

**IMPACT OF SMOKE-FREE LEGISLATION IN IRELAND ON LUNG CANCER  
INCIDENCE AND MORTALITY**

by

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A Dissertation

Submitted in Partial Fulfillment of the Requirements for the  
Master of Public Health.

School of Public Health  
in the College of Medicine and Health,  
National University of Ireland, Cork  
November 2018

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## **Journal Article Title Page**

### **FULL-LENGTH RESEARCH ARTICLE**

## **Impact of Smoke-Free Legislation In Ireland on Lung Cancer Incidence And Mortality**

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**Word Count:** 4026 (2 Tables, 5 Figures, 4 Supplementary Tables, 3 Supplementary Figures)

**Acknowledgements:** TLC acknowledges funding from the George J. Mitchell Scholarship program of the US-Ireland Alliance. He thanks the Ireland Environmental Protection Agency, Ireland Health Services Executive, National Cancer Registry Ireland, and the Central Statistics Office of Ireland for access to air quality, smoking prevalence, cancer incidence, and cancer mortality data (respectively). This paper was written as TLC's dissertation for a Master of Public Health degree, and he thanks the UCC School of Public Health faculty for their instruction and guidance in the MPH program.

## **Acknowledgements:**

Several people and institutions deserve my gratitude for this dissertation.

First and foremost, I would like to thank my dissertation adviser, Prof. Zubair Kabir, for his guidance and support. I would also like to thank my MPH instructors, including Prof. Kabir as well as Prof. Ivan Perry, Prof. Anthony (Tony) Fitzgerald, and Prof. Ali Khashan. I appreciate the financial support, experiences, and fellowship afforded to me by the George J. Mitchell Scholarship of the US-Ireland Alliance. Without the Mitchell Scholarship, I would not have been had the life-changing experience of spending a year in Ireland or the opportunity to pursue an MPH at UCC. The lessons I have learned from this course will serve me well as I pursue a career in health research.

I would also like to thank the National Cancer Registry Ireland for providing cancer incidence data, the Central Statistics Office for providing population estimates and cancer mortality data, the Health Services Executive for providing Irish smoking prevalence data, and the Ireland Environmental Protection Agency for providing air quality data. This project would not have been possible without the assistance of those institutions and the hard work of their employees.

I am grateful for the support of my friends and family. I greatly enjoyed all the coffee-and-study sessions I had at Café Eco with my classmate, Melanie. I appreciate the kindness and support my family (particularly my mother) has given me throughout my academic career.

Although not directly related to my dissertation or my study in Ireland, I would be remiss if I did not thank my doctors at Massachusetts General Hospital, Hospital of the University of Pennsylvania, and Saint Mary's Medical Center. I developed testicular cancer in my first semester at UCC, and I would not have been able to complete this degree without the compassionate care of Dr. Gabale, my urologist; Dr. Blute, my surgeon; and Dr. Vaughn, my oncologist.

In that vein, my dissertation is dedicated to all patients, survivors, and victims of cancer. Hopefully, this work will be used to improve tobacco control policy so that fewer individuals and families will have to suffer through the hardships of cancer.

**Main Text:****Abstract:**

**Background:** In 2004, Ireland became the first country worldwide to institute a comprehensive workplace smoking ban. Previous research has found that comprehensive smoking bans are associated with public health benefits, including significant reductions in the incidence and mortality of cardiovascular and respiratory disease. However, given the relative recent occurrences of smoking bans and the long latency of smoke's effect on lung cancer, the effect of smoking bans on lung cancer has not been well explored.

**Methods:** This study exploits the 2004 Irish Workplace Smoking Ban as a quasi-experiment to discern the effect of smoking bans on lung cancer incidence and mortality. Annual, age- and sex-specific incidence and mortality of lung cancer were calculated. Previous research suggests that a smoking ban was unlikely to have an immediate effect on lung cancer and so an appropriate lag time for a modelled interruption was calculated (2010 for lung cancer incidence, 2006 for lung cancer mortality). A one-sample, Poisson-based, interrupted time series analysis, adjusted for the confounding of smoking prevalence, was used to compare lung cancer incidence and mortality before and after the modelled interruption. Effect modification was evaluated by comparison of results from segmented regressions. Finally, the number of incident cases and mortalities were computed by comparing model-fitted to observed lung cancer incidence and mortality rates. To validate that the findings are due to the smoking ban, identical analyses were run for incidence and mortality of brain cancer, a cancer with no link to smoking or second-hand smoke exposure. Analyses were conducted in R ver. 3.5.0.

**Results:** Each year following the modelled interruptions, lung cancer incidence in Ireland decreased 3% (95%CI 2-5,  $p<0.01$ ) relative to the modelled counterfactual, and lung cancer mortality in Ireland decreased 1% (95%CI 0-2,  $p=0.01$ ) relative to the modelled counterfactual. In absolute terms, the 2004 Irish Workplace Smoking Ban was associated with an estimated 209 (95%CI 155-274) fewer lung cancer incident cases per year and 122 (95%CI 104-143) fewer lung cancer deaths per year. These estimates correspond to approximately 6.9% fewer lung cancer incident cases and 5.9% fewer lung cancer deaths post-the smoking ban.

**Discussion:** The 2004 Irish Workplace Smoking Ban avoided approximately 1,050 incident lung cancer cases and 1,100 lung cancer deaths. This is among the first studies to examine the effect of a comprehensive smoke-free policy on lung cancer in a comparable population setting. The findings add to the body of literature informing the public, policy-makers, and tobacco control advocates on the positive health effects of comprehensive smoke-free legislation.

## **Introduction:**

Ireland has become a global leader in tobacco control practices designed to reduce smoking prevalence and second-hand smoke exposure. This strategy has been successful, reducing the smoking prevalence from 29% to 18% in the past 15 years (1). A watershed moment for this movement in tobacco control was the 2004 Workplace Smoking Ban (2), through which Ireland became the first country globally to institute a comprehensive smoking ban in all workplaces, including restaurants, bars, and pubs (3). Previous research has shown the positive effect the Workplace Smoking Ban has had on workers; following the ban, Irish workers experienced improvements in bar-worker respiratory function and reductions in self-reported second-hand smoke and respiratory symptoms (4,5). Further, the level of particulate matter in bars and pubs decreased significantly following the ban (6). The effects of the Workplace Smoking Ban could also be observed on a broader level, as hospital admissions due to acute coronary syndrome (7) and acute pulmonary disease (8); mortality due to cardiovascular, cerebrovascular, and respiratory disease (9); and babies born small-for-gestational age (10) all decreased in Ireland following the Workplace Smoking Ban.

These positive health effects emerging from the Workplace Smoking Ban are in line with other similar evidence on smoking bans globally (11). Importantly, researchers have also found that possible counter-effects of smoke-free legislation are either negligible or non-existent. For example, researchers failed to find evidence of substantial changes in business revenues or operating expenses (12), including at bars and pubs (13). Further, studies suggest that smoking bans do not tend to affect the subjective wellbeing of smokers (14). The consistently positive health effects combined with negligible economic or well-being counter-effects have made smoking bans an attractive public health strategy; to date, 17 EU countries (15) and 26 US states (and the District of Columbia) (16) have adopted workplace smoking bans.

Still, there are potential areas of research around comprehensive workplace smoking bans that have yet to be thoroughly investigated. Perhaps most strikingly, the effect of smoking bans on lung cancer has not been thoroughly explored. Lung cancer is an important area in public health with substantial human and economic consequences in Ireland and globally (17). For example, lung cancer is the fifth most common form of cancer in Ireland, with an estimated 2,566 new cases annually (18). A recent economic evaluation estimates that lung cancer costs the Irish health-care system €619 million, amounting to approximately 4% of total health-care expenditures (19). Due to the massive impact lung cancer has on Ireland, even marginal changes to lung cancer incidence and/or mortality will have large absolute effects on population health.

Smoking is the single most preventable cause of lung cancer, as the Irish Cancer Society estimates that 9 of 10 cases of lung cancer in Ireland are caused by smoking (18). In addition to active smoking, there is evidence that second-hand smoking is also a contributing factor for lung cancer (20–22). The Workplace Smoking Ban has the potential to change both of these exposures; second-hand smoke exposure may be reduced (23) and/or the level of active smoking (i.e., prevalence, frequency, and intensity) may be decreased (24–26).

