



## PESTICIDES & SELECTED ONCOLOGY DIAGNOSES

PREPARED BY: OFFICE OF MEDICAL AFFAIRS

DATE : JUNE 6, 2025

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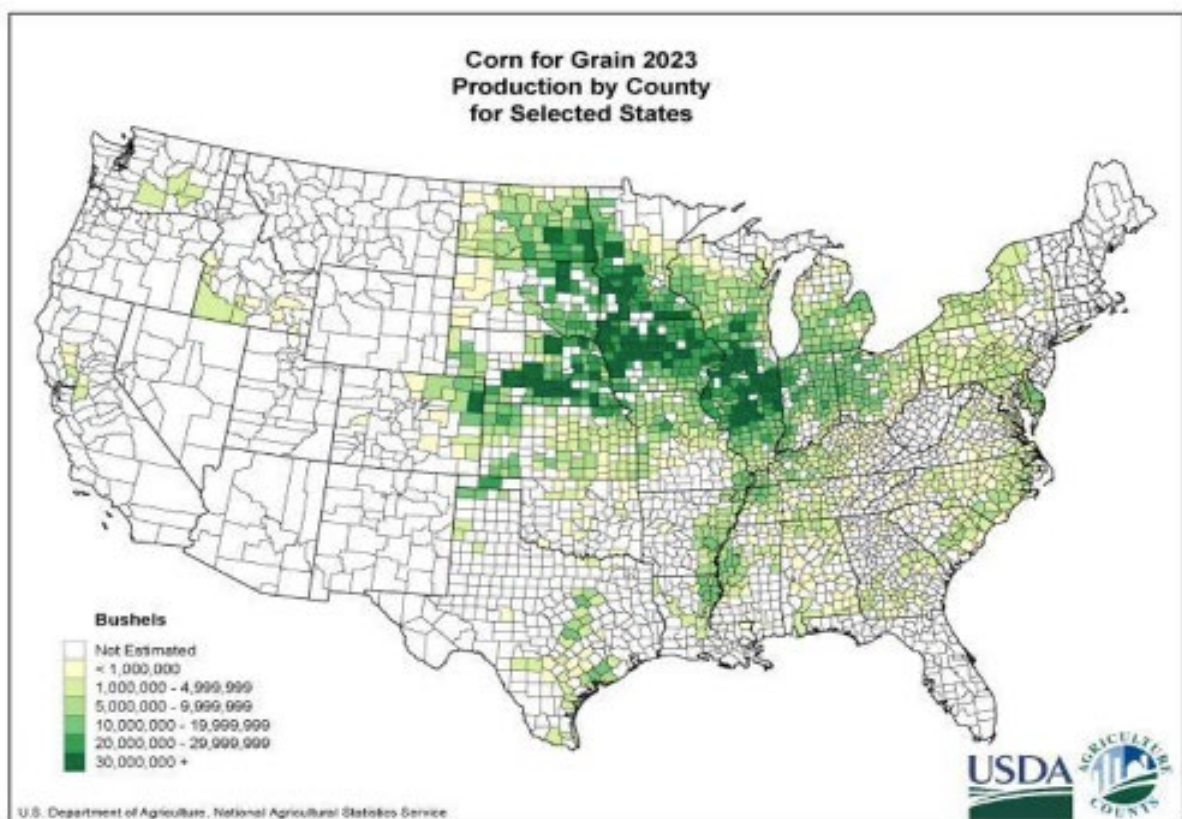


