1. **Relationship between smoking and lung cancer**

It is a widely accepted public opinion that smoking can cause lung cancer. This public opinion has been developed and supported by multiple research papers in the past 60-80 years. Smoking was first identified as a cause of cancer in 1950 [1] [2]. In 1957, in the United States a research came to the conclusion that "The sum total of scientific evidence establishes beyond reasonable doubt that cigarette smoking is a causative factor in the rapidly increasing incidence of human epidermoid carcinoma of the lung" [3]. In the following period, the accumulating scientific papers with similar conclusions had led to the acceptance of a similar viewpoint by responsible public health officials in Great Britain [4], the Netherlands, Norway, and the United States. Such studies were retrospective studies on men with lung cancer [5] [6] [7] and for woman [8]. The first results of a third large prospective study with 200,000 observed for 30 months reported similar findings supporting causality [9].

However, in 1959 [10], a more cautious artic was published, claiming that „The magnitude of the excess lung-cancer risk among cigarette smokers is so great that the results cannot be interpreted as arising from an indirect association of cigarette smoking with some other agent or characteristic, since this hypothetical agent would have to be at least as strongly associated with lung cancer as cigarette use, no such agent has been found or suggested”, leaving the option open for a common cause confounder not discovered, so far! An article published a decade later, in 1969 [11] aimed to uncover controversies of statistical inference with “special reference to the cigarette smoking and lung cancer controversy”. The article states three sources of confusion about the role of smoking in lung cancer: 1) lack of agreement in the definitions when implying a specific factor to be causing a disease, 2) the method of measuring the strength of the relationship in a 2X2 table and 3) the making of decisions and the subsequent formulation of actions based upon existing data. Nevertheless, a ban on cigarette advertisements on TV and radio went into effect in 1971.

Since then, smoking has been found to play a causative role in several types of cancers, including laryngopharyngeal, esophageal, gastric, hepatic, renal, cervical, and hematologic cancers [12] When breathing in tobacco smoke, thousands of chemicals enter the lungs, and many of these chemicals have the potential to damage the DNA in lung cells. The body will work to repair the damage that’s done by these chemicals, but over time, smoking can cause more damage than the body can heal, which may lead to the formation of cancer cells. A collection of key facts regarding smoking from recent year:

* tobacco smoke exposes the human body to roughly 7,000 types of chemicals, among which 70 are known to be cancer-causing chemicals [13]
* tobacco use is responsible for about 22% of cancer deaths [14]
* about 90 % of lung cancers can be attributed to smoking [15]
* People who quit smoking reduce risk of developing lung cancer by 30 to 50% 10 years after quitting, compared to people who continue to smoke [16]

While cigarette smoking has been indisputably established as a major risk factor for lung cancer, it is important to note that 10–15% of lung cancer patients have no history of smoking at all and that lung cancer is a leading cause of cancer death among non-smokers [17] [18].

1. **Effect of second hand smoking**

Knowing the mechanism helps draw further conclusions. Knowing that the smoke containing chemicals damage lung cells lead to the development of cancer cells allowed governments to restrict second-hand smoking. Such studies are scarce [13] but do exist. A 2018 review of studies found that exposure to secondhand smoke significantly increases the risk of cancer for non-smokers, especially the risk of developing lung and breast cancer in women [19]. Furthermore, sidestream smoke the by-products of cigarette smoking, including tobacco-specific nitrosamines that are the main cause of adenocarcinoma have been detected in the urine of non-smokers exposed to secondhand smoke [20] [21]. That is, there is good biological evidence supporting secondhand smoke as a risk factor for cancer in never smokers [13].

1. **Effect of restricting send hand smoking**

In 1975 the U.S. state of Minnesota enacted the Minnesota Clean Indoor Air Act, making it the first state to restrict smoking in most public spaces. Interestingly though, only in the late 1990s and 2000s did smoking bans become serious. A major milestone was the 9th of August, 1997, when President Bill Clinton issued Executive Order 13058 banning smoking in all interior spaces owned, rented, or leased by the Executive Branch of the Federal Government. Still, long-term exposure to secondhand smoke is attributed to about 7,000 lung cancer deaths in the United States each year according to the American Cancer Society [22].

