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Incidence and Case-Fatality Ratio of COVID-19 Infection in Relation to Tobacco Smoking, Access to Healthcare, Poverty, and Population Demographics in the USA

Yves Muscat Baron[1*] and Liberato Camilleri[2]

[1]Mater Dei Hospital Medical, School of Malta, University of Malta, Malta, UK
[2]Department of Statistics & Operations Research Faculty of Science, University of Malta, Malta, UK

Abstract

Background: Tobacco smoking has been shown to increase the severity of COVID-19 infection and the risk for intra-tracheal ventilation in smokers. Tobacco smoking exposes the user and nearby individuals to very high concentrations of particulate matter in a short period of time. Genes coding for SARS-CoV-2 have been found adherent to particulate matter which has been linked to COVID-19 related mortality PM2.5. The aim of the study was to observe the incidence of SARS-CoV-2 infection rates in the USA, comparing States differentiated by the degree of smoking bans, exploring a possible link between tobacco smoke-related particulate matter and SARS-CoV-2 transmission.

Methodology: Two groups of USA States, differentiated by the degree of smoking legislative restrictions, had a number of variables compared. Variables related to COVID-19 were obtained from the John Hopkins Coronavirus Resource Centre between the 20th and the 26th September 2020. The degree of smoking bans and the percentage of the smoking population in the USA States were obtained from the websites of the Nonsmokers Rights Foundation and the Centres of Disease Control database respectively. Population characteristics were obtained from databases concerning USA demographics.

Results: The incidence of COVID-19 infection in the States with limited bans on tobacco smoking was 2046/100,000 (sd+/-827) while the infection incidence in States with more restrictive rulings on tobacco smoking was 1660/100,000 (sd+/-686) ($p<0.038$). The population percentage of smokers in States with minor limitations to smoking was 18.3% (sd+/-3.28), while States with greater smoking restrictions had a smoking population percentage of 15.2% (sd+/-2.68) ($p<0.0006$). Significant correlations were noted between the percentage of the states' population which was below the poverty line and access to Healthcare. Population density correlated significantly with the case-fatality ratio ($R=0.66$ $p<0.0001$).

Conclusion: States in the USA with high levels of tobacco smoking and limited regulation had significantly higher rates of COVID-19 infection incidences than States with greater smoking restrictions. The State population percentage living in poverty, and access to healthcare were significantly different between both groups of States. Densely populated USA States with partial bans on tobacco smoking, with elevated percentages of the population living in poverty and with limited access to healthcare had high incidences of COVID-19 rates during the time period assessed.

Keywords: Tobacco smoking • COVID-19 Incidence • Case-fatality ratio • Access to healthcare • Poverty

Introduction

Tobacco smoking is associated with a significant proportion of global mortality. Of the worldwide burden of 8 million deaths per year, more that 85% of these deaths occur in smokers themselves [1]. Non-smokers are also at substantial risk, resulting in approximately one million deaths per annum due to second-hand smoking (WHO 2019). Second-hand smoking exposes these individuals to particulate matter and potentially to respiratory disease through smoke-induced infection transmission [2,3].

In an effort to curb smoking and reduce the adverse effects of second-hand smoking, several nations have introduced restrictive measures. In the USA there appears to be a divide, with some States applying restrictive smoking regulation while in others there exist partial smoking bans.

Smoking is the human activity which singularly exposes humans to significantly elevated levels of airborne particulate matter in a short period of time. Long-term exposure to particulate matter PM2 [4], in the USA has been linked to COVID-19 related mortality [5]. Particulate matter has been noted to have genes appertaining COVID-19 adherent to it. The possibility of a dual effect of reducing pulmonary defences and the carriage of COVID-19 by particulate matter has been explored [6].

This paper assesses whether smoking in USA varies across its member States some of which have less restrictive regulation on tobacco smoking than others. Concomitantly the incidence of COVID-19 across the USA was assessed in relation to the USA's States reviewed in an effort to find an incidence pattern and case-fatality ratio coinciding with COVID-19 infection. As a corollary the population density body mass index and age demographics were also assessed between both groups of States.