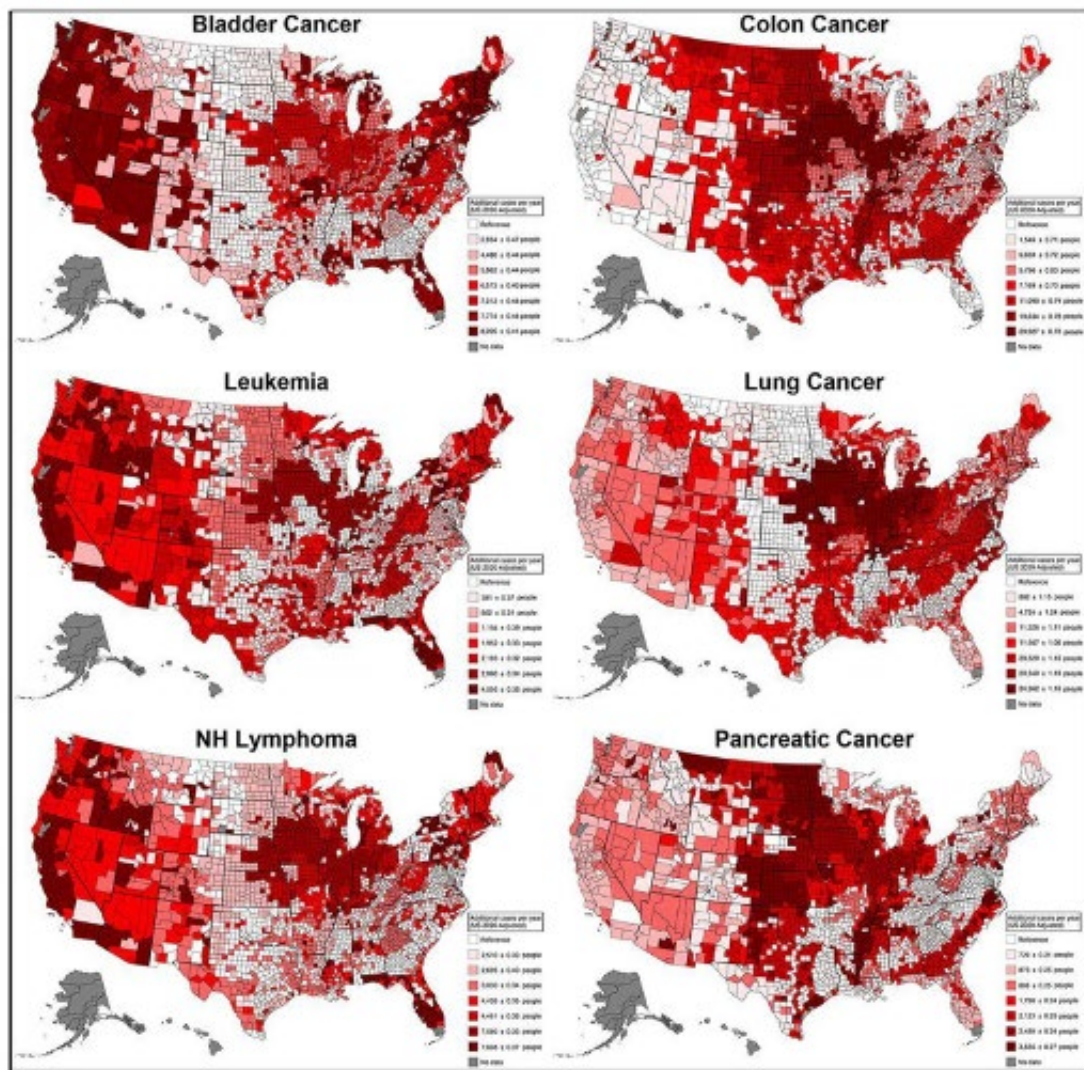
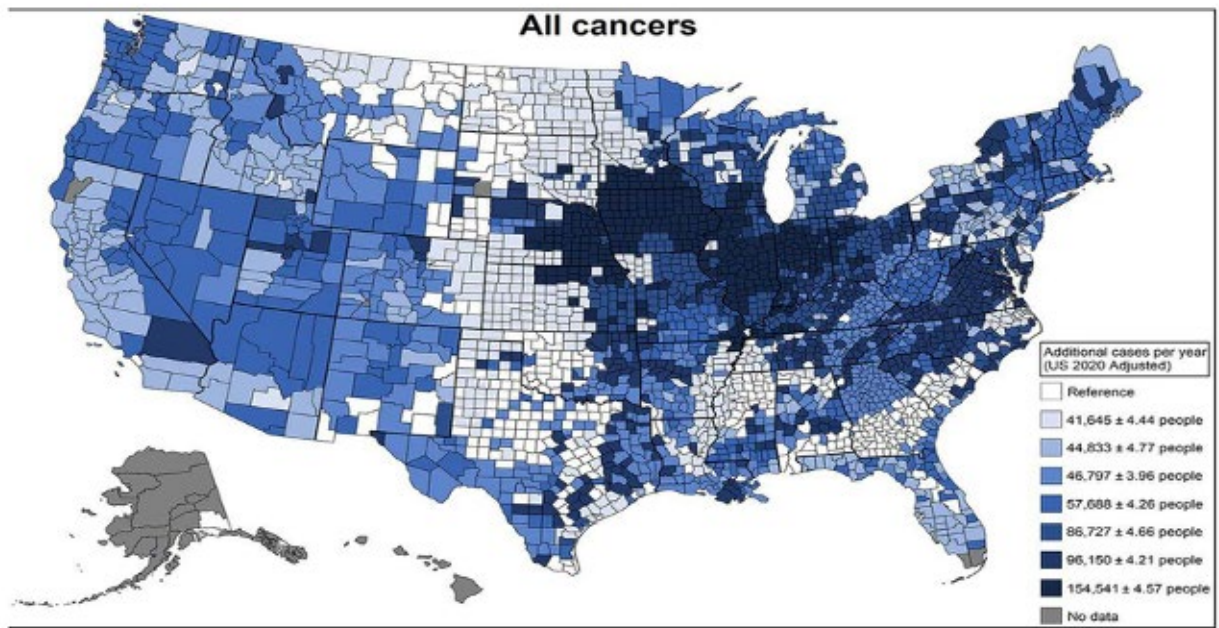
# Key Takeaway Notes