A picture containing plate, food, piece, dessert

Description automatically generatedText

Description automatically generated

*Current smoke bans globally*

The are discussions in public opinion and the scientific community in the extent of smoking bands have on reducing lung cancer. “Directly after the legislation, more people were trying to quit smoking, and more people succeeded because it’s much easier to avoid those situations,” says Hazel Cheeseman, Director of Policy at ASH (Action on Smoking and Health) in 2017, 10 years after the smoking ban in UK’s pubs and restaurants – For context, in 2006, 22 per cent of adults smoked, whereas in the latest statistics (2015) 18 % did.

Few research papers have been published on trying to reveal the effect of smoking bands on lung cancer.

* In 2004, Ireland became the first country to institute a comprehensive workplace smoking ban. A research was to compare lung cancer incidence and mortality before and after the modelled interruptions. An identical analysis was applied to brain cancer, a cancer with no known link to smoking or second-hand smoke exposure, as a validity check. The results showed that Each year following the modelled interruptions, lung cancer incidence and mortality in Ireland decreased 2% (95%CI 1–3, p<0.01) and 1% (95%CI 0–2, p=0.02) relative to the modelled counterfactual. In absolute terms, the smoking ban was associated with 32 (95%CI 14–52) fewer lung cancer incident cases per year and 113 (95%CI 96–131) fewer lung cancer deaths per year, equivalent to 1.36% of the post-interruption lung cancer incident cases and 6.03% of the post-interruption lung cancer deaths [23].
* In 2009, a report by the International Agency for Research on Cancer on the effects of smokefree laws concluded that 1) there is sufficient evidence that smokefree workplaces reduce cigarette consumption among people who continue to smoke, 2) there is strong evidence that smokefree workplaces lead to increased successful cessation among people who smoke, and 3) there is strong evidence that smokefree policies reduce tobacco use among youth,
* One of the most interesting study from 2021 has found that in Europe, an estimated 1·65 million lung cancer cases could be prevented over a 20-year period with the highest-level implementation of tobacco control policies. The study had “large variation was in European regions and countries reflecting the current level of tobacco control, with the largest potential for prevention in Western Europe (24·5%), Southern Europe (23·1%) and Eastern Europe (22·5%), and the lowest but still substantial potential for further prevention in Northern Europe (12·5%)” [24].

In our view, research papers are scarce in this topic as more time needs to pass for the effect to take place. To support this, I quote Professor Max Parkin, co-author of the report for Cancer Research UK: "We can see that lung cancer rates should continue to drop, but the number of cases will increase. This increase will mostly be in women, which reflects the peak rates of smoking among women back in the 1970s”. For our analysis, this suggests that taking as many lags as possible will be needed, and countries where bans were introduced just 3-5 years prior to the last data on lung cancer death will need to be dropped.

Also, the elongation of life is likely to be a confounder. “The actual number of people with lung cancer is set to rise, however, from 38,500 to more than 41,600 by 2024, as people live longer.”

[1] 2. Doll R., Hill A.B. Smoking and carcinoma of the lung; preliminary report. Br. Med. J. 1950;2:739–748. doi: 10.1136/bmj.2.4682.739.

[2] Wynder E.L., Graham E.A. Tobacco smoking as a possible etiologic factor in bronchiogenic carcinoma; a study of 684 proved cases. J. Am. Med. Assoc. 1950;143:329–336. doi: 10.1001/jama.1950.02910390001001.

[3] Smoking and Health. Joint Report of the Study Group on Smoking and Health. Science 125: 1129-1133, 1957

[4] Medical Research Council: Tobacco smoking and cancer of the lung. Brit. M. J. 1: 1523-1524, 1957.