Methodology

This study compared two groups of States in the USA, differentiated by

**Address for Correspondence:* Yves Muscat Baron, Mater Dei Hospital Medical, School of Malta, University of Malta, Malta, UK; E-mail: astridmbaron@gmail.com

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the gradation of legislative restrictions on tobacco smoking. The variables assessed include COVID-19 incidence during the week between the 20th and the 26th September 2020, case-fatality ratios, state population density and population percentages of individuals 65/75 years and older. The incidence of COVID-19 infection, prevalence of testing and case-fatality ratios was attained from the John Hopkins Resource Centre database [7]. The degree of smoking restrictions in the States assessed was obtained from the websites of the Non-smokers' Rights Foundation [8]. The legislative measures included in the study governed smoking related legal restrictions up to October 2018. The percentage of the state smoking was retrieved from the U.S. Centres of Disease Control database [9]. Population density, body mass index and population percentages of individuals 65/75 years and older were obtained from websites concerning USA demographics in 2018 and 2019 [10-12].

Results

COVID-19 infection incidences were significantly higher in the States with partial bans on tobacco smoking compared with highly regulated States ($p<0.038$). The incidence of COVID-19 infection in the States with partial bans on tobacco smoking was 2046/100,000 (sd+/-827), while the infection incidence in States with restrictive regulation on tobacco smoking was 1660/100,000 (sd+/-686) (Tables 1 and 2).

The percentage of the smoking population in the States with minimum regulation in 2018 was significantly higher than that of States with more severe prohibitions on tobacco smoking ($p<0.0006$). The percentage of smokers in States with minimal restrictions to smoking was 18.3% (sd+/-3.28) while States with greater smoking restrictions had a smoking population percentage of 15.2% (sd+/-2.68). Other factors that could affect the COVID-19 USA pandemic such as the state case-fatality ratio, population density, body mass index and the percentage of the state population aged 65 years or above and 75 years and above did not show any significant difference between both groups of States.

A number of significant correlations were obtained when comparing variables of all the US States together and when the two groups of States (restrictive and partial smoking ban groups) were assessed separately. The states' population density correlated significantly ($R=0.66$ $p<0.0001$) with the case-fatality ratio. The correlation of the population density/case fatality ratio still applied when the two groups of States were assessed separately (partial ban $R=0.58$ $p<0.003$ and restrictive regulation $R=0.74$ $p<0.0001$).

The case fatality ratio correlated with increasing age in the 75 years and over age group ($R=0.29$ $p<0.04$). No significant correlation between the 65 years and over age group and the case fatality ratio. In the 75 years and over age group the proportion of foreign born population (0.7% sd+/-0.57) was significantly higher in the States with restrictive smoking regulations compared to the population of States with limited smoking restrictions (0.45% sd+/-0.45). States with more restrictive tobacco regulations had significantly higher Healthcare Coverage (93.1% sd+/-2.3 *vs* 90.4% sd+/-3.2 $p<0.004$). Healthcare Coverage correlated negatively with COVID-19 incidence ($R=-0.39$ $p<0.004$) (Figure 1).

Table 1. COVID-19 Variables and population demographics in of states with strict smoking bans and lower smoking population rates.

	Percentage population of smokers	Percentage population of smokers	Percentage population of smokers	Percentage population of smokers	Percentage population of smokers
Wisconsin	16.4	1670	41	40.73	1.2
Michigan	18.9	1282	67	19.13	5.38
Nebraska	16	2124	9	236	1.09
Iowa	16.6	2544	21	121.14	1.58
Illinois	15.5	2181	89	24.51	3.12
Kansas	17.2	1808	14	129.14	1.12
Colorado	14.5	1125	20	56.25	3.09
Utah	9	1989	14	142.07	0.68
New York	12.8	2312	162	14.27	7.44
Maryland	12.5	1987	238	8.34	3.22
Vermont	13.7	274	26	10.53	3.37
Maine	17.8	377	16	6.61	2.72
Massachusetts	13.4	1850	336	5.505	7.38
Rhode Island	14.6	2229	394	5.657	4.57
New Jersey	13.1	2249	470	4.78	8.01
Delaware	16.5	2009	187	10.74	3.18
New Mexico	15.2	1315	6	219.166	3.07
Arizona	14	2925	23	127.17	2.56
California	11.2	1989	97	48.51	1.91
Oregon	15.6	719	16	44.937	1.71
Washington	12	1084	41	26.439	2.48
Montana	19.5	963	2	481.5	1.52
South Dakota	19	2113	4	528.25	1.05
North Dakota	19	2356	4	589	1.06
Alaska	19.1	933	1	933	0.65
Hawaii	13.4	805	86	9.36	1.05

