among women [1, 2]. These include sexually transmitted diseases and urinary tract infections, and more recently, women seem to be disproportionately positive for SARS-CoV-2, the virus that causes COVID-19 disease [3–5]. The Black population in Mississippi (MS) is 39% of the total population, the highest proportion in the USA. As of April 2021, the Black population in MS represented only one-third of COVID-19 cases, but over half of associated deaths [6]. Racial statistics are limited for other diseases, such as seasonal influenza virus due to being sparsely reported in 14 states [7]. Risk factors associated with increased morbidity and mortality for COVID-19 and other respiratory infections including influenza include a body mass index (BMI) of 30 or greater and advanced age [8–16]. Given that Mississippi has the highest prevalence of obesity (41%; obesity defined as BMI ≥ 30 [17]) in the USA, along with 46% of the Black population being obese or morbidly obese, the potential impact of respiratory disease is of concern. Additionally, sex differences in disease outcome are now coming to light, especially in COVID-19, indicating a larger risk of morbidity for men [18].

The inflammatory response during an infection can induce a fever that leads to an elevated heart rate [19]. For COVID-19, while there have been some studies to examine heart rate, none has identified a significant association with increased heart rate [20]. In contrast, other studies using wearable data monitoring devices that measure heart rate,

✉ Michael R. Garrett
  mrgarrett@umc.edu

1 Department of Pharmacology and Toxicology, University of Mississippi Medical Center, 2500 North State Street, Jackson, MS 39216, USA

2 Department of Medicine (Nephrology), University of Mississippi Medical Center, Jackson, MS, USA

3 Department of Pediatrics (Genetics), University of Mississippi Medical Center, Jackson, MS, USA

activity, and sleep have identified associations with influenza [21]. Early detection using these types of measurement have the potential to reduce risk of morbidity, mortality, and disease transmission through earlier intervention strategies. Thus, distinguishing patterns among vital signs, body temperature, pulse rate, respiration rate, and blood pressure, can help to more rapidly and accurately diagnose a potential respiratory virus.

The University of Mississippi Medical Center (UMMC) is Mississippi's only academic medical center and treats patients from across the state through its main campus, located in Jackson as well as two community hospitals. The objective of this study was to utilize UMMC's extensive clinical database to investigate the potential association between temperature, pulse rate, blood pressure, and respiration rate with COVID-19 and flu. In particular, the large Black population in Mississippi provides an opportunity to examine whether racial differences exist between these physiological parameters and respiratory diseases.

Materials and Methods

Data extracted from the UMMC Patient Cohort Explorer (PCE) [22] contains patient data derived from the electronic health record used on-site (EPIC) from January 1, 2013, through February 28, 2021. The data warehouse includes de-identified and date-shifted clinical information and does not include any protected health information (PHI). Pursuant to 45 CFR 46, use of this database does not meet the definition of human subjects' research and does not require IRB review.

COVID-19 patients were identified through the PCE COVID-19 Research Registry dashboard (March 3, 2020, to February 27, 2021), which were diagnosed as SARS-CoV-2 positive either by rapid antigen assay, reverse transcriptase polymerase chain reaction, or seropositivity. Patients with a diagnosis of flu were identified by the encounter diagnosis name "influenza A" or "influenza B," determined by rapid antigen assay, reverse transcriptase polymerase chain reaction, direct or indirect fluorescent staining, or viral culture. To note, diagnoses are only defined by a positive test and may not reflect a symptomatic state. The total number of flu patients (both influenza A and influenza B) from the 2017–2018 season is included in this study, October 1, 2017, to September 30, 2018. To control for variability for co-morbidities, flu diagnosed patients without any other previous diagnoses are compared to those previously diagnosed with essential (primary) hypertension (ICD-10 I10 [23]).

Mississippi population estimates of age, sex [24], race [25], and BMI [26] establish per capita frequencies. Chi-squared test ($\alpha = 0.05$) evaluates the association of positivity cases for disease diagnosis, age, sex, race, and BMI.

One-way ANOVA ($\alpha = 0.05$) assesses differences in office visit dimensions (BMI, diastolic blood pressure (BP), pulse rate, respiration rate, systolic BP, and temperature) among time relative to diagnosis, with post hoc tests Dunnett's multiple comparisons test ($\alpha = 0.05$) for differences between day of diagnosis and other time periods and Sidak's multiple comparisons test for differences among data within a time period.

Results

In total, 24,030 patients were identified as SARS-CoV-2 positive (COVID-19 diagnosis) from March 3, 2020, to February 27, 2021, and 4,050 patients were influenza A or influenza B positive (flu diagnosis) from October 1, 2017, to September 30, 2018 (Table S1). Patients with reported demographic dimensions (age, race, and sex) and office visit dimensions (BMI, diastolic blood pressure (BP), pulse rate, respiration rate, systolic BP, and temperature) for day of diagnosis and additional encounter visits within 60 days before and after first unique viral disease diagnosis are included in the analysis; 1,363 COVID-19 diagnosed patients and 507 flu diagnosed patients are ultimately included in the analysis (Table S2).