- Research demonstrates an association between pesticide exposure and the development of cancer
- Several pesticides are associated with several deadly forms of cancer
- Proper education, protection, and application are essential to reduce exposure risk
- Pesticide associated cancer risk reduction should be a routine part of our daily lives
- Do your commercial and industrial pesticide application practices concern you? Schedule an appointment with our management team here: <https://bit.ly/44Ec1CZ>

The US Department of Agriculture estimates that 96% of all corn production is treated with pesticides to ensure maximum crop yields. (Gerkin et al)

## Corn: Production Acreage by County





## Overview

In this article we will look to understand the association between pesticides and certain cancers. Cancer is complex. Risk factors for one type of cancer do not necessarily transfer to another. Additional factors include genetic, environmental, and behavioral causes etc. We will focus on associations with material impacts on health, financial and quality of life for individuals, communities and healthcare payers whether private or governmental.

The Journal of the National Cancer Institute publication describes the risks in a specific cohort. They examined the mortality rates of 3,827 men licensed to apply pesticides in Florida. They used the Standardized Mortality Ratio (SMR) to compare subgroups. An SMR of 1.0 means there is no increased or decreased risk. The subgroup analysis for risk of lung cancer, brain cancer, and acute myeloid leukemia were elevated. Cohorts were measured by years of professional licensure as a proxy for duration of pesticide exposure. There was only a 3% increase in risk or an SMR of 1.03. The association with lung cancer is compelling.

|                    | Years of License |             |           |
|--------------------|------------------|-------------|-----------|
| Years of Licensure | < 10 Years       | 10-20 Years | >20 Years |
| Lung SMR           | 1.01             | 1.55        | 2.89      |

They also note that there was an elevated association (SMR: 2.0) with an unspecified brain cancer. Acute myeloid leukemia was more than three times likely to occur in the cohort against a background rate of 0.9 expected for the cohort (Blair, PhD et al.).

