**Introduction**

Of all cancer types, lung cancer has the second highest incidence and is the leading cause of mortality in the world1. In the United States alone, approximately 228,280 people are projected to be diagnosed with it in 2020; 14,380 of which will be Texans2. The 5-year relative survival rate for lung cancer is 19%, which is one of the lowest, particularly when compared to prostate cancer (98%) and breast cancer (90%)2. As a result, it has become increasingly important to determine sub-populations and area-types that have an increased risk for the disease3. There are multiple practical options for both early detection (low-dose spiral CT screening, chest X-rays (CXR), sputum cytology, etc.) and treatment (resection, chemotherapy, etc.) for these individuals most at risk 3-5.

In December of 2019, the world was introduced to the novel COVID-19 virus, a pandemic that has taken thousands of lives and infected millions worldwide; in the United States, medical institutions and resources have become overwhelmed, leading to a state of emergency across the nation6. The CDC has officially stated that cancer increases one’s risk of severe illness from COVID-197. Previous work has suggested that cancer patients have a higher death rate from coronavirus8, particularly lung cancer patients who are typically older in addition to having cardiovascular/ respiratory comorbidities, smoking-related lung damage, abnormalities in airway/ pulmonary tissue, and are on immunosuppressing treatment9.

Previous studies have indicated evidence of spatiotemporal relationships among lung cancer in Maine, South Carolina and Kentucky10-13. The goal of this analysis was to determine (1) spatiotemporal relationships and trends; (2) correlations with and effects of the COVID-19 pandemic; (3) county-level socioeconomic risk factors for lung cancer in Texas. Finally, an easy-to-use interactive dashboard app was created to visualize the results of the study, which can be accessed by the following link: . Such information will be vital for policy and health leaders to best understand lung cancer and efficiently utilize early detection/ treatment resources.

**Data Collection & Preparation**

Lung cancer data for every year between 1995 and 2017 was collected from the Texas Cancer Registry (TCR) and processed via SEER\*Stat, a software that ensures strict data quality measures14. State law requires that health care professionals and institutions report information regarding cancer diagnoses and treatments to the TCR, suggesting the data is as exhaustive as possible within Texas15. The analysis was conducted by histologic type as each is hypothesized to have a unique etiology, onset, and effect on the patient. The gray boxes in **Fig 1** detail the four histologic types that were used to divide the lung cancer dataset.

**Figure 1:** Relative Distribution of Lung Cancer Diagnoses in the U.S. from 2013-2017 by Histologic Type16

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The following were the histologic codes, as determined by the third edition of the *International Classification of Diseases for Oncology* (ICD-0-3) used in the analysis17. Only microscopically conformed invasive/ metastatic lung cancer cases were considered (“/3”). Lung cancer was defined by the ICD-0-3/WHO 2008 site classification “Lung and Bronchus” within the SEER\*Stat software. Small cell carcinoma was classified under 8002 and 8041-5. Adenocarcinoma was classified under 8050, 8140-1, 8143-4, 8145, 8147, 8201, 8250-5, 8260, 8262, 8290, 8310, 8320, 8323, 8333, 8401, 8441, 8470, 8480-1, 8490, 8507, 8550-1 and 8570-6. Squamous cell carcinoma was classified under 8051-2, 8070-6, 8083-4, 8094, 8120, 8123 and 8130. Adenocarcinoma and squamous cell carcinoma are the two major types of non-small cell histologic types. Other non-small cell carcinoma were classified under 8003-4, 8012-4, 8021-2, 8030-3, 8046, 8082, 8200, 8240-6, 8249, 8430, 8560 and 8562. Sarcomas, non-specified carcinomas, and other specified types were excluded due to their limited prevalence among the population and lack of relation to the four categories defined above.

Population count data in 1995, 2000, 2005, 2010, and 2015 was collected from the US Census18. These were the years used for the socioeconomic associations’ analysis. The county-level socioeconomic factors included in the analysis were poverty and rurality. Poverty rate data was collected from the US Decennial Census and, for most recent years, the 5-year American Community Survey (ACS)19. County-level poverty rates for the years of 1995 and 2005 were extrapolated by taking the average of the 1990 and 2000 data/ 2000 and 2010 data, respectively. Quantifying the rurality of each county in Texas was conducted by utilizing their “Rural Urban Continuum Codes”, which are calculated by population and commuter data as well as adjacency to nearby metropolitan areas21-22. Because the scores are only available for the years 1993, 2003, and 2013, the most recent year before the desired year of analysis was used. Data regarding the frequency of COVID-19 cases and fatalities by county in Texas was collected from the TX DSHS, which has been updated daily since March 4th, 202022. These datasets were cleaned and processed (accounting for inconsistences/ missing data and reformatting to make the process of analysis more efficient) via both Excel and R.