General Patient Demographics for COVID-19 and Flu

Patients diagnosed with COVID-19 or flu are stratified based on age or BMI (Fig. 1). During the time period studied, the peak of COVID-19 diagnosis occurs in 50–64-year-olds, which is approximately double the number of patients at the tail ends of the age spectrum. In contrast, there is no apparent association between flu diagnosis and age, as diagnosis was similar across all the age groups. Patients with COVID-19 or flu diagnoses are disproportionately obese, with 93% of COVID-19 and 79% of flu patients having a BMI $\geq$ 30.

The diagnoses grouped by race and sex reveal that more Black females have a diagnosis of COVID-19 or flu compared to White females, while Black males have a diagnosis of COVID-19 twice that compared to white males (Fig. 2A and C). Black female patients ages 50–64 disproportionately represent infected patients in the Black population, with 18% COVID-19 diagnosis and 13% flu diagnosis. Additionally, 70% of COVID-19 and 53% of flu patients are Black with a BMI $\geq$ 30 and 60% of COVID-19 and 54% of flu patients are females with BMI $\geq$ 30 (Fig. 2B and D). Black female patients have the most diagnosis for COVID-19 and have BMI > 40 (22%) and for flu have BMI between 30 and 39 (17%).

Overall, there are disproportional diagnoses in Black female patients composing the highest number of COVID-19 (51%) and flu (45%) patients. Additionally,

Fig. 1 Respiratory virus patient demographics. COVID-19-positive patients ($n = 1363$) and flu-positive patients ($n = 507$) stratified by age (**A**) and BMI (**B**). Chi-square analysis shows a significant association of virus diagnosis with BMI ($p < 0.0001$) and age (0.002)
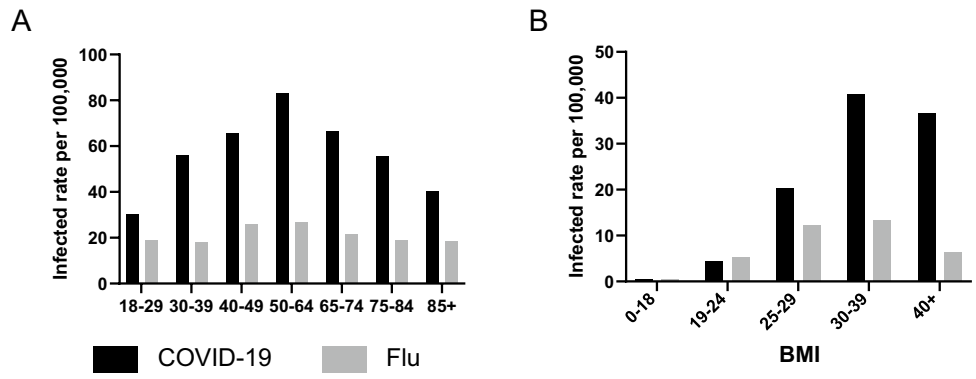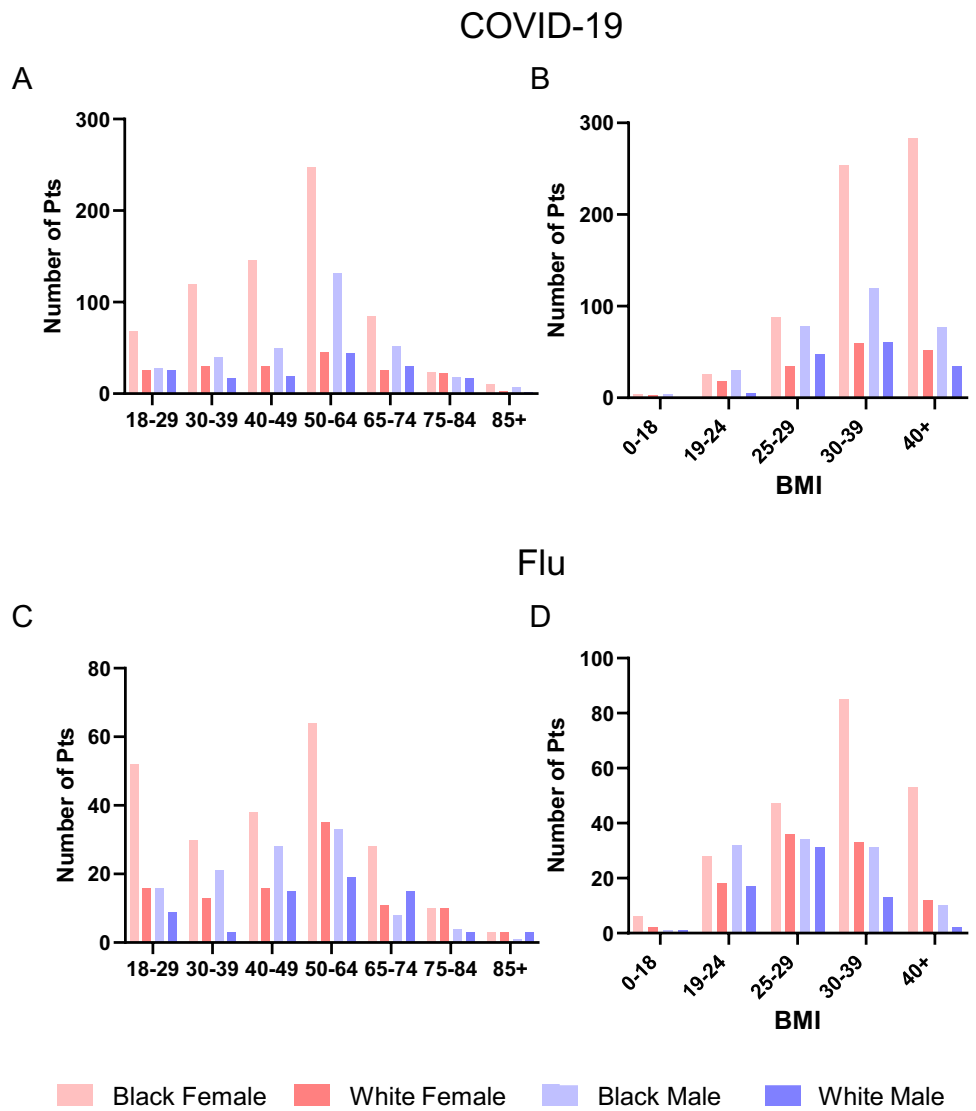
Fig. 2 Distribution of age by sex and race for COVID-19 positive patients (**A**) and flu positive patients (**C**) and distribution of BMI by sex and race for COVID-19 positive patients (**B**) and flu positive patients (**D**)