Table 2. More variables assessed of states with strict smoking regulation and lower smoking population rates.

of	Percentage population Age>65 yr	Percentage population Age>75 yrs native born	Percentage population Age>75 yrs foreign born	Total percentage population Age>75 \yrs	Percentage of population overweight or obese
Minnesota	16.3	6.38	0.35	6.73	67.3
Wisconsin	17.5	6.82	0.32	7.14	68.4
Michigan	17.6	6.62	0.49	7.11	68.2
Nebraska	16.1	6.58	0.22	6.8	73.7
Iowa	17.5	7.4	0.16	7.56	72
Illinois	16.1	5.73	0.92	6.65	65.8
Kansas	16.3	6.58	0.23	6.81	70.5
Colorado	15.6	4.91	0.45	5.36	61.9
Utah	11	4.12	0.28	4.4	65.2
New York	16.9	5.25	1.92	7.17	57.2
Maryland	15.9	5.53	0.84	6.37	66.5
Vermont	20	7.12	0.56	7.68	66.9
Maine	21.2	8	0.38	8.38	66.4
Massachusetts	16.8	5.77	1.2	6.97	62.1
Rhode Island	17.7	6.56	0.94	7.5	64.4
New Jersey	16.6	5.48	1.55	7.03	65.9
Delaware	19.4	7.03	0.5	7.53	65.9
New Mexico	18	6.44	0.59	7.03	62.8
Arizona	18	6.54	0.86	7.4	66.3
California	14.8	3.93	2.1	6.03	58.5
Oregon	18	6.35	0.61	6.96	64.6
Washington	15.9	5.16	0.86	6.02	63.7
Montana	19.3	7.21	0.24	7.45	60.1
South Dakota	17.1	6.88	0.07	6.95	72.4
North Dakota	15.8	6.81	0.09	6.9	76.9
Alaska	12	3.38	0.47	3.85	72.9
Hawaii	18.9	5.98	1.91	7.89	72.9

States with more restrictive bans on tobacco smoking had lower percentages of the states' population below the poverty line compared with states with limited regulation (12.4% sd+/-2.3 *vs* 15.2% sd+/-2.7 p<0.05). Higher state poverty percentages correlated with COVID-19 incidences (R=0.4 p<0.005) (Figure 2).

There was no significant difference in and the median household income between both groups of states. There was no difference when comparing the proportion of native born to the foreign born cohorts when the both groups of States were combined in both the 75+ year age group. The correlation between the percentage smoking population and case-fatality

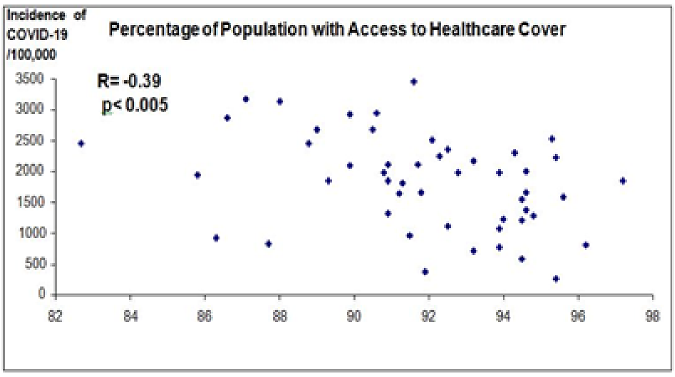

Figure 1. Percentage of population with access to healthcare.

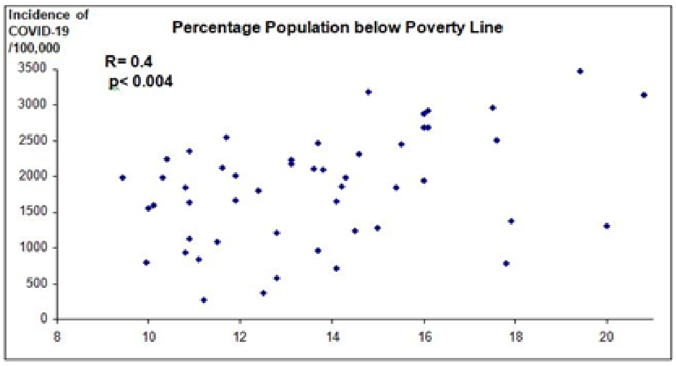

Figure 2. Percentage population living in poverty.

ratio just missed statistical significance ($R=0.27$ $p<0.056$). There was no significant correlation between the incidence of COVID-19 and case-fatality ratio (Tables 3 and 4).