Despite the intuition that a smoking ban may impact lung cancer incidence and mortality, only two previous studies have explicitly measured lung cancer (hospital admissions and mortality) before and after a smoking ban. The first study (27) followed lung cancer mortality before and after the 2007 Hong Kong smoking ban. Though the authors found a significant reduction in lung cancer mortality immediately following the ban, they cautioned against interpreting this finding as an effect of the ban, given the long latency period for lung cancer relative to the short follow-up period of the study (two years after the ban). The second study (28) measured lung cancer incidence in relation to municipal smoke-free ordinances in the US state of Kentucky, finding that individuals living in communities with comprehensive smoke-free ordinances were 7.9% less likely to be diagnosed with lung cancer. Because the studied municipal smoke-free ordinances were implemented at different times (ranging from 2004-2013), the authors may not have had sufficient follow-up data for several of the municipalities; indeed, the authors state their results are preliminary and may not capture the full-term effects of the ordinances.

While these past studies are informative indicating the magnitude and direction of the impact of smoking ban on lung cancer, the full effects of smoking bans on lung cancer is yet to be determined in terms of a longer follow-up study. Therefore, this study, using the oldest national smoking ban (Ireland's in 2004) and the latest available data (up to 2015), has the potential to add to the body of evidence in relation to a critically important public health strategy. This research will be useful both in evaluating the effectiveness of a comprehensive smoking ban and informing the public and the policy-makers alike in other comparable countries on the potential benefits or consequences of adopting comprehensive smoking bans.

### **Research Question:**

This study seeks to answer the following research question:

What was the effect of the 2004 Irish Workplace Smoking Ban on lung cancer incidence and mortality when compared to a counter-factual scenario?

### **Methods:**

#### *Study Design:*

The study design was a quasi-experimental interrupted time-series study based upon Poisson regression, using the pre-ban period as historical controls.

#### *Data sources:*

Aggregated cancer incidence data from 1994 to 2014 were extracted from the National Cancer Registry of Ireland (NCRI). In this case, incidence refers to the number of cases of lung cancer discovered among members of a given demographic age-sex group in a given year. The NCRI captures the near universe of cancer incidence in Ireland, as validated in a recent study (29). Individual age groups in certain years with fewer than five cases were coded as "<5" rather than

a specific number; when that occurred, the number of cases was recoded to 2, the median of 0 to 4. (The data abstraction form submitted to the NCRI is appended at the end of this document).

Quarterly (aggregate) cancer mortality data from 1994 to 2015 was extracted from the Deaths Occurring by Sex, Cause of Death, Age at Death and Year dataset (VSA08) from the StatBank of Irish Central Statistics Office (CSO). The VSA08 is a validated record of cause of death in Ireland(30).

Irish population data by age and sex was extracted from the Population and Migration Estimates from the CSO. Cigarette smoking prevalence data by age and sex from 2002 to 2018 was extracted from the Health Service Executive's (HSE) Ipsos MRBI's Omnipoll.

Because the study sample and target population for lung cancer incidence and mortality are nearly one in the same, it is unlikely that selection bias will play a significant role in the study.

#### *Confounders:*

Lung cancer incidence and mortality was adjusted by annualized percentage of smokers in Ireland. Previous studies indicate Irish smoking prevalence was not impacted by the smoking ban (9,31,32), so smoking prevalence is unlikely to be a mediator between the smoking ban and lung cancer incidence and mortality.

Irish smoking prevalence data is only available for 2002-2018. Similar to previous analyses, a linear time trend was fit through this data and prevalence before 2002 was imputed based upon this linear trend model. Because age-sex cell sizes were small for smoking prevalence (some had less than 10 respondents) and substantial imputation had to be conducted to account for years before 2002, overall smoking prevalence was used as a confounder in the main model. A supplementary analysis using age-sex specific smoking prevalence rates as a confounder was also computed.

Air quality is another potential confounder, as there is significant evidence that high particulate matter concentration is associated with lung cancer (33). However, scarce Irish Environmental Protection Agency data on particulate matter made the analysis unreliable, and so air quality was not included as a confounder in the main results. An explanation of the effect of adding particulate matter to the data is included in Supplement 1.

The model can be visualized in the following Directed Acyclic Graph (Figure 1).

[Figure 1 Near Here]

#### *Statistical Analysis:*

Poisson regression with one-sample interrupted time-series analysis (34–37) was used to calculate the difference in annual lung cancer mortality and incidence before and after an interruption. That is, for each year-age-sex combination, the number of mortality and incidence cases within that group was regressed against an indicator for pre- vs. post-interruption, with an offset for the population of the age-sex group.

There is some evidence that an effect on lung cancer may be observed after 1-year of a comprehensive smoking ban (38), however, this evidence is not conclusive. Consequently,



interruption points 0, 1, 2, 3, 4, 5, and 6 years after the 2004 ban were tested using a forward stepwise regression, and the most significant break point (measured by the absolute value of the t-statistic) was used as the interruption. This protocol is in line with previous studies on tobacco control interventions with unknown lag periods for observable outcomes (38,39). The break interruption used for lung cancer incidence was 2010 and the interruption used for lung cancer mortality was 2006.

A linear time trend was included to detect underlying linear trends in incidence or in mortality. A Durbin-Watson statistic revealed significant autocorrelation in both the incidence and mortality data, and so significant lag time effects were included in each model (a 2-year lag for incidence; 1-, 2-, and 3- year lags for mortality).

In formulaic terms, the model was specified as follows:

$$\ln(E(Y_{t,s,a})) = \beta_0 + \beta_1 T_{t,s,a} + \beta_2 X_{t,s,a} + \beta_3 X_{t,s,a} T_{t,s,a} + \beta_4 C_{t,s,a} + \epsilon_{t,s,a}$$

In this model, the subscript  $t$  refers to the year, subscript  $s$  to sex, subscript  $a$  to age group,  $Y_t$  to the aggregated annual rate (either incidence or mortality),  $T_t$  to the years since the beginning of the study period (1994),  $X_t$  to an indicator variable for whether the observation is before or after the intervention, and  $C_t$  to a matrix of time-varying confounders. The  $\beta$ 's are parameter estimates, and  $\epsilon_t$  is an error term. The lag terms,  $\epsilon_t$ , are modelled as:

$$\epsilon_{t,s,a} = \rho \epsilon_{t-Q,s,a} + u_{t,s,a}$$

where  $Q$  is equal to the number of lagged years and  $\rho$  is the correlation coefficient between adjacent error terms.

In this model,  $\beta_2$  captures immediate shifts after the interruption, while  $\beta_3$  captures slope (i.e., gradual) shifts after the interruption.

To validate that the observed shifts are attributable to the smoking ban, an identical analysis was conducted with incidence and mortality of brain cancer as the dependent variable. Brain cancer is unrelated to smoking (either active or passive) and so there should be no impact of the smoking ban on brain cancer incidence or mortality.

To detect effect modification, segmented regression analyses were conducted based upon age group and sex.

For each analysis, risk ratios and 95% confidence intervals for both immediate effects ( $\beta_2$ ) and gradual effects ( $\beta_3$ ) were reported by exponentiating the Poisson regression coefficients and confidence intervals. P-values were also reported.

#### *Total Number of Cases Avoided:*

In addition to the regression analysis, the total number of cases avoided from the smoking ban was calculated by subtracting the observed number of cases from the number of cases predicted over the post-interruption time period using the pre-interruption slope and intercept (40). A 95% confidence interval was computed through bootstrapping the difference between the number of cases predicted versus the number of cases observed, in line with previous studies (41).

All data analyses were conducted in R ver. 3.5.0 using a two-sided alpha of 0.05.

## Results:

The 2004 Irish Smoking Ban significantly reduced the incidence and mortality of lung cancer in Ireland. In line with previous studies, the smoking ban was most strongly associated with a decline in lung cancer mortality 2 years after the smoking ban (interruption modelled at 2006); further, a decline in lung cancer incidence was observed 6 years after the smoking ban (interruption modelled at 2010). Specifically, in each year after these modelled interruptions, the lung cancer incidence decreased 3% (95%CI 2-5,  $p<0.01$ ) relative to the modelled counterfactual (Figure 2) and lung cancer mortality decreased 1% (95%CI 0-2,  $p=0.01$ ) relative to the modelled counterfactual (Figure 3).