Black female patients with BMI ≥ 30 are the majority infected with both COVID-19 (42%) and flu (30%). Black female patients with the highest number of diagnoses are 50–64 years old with BMI ≥ 30 with 15% of

total COVID-19 and 12% of total flu patients being Black female of 50–64 years old with BMI ≥ 30.

Disease Dynamics Based on Vital Signs

The data of vital sign measurements are presented relative to first unique viral diagnosis and grouped into − 60 to − 31 days before diagnosis (− 2 months), − 30 to − 1 days before diagnosis (1 month), day of diagnosis (0), 1 to 30 days after diagnosis (1 month), and 31 to 60 days after diagnosis (2 months). For temperature in COVID-19 patients, there is a significant difference among the time points ($p < 0.0001$; one-way ANOVA ($\alpha = 0.05$)) with day of diagnosis significantly different from every other time point (vs − 2 months and − 1 month $p < 0.0001$ and vs 1 month and 2 months $p = 0.0001$ and 0.0002, respectively; Dunnett's multiple comparisons test ($\alpha = 0.05$); Fig. 3a). COVID-19 patients have an average increase of 0.54°F from the average temperature throughout the timeline; pre- and post-diagnosis temperature range from 93.2 to 103.1°F and day of diagnosis temperatures range from 96.0 to 101.6°F (Fig. 3b). Temperature is also significantly different for flu patients, $p < 0.0001$, with the day of diagnosis having statistical difference between every other time point ($p < 0.0001$ for all;

Fig. 3c). Flu patients have an average increase of 1.00°F from the average temperature throughout the timeline; pre- and post-diagnosis temperature range from 95.1 to 100.7°F and day of diagnosis temperatures range from 96.1 to 103.0°F (Fig. 3d).

COVID-19 diagnosed patients do not have significant differences in pulse rate across the time of study. For flu patients, there is a significant difference within the timeline ($p < 0.0001$) with day of diagnosis being significantly different from every time point ($p < 0.0001$ for all, Fig. 4a). Flu patients have an average increase of 7.6 beats per minute (bpm) from the average pulse rate throughout the timeline; pre- and post-diagnosis pulse rate range from 51.0 to 146.4 bpm and day of diagnosis pulse rate ranges from 53.0 to 164.0 bpm (Fig. 4b).

Demographic Biases in Diagnosis Dynamics

Given the potential impact of patient demographics on diagnosis as described above, we examined clinical parameters striated by sex and race at each time point. This analysis was focused on flu patients due to more office visit dimension data available for patients before, during, and after flu diagnosis.