The correlation of the integer dividing the incidence of COVID-19 by the State population density compared to the case-fatality ratio was also carried out. The incidence of COVID-19 infection when factored with State population density as a denominator, significantly correlated ($R=0.67$ $p<0001$) with the case-fatality ratio. This latter correlation also applied for both the States with partial smoking bans ($R=0.57$ $p<0.003$) and more strict regulation ($R=0.75$ $p<0.0001$) of tobacco smoking.

Regression analysis indicated that population density, poverty, limited access to healthcare and living in a State with partial bans on tobacco smoking increased the incidence of COVID-19. For every unit increase in the population density, the incidence of COVID-19 Infection/100,000 increased by 4.413. With every 1% increase in the percentage population in poverty, the rate of COVID-19 increased by 116.1. In States with restrictive smoking bans the mean incidence of COVID-19 Infection/100,000 is 117.3 less than in States where smoking is partially banned.

Table 3. Variables assessed of States with partial smoking bans and higher smoking population rates.

	Percentage population of smokers	Incidence of COVID-19 infection/100,000	Population density individuals per Km^2	COVID-19 incidence /population density
Indiana	21.1	1656	71	23.32
Missouri	19.4	1860	34	54.7
Oklahoma	19.7	1941	22	88.22
Arkansas	22.7	2509	22	114.04
Tennessee	20.7	2687	61	44.04
Kentucky	23.4	1377	43	32.02
Ohio	20.5	1234	109	11.32
Pennsylvania	17	1210	110	11
New Hampshire	15.6	584	57	10.24
Connecticut	12.3	1557	286	5.44
Virginia	14.9	1644	81	20.29
North Carolina	17.4	1845	79	23.35
South Carolina	18	2687	62	43.338
Georgia	16.1	2883	68	42.397
Florida	14.5	3183	145	21.95
Alabama	19.2	2956	37	79.89
Missisippi	20.5	3137	24	130.708
Louisiana	20.5	3467	41	84.56
Texas	14.4	2458	40	61.45
Nevada	15.7	2461	10	246.1
Idaho	14.7	2097	7	299.57
Wyoming	18	841	2	420.5
West Virginia	25.2	785	29	481.5

Table 4. More variables assessed of States with partial smoking bans and higher smoking population rates.

	Percentage population age>65yr	Percentage population Age>75yr native born	Percentage population Age>75yr foreign born	Total percentage population Age >75yr	Percentage of population overweight or obese
Indiana	16.1	6.32	0.22	6.54	68.4
Missouri	17.3	6.97	0.19	7.16	68.5
Oklahoma	16.1	6.31	0.23	6.54	71.9
Arkansas	17.4	6.88	0.12	7	71.2
Tennessee	16.7	6.4	0.19	6.59	69.7
Kentucky	16.8	6.48	0.14	6.62	69.8
Ohio	17.5	6.85	0.37	7.22	69.2
Pennsylvania	18.7	7.5	0.48	7.98	67.7
New		Minnesota	Minnesota	Minnesota	Minnesota
Hampshire	18.6	6.67	0.6	7.27	66.5
Connecticut	17.7	6.53	1.03	7.56	61.5
Virginia	20.5	5.7	0.62	6.32	66.2
North Carolina	16.7	6.2	0.3	6.5	68.2
South Carolina	18.2	6.5	0.32	6.82	66.7
Georgia	14.3	4.88	0.44	5.32	66.4
Florida	20.9	7.12	2.06	9.18	65.7
Alabama	17.3	6.7	0.18	6.88	68.6
Missisippi	16.4	6.25	0.12	6.37	65.8
Louisiana	15.9	5.93	0.21	6.14	69.3
Texas	12.9	4.19	0.77	4.96	67.2
Nevada	16.1	4.8	1.2	6	66.4
Idaho	16.2	6.05	0.28	6.33	67.8
Wyoming	17.1	6.3	0.12	6.42	61.5
West Virginia	19.7	7.95	0.135	8.085	70

Table 5. More variables assessed of States with strict smoking regulation and lower smoking population rates.

