Health-care workers with COVID-19 living in Mexico City: clinical characterization and related outcomes

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Commentary: We explored prevalence of SARS-CoV-2, symptoms, and risk factors associated with adverse outcomes in HCWs in Mexico City. Particular attention should focus on HCWs with risk factors to prevent adverse outcomes and reduce infection risk.

ABSTRACT

BACKGROUND: Health-care workers (HCWs) could be at increased occupational risk for SARS-CoV-2 infection. Information regarding prevalence and risk factors for adverse outcomes in HCWs is scarce in Mexico. Here, we aimed to explore prevalence of SARS-CoV-2, symptoms, and risk factors associated with adverse outcomes in HCWs in Mexico City.

METHODS: We explored data collected by the National Epidemiological Surveillance System in Mexico City. All cases underwent real-time RT-PCR test. We explored outcomes related to severe COVID-19 in HCWs and the diagnostic performance of symptoms to detect SARS-CoV-2 infection in HCWs.

RESULTS: As of July 5th, 2020, 35,095 HCWs were tested for SARS-CoV-2 and 11,226 were confirmed (31.9%). Overall, 4,322 were nurses (38.5%), 3,324 physicians (29.6%), 131 dentists (1.16%) and 3,449 laboratory personnel and other HCWs (30.8%). After follow-up, 1,009 HCWs required hospitalization (9.00%), 203 developed severe outcomes (1.81%), and 93 required mechanical-ventilatory support (0.82%). Lethality was recorded in 226 (2.01%) cases. Symptoms associated with SARS-CoV-2 positivity were fever, cough, malaise, shivering, myalgias at evaluation but neither had significant predictive value. We also identified 341 asymptomatic SARS-CoV-2 infections (3.04%). Older HCWs with chronic non-communicable diseases, pregnancy, and severe respiratory symptoms were associated with higher risk for adverse outcomes. Physicians had higher risk for hospitalization and for severe outcomes compared with nurses and other HCWs.

CONCLUSIONS: We report a high prevalence of SARS-CoV-2 infection in HCWs in Mexico City. No symptomatology can accurately discern HCWs with SARS-CoV-2 infection. Particular attention should focus on HCWs with risk factors to prevent adverse outcomes and reduce infection risk.

Keywords: COVID-19; SARS-CoV-2; Health-Care Workers; Mortality; Mexico

INTRODUCTION

The pandemic caused by the SARS-CoV-2 has created new challenges in health-care systems worldwide (1). Recently, the pandemic has had significant increases in the number of cases in the Americas, where it has caused considerable pressure on health-care facilities and led to a substantial number of deaths (2,3). Health-care workers (HCWs) have a fundamental role in caring and managing patients with COVID-19, being the primary workers involved in the daily management of the pandemic at an individual level. Notably, this population could be at increased occupational risk of acquiring SARS-CoV-2 infection, which ultimately could lead to an increased risk of associated COVID-19 complications. Although it has been emphasized that HCWs with respiratory symptoms should be isolated as soon as possible and protective equipment has been provided in several facilities, there is no consensus on the essential symptoms to promptly identify positive cases to mitigate transmission risks (4). This was previously reported in the Influenza A(H1N1) pandemic in 2009 with increased risk for influenza in early periods of the pandemic for HCWs, which alongside social disparities could represent a challenge to HCWs, particularly in developing countries (5,6).

The situation in Mexico is complex, given that SARS-CoV-2 infections coexist with a high prevalence of comorbidities associated with COVID-19 complications in a large proportion of patients, including HCWs. Furthermore, healthcare systems within Mexico are highly fragmented and quality of care and the ability to protect HCWs within each institution is highly heterogeneous due to structural inequalities, which overall could increase the disparities in risk among HCWs within marginalized communities (7). Given these fundamental differences, HCWs living in Mexico are at a substantial risk for SARS-CoV-2 infection and adverse COVID-19 outcomes. There is a need to understand these trends and outcomes related to COVID-19 in HCWs to generate evidence which could inform public policy and promote development of recommendations to improve work environments amongst HCWs by reducing transmission risk and, ultimately improve quality of care. Here, we sought investigate the epidemiology of SARS-CoV-2 infection within HCWs and its

related outcomes in Mexico City. We also assessed the predictive ability of individual symptoms and comorbidities to identify HCWs with SARS-CoV-2 infection for prompt isolation of affected cases.