Other research helps us understand the even higher risks for developing cancer when pesticides applicators are not following industry standards. In one study there was a 500% higher risk of developing lung cancer. Poor education, in-service updates, lack of PPE use were cited as drivers. (Luqman et al)(Kim et al.)(Kangkhetrn and Juntarawijit)

Other research supports this association with lung cancer. The Agricultural Health Study analyzed a prospective cohort of 57,284 applicators and 32,333 spouses of farmers without a history of lung cancer. The enrollment period 1993-1997 through the end of 2001. The baseline incidence of lung cancer in this population was 0.44 which was attributed to a low cigarette smoking prevalence. A pattern appeared in five exposure categories. (Alvavanja et al.) In the highest exposure categories the risk for developing lung cancer ranged from 200% up to 500% higher. Spouses had no excess risk. (Alvavanja et al.) See table below.

|               | Exposure Categories (1-4 lowest to highest) |        |        |        |
|---------------|---------------------------------------------|--------|--------|--------|
|               | 1                                           | 2      | 3      | 4      |
| Metolachlor   | OR 1.0                                      | OR 1.6 | OR 1.2 | OR 5.0 |
| Pendimethalin | OR 1.0                                      | OR 1.6 | OR 2.1 | OR 4.4 |
| Chlorpyrifos  | OR 1.0                                      | OR 1.1 | OR 1.7 | OR 1.9 |
| Diazinon      | OR 1.0                                      | OR 1.6 | OR 2.7 | OR 3.7 |

Researchers examined a prospective cohort of 57,310 pesticide applicators from Iowa and North Carolina. Using survey instruments, lifetime exposure and other potentially relevant factors and statistical analysis, lung cancer Hazard Ratios were calculated. After adjusting for smoking, they were elevated in selected chemicals. Three pesticides had the most significant elevated association with lung cancer: pendimethalin was associated with a 1.50 HR, dieldrin HR 1.93 and chlorimuron ethyl 1.74. (Bonner et al.)

A research paper using US Dept. of Agriculture data asserts that pesticide application is ubiquitous and that in 2021 96% of the 93.4 million acres where corn is planted had pesticides applied. This paper used county-wide agricultural datasets to provide a population or public health cancer risk

perspective. The hypothesis: “more pesticide use leads to higher cancer incidence” as the opposite idea is not supported by evidence. Using a Penn State University model called Latent Class Analysis (LCA) they were able to see patterns of association in 69 different pesticides in use. (Gerkin et al.)

The LCA methodology grouped agricultural pesticide use that represent crop types and agricultural industry in the county. Corn production can be for human and livestock consumption or for biofuel. They retrieved additional data from various federal databases for cancer incidence, smoking rates, and social vulnerability index (SVI). The SVI measures county level disaster impact risk. These registries provided cancer surveillance data: CDC’s National Program of Cancer Registries, National Cancer Institute’s Surveillance, Epidemiology, and End Results Program and the CDC’s National Center for Health Statistics. The researchers demonstrated the following patterns.

- **Atrazine:** consistently high correlation in regions with high added risk for all cancers and colon cancers specifically.
- **Boscalid:** consistently high correlation in high added risk regions for leukemia, non-Hodgkin’s lymphoma, and pancreatic cancer.
- **Dimethomorph:** high added risk of leukemia and non-Hodgkin’s lymphoma but also regions with a low added risk of colon cancer.
- **Dicamba:** high added risk of colon cancer and pancreatic cancer.
- **Dimethenamid:** low added risk of bladder cancer, but in combination with dimethenamid-P: high added risk of pancreatic cancer.
- **Dinotefuran:** was at the top in regions with high leukemia and non-Hodgkin’s lymphoma on the opposite end for colon cancer.
- **Glyphosate:** consistently at the top, high added risk of colon and pancreatic cancer.
- **Imazethapyr:** similar risk of colon and lung cancer.
- **Metolachlor and metolachlor-S:** the combination was a consistent top contributor for regions with higher added risk of colon and pancreatic cancer. (Gerkin et al.)