	Household income annual $	Poverty % population	Healthcare coverage % population
Minnesota	70,315	10.1	95.6
Wisconsin	60,773	11.9	94.6
Michigan	56,697	15	94.8
Nebraska	59,566	11.6	91.7
Iowa	59,955	11.7	95.3
Illinois	65,030	13.1	93.2
Kansas	58,218	12.4	91.3
Colorado	71,953	10.9	92.5
Utah	71,414	10.3	90.8
New York	67,844	14.6	94.3
Maryland	83,242	9.44	93.9
Vermont	60,782	11.2	95.4
Maine	55,602	12.5	91.9
Massachusetts	79,835	10.8	97.2
Rhode Island	64,340	13.1	95.4

New Jersey	81,740	10.4	92.3
Delaware	64,805	11.9	94.6
New Mexico	47,169	20	90.9
Arizona	59,246	16.1	89.9
California	75,277	14.3	92.8
Oregon	63,426	14.1	93.2
Washington	74,073	11.5	93.9
Montana	55,328	13.7	91.5
South Dakota	56,274	13.6	90.9
North Dakota	63,837	10.9	92.5
Alaska	74,346	10.8	86.3
Hawaii	80,212	9.94	96.2

Table 6. More variables assessed of States with partial smoking bans and higher smoking population rates.

	Household income $	Poverty% population	Healthcare coverage% population
Indiana	55,746	14.1	91.8
Missouri	54,478	14.2	90.9
Oklahoma	51,924	16	85.8
Arkansas	47,062	17.6	92.1
Tennessee	52,375	16.1	90.5
Kentucky	50,247	17.9	94.6
Ohio	56,111	14.5	94
Pennsylvania	60,905	12.8	94.5
New Hampshire	60,905	12.8	94.5
Connecticut	76,348	10	94.5
Virginia	72,577	10.9	91.2
North Carolina	53,855	15.4	89.3
South Carolina	52,306	16	89
Georgia	58,756	16	86.6
Florida	55,462	14.8	87.1
Alabama	49,861	17.5	90.6
Missisippi	44,717	20.8	88
Louisiana	47,905	19.4	91.6
Texas	60,629	15.5	82.7
Nevada	58,646	13.7	88.8
Idaho	55,583	13.8	89.9
Wyoming	61,584	11.1	87.7
West Virginia	44,097	17.8	93.9

DISCUSSION

The incidence of respiratory infection increases with tobacco smoking. Moreover tobacco smoking exacerbates the severity of pulmonary infections. The risk for mortality from tuberculosis has been shown to increase nine-fold in tobacco smokers [13]. Legionella infection is known to increase up to 121% increased risk of legionella pneumonia with every packet of cigarettes smoked. Similarly Mycoplasma and viral infections such as the influenza are more common in tobacco smokers [14]. Smokers have also been noted to have had higher mortality in the 2012 MERS-CoV outbreak [15]. In a similar fashion COVID-19 is a highly infectious viral disease that affects the respiratory system leading to a myriad of presentations and complications (Tables 5 and 6).

Smoking impairs pulmonary defences against lung infection and may be implicated in the transmission of COVID-19. The immune system is adversely affected by the components of tobacco smoking including particulate matter element [16]. Tobacco smokers through their smoking habits are exposed to very high concentrations of particulate matter [17].

The impact of particulate matter PM2.5 on the immune response influences macrophage function and the modulation of the cytokine response. PM2.5-induced inflammation may result in an increase in the number of pulmonary neutrophils, eosinophils, T cells and mastocytes [18,19]. This cellular reaction can result in inflammatory cytokine production and the resultant cytokine storm has been responsible for a significant number of COVID-19 related deaths [20].