Fig. 3 Temperature dynamics during COVID-19 and flu diagnoses. Temperature for each patient was grouped relative to day of diagnosis − 60 to − 31 days before diagnosis (− 2 months), − 30 to − 1 days before diagnosis (1 month), day of diagnosis (0), 1 to 30 days after diagnosis (1 month), and 31 to 60 days after diagnosis (2 months) for COVID-19 (**A**) and flu (**C**) diagnosed patients; mean denoted by cross (* *p*-value < 0.0001). The average temperature for each day within − 60 to 60 days post diagnosis (grey circles) and 7-day moving average (Black line) shows the time course of temperature dynamics in COVID-19 (**B**) and flu (**D**) diagnosed patients
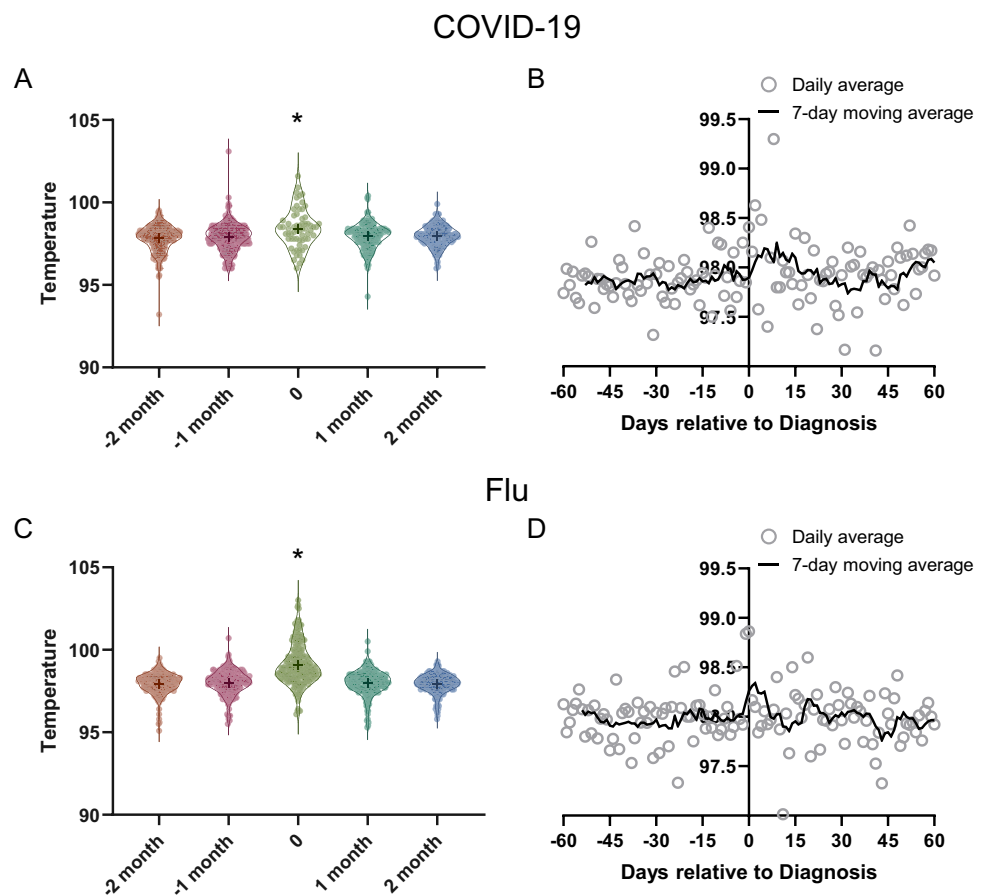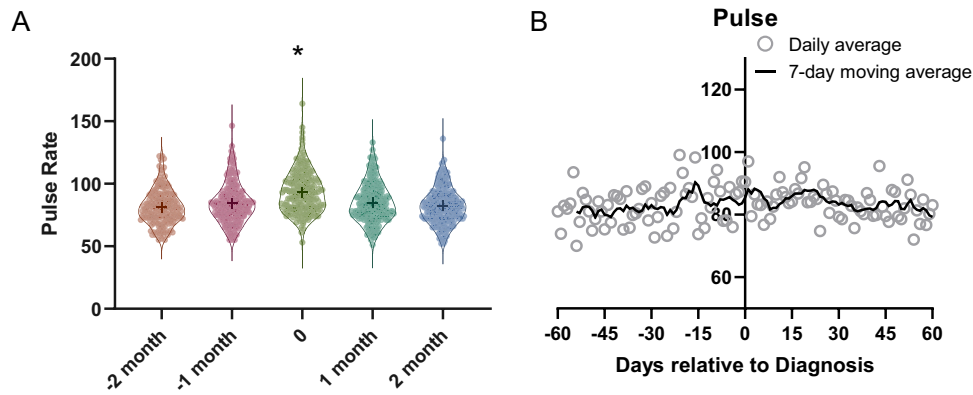
Fig. 4 Pulse rate dynamics during flu diagnosis. Pulse rate for each patient was grouped relative to day of diagnosis − 60 to − 31 days before diagnosis (− 2 months), − 30 to − 1 days before diagnosis (1 month), day of diagnosis (0), 1 to 30 days after diagnosis (1 month), and 31 to 60 days after diagnosis (2 months) (**A**); mean denoted by cross (* *p*-value < 0.0001). The average temperature for each day within − 0 to 60 days post diagnosis (gray circles) and 7-day moving average (black line) show the time course of pulse rate dynamics in flu diagnosed patients (**B**)

The average and standard deviation of the office visit dimensions were calculated for each of the discrete time points for four sex and race groups (Black female, White female, Black male, and White male) and tested for statistical difference using one-way ANOVA independently (Table 1). For temperature, all four groups are statistically

Table 1 Average and standard deviation (in parenthesis) are reported for each office visit dimension for each sex and race group for the discrete time periods of − 60 to − 31 days before diagnosis (− 2 months), − 30 to − 1 days before diagnosis (1 month), day of diagnosis (0), 1 to 30 days after diagnosis (1 month), and 31 to 60 days after diagnosis (2 months). One-way ANOVA ($\alpha = 0.05$) was performed for each office visit dimension to obtain *p*-value