A strong correlation has been reported in the scientific literature between pesticides and bladder cancer. Lucchesi et al describe how cancer begins, spreads and becomes resistant. The paper describes how pesticides exposure lead to DNA damage. The article describes in great detail how pesticides alter molecular pathways leading to the genetic damage at the root of bladder cancer. They further state this also allows cancer to spread throughout the body, evade the immune system, and adapt to new sites in the body. Pesticides having an association with bladder cancer are DDT,

Imazethapyr, 2,4-Dichlorophenoxyacetic acid, Bentazon, Bromoxynil, Chloramben, Diclofop-methyl, Imazaquin, and Heptachlor. (Lucchesi et al.)

Koutros et al describes the excess risk for bladder cancer. Using the Agricultural Health Study data and a Rate Ratio (RR) researchers could determine if an association exists between 65 pesticides and the 321 bladder cancer cases in the study cohort and two subgroups: exposure and smoker. The 'ever used' group for imazaquin had an RR of 1.54. The excess risk became clearer in a never-smoker group. The RR rose to 3.03. Similar patterns in never smokers and several chlorinated pesticides and organochlorine insecticides were also seen. (Koutros et al.)

Researchers conducted a meta analysis of 9 epidemiologic, 7 case control, and 3 cohort studies. Bladder cancer and high pesticide carried increased risk in America RR 1.74. Other subgroups did not demonstrate this elevated risk. (Liang et al.)



Pesticide application and brain cancer has been researched and similar patterns of increased risk were seen. The authors revisited a meta-analysis conducted in 1998 and provided evidence from over 40 years of literature that continues to support an increased risk for brain cancers in farmers with exposure to pesticides. Fifty two studies assessed. The range of positive association between farming, pesticide use and brain cancer spanned from minimal (1.03) up to marked elevated risk at 6.53. (Gatto et al.) The authors cite numerous studies that support an increased risk. (Acqualella, PhD et al.)

Ruder et al assessed workplace practices and found an elevated risk for the brain cancer glioma in farmers. The OR for farmers who 'never immediately washed up' was 3.08 and for those who 'never changed clothes' it was 2.84. (Ruder et al.)

An article in Occupational & Environmental Medicine researched the OR for glioma in farming and the use of individual and chemical pesticide classes. Two herbicides and three insecticides carried an elevated OR: metribuzin (3.4), paraquat (11.1), bufencarb (18.9), chlorpyrifos (22.6), and coumaphos (5.9). (Lee et al.)

UCLA published a study examining the association between childhood cancers and agricultural pesticide exposure by proximity (4000m) to pesticide application locations. They state 5% of childhood brain cancers are attributable to inherited genetic disorders. Searching through several databases compiling pesticide application amounts and a statewide cancer registry they found 667 cases of childhood (<6yo) brain cancer that were matched to 123,158 controls. The OR for brain cancer are listed in the table below: (Lombardi et al.)

|                 | Bromacil | Thiophanate-methyl | Triforine | Kresoxim -methyl | Chlorothalonil | Propiconazole | Dimethoate | Linuron |
|-----------------|----------|--------------------|-----------|------------------|----------------|---------------|------------|---------|
| Astrocytoma     | OR 2.12  | OR 1.64            | OR 2.38   | OR 2.09          | -              | -             | -          | -       |
| Medulloblastoma | -        | -                  | -         | -                | OR 1.78        | OR 1.60       | OR 1.60    | OR 2.52 |
| Ependymoma      | -        | OR 1.72            | -         | -                | -              | -             | -          | -       |

The US has brain and central nervous system (CNS) as the most common solid tumors and the second leading cause of death in children from ages 0 - 14 years old, according to an Environmental International paper. Treatments vastly improve life spans in many childhood cancer diagnoses. The quality of life and financial impacts are large. (Van Maele-Fabry et al.)