While effect modification could not be formally tested with an interaction term, there is little evidence to suggest that the effect is modified by either age group or sex. For both lung cancer incidence (Table 1) and mortality (Table 2), the effect of the smoking ban was similar among males and females and all age groups ranging from 40-44 years old to 85+. For example, both males and females saw a 2% decrease (95%CI 1-4,  $p=0.01$  for males; 95%CI 1-4,  $p<0.01$  for females) in lung cancer incidence each year following the modelled interruption, and males and females saw a 1% and 2% decrease (95%CI 0-3,  $p=0.02$  for males; 95%CI 0-2,  $p=0.02$  for females) in lung cancer mortality each year following the modelled interruption. There were few indications of effect modification among different age groups, with most age groups having similar gradual effects sizes for lung cancer incidence and lung cancer mortality. One potential exception is that, while the results indicated immediate increases in lung cancer mortality occurred for most age groups, there was a significant immediate decline in lung cancer mortality for those aged 85 and older (Table 2).

The total number of incident cases avoided due to the smoking ban was approximately 1,050 (95%CI 780-1370) or 209 (95%CI 155-274) per year following the 2010 modelled interruption, representing 6.9% of incident cases observed since 2010. The total number of mortalities avoided due to the smoking ban was approximately 1,100 (95%CI 930-1290) or 122 (95%CI 104-143) per year following the 2006 modelled interruption, representing 5.9% of incident cases observed since 2006.

The model showed an increase in both lung cancer incidence and mortality immediately following the modelled interruptions. Lung cancer incidence was 76% higher than expected in 2010 (95%CI 42-117,  $p<0.01$ ), and cancer mortality was 13% higher than expected in 2006 (95%CI 1-26,  $p=0.03$ ).

Using age-sex specific smoking prevalence rates as a confounder (rather than the overall Irish smoking prevalence) did not meaningfully impact these results. In that model, in each year after these modelled interruptions, the lung cancer incidence (Supplementary Table 1) decreased 3% (95%CI 2-4,  $p<0.01$ ) relative to the modelled counterfactual and lung cancer mortality

(Supplementary Table 2) decreased 1% (95%CI 0-2,  $p=0.03$ ) relative to the modelled counterfactual. Similarly, including particulate matter 2.5 concentration as a confounder did not significantly alter the results (see Supplement 1).

There was no significant effect of the smoking ban on brain cancer (Figures 4 and 5). Brain cancer incidence increased 39% (95%CI -24 – 154,  $p=0.28$ ) immediately following the ban and fell 2% each year after the smoking ban (95%CI -5 – 1,  $p=0.20$ ), but neither of these findings were significant at an alpha of 0.05 (Supplementary Table 3). Similarly, brain cancer mortality increased by 26% immediately following the ban (95%CI -7 – 70,  $p=0.14$ ) and fell 1% each year after the smoking ban (95%CI -3 – 1,  $p=0.39$ ). Again, neither of these results were significant at an alpha of 0.05 (Supplementary Table4).

[Table 1-2 & Figure 2-5 Approximately Here]

## **Discussion:**

The 2004 Irish Workplace Smoking Ban significantly reduced the public health burden associated with lung cancer. Both lung cancer incidence and mortality fell relative to observed rates, resulting in approximately 1,050 fewer incident cases and 1,100 fewer deaths so far. While effect modification was not formally tested, there is little evidence to suggest that the effect was modified by either age or sex. These results were robust to sensitivity analyses, including using age-sex specific smoking prevalence rates or including air quality as a confounder. Further, that these results were due to the smoking ban was validated by the lack of significant findings when applying the same analyses to incidence and mortality due to brain cancer, a cancer unrelated to smoking or second-hand smoke exposure.

That lung cancer incidence and mortality increased immediately following the modelled interruptions is surprising. It is unlikely these statistically significant findings can be explained by the smoking ban, as there is no known reason to believe a smoking ban would increase lung cancer incidence or mortality. Instead, these immediate increases are more likely artefacts of using a stepwise regression to choose the interruption with the maximally significant gradual effect and applying linear models to data that is not precisely linear. Regardless, the positive effect of the smoking ban on both lung cancer incidence and mortality was significant over the entire available timeframe, as demonstrated by the positive number of incidence cases and deaths avoided due to the smoking ban. That is, the gradual decreases in lung cancer incidence and mortality outweighed the immediate increases, leading to a significantly positive public health effect over the studied timeframe. While these statistical anomalies may impugn the results of the study altogether, it is reassuring that a robustness test applying the same method to brain cancer showed no effect of the smoking ban. That these modelled interruptions were associated with reductions in tobacco-related cancers but not with tobacco-unrelated cancers supports the notion that the modelled interruptions represent the effect of the smoking ban.

There appears to be a longer latency in incidence than mortality. This study treated incidence and mortality as separate outcomes as we had insufficient data to measure the path from discovery (i.e., incidence) to death (i.e., mortality). Consequently, a definitive explanation cannot be

offered. However, several possible explanations exist. For example, lung cancer mortality may be exacerbated by other causes such as infection or injury, and it is possible there were changes in those other causes. Further, medical testing or early detection practices could have changed over the study period. From this perspective, mortality is perhaps a better outcome variable than incidence, as incidence is a function of both testing and onset of the disease. Future research utilizing individual-level, longitudinal data may provide better insight into this phenomenon.

The observed effect of the smoking ban appeared relatively consistent among sex and age-groups. While effect modification could not be formally tested with an interaction term, the effect sizes appeared similar among the groups, with substantial overlap in confidence intervals. The one potential exception noted is that the point estimate for those aged 85 years or older indicated an immediate decrease in lung cancer mortality while the point estimates for other age groups indicated an immediate increase. Some may hypothesize that this observed effect is indicative of the phenomenon known as “harvesting”, in which improvements to air quality postpone mortality among the very ill in the very short-term without having much of a public health impact (42). However, because of the significant lag time between the smoking ban and the modelled interruption, it is more likely this is simply due to random variation than to harvesting. Of course, the immediate effect is not significantly different from no effect for all age groups, and future research with richer data would have to discern whether this type of effect modification occurs at all.

Only a few studies have investigated the effect of the smoking ban on lung cancer. Within this limited literature, the current results appear to be in line with past evidence. Perhaps the most comparable past study investigated the impact of comprehensive smoking bans on lung cancer incidence in Kentucky. The authors found that in comprehensive smoking bans, lung cancer incidence rates were 7.9% lower than would otherwise be expected; the present study found that the smoking ban in Ireland reduced lung cancer incidence by 6.9%.

#### *Strengths and Limitations:*

To my knowledge, this is the first study to investigate the effect of a smoking ban on lung cancer within Ireland. Ireland had the first nation-wide smoking ban in the world and, consequently, there are more years of data on the effect of Ireland’s smoking ban than any others. Previous research teams investigating the connection between smoking bans and lung cancer have admitted they were unable to estimate the full effect of the smoking ban on lung cancer due to the long latency of second-hand smoke on lung cancer. While it is possible that the effect of Ireland’s smoking ban on lung cancer will continue to evolve in the future, this study at least provides results using data more than 10 years after the implementation of the ban. Therefore, this study contributes to the literature a better understanding of the medium- to long-term effects of smoking bans on lung cancer.

This study is not without limitations. Due to institutional disagreements related to the European Union’s General Data Protection Regulation of 2016/2017, I was unable to procure individual-level data on lung cancer incidence, potentially reducing the precision of my analysis. Further, that Ireland enacted its workplace smoking ban all at once implies that there is no contemporary control group. The one-sample interrupted time series design exploits patterns in the data from

before the modelled interruption to patterns after the modelled interruption, essentially treating the pre-interruption data as a control for the post-interruption treatment group. While this approach has been frequently used in the literature (9), the possibility remains that an external event could have impacted lung cancer at roughly the same time as the modelled interruption. In that case, the effect of the smoking ban on lung cancer incidence and mortality would be unclear; the effect reported here could be overstated if the external event reduced lung cancer incidence and/or mortality, and the effect reported here could be understated if the external event increased lung cancer incidence and/or mortality. After intensively examining the tobacco control landscape in Ireland, however, I could not find a significant event near either of the modelled interruptions that could convincingly explain a significant effect on lung cancer, though it is possible interventions such as media campaigns, health promotional activities, and the point-of-sale advertising ban in 2009 could play a role. Further, a robustness test was conducted that applied an identical analysis to data on brain cancer. Brain cancer is unrelated to smoking and so it was expected that the smoking ban would have no effect on brain cancer incidence or mortality; indeed, the smoking ban appears to have had no significant effect. While this robustness test does not completely rule out the possibility of an external event that affected lung cancer, it mitigates the possibility that a broader event on cancer or public health is the true cause of the observed decline in lung cancer incidence and mortality.