	− 2 months	− 1 month	0	1 month	2 months	*p*-value
Female Black or African American (*n* = 225)						
Temperature (F)	98.02 (0.58)	98.05 (0.64)	99.36 (1.19)	98.07 (0.73)	98 (0.52)	< 0.0001
Pulse rate	81.98 (11.67)	83.71 (14.86)	94.74 (14.88)	83.12 (12.45)	82.38 (12.63)	< 0.0001
Systolic BP	134.7 (17.61)	134.1 (25.49)	134.5 (19.49)	129 (19.94)	131.3 (21.58)	0.2234
Diastolic BP	78.33 (11.47)	78.27 (13.61)	80.44 (13.23)	77.02 (11.92)	75.94 (12.05)	0.1302
Respiration rate	18.54 (2.15)	17.83 (1.99)	17.74 (1.94)	17.8 (2.1)	18.25 (1.81)	0.1756
Female White or Caucasian (*n* = 104)						
Temperature (F)	97.93 (0.67)	97.92 (0.84)	98.86 (1.26)	97.95 (0.63)	97.9 (0.5)	< 0.0001
Pulse rate	79.2 (13.75)	82.44 (13.67)	96.4 (18.61)	81.84 (13.18)	79.93 (14.66)	< 0.0001
Systolic BP	130 (19.48)	129.7 (22.37)	127.6 (13.46)	129.2 (15.67)	131.2 (16.08)	0.3626
Diastolic BP	73.36 (12.9)	73 (12.36)	76.25 (9.71)	72.72 (12.83)	75.18 (10.75)	0.4004
Respiration rate	17.95 (1.76)	18.5 (2.26)	18.2 (1.53)	19.05 (2.55)	18.83 (1.65)	0.279
Male Black or African American (*n* = 111)						
Temperature (F)	97.89 (0.67)	98.9 (1.13)	97.99 (0.83)	97.99 (0.83)	97.83 (0.68)	< 0.0001
Pulse rate	86.91 (15.99)	89.95 (18.4)	88.61 (15.48)	90.75 (17.17)	87.52 (12.46)	0.7405
Systolic BP	125.8 (16.61)	131.6 (16.49)	132.9 (19.83)	129 (17.59)	130.1 (15.99)	0.3316
Diastolic BP	76.75 (8.67)	77.66 (11.99)	80.25 (12.65)	80.45 (10.47)	79.58 (11.77)	0.4029
Respiration rate	18.38 (1.26)	18.59 (2.16)	18.33 (1.98)	18.33 (1.98)	18.46 (1.61)	0.9796
Male White or Caucasian (*n* = 67)						
Temperature (F)	97.76 (0.73)	97.96 (0.81)	98.82 (1)	97.86 (0.69)	98.11 (0.52)	< 0.0001
Pulse rate	73.52 (40)	79.52 (40)	85.8 (40)	82.54 (40)	78.67 (40)	0.0546
Systolic BP	131.9 (12.01)	126.4 (15.43)	127.2 (19.9)	133.5 (16.53)	126.7 (17.15)	0.3894
Diastolic BP	76.37 (9.11)	75 (11.86)	77.61 (12.35)	78.35 (13.02)	71.11 (10.11)	0.0942
Respiration rate	17.84 (2)	18 (1.71)	18.84 (1.99)	19.15 (1.14)	18 (2.37)	0.2686

significant ($p < 0.0001$, for all). Comparison among the groups within a time point, using Sidak's multiple comparisons test ($\alpha = 0.05$), shows that White males have a significantly higher temperature at -1 month before flu diagnosis than all other groups. At day of diagnosis, White females and white males are not significantly different from each other, yet Black females and Black males are significantly different from all other groups.

For pulse rate, only the female groups have a significant difference in pulse rate ($p < 0.0001$) while the male groups are not significantly different (Fig. 5). Black females and White females have an average increase of 12.0 and 15.6 bpm, respectively, from the average pulse rate throughout the timeline; pre- and post-diagnosis pulse rates range from 55.0 to 130.0 bpm (Black females) and 54.0 to 116.0 bpm (White females) and day of diagnosis pulse rates range from 72.0 to 164.0 bpm (Black females) and 69.0 to 145.0.0 bpm (White females). Additionally, comparison among the groups within a time point shows differences in race and/or sex at -2 months, day of diagnosis, and 1 month (Fig. 5). Overall, White females have a greater increase in pulse rate at day of diagnosis while Black females have a larger range or increased pulse rates at day of diagnosis. Blood pressures and respiration rate were not significantly different at day of diagnosis for any of the groups.

To determine if pre-existing diseases could bias office visit dimensions, patients with no pre-existing diagnosis ($n = 57$) were compared to those with essential (primary) hypertension ($n = 234$). There is a significant difference in systolic BP at day of diagnosis, with CVD having an average systolic BP of 131.29 compared to 138.90 of flu only patients. Temperature is significantly lower in CVD patients -1 month and day of diagnosis compared to flu only patients; the difference in temperature increase from average across the timeline for CVD patients was 1.10°F while flu

only patients had an average increase of 1.13°F. Pulse rate significantly changed across visits, peaking at diagnosis, but was not significantly different between those with flu only compared to flu and CVD (Table S3). The average increase in pulse rate for CVD patients was 11.42, slightly higher than flu only patients which was 8.30. Thus, we found no significant evidence that pre-existing diseases affect office dimensions.