METHODS

Data sources

We analyzed data collected within the National Epidemiological Surveillance System database in Mexico City, which is an open-source dataset comprising daily updated suspected COVID-19 cases that have been tested using real-time RT-PCR to confirm SARS-CoV-2 according to the Berlin Protocol (8), and were certified by the National Institute for Diagnosis and Epidemiological Referral (9,10).

Definitions of COVID-19 cases, predictors, and outcomes

Health-care related professions included subjects whose occupations were reported as physicians, nurses, dentists, laboratory personnel and other involved HCWs. Demographic and health data were collected and uploaded to the epidemiologic surveillance database by personnel from each corresponding health-care facility. Available variables include age, sex, nationality, state and municipality where the case was detected, immigration status as well as identification of individuals who self-identify as indigenous. Health information includes the status of diabetes, obesity, chronic obstructive pulmonary disease (COPD), immunosuppression, pregnancy, arterial hypertension, cardiovascular disease, chronic kidney disease (CKD), and asthma. Evaluated symptoms included fever, cough, odynophagia, dyspnea, irritability, diarrhea, chest pain, shivering, headache, myalgia, arthralgia, malaise, rhinorrhea, polypnea, vomiting, abdominal pain, conjunctivitis, cyanosis, and sudden onset of symptoms. Date of symptom onset, hospital admission, and death are available for all cases as are outpatient or hospitalized status, information regarding the diagnosis of clinical pneumonia, ICU admission, and whether the patient required mechanical ventilation support (MVS). Severe outcome was defined as a composite definition comprising death, requirement for MVS or ICU admission (11).

Statistical analysis

Study population

Categorical variables are presented in frequency distribution with their respective percentage. Continuous variables are presented in mean (standard deviation) or median (interquartile range) wherever appropriate. We compared characteristics of HCWs with positive and negative SARS-CoV-2 infections, using chi-squared tests for categorical variables and Student's t-test or Mann-Whitney's U for continuous variables depending on variable distribution.

Conditions and symptoms related to SARS-CoV-2 positivity

We aimed to investigate comorbidities and symptoms associated with SARS-CoV-2 positivity using a mixed effects logistic regression model, including facility of treatment as a random effect to account for the variability in case distribution and treatment across healthcare facilities. We excluded HCWs who were suspected cases at the time of inclusion without a definitive result for SARS-CoV-2. Two separate models were designed to explore separately comorbidities and symptoms associated with SARS-VoV-2 positivity. We further explored the diagnostic test capacity, area under the curve, sensitivity, specificity, positive and negative predictive values (VPP, VPN, respectively) of each symptom to predict SARS-CoV-2 positivity.

COVID-19 mortality risk and clinical outcomes

We fitted Cox Proportional risk regression models to explore risk factors associated to COVID-19 related 30-day lethality, hospitalization, or severe outcome estimating time from symptom onset up to death, clinically reported outcome, or censoring, whichever occurred first. Factors associated with using mechanical ventilation support (MVS) were evaluated using a mixed effects logistic regression model. We also performed a Kaplan-Meier analysis to assess differences in COVID-19 outcomes comparing physicians and other HCWs using the Breslow-Cox test. We evaluated Cox Proportional risk regression model performance using Harrel's c-statistic and model assumptions were verified using Schöenfeld residuals. Logistic regression model performance was evaluated using the Nagelkerke R^2 and the

Hosmer-Lemeshow test. A p-value <0·05 was considered as statistical significance threshold. All analyses were performed using R software version 3.6.2.