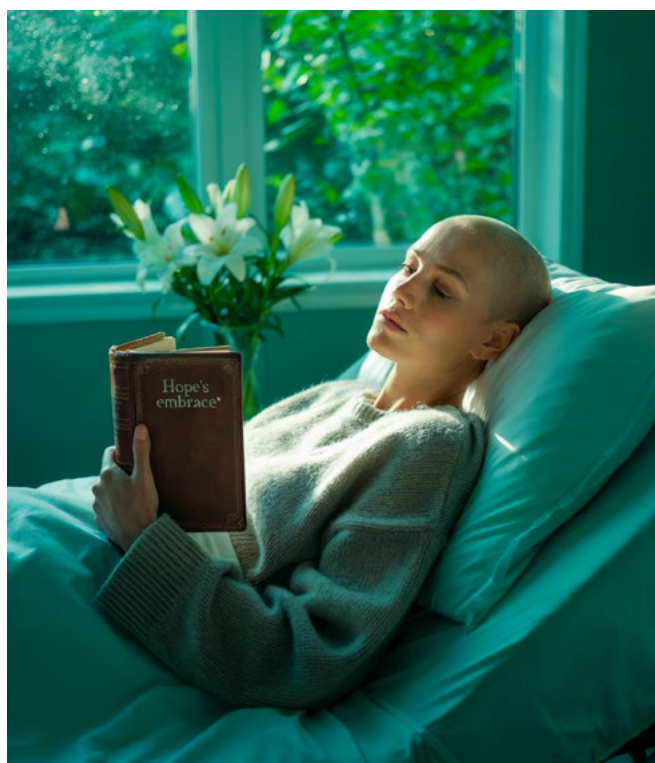
In France, a group of researchers studied whether exposure to pesticides resulted in a higher risk of developing brain cancer. They enrolled 221 people with brain tumours and 442 matched controls from May 1999 to April 2001. Their findings were somewhat mixed. A significant association was found when lifelong cumulative exposure was isolated. In the highest quartile of exposure the risk for brain tumors was statistically significant with an OR of 2.16 for all brain tumors and 3.21 for gliomas. An additional finding of elevated OR was found in the pesticide use for home plants (OR 2.24) (Provost et al.)

## Cost of Care

A JAMA Oncology article on the global cost of treating cancers published in 2023 based on 2016 healthcare data. This table shows the national financial burden for selected cancers. The cost of care for pesticide associated cancers will be a subset of these numbers. (Chen, ScD et al.)

As advances in healthcare and more specifically cancer care bring better outcomes they also come with great costs. A paper from Cancer, Epidemiology, Biomarkers and Prevention created models and forecasts to better understand the current and future cost of cancer treatment in the United States. Several factors affect the intensity of treatment and cost. Costs are highest in the early initial treatment followed by end of life care. They cite earlier data from 2010 estimating the national cost of care for colorectal at \$14.1B, lymphoma \$12.1B, and lung \$12.1B. There are indirect costs to be considered such as lost productivity (disability, absenteeism, and presenteeism),

caregiver time impacts, non-medical costs to obtain care, and familiar wage earner losses. They estimate the national value of life lost to early death attributed to cancer to be \$115.8B and forecasted to be \$147.6B in 2020 with the surge attributed to population growth and longer life spans in general. They note, more than 2 million cancer survivors did not receive medical care due to an inability to afford the treatment options. (Yabroff et al.)



|                        | National Cost of Treatment 2016 |                            |                            |
|------------------------|---------------------------------|----------------------------|----------------------------|
|                        | Medium Treatment Cost           | Lower Bound Treatment Cost | Upper Bound Treatment Cost |
| Lung*                  | \$7.3B                          | \$6.3B                     | \$8.4B                     |
| Colon**                | \$10.5B                         | \$9.3B                     | \$11.7B                    |
| Non-Hodgkin's Lymphoma | \$11.8B                         | \$10.4B                    | \$13.4B                    |
| Leukemia               | \$12B                           | \$10.7B                    | \$13.6B                    |
| Bladder                | \$2.6B                          | \$2.3B                     | \$2.9B                     |
| Pancreatic             | \$2.5B                          | \$2.2B                     | \$2.8B                     |

\* Includes tracheal and bronchial cancers \*\* Includes rectal cancer (Chen, ScD et al.)