Discussion

For Mississippi, COVID-19 cases and deaths are reported by race but not for flu virus at either the country (CDC) or state (MSDH) levels. Age, sex, and race seem to play a vital role in diagnosis population statistics, and more complete demographic reports are necessary to understand the role of disparities. Factors, such as reported BMI, show a vital role in COVID-19 and flu patients. Obesity was a risk factor for severe morbidity or mortality upon infection for COVID-19 [10] and the 2009 pandemic H1N1 virus [27–33] as well as an increasing risk of hospitalization for both pandemic and non-pandemic flu infections with an increase in BMI [34, 35]

Global data shows little difference of COVID-19 case numbers based on sex [36], yet in this study (during the period studied), we found that women in Mississippi have the highest number of COVID-19 and flu diagnoses. Taking into account sex disparities across racial groups, we found overall that Black women have the greatest number of diagnoses for both viruses further showing the limitation of unidimensional reporting that relies on only sex or racial statistics alone (also highlighted by [37]). This study adds another example of how Black women in the US continue

Fig. 5 Pulse rate dynamics during flu diagnosis for 4 sex and race groups. Pulse rate for each patient was grouped relative to day of diagnosis -60 to -31 days before diagnosis (-2 months), -30 to -1 days before diagnosis (1 month), day of diagnosis (0), 1 to 30 days after diagnosis (1 month), and 31 to 60 days after diagnosis (2 months); mean denoted by cross. Comparison among the groups within a time point was completed with Sidak's multiple comparisons test ($\alpha = 0.05$), * p-value < 0.05
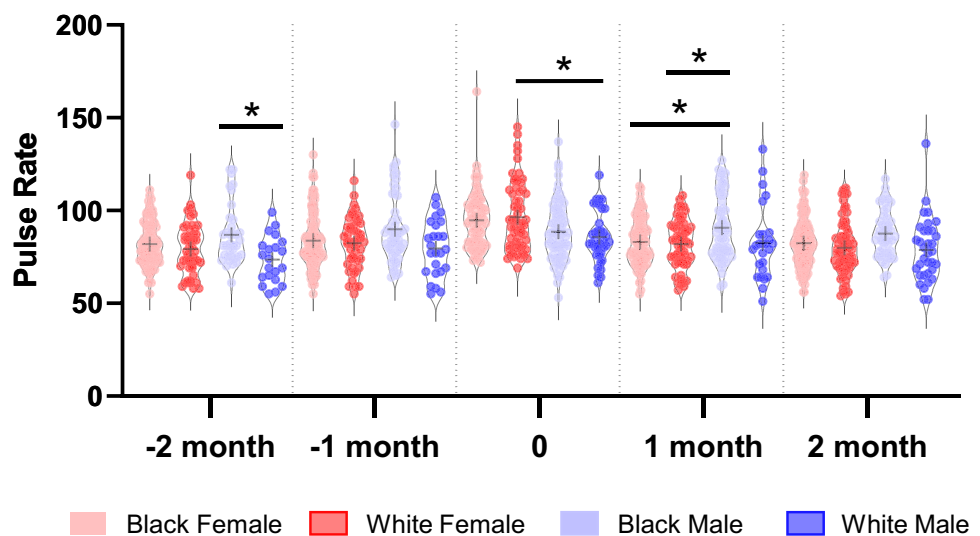
to have health inequalities that contribute to greater burden of disease [38].

Social distancing has been recommended in past pandemics, including influenza virus, to limit or stop the spread of highly transmissible diseases [39, 40]. Those groups with less social isolation and social distancing may be more likely to be infected with highly transmissible viruses. This could be the case with middle-aged women in this study with the most diagnosis. Higher social interactions, deferring from CDC guidelines for slowing the spread of COVID-19 [41], and coming into contact with children and teenagers have all been noted to play an important role in disease transmission [42]. In all data, for COVID-19, there were 190 patients diagnosed with pregnancy or postpartum with age ranging from 14–42 and for flu, there were 114 patients diagnosed with pregnancy or postpartum in the 18–38 age range. However, all these patients were excluded from this study due to lack of office visit dimensions. Additionally, with the majority of diagnosis being infected women ranging from 50 to 64 years old age group, one factor that is not addressed in the PCE database is if these women are currently in menopause. Menopause, typically occurring between ages of 50 and 52, has been linked, albeit in lean women, lower lung function in menopausal women [43]. Although there is no racial difference in the start of menopause, there is a significant difference in location with those in southern states which have earlier menopause than the rest of the USA [44].

The overarching goal for the identification of vital signs using non-invasive monitoring is to be able to determine a viral infection before symptom onset. Asymptomatic infections are common in COVID-19 and flu, and transmission still occurs to naïve individuals [45–47]. Faster application of interventions can reduce virus replication and spread; for example, the commonly used anti-flu drug oseltamivir (Tamiflu) is more effective when taken within 48 h of symptom onset [48], yet most do not seek clinical intervention until 3–8 days post symptom onset [49].