RESULTS

COVID-19 in health-care workers

As of the writing of this report (July 5th, 2020) we identified 35,095 HCWs assessed for SARS-CoV-2. Amongst them, 11,226 (31.9%) had confirmed SARS-CoV-2 infection. Overall, positive cases have been increasing since late February, with a notable peak of confirmed cases in late May and early June (**Supplementary Figure 1**). In the group of confirmed cases 4,322 (38.5%) were nurses, 3,324 (29.6%) physicians, 131 (1.16%) dentists, 299 (2.66%) laboratory personnel and 3,150 (28.1%) referred as supportive HCWs. COVID-19 outcomes included 1,009 (9.00%) HCWs who required hospitalization, 203 with a severe outcome (1.81%), and 93 who required MVS (0.82%). Lethality attributable to COVID-19 was recorded in 226 (2.01%) HCWs. Overall, 341 (3.04%) HCWs referred no associated symptomatology but tested positive for SARS-CoV-2. Compared with negative cases, those with confirmed SARS-CoV-2 test were older, predominantly female, and with a higher prevalence of diabetes and obesity. As expected, confirmed cases had a higher rate of adverse clinical outcomes (**Table 1**).

Associated symptoms and conditions in health-care workers with SARS-CoV-2 positivity

Symptoms associated with increased probability of SARS-CoV-2 positivity in HCWs included fever, cough, malaise, shivering, myalgias, arthralgias, rhinorrhea, chest pain, and polypnea at the time of clinical assessment. Diarrhea, sudden onset of symptoms, irritability, headache were all associated with decreased likelihood of having a positive SARS-CoV-2 test. Next, we sought to investigate the predictive performance of each symptom to predict SARS-CoV-2 positivity; as expected, all symptoms were highly unspecific. Nevertheless, cases reporting headache, cough, and fever had a higher sensitivity for a positive SARS-CoV-2 test; cyanosis, polypnea, and dyspnea had greatest specificity but with poor sensitivity (**Supplementary Table 1**). We found that pregnancy, male sex, prolonged time for clinical assessment (≥7 days since beginning of symptoms), obesity, and diabetes were conditions

which increased likelihood of SARS-CoV-2 positivity; whilst active smoking and puerperium had a decreased likelihood of being positive cases (**Figure 1**).

Predictors for COVID-19 related outcomes in health-care workers

In confirmed SARS-CoV-2 cases, we found that symptoms at clinical assessment which increased risk for hospitalization were dyspnea, fever, and polypnea; while HCWs with diarrhea, odynophagia, and conjunctivitis had a decreased risk for this outcome. Exploring for conditions related to hospitalization, we found that cases with age ≥65 years, HIV/AIDS, diabetes, obesity, and arterial hypertension had increased risk of being hospitalized. HCWs with age ≥65 years, dyspnea, fever, or polypnea at the moment of clinical assessment had increased risk for severe outcome. Moreover, age ≥65 years, diabetes, and dyspnea at evaluation were conditions associated with MVS. Predictors of lethality in HCWs were clinical pneumonia at evaluation, age ≥65 years, diabetes, and obesity (**Figure 2**).

COVID-19 related outcomes of amongst groups of health-care workers.

Overall, compared with non-HCWs with positive SARS-CoV-2 test living in Mexico City, HCWs had a decreased risk for hospitalization (HR 0.47, 95%CI 0.44-0.53), severe outcome (HR 0.41, 95%CI 0.35-0.47) and lethality (HR 0.38, 95%CI 0.32-0.43) (**Figure 3**). Moreover, when we compare HCWs with clinical pneumonia at clinical assessment, we found that this group had a decreased risk for lethality compared with all non-HCWs with or without pneumonia (Breslow-Cox <0.001, **Supplementary Figure 2**). As a secondary analysis, we sought to explore risk of COVID-19 related outcomes in subgroups of HCWs. Characteristics among physicians, nurses and other HCWs are presented in **Supplementary Table 2**. Although the group of physicians had a decreased likelihood to have a positive SARS-CoV-2 test (OR 0.75, 95%CI 0.71-0.79) compared with the group of nurses and other HCWs, this group had an increased risk for hospitalization (HR 1.22, 95%CI 1.06-1.40) and severe outcome (HR 1.56, 95%CI 1.17-2.10,) after adjusting for sex, age and comorbidities compared with the group including nurses and other HCWs. Univariate Cox regression model also shown that physicians had an increased lethality risk (HR 1.53, 95%CI 1.17-2.01), which did not sustain significance after adjustment for previously mentioned