Another publication using Medicare costs demonstrates this three phase pattern for cancer treatments cost in the Initial, Continuing Care, and Last Year of Life segments. Excerpted data is shown in the table immediately below. They used annualized costs on a per person basis in 2020 dollars for medical services.

There is a marked lag on the order of years to decades, between chronic pesticide exposure, disease development, diagnosis, and the rise in cost of treatment. This separation in time allows for the dissociation between the application, exposure risk, and the time needed for the metabolic pathway derangements to result in disease. This pushes out the associated costly treatments and ultimately the payment for the cost of care coming from sources that were not associated with the original pesticides application. (National Cancer Institute)

| Medical Treatment Costs Per Patient | Segmented Phases of Cancer Treatment and Costs |             |                   |
|-------------------------------------|------------------------------------------------|-------------|-------------------|
|                                     | Initial                                        | Continuing  | Last Year of Life |
| Bladder                             | \$26,442.80                                    | \$5,517.60  | \$109,727.30      |
| Brain                               | \$139,813.80                                   | \$17,385.60 | \$176,354.90      |
| Colorectal                          | \$66,523.50                                    | \$6,246.3   | \$110,143.70      |
| Leukemia*                           | \$297,950.20                                   | \$60,485.50 | \$635,252.40      |
| Lymphoma**                          | \$150,536.70                                   | \$22,590.90 | \$273,693.60      |
| Lung***                             | \$220,808.00                                   | \$39,456.10 | \$337,406.30      |
| Pancreatic                          | \$108,165.70                                   | \$18,426.70 | \$125,030.80      |

\*Sum of Leukemia types \*\* Sum of Lymphoma types \*\*\* Sum of Lung types  
(National Cancer Institute)

| Drug Costs Per Patient | Segmented Phases of Cancer Treatment and Costs |             |                   |
|------------------------|------------------------------------------------|-------------|-------------------|
|                        | Initial                                        | Continuing  | Last Year of Life |
| Bladder                | \$624.60                                       | \$520.50    | \$1,353.40        |
| Brain                  | \$2,394.40                                     | \$1,353.40  | \$1,873.90        |
| Colorectal             | \$416.40                                       | \$208.20    | \$1,353.40        |
| Leukemia*              | \$49,137.90                                    | \$58,507.30 | \$23,111.50       |
| Lymphoma**             | \$3,581.90                                     | \$1,145.10  | \$23,111.50       |
| Lung***                | \$9,681.80                                     | \$6,662.90  | \$11,451.70       |
| Pancreatic             | \$5,517.60                                     | \$3,851.90  | \$5,829.90        |

\*Sum of Leukemia types \*\* Sum of Lymphoma types \*\*\* Sum of Lung types  
(National Cancer Institute)

The researchers Chen et al published a methodology to better understand and quantify the impact on GDP generated by important disease categories. They forecast trends for important disease categories and the GDP gains by reducing the prevalence of the negative GDP factors. For cancer alone, a 10% reduction in prevalence would yield a \$1T benefit to GDP.