In this study, we primarily saw significant variations from the average at the day of disease diagnosis but not before. We show a significant difference from baseline in pulse rate of flu diagnosed patients, similar to other findings [50], but no significant difference in COVID-19 diagnosed patients as others were unable to find as well [20]. On the other hand, increased temperature is a well-known marker for infection. A fever is defined as a temperature at or above 100.4°F, yet the average oral temperature has decreased from 98.6 to 97.9°F without a change in guidelines for fever. As found here, an increase of 0.5°F for COVID-19 and 1.0°F for flu could be substantial enough to suspect a viral infection.

We do not see a significant change in blood pressure before and after diagnosis from date of diagnosis. This could be due to multiple factors including direct and indirect interventions, including cold medicines and blood pressure medicines, respectively, that could potentially stabilize blood pressure from increasing during infection. Those with CVD and flu diagnosis do have higher BP than those with flu diagnosis only, yet there is still no difference in BP on day of diagnosis compared to their BP before and after diagnosis.

Importance of disease outcome, including mortality, could further inform about differences found at day of diagnosis, leading to information for prognosis prediction. One major caveat to consider in this study relates to lack of patient death information. Neither date of death nor cause of death is logged; additionally, death is only added into EPIC if mortality is reported to the hospital, or the patient has died within the hospital umbrella system. With this in mind, we are unable to assess risk of disease fatality in this study and their relation to difference found at day of diagnosis in order to compare to national averages for COVID-19 and flu found by others [51–53].

Conclusions

Our findings show the need for more complete demographic and office visit dimension data from patients during epidemic and pandemic events. In this study, we find that disease burden is greater in Black women in 50–64 age group for COVID-19 and flu virus in the Mississippi population. For all patients at the time of diagnosis, temperature is significantly increased for both respiratory viruses and pulse rate is significantly increased for flu virus diagnosis. This data is consistent with previous research and supports the idea that these vital sign measurements could provide early indication of infection with application of wearable devices.

Declarations

Conflict of Interest The authors declare no competing interests.

References

1. Jones CP, Ogbara T, Braveman P. Disparities in infectious diseases among women in developed countries. Emerg Infect Dis. 2004;10(11):e20–e20.

2. Vahidy FS, et al. Racial and ethnic disparities in SARS-CoV-2 pandemic: analysis of a COVID-19 observational registry for a diverse US metropolitan population. BMJ Open. 2020;10(8):e039849.

3. Davido B, et al. Post–COVID-19 chronic symptoms: a postinfectious entity? Clin Microbiol Infect. 2020;26(11):1448–9.

4. Torjesen I. Covid-19: Middle aged women face greater risk of debilitating long term symptoms. BMJ. 2021;372:n829.

5. Evans RA et al. Physical, cognitive and mental health impacts of COVID-19 following hospitalisation – a multi-centre prospective cohort study. medRxiv. 2021: 2021.03.22.21254057.

6. MSDH. Mississippi State Department of Health: Coronavirus Disease 2019 (COVID-19). 2021.

7. Chaves SS, et al. The US influenza hospitalization surveillance network. Emerg Infect Dis. 2015;21(9):1543–50.

8. Malik VS, et al. Higher body mass index is an important risk factor in COVID-19 patients: a systematic review and meta-analysis. Environ Sci Pollut Res Int. 2020;27(33):42115–23.

9. Philipose Z et al. Obesity, old age, and frailty are the true risk factors for COVID-19 mortality and not chronic disease or ethnicity. medRxiv. 2020: 2020.08.12.20156257.

10. O'Hearn M, et al. Coronavirus disease 2019 hospitalizations attributable to cardiometabolic conditions in the United States: a comparative risk assessment analysis. J Am Heart Assoc. 2021;10(5):e019259.

11. Control, C.f.D. People with certain medical conditions. 2021 June 21, 2021; Available from: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html.

12. Hendren NS, et al. Association of body mass index and age with morbidity and mortality in patients hospitalized with COVID-19. Circulation. 2021;143(2):135–44.

13. Moser J-AS, et al. Underweight, overweight, and obesity as independent risk factors for hospitalization in adults and children from influenza and other respiratory viruses. Influenza Other Respir Viruses. 2019;13(1):3–9.

14. Honce R, Schultz-Cherry S. Impact of obesity on influenza a virus pathogenesis, immune response, and evolution. Front Immunol. 2019;10:1071.

15. Han Y-Y, et al. Obesity and rhinitis in a nationwide study of children and adults in the United States. J Allergy Clin Immunol. 2016;137(5):1460–5.

16. Baik I, et al. A prospective study of age and lifestyle factors in relation to community-acquired pneumonia in US men and women. Arch Intern Med. 2000;160(20):3082–8.

17. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: executive summary. Expert panel on the identification, evaluation, and treatment of overweight in adults. Am J Clin Nutr. 1998;68(4):899–917.

18. Peckham H, et al. Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ITU admission. Nat Commun. 2020;11(1):6317.

19. Karjalainen J, Viitasalo M. Fever and cardiac rhythm. Arch Intern Med. 1986;146(6):1169–71.

20. Quer G, et al. Wearable sensor data and self-reported symptoms for COVID-19 detection. Nat Med. 2021;27(1):73–7.

21. Radin JM, et al. Harnessing wearable device data to improve state-level real-time surveillance of influenza-like illness in the USA: a population-based study. Lancet Digit Health. 2020;2(2):e85–93.