covariates (**Figure 3**). Finally, a particular group of interest was those HCWs who belonged to an indigenous group, which had up to 11-fold increased risk for COVID-19 lethality (HR 11.44 95%CI 3.57-36.) after adjusting for covariates, although no differences were found in the risk for hospitalization and severe outcome.

DISCUSSION

In this work, we report the prevalence of SARS-CoV-2 infection, related symptomatology, and COVID-19 clinical outcomes using a city-wide based surveillance reports of HCWs living in Mexico City. Amongst health-care workers, the group of physicians tend to have an increased risk of severe COVID-19 outcomes, which is a remarkable occupational risk. Moreover, certain factors, such as associated comorbidities and symptoms at the time of evaluation may predispose an increased risk of adverse outcomes. These findings should be considered by authorities in relation to relevant occupational hazards in HCWs, particularly in physicians; given the vital role of HCWs in managing the impact of the pandemic on individual patients, promoting the application of stricter regimes to reduce the probability of infection and adverse outcomes attributable to COVID-19 amongst HCWs is of paramount importance.

HCWs have increased occupational hazard to acquire SARS-CoV-2 infection compared with general population, attributable to direct contact during care of hospitalized patients. Prevalence and lethality rates of SARS-CoV-2 infections reported in our population are slightly higher compared with previous reports in China, Europe and the United States (4,12–17). Similarly, in Mexico the number of positive cases reported in HCWs has increased since the first confirmed cases were reported in late February. To reduce transmissibility and improve outcomes, it has been proposed that HCWs who develop respiratory symptoms should be isolated to mitigate the spread between peers. However, as

our results confirm and based on previous reports, there is no sustainable evidence which allows using specific symptoms to identify SARS-CoV-2 positive cases in a clinical context (4). Hence, global and local authorities should instead steadily encourage the rational use of personal protective equipment in HCWs, regardless of contact and care for patients with SARS-CoV-2 and systematic testing amongst HCWs to identify asymptomatic cases. Although previous reports have shown the effectiveness of personal protective equipment, there is still insufficient evidence if this strategy could mitigate the infection amongst all HCWs at long-term, which sets an area of opportunity for further studies (18,19).

Our results also show that comorbidities in HCWs, particularly those related to chronic non-communicable diseases (e.g., diabetes, obesity and arterial hypertension), and the presentation of severe respiratory symptoms at the time of clinical assessment, increases the risk of adverse COVID-19 outcomes. Certain groups, such as pregnant women, older workers, and those referred to belong to an indigenous group, are at higher risk for severe related outcomes. Previous reports by our group had shown the relationship between the presence of cardiometabolic diseases and risk of complications associated with SARS-CoV-2 infection in Mexico (20–23). Although not completely understood, this relationship could be explained by immunological over responsiveness observed in confirmed cases with diabetes and obesity (20,23,24), particularly given recent evidence relating changes associated with an enhanced immune response to SARS-CoV-2 with risk of respiratory and multi-organ failure (23,25). Conversely, in patients with prior immunosuppression, an increased risk for associated co-infections has been reported, which could explain risk for adverse outcomes in HCWs with HIV/AIDS or pregnancy (26,27).

Finally, we found that physicians are a group of risk for developing adverse events compared to other HCWs. This is consistent with a previous report, as it has been shown that physicians tend to spend more time in areas where patients with SARS-CoV-2 are assisted (28). Furthermore, prolonged shift times, work overload, phycological distress and exposure to probable cases amongst peers could lead physicians to be considered a group with significant occupational risk for developing COVID-19 related outcomes (29–31).