**Analysis**

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Description automatically generatedThe risk of lung cancer was assumed to be different for various demographic groups. This is because lung cancer rates tend to vary by age, sex, and race. In order to take this into consideration, every year, Texas’ population data was divided into 30 groups that were formed assuming 3 age-groups (<55 Years, 55-74 Years, 75+ Years), 2 genders (Male, Female), and 5 race groups (White, Black, American Indian, Asian and Pacific Islander, and Hispanic). For example, one demographic group was “black females between 55 and 74 years of age”. Based on state-wide lung cancer data, a general lung cancer rate was calculated for each demographic group. This rate was then used to calculate the expected number of lung cancer diagnoses in each county based on the number of people in each demographic group living in that county. Finally, the true number of lung cancer cases in each county were used to find its standardized incidence ratio (SIR). SIRs are useful because they have a straightforward interpretation. A value greater than 1 indicates a potential high incidence county or “hot spot” that may be at particular risk for lung cancer. A value less than 1, on the other hand, indicates a “cold spot”. Assuming demographic group *k* and county *i* in year *j*, SIR was calculated by the following formulas23:

**Figure 4:** Model-based RR & Observed SIR from 1995-2015

*Dallas County (Pop. = 2,600,000)*

*Andrews County (Pop. = 18,000)*

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**Model Selection & Implementation**

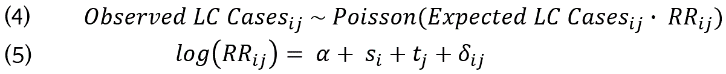
Independence between each possible pair of observations is an unfair assumption in this analysis because there exist three types of correlations in county-level lung cancer data that must be taken into consideration in a model:

(1) Spatial: Counties that are close to one another often share socioeconomic traits and topographies.

(2) Temporal: Various events/ anomalies happen in certain years that influence counties’ rates

(3) Spatiotemporal: The two effects above may interact with one another and contribute to additional variation

For this project’s analysis, a combination of the Bernardinelli Model24 and Leroux Model25 was used to model the relative risk of lung cancer for county *i* in year *j*:



where **α** is the intercept; **s** represents the spatial effects via a neighborhood matrix and Leroux parameter to determine the spatial dependency of the data; **t** represents the temporal effects via a Markovian random-walk model of order two; and **𝛿** represents the spatiotemporal effects via a completely random, independent and identically distributed model. This model was selected after calculating the information loss (sum of WAIC, DIC, and -∑ log (CPO)) of seven variations of the model for the lung cancer data of each histologic type26. Interestingly, the model with the least information loss of the original data varied by histologic type. The model options and their information loss can be found in the Appendix (**Figs 2-3**). The models were implemented through the R-INLA27 software by the methods outlined in both Moraga28 and Rubio-Gomez V29. By getting rid of uncertainty and unnecessary noise, model-based relative risk (RR) provides a smoothed version of SIR, is less vulnerable to abnormalities, and is generally considered more accurate. **Fig 4** helps visualize the effects of modeling – the significant yearly variation in the SIR for smaller counties tends to be due to small sample size, which is why modeled relative risk fluctuates less in the less populated Andrews County.

**Results**

Detailed results by demographic group & county can be found by the interactive dashboard (link in introduction).

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*General* – For all histologic cancer types, **Fig 5** shows that lung cancer rates in Texas increased and then decreased between 1995 and 2015, all trends being mostly driven by the elderly. Males and females had very similar patterns for small cell carcinoma and “other” non-small cell carcinomas. The gap between genders has decreased in recent years, a result that has been seen throughout the US21. However, although squamous cell carcinoma rates have decreased significantly among men, the rate has stayed relatively stagnant among women. Adenocarcinoma rates, on the other hand, have remained relatively stagnant among men but increased significantly among females. **Fig 7** shows this concerning trend, which is mainly driven by women above the age of 75. Rates for different histologic types and demographic groups can be found on the dashboard. **Fig 8** visualizes the spatiotemporal trends across counties in Texas by relative risk, which is a modeled version of SIR. Redder counties are at particularly high risk for lung cancer. **Figs 9-12** in the Appendix show these trends by histologic type.

**Figure 8**: Modeled (Eq. 4 & 5) Relative Risk (RR) by County in 1995, 2000, 2005, 2010 & 2015 for All Histologic Types

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**Figure 13**: Rurality Score by County in TX in 2015

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*Socioeconomic* – Rurality (**Fig 13**) and poverty (**Fig 14**) were two county-level characteristics hypothesized to be related to lung cancer. A modification of the model (Eq 5) was made to incorporate these two datasets as components of α:



**Figure 14**: Poverty Rate (%) by County in TX in 2015

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Description automatically generated **Figure 16**: 95% Confidence Intervals for the Poverty and Rurality Parameter Distributions by Histologic Type

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**Fig 15** (in the Appendix) visualizes the relative risk (RR) by county in Texas assuming the modified model (Eq 6). It is interesting to note that county-level poverty rate had an insignificant effect on lung cancer risk. Non-informative priors were assumed for both parameters in the analysis. As outlined in **Fig 16**, the parameter distributions yielded from the model (Eq 6) included 0 in their 95% CI’s for most histologic types. However, there were significant negative relationships between poverty and all lung cancer, small cell carcinoma, and adenocarcinoma. This implies that adenocarcinoma and small cell carcinoma rates tend to be higher in less rural and more metropolitan counties.

*COVID-19* – As described above, it was of interest to investigate potential relationships between COVID-19 and lung cancer, particularly how the pandemic has stressed Texas’ oncological resources. As shown in **Fig 17**, there do not appear to be notable similarities in how the two have affected the state. For example, lung cancer rates appear to be lowest in the southern tip of Texas, but the same area has some of the highest relative incidences of COVID-19. In addition, as evidenced by the parameter distributions in **Figs 18-21** (in the Appendix), there do not appear to be any statistically significant spatiotemporal relationships between how lung cancer and COVID-19 have affected Texas counties. Each of these models takes into consideration both death rates (i.e. how successfully healthcare institutions can care for their patients) and case rates (i.e. areas where people are most at risk).

**Figure 17**: COVID-19 Cases & Lung Cancer Diagnoses per 100k Texans by County

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**Discussion**

Bala blab la

**Conclusion**

Bla bla so close

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