Most of the early studies linking smoking to COVID-19 infection were carried out in mainland China. Zhou et al. assessed 191 patients infected with COVID-19, 54 of who succumbed to the infection, while the other 137 survived resulting in a case-fatality ratio of 28.3% [21]. The high case-fatality ratio suggests that this cohort (191) were seriously ill with COVID-19. A non-significant proportion (9%) of those who succumbed to the infection was currently smoking as opposed to 4% smokers among those who survived. Similar no significant results were obtained by Zhang et al. [22]. Out of 140 patients with COVID-19, 58 had severe infection. Of the patients with severe infection 3.4% were current smokers and 6.9% were smokers in the past, while in the less severe group none were presently smoking and only 3.7% were previous smokers. The largest study performed in China recruited 1,099 patients with COVID-19 infection [23]. The proportion of patients with severe symptoms comprised 15.7%. Of the patients presenting with severe symptomatology, 16.9% were recent smokers and 5.2% were ex-smokers, while in the group with minimal COVID-19 symptoms 11.8% were currently smoking and 1.3% smoked in the past.

Meta-analysis of several studies from various centres was carried out in the months following the outbreak in China. One meta-analysis analysing 11,590 hospitalized patients, indicated that which 2,133 (18.4%) developed severe disease. Disease severity occurred in 29.8% of patients who smoked currently or in the past compared with 17.6% of non-smokers (OR=1.91; 95% CI: 1.42-2.59). Another meta-analysis by Simons et al. assessed 102 studies investigating the connection between disease progressions and smoking status. Patients who were currently smoking were more likely to experience disease progression as opposed to non-smokers (RR=1.39; 95% CI: 1.09–1.77) [24,25].

This study indicated that States in the USA with high levels of tobacco smoking and partial regulation had significantly higher rates of COVID-19 infection incidences than states with more severe smoking bans. As described earlier this could be attributed to the reduced respiratory immunity due to the toxicity of tobacco smoking including particulate matter. Alternatively besides impaired pulmonary defences, transmission of COVID-19 infection through viral carriage by surface particulate matter has been alluded to by Comunian et al. Tobacco smoking has the attribute of exposing both smokers and bystanders to very high concentrations of particulate matter in a short period of time. This has been noted not only indoors with adequate ventilation, but also in the open air.

Studies have shown that average levels of PM2.5 in open-air smoking venues exceed the WHO recommendation of 25 μg/m^3. These levels varied from 8.32 μg/m^3 to 124 μg/m^3 at open-air settings where tobacco smoke was present. Extremely elevated levels of 1,000 μg/m^3 have been noted in some smoking venues. These elevated levels of PM2.5 are more likely in densely packed areas with poor ventilation, in the presence of smokers. Confirming the risks of PM2.5 exposure due to passive smoking, even smoke-free venues close to open-air smoking settings also had potentially high PM2.5 concentrations, with levels ranging from 4 μg/m^3 to 120.51 μg/m^3. Setti et al. have shown increased COVID-19 transmission has been noted was noted to coincide with elevated peaks of particulate matter. The same authors have suggested that the recommended social distance of 2 metres is only effective if masks are worn because particulate matter can travel up to distances of 10 metres and more [26]. The importance of face protection with masks cannot be understated, as Zhang et al. have shown that the use of masks was crucial in determining the disease spread in Wuhan, Italy and New York. Wearing of masks has been estimated to have reduced the number of COVID-19 infections by more than 78,000 in Italy and over 66,000 in New York City during the months of April and May 2020 [27].

In a paper linking subway particulate matter and COVID-19, it was hypothesized that the haematite-rich particulate matter may be a superior vector to surface particulate matter as it creates a microenvironment suitable for COVID-19 persistence [28,29]. Whereas surface carbon-rich particulate matter has adsorbing properties on adherent substances, subway haematite-rich particulate matter may easily release any adherent COVID-19. Moreover COVID-19 has been noted to have persisted on steel objects for up to 72 hours [30].

Ambient salinity and the sodium chloride component in PM2.5 have been touted as protective factor against COVID-19 [31]. The particulate matter sodium chloride component has the propensity to attract water which may deter the hydrophobic C-terminal protein in the COVID-19 Spike Protein [32]. This protective effect did not apply to the pandemic in the salinity-rich East Coast of USA. Although the states of New Jersey, Connecticut and Massachusetts have high levels of ambient salinity [33], the incidence and case-fatality ratio was still elevated. The role of subway commuter congestion, interconnectivity and elevated subway PM2.5 levels may have eclipsed any saline related protective factors, causing high death rate in New York State [34] and the adjacent states of Connecticut, New Jersey and Massachusetts. Similarly the exhaled tobacco derived particulate matter is devoid of any exposure to ambient salinity. In a similar manner, the protective effect of sodium chloride may not be available to particulate matter originating from exhaled tobacco fumes.