[5] STOCKS, P.: Report on cancer in North Wales and Liverpool region. Brit. Empire Cancer Campaign. Thirty-fifth Annual Report 1957, Supp. to Part II.

[6] SCHWARTZ, D. and DENOIX, P.: L'enquette francaise sur l'etiologie du cancer broncho-pulmonaire: role due tabac. La Semaine des Hopitaux de Paris 33: 424-437, 1957.

[7] SEGI, M., FUKUSHIMA, 1., FUGISAKU, S., KURIHARA, M., SAITO, S., ASANO, K., and KAMOI, M.: An epidemiological study on cancer in Japan. Gann 48: Supp. 1957, 63 pp.

[8] HAENSZEL, W., SHIMKIN, M., and MANTEL, N.: A retrospective study of lung cancer in women. J. Nat. Cancer lnst. 21: 825-842, 1958.

[9] DORN, H.: Tobacco consumption and mortality from cancer and other diseases. Acta Unio internat. contra cancrum. In press.

[10] Smoking and Evidence and Questions 1 Lung Cancer: Recent a Discussion of Some JEROME CORNFIELD,2,3 WILLIAM HAENSZEL,4 E. CUYLER HAMMOND,5 ABRAHAM M. LILIENFELD,2 MICHAEL B. SHIMKIN,4 and ERNST L. WYNDER 6

[11] PROBLEMS OF STATISTICAL INFERENCE IN HEALTH WITH SPECIAL REFERENCE TO THE CIGARETTE SMOKING AND LUNG CANCER CONTROVERS

[12] 4. Sasco A.J., Secretan M.B., Straif K. Tobacco smoking and cancer: A brief review of recent epidemiological evidence. Lung Cancer. 2004;45(Suppl. 2):S3–S9. doi: 10.1016/j.lungcan.2004.07.998

[13] Exposure to Secondhand Smoke and Risk of Cancer in Never Smokers: A Meta-Analysis of Epidemiologic Studies. A-Sol Kim,1 Hae-Jin Ko,2,\* Jin-Hyun Kwon,3 and Jong-Myung Lee4

[14] Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015

[15] Lung Cancer, Faraz Siddiqui; Sarosh Vaqar; Abdul H. Siddiqui

[16] Cigarette Smoking: Health Risks and How to Quit (PDQ®), Bethesda (MD): National Cancer Institute (US); 2002-

[17] Thun M.J., Henley S.J., Burns D., Jemal A., Shanks T.G., Calle E.E. Lung cancer death rates in lifelong nonsmokers. J. Natl. Cancer Inst. 2006;98:691–699. doi: 10.1093/jnci/djj187.

[18] Centers for Disease Control and Prevention Annual smoking-attributable mortality, years of potential life lost, and productivity losses–United States, 1997–2001. Morb. Mortal. Wkly. Rep. 2005;54:625–628

[19] Exposure to Secondhand Smoke and Risk of Cancer in Never Smokers: A Meta-Analysis of Epidemiologic Studies

[20] Hecht S.S., Carmella S.G., Murphy S.E., Akerkar S., Brunnemann K.D., Hoffmann D. A tobacco-specific lung carcinogen in the urine of men exposed to cigarette smoke. N. Engl. J. Med. 1993;329:1543–1546. doi: 10.1056/NEJM199311183292105.

[21] Maclure M., Katz R.B., Bryant M.S., Skipper P.L., Tannenbaum S.R. Elevated blood levels of carcinogens in passive smokers. Am. J. Public Health. 1989;79:1381–1384. doi: 10.2105/AJPH.79.10.1381

[22] <https://www.cancer.org/cancer/lung-cancer/causes-risks-prevention/risk-factors.html>

[23] <https://jech.bmj.com/content/73/Suppl_1/A44.2>

[24] Impact of tobacco control policies implementation on future lung cancer incidence in Europe: An international, population-based modeling study