#### *Implications for Policy-Makers and Future Research:*

This study has important implications for policy-makers, tobacco control practitioners, and researchers. Research into the effects of smoking bans on public health broadly and lung cancer specifically is crucially important. Smoking bans are still a relatively new policy invention, and policy-makers still must defend smoking bans to critics (43). Further, there is still an enormous portion of the developed world living without comprehensive smoking bans. Twenty-four US states and 11 European Union countries do not yet have comprehensive smoking bans (16,44). In each of these jurisdictions, lung cancer and other ailments related to smoking levy an enormous burden. This research contributes to the body of evidence that smoking bans have the potential to significantly improve population health and well-being.

Policy-makers can use this study as evidence that the smoking ban avoided approximately 1,050 cases of lung cancer and saved approximately 1,100 lives since its implementation in 2004. Combining the results of this study with previous research on the other positive health effects of the smoking ban, such as reduced cardiovascular disease, along with studies failing to show a negative economic effect of smoking ban, policy-makers now have an arsenal of validated research to support the adoption (or retention (43)) of smoking bans. Similarly, tobacco control practitioners can use these results to recommend smoking bans in smaller jurisdictions and even individual establishments. In the coming years, there will be medium- and long-term data on national smoking bans adopted shortly after Ireland's, such as those in Norway (2004), New Zealand (2004), and the United Kingdom (2007). Researchers can explore whether smoking bans have a similar effect on lung cancer within different cultures and different tobacco control regimes as these data become available. Of course, even though this study utilizes data from more than a decade after the implementation of the Irish smoking ban in 2004, the study's empirical strategy revealed significant delays in its effect on lung cancer. Therefore, the study's

time frame after the modelled interruptions (2010 for incidence and 2006 for mortality) leave less post-interruption time to analyze; future researchers can explore even longer-term results as data become available.

In summary, the 2004 Irish Workplace Smoking Ban has been shown to have had several public health benefits, including reductions in lung cancer incidence and mortality. Longer follow-up studies are essential to fully understand the biological and policy implications of a comprehensive smoke-free policy.

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**Tables:**

**Table 1. Overall effect estimates of the Smoking Ban on Lung Cancer Incidence in the time period studied (1994-2014) by age-groups in Ireland**

	Immediate Effect			Gradual Effect		
	RR	95%CI	p	RR	95%CI	p
Total	1.76	(1.42 to 2.17)	0.00	0.97	(0.95 to 0.98)	0.00
40-44 years	1.88	(0.18 to 18.65)	0.59	0.96	(0.84 to 1.09)	0.48
45-49 years	2.63	(0.57 to 12.08)	0.21	0.93	(0.85 to 1.01)	0.10
50-54 years	2.77	(1.00 to 7.64)	0.05	0.95	(0.90 to 1.01)	0.11
55-59 years	1.16	(0.53 to 2.52)	0.70	0.99	(0.95 to 1.03)	0.60
60-64 years	1.35	(0.76 to 2.40)	0.30	0.98	(0.95 to 1.02)	0.35
65-69 years	2.26	(1.11 to 4.61)	0.03	0.95	(0.91 to 1.00)	0.03
70-74 years	1.09	(0.63 to 1.90)	0.75	1.00	(0.97 to 1.03)	0.87
75-79 years	1.14	(0.68 to 1.90)	0.63	0.99	(0.96 to 1.02)	0.51
80-84 years	1.86	(0.99 to 3.47)	0.05	0.96	(0.93 to 1.00)	0.04
85+ years	2.05	(0.95 to 4.42)	0.07	0.97	(0.92 to 1.01)	0.14
Female	1.51	(1.14 to 1.99)	0.00	0.98	(0.96 to 0.99)	0.00
Male	1.54	(1.10 to 2.15)	0.01	0.98	(0.96 to 0.99)	0.01

**Table 2. Overall effect estimates of the Smoking Ban on Lung Cancer Mortality in the time period studied (1994-2014) by age-groups in Ireland**

	Immediate Effect			Gradual Effect		
	RR	95%CI	p	RR	95%CI	p
Total	1.13	(1.01 to 1.26)	0.03	0.99	(0.98 to 1.00)	0.01
40-44 years	1.51	(0.37 to 5.83)	0.55	0.95	(0.85 to 1.05)	0.28
45-49 years	1.61	(0.71 to 3.58)	0.25	0.96	(0.91 to 1.03)	0.25
50-54 years	1.20	(0.66 to 2.15)	0.55	1.01	(0.96 to 1.05)	0.76
55-59 years	1.37	(0.90 to 2.07)	0.14	0.99	(0.95 to 1.02)	0.40
60-64 years	1.37	(0.98 to 1.90)	0.06	0.98	(0.95 to 1.01)	0.12
65-69 years	1.19	(0.83 to 1.71)	0.34	0.99	(0.96 to 1.02)	0.38
70-74 years	1.06	(0.81 to 1.38)	0.67	0.99	(0.97 to 1.01)	0.37
75-79 years	1.25	(0.96 to 1.63)	0.10	0.97	(0.95 to 0.99)	0.01
80-84 years	1.28	(0.92 to 1.78)	0.14	0.98	(0.95 to 1.01)	0.11
85+ years	0.58	(0.32 to 1.04)	0.07	1.04	(1.00 to 1.10)	0.07
Female	1.20	(1.01 to 1.43)	0.04	0.98	(0.97 to 1.00)	0.02
Male	1.15	(0.99 to 1.33)	0.06	0.99	(0.98 to 1.00)	0.02

**Supplementary Table 1. Overall effect estimates of the Smoking Ban on Lung Cancer Incidence in the time period studied (1994-2014) by age-groups in Ireland, using age-sex specific smoking prevalence as a confounder**

	Immediate Effect			Gradual Effect		
	RR	95%CI	p	RR	95%CI	p
Total	1.66	(1.37 to 2.00)	0.00	0.97	(0.96 to 0.98)	0.00
40-44 years	1.74	(0.21 to 14.05)	0.60	0.96	(0.85 to 1.08)	0.48
45-49 years	2.53	(0.50 to 12.82)	0.26	0.93	(0.85 to 1.02)	0.14
50-54 years	3.49	(1.38 to 8.79)	0.01	0.94	(0.89 to 0.99)	0.02
55-59 years	0.91	(0.46 to 1.80)	0.79	1.00	(0.96 to 1.04)	0.88
60-64 years	1.46	(0.87 to 2.46)	0.15	0.98	(0.95 to 1.00)	0.10
65-69 years	2.24	(1.20 to 4.19)	0.01	0.96	(0.92 to 0.99)	0.02
70-74 years	0.80	(0.48 to 1.32)	0.38	1.02	(0.99 to 1.05)	0.27
75-79 years	1.23	(0.78 to 1.94)	0.37	0.99	(0.96 to 1.01)	0.27
80-84 years	2.40	(1.38 to 4.18)	0.00	0.95	(0.92 to 0.98)	0.00
85+ years	2.41	(1.22 to 4.75)	0.01	0.95	(0.92 to 0.99)	0.02
Female	1.62	(1.26 to 2.07)	0.00	0.97	(0.96 to 0.99)	0.00
Male	1.42	(1.06 to 1.91)	0.02	0.98	(0.96 to 1.00)	0.01

**Supplementary Table 2. Overall effect estimates of the Smoking Ban on Lung Cancer Mortality in the time period studied (1994-2014) by age-groups in Ireland, using age-sex specific smoking prevalence as a confounder**