22. University of Mississippi Medical Center, C.f.I.a.A., Patient cohort explorer. 2020.

23. Organization, W.H. International statistical classification of diseases and related health problems (10th ed.). 2016.

24. U.S. Census Bureau, P.D. Annual Estimates of the Resident Population for Selected Age Groups by Sex for Mississippi: April 1, 2010 to July 1, 2019 (SC-EST2019-AGESEX-28). 2020.

25. U.S. Census Bureau, P.D. Annual Estimates of the Resident Population by Sex, Race, and Hispanic Origin for Mississippi: April 1, 2010 to July 1, 2019 (SC-EST2019-SR11H-28). 2020.

26. CDC. Behavioral risk factor surveillance system. 2019.

27. Flegal KM, et al. Prevalence and trends in obesity among US adults, 1999–2008. JAMA. 2010;303(3):235–41.

28. Gill JR, et al. Pulmonary pathologic findings of fatal 2009 pandemic influenza A/H1N1 viral infections. Arch Pathol Lab Med. 2010;134(2):235–43.

29. Morgan OW, et al. Morbid obesity as a risk factor for hospitalization and death due to 2009 pandemic influenza A(H1N1) disease. PLoS One. 2010;5(3):e9694.

30. Thompson DL, et al. Risk factors for 2009 pandemic influenza A (H1N1)-related hospitalization and death among racial/ethnic groups in New Mexico. Am J Public Health. 2011;101(9):1776–84.

31. Vaillant L. et al. Epidemiology of fatal cases associated with pandemic H1N1 influenza 2009. Euro Surveill. 2009;14(33).

32. Venkata C, Sampathkumar P, Afessa B. Hospitalized patients with 2009 H1N1 influenza infection: the Mayo Clinic experience. Mayo Clin Proc. 2010;85(9):798–805.

33. Louie JK, et al. Factors associated with death or hospitalization due to pandemic 2009 influenza A(H1N1) infection in California. JAMA. 2009;302(17):1896–902.

34. Cocoros NM, et al. Obesity as a risk factor for severe influenza-like illness. Influenza Other Respir Viruses. 2014;8(1):25–32.

35. Martín V, et al. High body mass index as a risk factor for hospitalization due to influenza: a case-control study. Arch Bronconeumol. 2016;52(6):299–307.

36. 5050. G.H. COVID-19 sex disaggregated data tracker. 2020 June 23, 2021; Available from: https://globalhealth5050.org/covid19/sex-disaggregated-data-tracker.

37. Rushovich T, et al. Sex disparities in COVID-19 mortality vary across US racial groups. J Gen Intern Med. 2021;36(6):1696–701.

38. Chinn JJ, Martin IK, Redmond N. Health equity among Black women in the United States. J Womens Health. 2020;30(2):212–9.

39. Markel H, et al. Nonpharmaceutical interventions implemented by US cities during the 1918–1919 influenza pandemic. JAMA. 2007;298(6):644–54.

40. Control, C.f.D. Social Distancing. 2020 June 22, 2021; Available from: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/social-distancing.html#:~:text=Since%20people%20can%20spread%20the,severe%20illness%20from%20COVID%2D19.

41. CDC. How to protect yourself & others. 2021.

42. Glass RJ, et al. Targeted social distancing design for pandemic influenza. Emerg Infect Dis. 2006;12(11):1671–81.

43. Real FG, et al. Lung function, respiratory symptoms, and the menopausal transition. Journal of Allergy and Clinical Immunology. 2008;121(1):72-80.e3.

44. McKnight KK, et al. Racial and regional differences in age at menopause in the United States: findings from the REasons for Geographic And Racial Differences in Stroke (REGARDS) study. Am J Obstet Gynecol. 2011;205(4):353.e1-353.e3538.

45. World Health Organization Writing, G., et al. Non-pharmaceutical interventions for pandemic influenza, international measures. Emerg Infect Dis. 2006;12(1):81–7.

46. Hayward AC, et al. Comparative community burden and severity of seasonal and pandemic influenza: results of the Flu Watch cohort study. Lancet Respir Med. 2014;2(6):445–54.

47. Sah P, et al. Asymptomatic SARS-CoV-2 infection: a systematic review and meta-analysis. Proc Natl Acad Sci. 2021;118(34):e2109229118.

48. CDC. Influenza antiviral medications: summary for clinicians. 2021 November 11, 2021; Available from: https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm.

49 Radin JM, et al. Epidemiology of pathogen-specific respiratory infections among three US populations. PLOS ONE. 2015;9(12):e114871.

50. Williams DP, et al. Heart rate variability and inflammation: a meta-analysis of human studies. Brain Behav Immun. 2019;80:219–26.

51. Wong JY, et al. Case fatality risk of influenza A (H1N1pdm09): a systematic review. Epidemiology (Cambridge, Mass). 2013;24(6):830–41.

52. Elezkurtaj S, et al. Causes of death and comorbidities in hospitalized patients with COVID-19. Sci Rep. 2021;11(1):4263.

53. Faust JS, del Rio C. Assessment of deaths from COVID-19 and from seasonal influenza. JAMA Intern Med. 2020;180(8):1045–6.