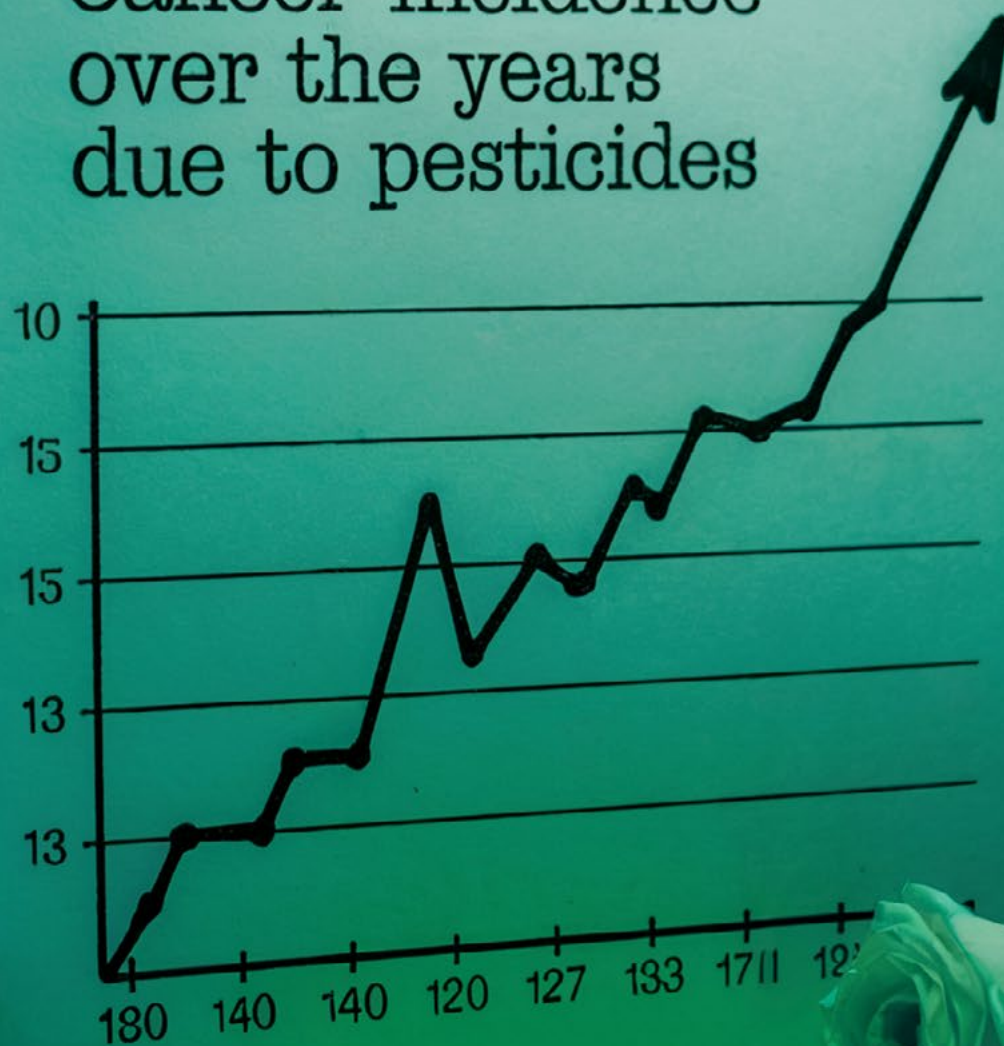
## Summary Statement

The available evidence to be considered makes a compelling argument when one examines the association between pesticide application and several important cancer types. The author acknowledges that there are confounding factors that lead to an individual having cancer. Reducing pesticide exposure or using ones with lower exposure risk could realize large dividends to be recognized as the population grows, ages, and cancer treatment costs rise.

Reasonable attempts to reduce the incidence and prevalence of these, and other, cancer diagnoses would lower the overall cost of care borne by all affected. This common sense and simple approach advocates for new thinking and directions in order to reduce the grave impact that a cancer diagnosis carries on an individual's health and the impact on those around the patient (family, community, payers, state, and federal government) agencies.

**Are you concerned about the safety  
of the pesticides applied on your  
commercial, industrial, public or  
government facilities?  
Schedule an appointment  
here: <https://bit.ly/44Ec1CZ>**

# Cancer incidence over the years due to pesticides



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