	Immediate Effect			Gradual Effect		
	RR	95%CI	p	RR	95%CI	p
Total	1.13	(1.04 to 1.24)	0.01	0.99	(0.98 to 1.00)	0.03
40-44 years	1.66	(0.59 to 4.69)	0.34	0.95	(0.85 to 1.07)	0.44
45-49 years	0.96	(0.48 to 1.90)	0.91	0.98	(0.91 to 1.06)	0.57
50-54 years	0.87	(0.56 to 1.35)	0.54	1.02	(0.97 to 1.08)	0.36
55-59 years	1.28	(0.87 to 1.88)	0.21	0.97	(0.93 to 1.01)	0.13
60-64 years	1.34	(0.98 to 1.84)	0.07	0.97	(0.93 to 1.01)	0.13
65-69 years	1.19	(0.87 to 1.62)	0.28	0.99	(0.96 to 1.03)	0.65
70-74 years	1.19	(0.97 to 1.47)	0.10	0.97	(0.95 to 1.00)	0.02
75-79 years	1.24	(1.01 to 1.53)	0.04	0.99	(0.97 to 1.01)	0.38
80-84 years	1.28	(0.95 to 1.73)	0.10	0.98	(0.94 to 1.01)	0.20
85+ years	0.72	(0.45 to 1.14)	0.16	1.03	(0.99 to 1.08)	0.15
Female	1.16	(1.00 to 1.34)	0.05	0.99	(0.97 to 1.01)	0.26
Male	1.17	(1.04 to 1.32)	0.01	0.98	(0.97 to 1.00)	0.01

**Supplementary Table 3. Overall effect estimates of the Smoking Ban on Brain Cancer Incidence in the time period studied (1994-2014) by age-groups in Ireland**

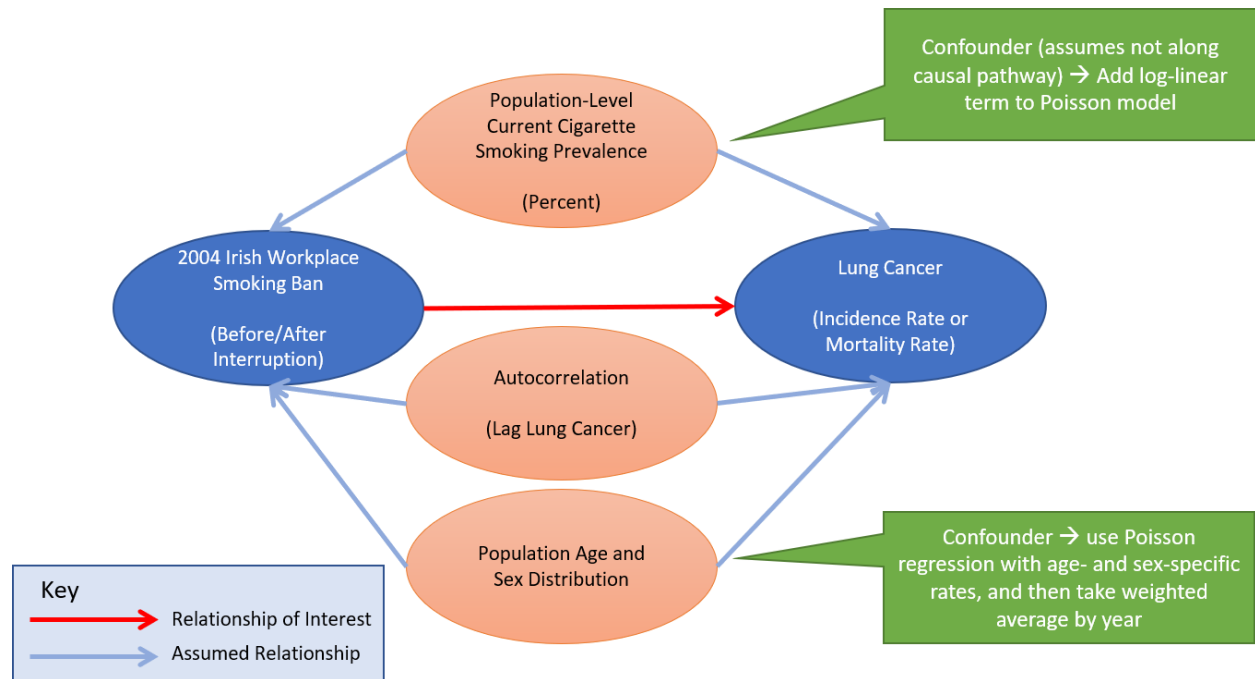
	Immediate Effect			Gradual Effect		
	RR	95%CI	p	RR	95%CI	p
Total	1.39	(0.76 to 2.54)	0.28	0.98	(0.95 to 1.01)	0.20
40-44 years	1.29	(0.09 to 16.73)	0.85	0.98	(0.84 to 1.13)	0.75
45-49 years	0.32	(0.03 to 3.29)	0.34	1.07	(0.94 to 1.23)	0.30
50-54 years	1.54	(0.20 to 11.62)	0.68	0.97	(0.86 to 1.09)	0.62
55-59 years	2.01	(0.33 to 11.91)	0.45	0.97	(0.87 to 1.07)	0.49
60-64 years	1.05	(0.21 to 5.13)	0.95	0.99	(0.91 to 1.09)	0.87
65-69 years	0.82	(0.17 to 3.97)	0.81	1.01	(0.93 to 1.11)	0.79
70-74 years	0.92	(0.17 to 4.71)	0.92	1.00	(0.91 to 1.09)	0.94
75-79 years	1.69	(0.27 to 10.41)	0.58	0.97	(0.88 to 1.08)	0.61
80-84 years	4.87	(0.55 to 41.36)	0.15	0.90	(0.80 to 1.02)	0.11
85+ years	7.02	(0.35 to 130.33)	0.20	0.88	(0.74 to 1.04)	0.12
Female	0.83	(0.37 to 1.84)	0.64	1.00	(0.96 to 1.05)	0.84
Male	2.96	(1.18 to 7.38)	0.02	0.94	(0.89 to 0.99)	0.02

**Supplementary Table 4. Overall effect estimates of the Smoking Ban on Brain Cancer Mortality in the time period studied (1994-2014) by age-groups in Ireland**

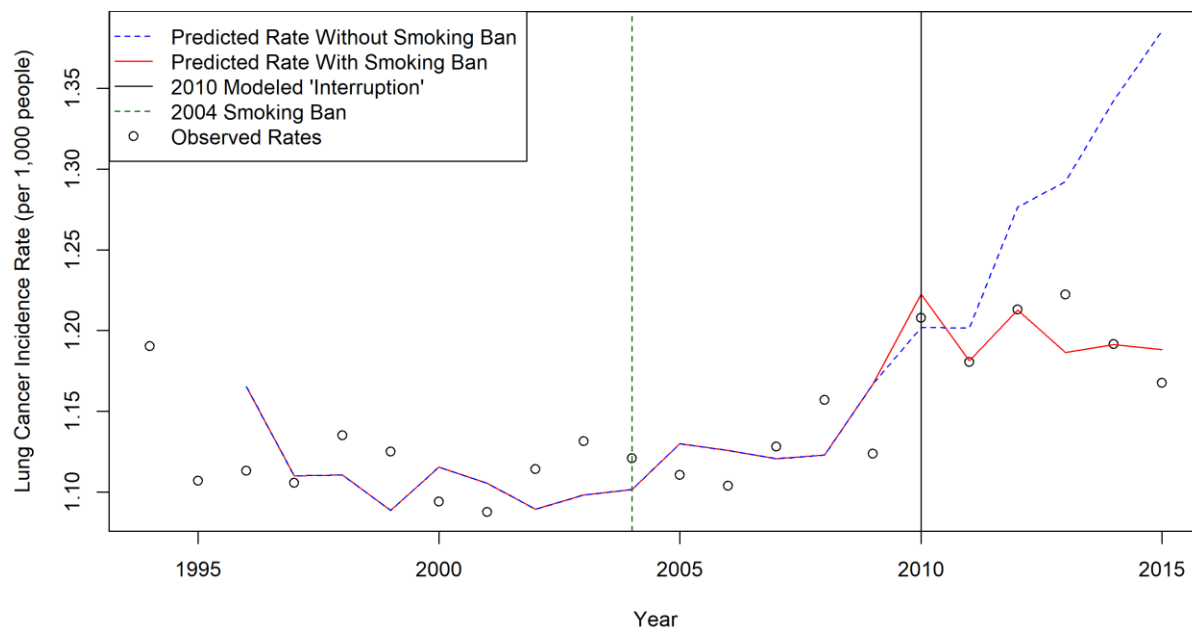
	Immediate Effect			Gradual Effect		
	RR	95%CI	p	RR	95%CI	p
Total	1.26	(0.93 to 1.70)	0.14	0.99	(0.97 to 1.01)	0.39
40-44 years	0.80	(0.17 to 3.46)	0.77	1.03	(0.90 to 1.16)	0.69
45-49 years	0.97	(0.27 to 3.31)	0.97	1.05	(0.95 to 1.16)	0.31
50-54 years	1.24	(0.31 to 4.82)	0.76	0.95	(0.87 to 1.05)	0.35
55-59 years	0.60	(0.24 to 1.41)	0.25	1.06	(0.99 to 1.13)	0.11
60-64 years	1.11	(0.43 to 2.86)	0.83	1.01	(0.93 to 1.09)	0.87
65-69 years	0.47	(0.18 to 1.17)	0.11	1.06	(0.99 to 1.14)	0.07
70-74 years	1.06	(0.46 to 2.38)	0.89	0.99	(0.93 to 1.05)	0.71
75-79 years	2.21	(0.88 to 5.38)	0.09	0.95	(0.89 to 1.02)	0.14
80-84 years	3.36	(1.17 to 9.44)	0.02	0.95	(0.87 to 1.04)	0.25
85+ years	24.02	(4.59 to 130.76)	0.00	0.80	(0.69 to 0.91)	0.00
Female	1.28	(0.79 to 2.05)	0.32	0.99	(0.95 to 1.03)	0.57
Male	1.27	(0.85 to 1.88)	0.24	0.99	(0.96 to 1.02)	0.49