Nevertheless, HCWs have overall a lower risk of having a positive test and adverse outcome, compared with other professions. This could be explained by potential factors such as prompt and appropriate medical attention and social assurance which could be provided to HCWs. Interestingly, we also found that groups of physicians who self-reported as belonging to an indigenous community were at increased risk of death attributable to COVID-19. Although preliminary, these results may denote an inequality of access to timely care given the significant social discrepancies reported in Mexico (7,32,33). More studies should focus on the risk of adverse outcomes attributable to social conditions in medical personnel.

Our study had some strengths and limitations. First, we analyzed a large dataset which included information on confirmed positive and negative SARS-CoV-2 cases in Mexico City, providing a unique opportunity to investigate COVID-19 specific risk factors in HCWs. A potential limitation of this study is the use of data collected from a sentinel surveillance system model, which is skewed towards investigating high-risk cases or only those with specific risk factors which on the one hand increases power to detect the effect of comorbidities and on the other hand might not be representative of milder cases of the disease. This is particularly true for asymptomatic cases amongst HCWs, which were heavily underrepresented in our study and its prevalence must be assessed with widespread testing amongst HCWs to reduce in-hospital transmission amongst HCWs. Furthermore, the reduced odds of SARS-CoV-2 positivity could be related to a higher number of tests being carried out amongst medical personnel compared to the general population, which is consistent with the positivity rate (). Another potential limitation of our study is that our assessment of HCWs is limited to those living in Mexico City, which may not capture the whole picture in the country or the large socio-economic inequalities which might lead to higher rates of infection amongst HCWs in disadvantaged areas.

In summary, we present the first report of a city-wide based surveillance system which assessed clinical symptomatology and related outcomes attributable to COVID-19 in HCWs living in Mexico City. We found that no specific symptoms can accurately discern among

HCWs with SARS-CoV-2 infection; furthermore, there is a considerable but underreported prevalence of positive asymptomatic infections. We show that comorbidities, presence of respiratory symptoms at clinical assessment, and susceptible groups of HCWs, could have increase the risk of severe outcomes. Our results could inform policies within the health-care systems on the rational use of personal protective equipment, early isolation of probable cases regardless the symptoms, exclusion of risk groups in areas where patients with SARS-CoV-2 are routinely assisted and consideration of intrinsic inequalities between workers, which overall, could bring to a better quality of life for HCWs during the COVID-19 pandemic.

AUTHOR CONTRIBUTIONS

Research idea and study design: NEAV, OYBC; data acquisition: NEAV, OYBC; data analysis/interpretation: NEAV, OYBC, AVV, CAFM, AMS, JPBL; statistical analysis: NEAV, OYBC; manuscript drafting: OYBC, NEAV, AVV, CAFM, AMS, JPBL; supervision or mentorship: OYBC. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions about the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

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TABLES

TABLE 1: Characteristics of health-care workers with and without positive COVID-19 living in Mexico. *Abbreviations*: COPD= Chronic obstructive pulmonary disease; HIV/AIDS= Human immunodeficiency virus and/or acquired immunodeficiency syndrome; CKD= Chronic kidney disease.

Parameter	Health-Care Workers with COVID (n=11,226)	Health-Care Workers without COVID (n=23,869)	P value
Female sex (%)	6,723 (59.9)	15,379 (64.4)	<0.001
Age (years)	40.2 (±10.7)	39.9 (±10.9)	<0.001
Physicians (%)	3,324 (29.6)	8,094 (33.9)	<0.001
Nurses (%)	4,322 (38.5)	8,305 (35.6)	<0.001
Dentists (%)	131 (1.16)	366 (1.53)	0.007
Laboratory personnel (%)	299 (2.66)	491 (2.06)	<0.01
Other HCWs (%)	3,150 (28.1)	6,436 (26.9)	0.020
Mortality (%)	226 (2.01)	100 (0.42)	<0.001
Hospitalizacion (%)	1,009 (9.00)	936 (3.93)	<0.001