This study also indicated that population density and age beyond 75 years and over was a significant factor in the case-fatality ratio. It has been shown that the case-fatality ratio varies according to the population demographics the older the population the greater the case fatality ratio. The population in Northern Italy aged 65 years and over constituted 25% of the Lombardy population. Consequently the case-fatality ratio in Italy was 9.3%. Similarly the Netherlands had a case-fatality ratio of 7.4% with a background 65+years population of 20% [35]. It is therefore biologically plausible that tobacco smoking in densely packed areas with elderly and vulnerable persons in the vicinity put these individuals at greater risk.

Similar to other studies access to Healthcare and the poverty index were related to the incidence of SARS-CoV-2 infection rates. Populations living in more deprivation counties in the United States had a larger number of confirmed SARS-CoV-2 cases and related mortality. Following April 2020 the pattern of COVID-19 incidence changed whereby more affluent counties had more confirmed SARS-CoV-2 cases. Risk of infection increased 2-fold in disadvantaged areas (weighted OR=2.08; 95% [CI]=1.99-2.17) and 3-fold greater (weighted OR=3.11; 95% CI=2.98-3.24) in very highly-disadvantaged areas, compared with more affluent areas [36,37]. It is interesting to note that at the time of the study, Utah, the only state with a single digit percentage US smoking population had a relatively elevated COVID-19 incidence. The percentage population who smoke in Utah is 9% and its incidence was 1989/100,000 which is high for a State with a restrictive smoking regulation. The presence of neighbouring partial ban States such as Nevada, Idaho and Wyoming may explain Utah's COVID-19 incidence. However Utah's case-fatality ratio was the lowest in the USA, possibly due to the combined factors of low smoking prevalence, low population density and low percentage cohorts in both the 65+(11%) and 75+(4.4%) age groups.

Tobacco smoking has also been linked to the expression of the ACE-2 receptor the viral point of entry into the pulmonary host cell. Cai et al. have demonstrated that increased ACE2 expression in single-cell transcriptomics of bronchial epithelium cells in current smokers compared to non-smokers'. This may have been particularly relevant to the origin and rapid transmission of SARS-CoV-2 in China, as 66% of Chinese males are smokers and 70% of the Chinese population is exposed to 2nd hand smoking [37].

There a number of limitations to the observations noted in this paper. There is some asynchrony in a number variables assessed. The population percentage of smokers was derived from 2018 data from the Centre of Disease Centre and Prevention. This also applies to the States' population, population density and percentage of individuals deemed overweight or obese. The incidence of co-morbidities was not available however the absence of age and body mass index differences between the two groups of states assessed may mitigate this deficiency to some extent. The data regarding incidence of COVID-19 infection, case-fatality ratio and testing frequency were collected over the period between the 20th and 26th September so as to reduce the bias for the constantly evolving fluctuations. Testing frequency was not available for all States; however there did not appear a significant difference of the testing frequency between both groups of states in the data available. Not all the required data from the District of Columbia, Puerto Rico, American Samoa and North Mariana Islands was available for assessment, so these territories were excluded from this study. These four regions constitute 1.37% of the whole USA population. Moreover the State bans considered were those imposed in 2018 and since then smoking regulations may have been altered. This study presupposes the unlikely assumption that adherence to smoking bans is enacted across the USA uniformly and admittedly this is unlikely to occur as has been shown in other countries such as Israel [38].

Conclusion

This paper suggests that States in the USA with elevated levels of tobacco smoking and limited smoking bans had significantly higher rates of COVID-19 infection incidences than States with more severe smoking restrictions. As shown in other papers, poverty, access to healthcare, population density and individuals aged 75 years and over demonstrated a significant correlation with the case-fatality ratio. Adjacent State smoking ban status could affect neighbouring state COVID-19 incidence. Besides the adverse effects of tobacco smoking on pulmonary defences and the propagation of the pulmonary ACE-2 and TMPRSS-2 receptor (viral point of host cell entry), it would be interesting to explore the possibility of infection transmission via COVID-19 laden particulate matter from exhaled fumes derived from tobacco smoking. Second-hand smoking may be implicated in COVID-19 transmission.

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