## Figures

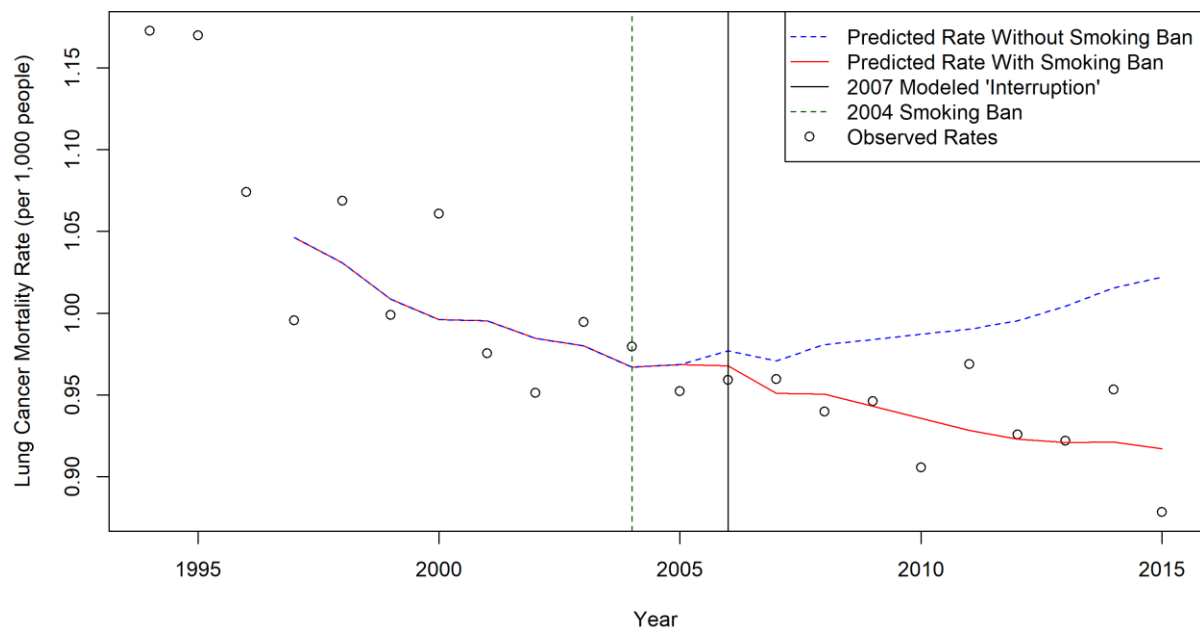


**Figure 1. Directed Acyclic Diagram Graph**



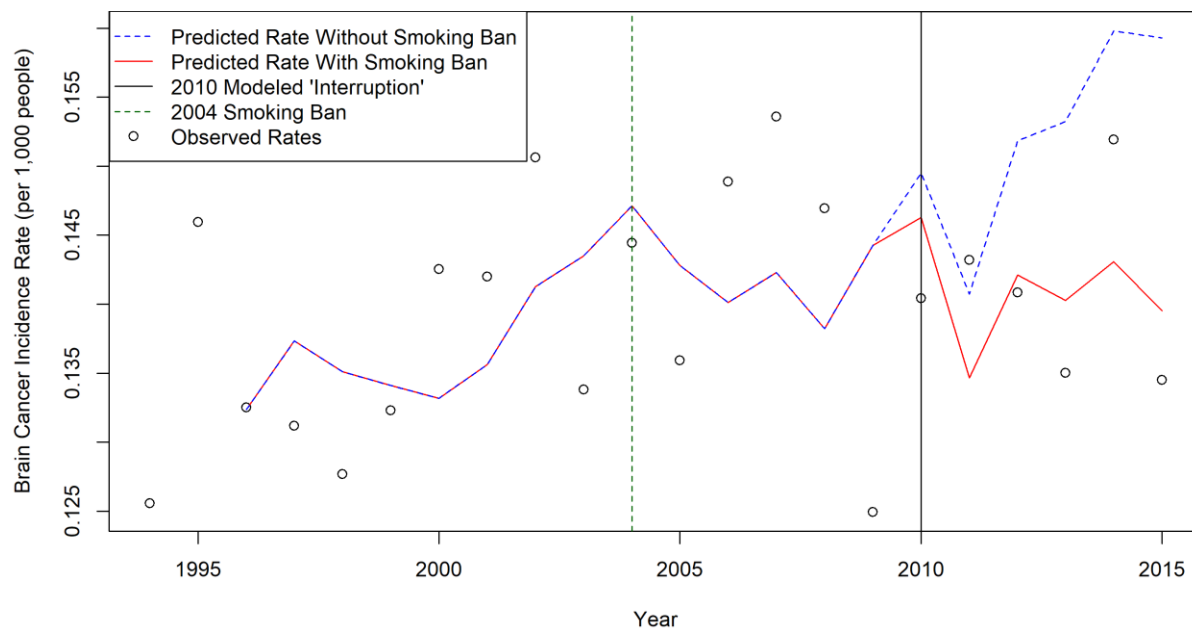
**Figure 2. Lung Cancer Incidence With and Without Smoking Ban**

The predicted lung cancer incidence rate is adjusted for the age- and sex- distribution of the Irish population, national smoking prevalence, and appropriate lag effects.