Severe Outcome	203 (1.81)	182 (0.76)	<0.001
Clinical pneumonia (%)	1,240 (11.1)	1,212 (5.10)	<0.001
Mechanical-Ventilation (%)	93 (0.82)	58 (0.24)	<0.001
≥7 days since beginning of symptoms (%)	2,266 (20.2)	3,714 (15.5)	<0.001
Diabetes (%)	785 (7.0)	1,297 (5.54)	<0.001
COPD (%)	60 (0.55)	131 (0.55)	0.926
Asma (%)	440 (3.92)	1,021 (4.28)	0.255
HIV/AIDS (%)	32 (0.28)	87 (0.36)	0.493
Obesity (%)	2,079 (18.5)	3,575 (15.0)	<0.001
Smoking status (%)	1,063 (9.48)	2,351 (9.84)	0.149
CKD (%)	62 (0.55)	105 (0.43)	0.213
Pregnant women (%)	38 (0.34)	49 (0.21)	0.243
Indigenous (%)	40 (0.36)	102 (0.43)	0.203

FIGURES

Figure 1: Associated symptoms (A) and conditions (B) at clinical assessment of COVD-19 in Health-Care Workers. *Abbreviations*: OR= Odds ratio; 95%CI= 95% confidence interval.

Figure 2: Risk factors associated to hospitalization (A), severe outcome (B), MVS (C) and lethality associated to COVID-19 in health-care workers with SARS-CoV-2 in Mexico City. Abbreviations: MVS= Mechanical ventilation support.

Figure 3: Kaplan-Meier survival plot to identify the risk of hospitalization (A-D), severe outcome (B-E) and lethality (C-F) in HCWs compared with other non-HCWs and between physicians and nurses and other HCW.