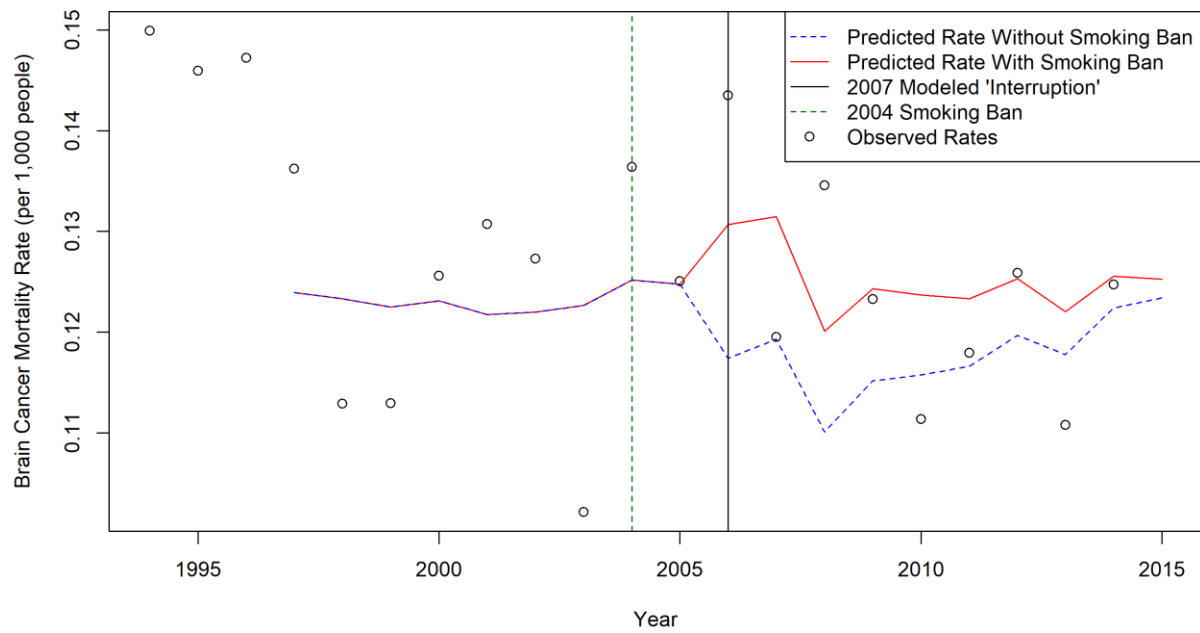
**Figure 3. Lung Cancer Mortality With and Without Smoking Ban**

The predicted lung cancer mortality rate is adjusted for the age- and sex- distribution of the Irish population, national smoking prevalence, and appropriate lag effects.



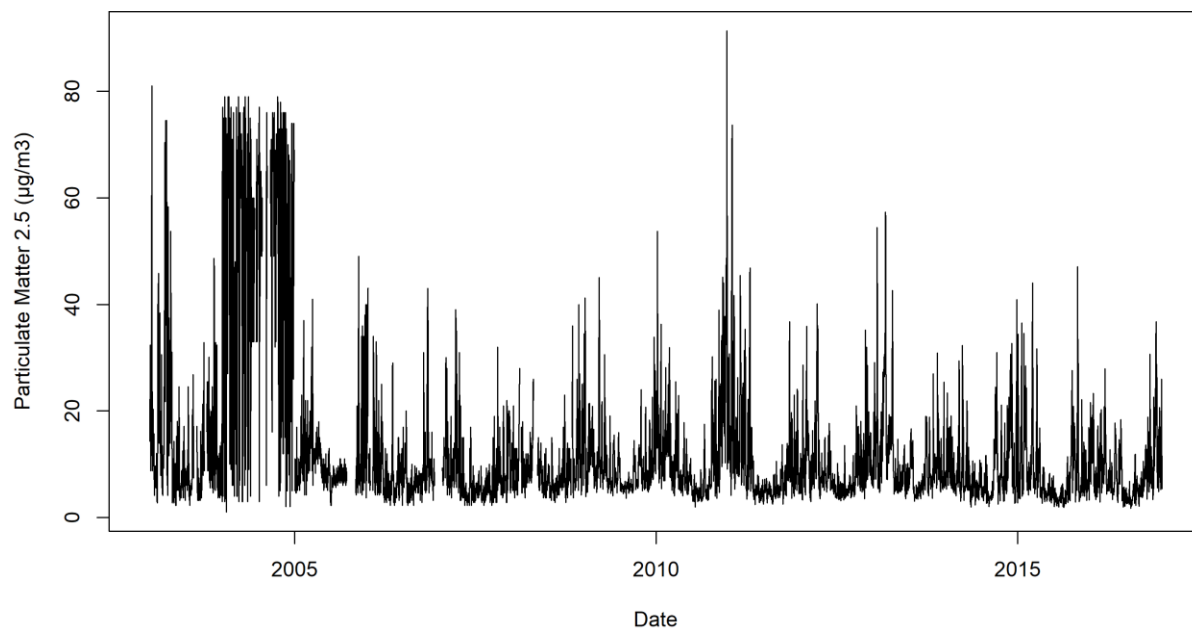
**Figure 4. Brain Cancer Incidence With and Without Smoking Ban**

The predicted brain cancer incidence rate is adjusted for the age- and sex- distribution of the Irish population, national smoking prevalence, and appropriate lag effects.

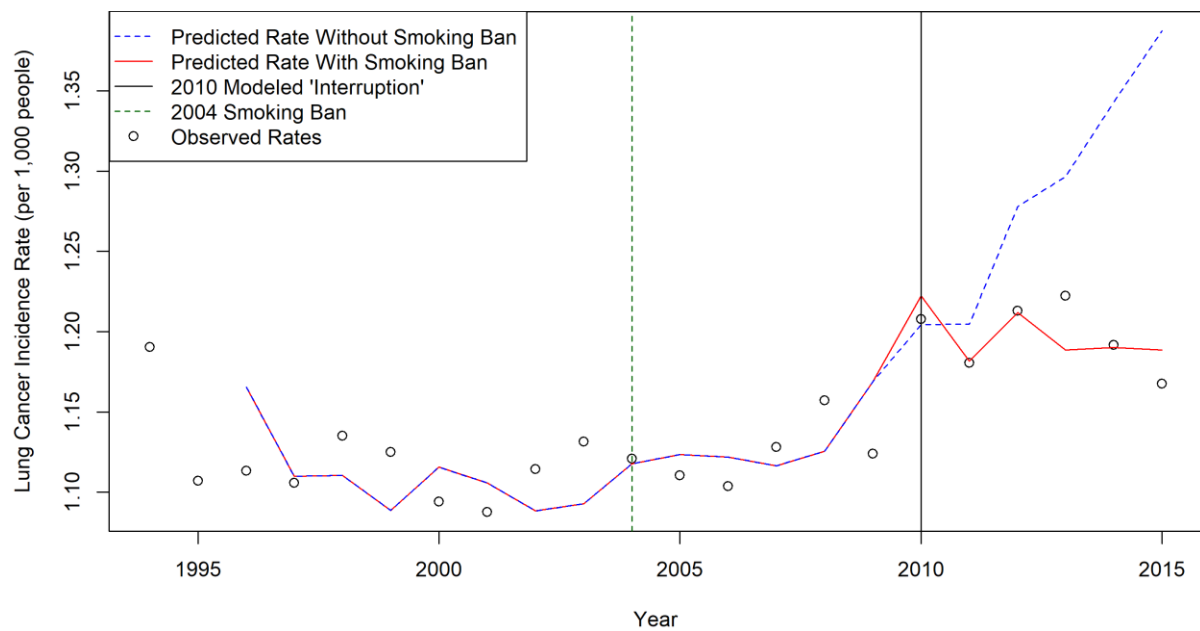


**Figure 5. Brain Cancer Mortality With and Without Smoking Ban**

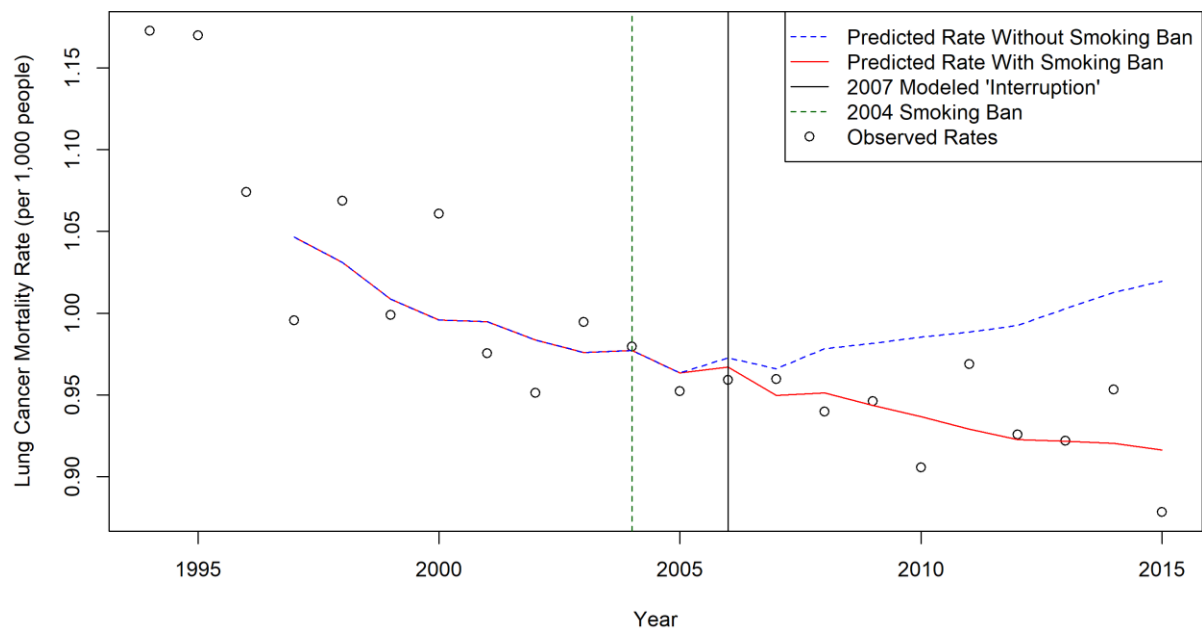
The predicted brain cancer mortality rate is adjusted for the age- and sex- distribution of the Irish population, national smoking prevalence, and appropriate lag effects.



**Supplement Figure 1: Average Particulate Matter 2.5 Concentration in Ireland**



**Supplement Figure 2: Lung Cancer Incidence With and Without Smoking Ban, Including Air Quality Data**



**Supplement Figure 3: Lung Cancer Mortality With and Without Smoking Ban, Including Air Quality Data**



## Supplement 1: Air Quality

There is a known connection between Particulate Matter 2.5 and lung cancer (33). However, Ireland's Environmental Protection Agency (EPA) data on the concentration of Particulate Matter 2.5 (PM2.5) (45) is inconsistently available for the relevant timeframe for this analysis. Apart from PM2.5 data from the Cork Oldstation Road site, all data on PM2.5 made available by the Irish Environmental Protection Agency was collected after January 1, 2009, three years after the mortality modelled interruption and one year before the incidence modelled interruption. Given this constraint in data availability, air quality has limited value to the analysis. Further, including air quality in the analysis would necessitate imputing values for several years on the same side of the interruption, which could bias the results. In the interest of completeness, however, the model including air quality data is shown here.

All datasets available in the EPA Ireland Archive of PM 2.5 Monitoring Data were extracted using a custom web-scraped built using Selenium in Python. These datasets included PM2.5 data from the following analysis sites: Clare Ennis, Cork Heatherton, Cork Oldstation, Dublin Marino, Dublin Coleraine Street, Dublin Finglas, Dublin Rathmines, Longford Town, May Claremorris, and Wicklow Bray. These datasets were merged, and for each date in the dataset (ranging from 2003 January 1 to 31 December 2016), the simple average PM2.5 concentration ( $\mu\text{g}/\text{m}^3$ ) was calculated (Supplement Figure 1). These values were further averaged across years and added to the model as a confounder.

[Supplement Figure 1 Near Here]

As evident in Supplement Figures 2 and 3, the results are essentially unchanged. Lung cancer incidence still decreased 3% and mortality 1%, identical to the main analysis results. Therefore, our results persist even when accounting for air quality as a confounder.

[Supplement Figures 2-3 Near Here]

## Supervisor Meeting Records:



School of  
Public Health

### Master of Public Health

#### Record of meeting between student and the project supervisor

*(A minimum of four records must be included in Appendices of submitted Dissertation)*

Name of Student: Theodoro Caputi

Name of Supervisor: Dr. Zubair Kabir

Project Title: Smoke-free Legislation and Lung Cancer

Project Aim: Measure the effect of the workplace smoking ban on lung cancer

Project Objectives: Determine change in lung cancer incidence/mortality after smoking ban

Date of Meeting: 21 February 2018 (E-mail Exchange)

#### **Issues Discussed:**

1. Talked about two different project ideas -- e-cigarette modelling and lung cancer incidence
2. Talked about a recent paper regarding Kentucky's smoking ban
3. Discussed the methodologies that would be used for both
- 4.

#### **General Comments**

#### **Agreed Goals for next meeting**

1. Correspond with Dr. David Levy at Georgetown
2. Correspond with Dr. Luke Clancy at TobaccoFree Research Institute Ireland
3. Look into where to procure data on lung cancer incidence/mortality and confounders
- 4.
- 5.

Signature of student: *Theodoro Caputi*

Signature of Supervisor: \_\_\_\_\_

Date and time of next meeting: Follow up via e-mail

**Master of Public Health**

**Record of meeting between student and the project supervisor**

*(A minimum of four records must be included in Appendices of submitted Dissertation)*

**Name of Student:** Theodore Caputi

**Name of Supervisor:** Dr. Zubair Kabir

**Project Title:** Smoke-free Legislation and Lung Cancer

**Project Aim:** Measure the effect of the workplace smoking ban on lung cancer

**Project Objectives:** Determine change in lung cancer incidence/mortality after smoking ban

**Date of Meeting:** 1 June 2018 (E-mail Exchanges)

**Issues Discussed:**

1. Talked about using Joinpoint versus Interrupted Time Series
2. Talked about using Stan Glantz's methodology using lag times
- 3.
- 4.

**General Comments**

**Agreed Goals for next meeting**

1. We said that Joinpoint would work for preliminary analyses, but we should use interrupted time series for the final paper
2. I will create a model adapted from Stan Glantz's that uses lag times and confounders in the interrupted time series.
- 3.
- 4.
- 5.

**Signature of student:** Theodore L. Caputi

**Signature of Supervisor:** \_\_\_\_\_

**Date and time of next meeting:** Follow up by e-mail

**Master of Public Health**

**Record of meeting between student and the project supervisor**

*(A minimum of four records must be included in Appendices of submitted Dissertation)*

**Name of Student:** Theodore L. Caputi

**Name of Supervisor:** Dr. Zubair Kabir

**Project Title:** Smoke-free Legislation and Lung Cancer

**Project Aim:** Measure the effect of the workplace smoking ban on lung cancer

**Project Objectives:** Determine change in lung cancer incidence/mortality after smoking ban

**Date of Meeting:** 15 June 2018 (E-mail Exchanges)

**Issues Discussed:**

1. Smoking prevalence as a confounder
2. Including a DAG in the paper
- 3.
- 4.

**General Comments**

**Agreed Goals for next meeting**

1. We decided to include smoking prevalence as a confounder in the model, so I will work on procuring this data
2. I will speak with Prof. Daahy about DAGs
- 3.
- 4.
- 5.

**Signature of student:** Theodore L. Caputi

**Signature of Supervisor:** \_\_\_\_\_

**Date and time of next meeting:** In touch via e-mail

**Master of Public Health**

**Record of meeting between student and the project supervisor**

*(A minimum of four records must be included in Appendices of submitted Dissertation)*

Name of Student: Theodoro L. Caputi

Name of Supervisor: Dr. Zubair Kabir

Project Title: Smoke-free Legislation and Lung Cancer

Project Aim: Measure the effect of the workplace smoking ban on lung cancer

Project Objectives: Determine change in lung cancer incidence/mortality after smoking ban

Date of Meeting: 17 September 2018

**Issues Discussed:**

1. Discussed the idea of harvesting to explain the effect on the elderly
2. Discussed wording of "averted" vs. "avoided"
3. Thought about adding Joinpoint regression results to the appendix
- 4.

**General Comments**

**Agreed Goals for next meeting**

1. Add explanation of harvesting to the discussion
2. Change avoided/averted wording
3. Consider whether Joinpoint would be appropriate for the appendix
- 4.
- 5.

Signature of student: Theodoro L. Caputi

Signature of Supervisor: \_\_\_\_\_

Date and time of next meeting: \_\_\_\_\_

**Declaration:**

**University College Cork**

**Department of Epidemiology and Public Health**



**Student Name: Theodore L. Caputi**

**Student Number: 35022566**

**Title of Assignment: IMPACT OF THE 2004 IRISH WORKPLACE SMOKING BAN ON LUNG CANCER INCIDENCE AND MORTALITY**

**Module Code: EH6043 (Dissertation in Epidemiology)**

**I declare that the content of this assignment is all my own work. Where the work of others has been used to augment my assignment it has been referenced accordingly.**

Signed Theodore L. Caputi Date 1 November 2018

Word Count 4026