Figure 1

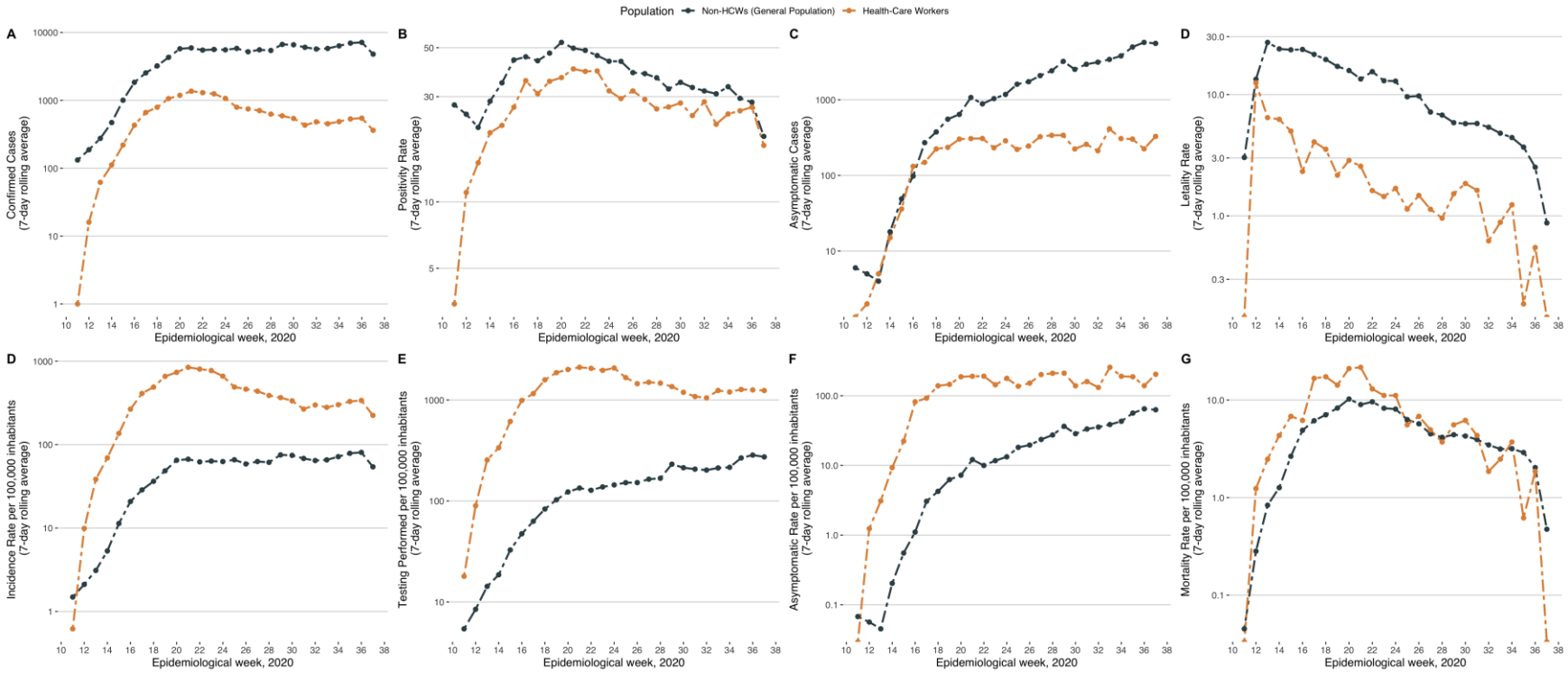

Figure 2

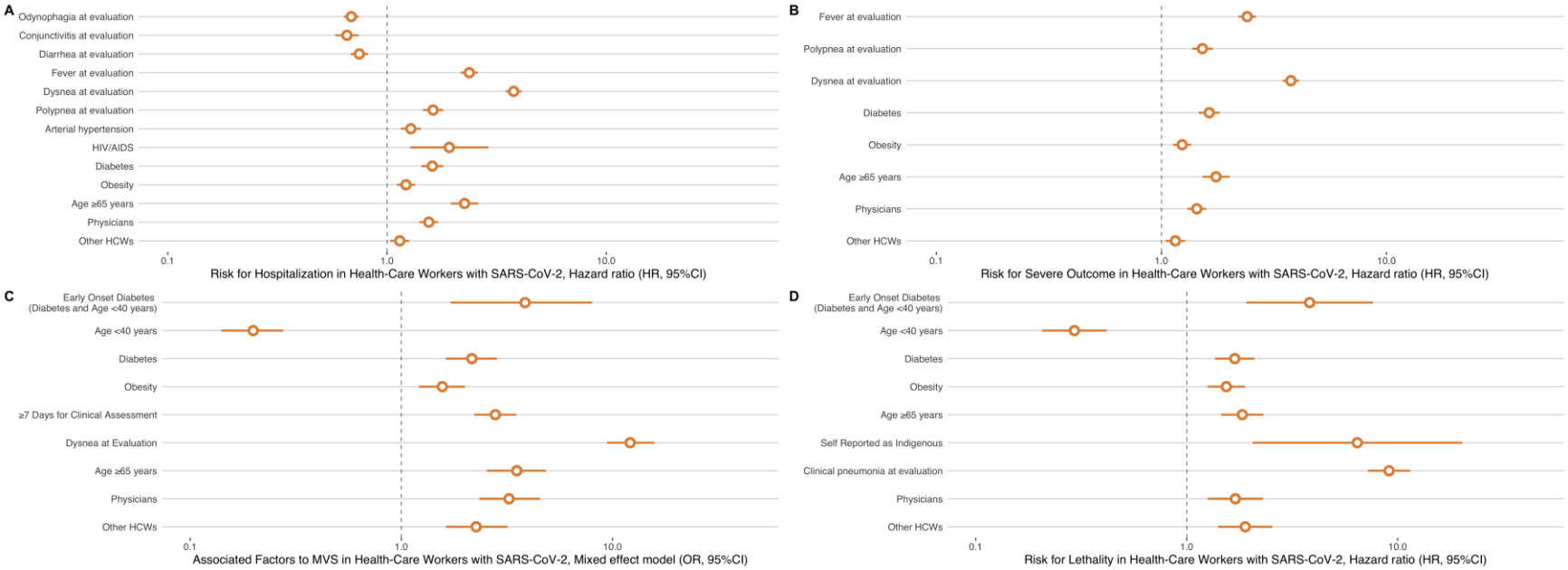

Figure 3