Assessing The Correlation Between Per- And Polyfluoroalkyl Substances (pfas) Exposure And Cancer Incidence In The U.s.

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Assessing the Correlation between Per- and Polyfluoroalkyl Substances (PFAS) Exposure and Cancer Incidence in the U.S.

Xiaoqing Zhang
Abstract

The study seeks to understand the relationship between key PFAS contaminants and their potential to cause cancer in the United States. It also aims to find out how different PFAS exposures affect different types of cancer and how food can increase or decrease the risk of getting cancer. The study used secondary data from the government and other reliable sources. The process looked at PFAS exposure, food malnutrition, and cancer rates in the population by using both descriptive and inferential statistics. After looking at socio-economic factors and their health effects on the public, the results showed that PFOS, PFHxS, and PFOA are the most common types of environmental pollutants. In urban areas, these contaminants are negatively linked to undernutrition. There was no significant link between PFAS exposure and thyroid, prostate, or non-Hodgkin's lymphoma, but there were weak links found in breast, ovary, and bladder cancer. This link suggests that PFAS has a complex effect on the incidence of cancer. The study also showed that diet, especially not eating enough fruit, plays a big role in the risk of getting cancer. In conclusion, the study says that a multifaceted plan to prevent cancer that includes improving diet and lowering environmental pollution should be used. This is because the links between eating habits, environmental pollution, and cancer development are complicated.

Keywords: PFAS contaminants, cancer risk, environmental pollutants, nutritional intake, public health, PFOS, PFHxS, PFOA, urban malnutrition, thyroid cancer, prostate cancer, non-Hodgkin's lymphoma, breast cancer, ovarian cancer, bladder cancer, dietary factors, fruit malnutrition, environmental pollution
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Chapter 1: Introduction

1.1. Background

Sources of Human Exposure

PFAS, a category of synthetic chemicals that are highly resistant to water, oil, and heat, have been widely employed in numerous fields, from non-stick cookware to firefighting foams. The chemical stability that serves as the basis for the application of PFAS in industries, also makes them persistently present in the environment and in biological systems, leading to their classification as forever chemicals (Jain, 2018). This persistence, as well as their common use, in turn, has resulted in almost acute environmental contamination and human exposure. Particularly, the data obtained from the US from 2013 to 2015 showed levels of PFAS above the minimum reporting levels in many public water sources (Hu et al., 2016).

Health Outcomes and Regulatory Responses

The rising awareness of health risks associated with per- and polyfluoroalkyl substances (PFAS) can be attributed to their environmental longevity and ubiquity in many mediums, such as drinking water, indoor dust, indoor air, and food. The chemicals have been found to be associated with a wide range of harmful health effects. Public management and manufacturing changes are responsible for the lowering of blood concentrations of decommissioned chemicals like perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) in the United States and European populations, which were frequently used in industrial and consumer applications (Steenland & Winquist, 2021). Consumers and manufacturers from the US and Europe are no longer using PFOA and PFOS either because of the new rules or changes in manufacturing. However, while the number of newer PFAS in the human body decreased, the concentrations of the older PFAS either remained stable or increased, suggesting that populations around the globe are still exposed to chemicals.

Evidence of Carcinogenic Effect

PFAS exposure is a severe concern because its health effects can be potentially detrimental. Of all these, cancer is considered the key one to be investigated intensively. Animal studies have demonstrated that PFAS can cause various cancers when animals are exposed to it, including Leydig cell adenomas, pancreatic acinar cell adenomas, hepatocellular adenomas or carcinomas in rats, and liver tumors in rainbow trout (Chang et al., 2014). Thus, it is plausible
that PFAS could be linked to carcinogenicity in humans. The primary sources of human PFAS exposure are likely to be drinking water, indoor air, and dust, possibly including food contaminated by food packaging (Sunderland et al., 2019). Accordingly, 6 million of the people who used these systems were exposed to the current EPA levels of PFOA and PFOS (Hu et al., 2016). Such widespread availability of indispensable services as drinking water makes it possible to pay close attention to the level of PFAS pollution in nature and human belongings.

**Global Variations in PFAS Levels**

The differences in geographical areas and time with regard to the concentrations of PFAS in serum clearly demonstrate that during these periods there have been active production, use, and the introduction of environmental and health standards. For instance, the reduction in the serum levels of PFOA and PFOS in the US and Europe after they were taken off the market by the major producers is in sharp contrast to the increased levels of these chemicals in some parts of China and the stable levels of other PFAS forms in certain regions in Europe (Land et al., 2018; Bao et al., 2017). Some PFAS compounds, such as perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS), were phased out in the U.S., which reduced serum concentrations in the general population. More than 98% of American adults have trace levels of a variety of PFAS in their blood, which emphasizes that the exposure is pervasive (Jain, 2018). This illustration highlights the significance of taking a decisive action that would help in preventing PFAS pollution and allow adequate exposure. PFAS have been recorded as residing in environmental compartments for a long time, and experimental evidence suggests that they can also cause cancer in animals. Through these, it is necessary to determine whether PFAS exposure and cancer in humans are associated, especially among the groups that are exposed to these chemicals at high or long-term levels. The purpose of this study is to fill the existing knowledge gap relating to the health effects of PFAS exposure on people across the United States.

**Role of Malnutrition in Cancer Development**

Malnutrition, which is nearly a consensus among health experts, can cause cancer growth. It can then become a crucial confounding factor when research studies aim at looking into connections between environmental pollutants like PFAS and cancer risk. A poor diet may weaken the immune system, increase the body's difficulty in detoxifying harmful poisonous substances, and change cell metabolism, which may eventually increase the risk of getting cancer (Fan et al., 2022). Malnutrition is defined as a lack or excess of nutrients in the diet that
may result in dietary deficiencies, overnutrition, obesity, and cancer risk mediated through inflammatory pathways (Beier, 2021). As a consequence, the nutritional level of the population determines cancer development and the persistence or suppression of the direct effects of green pollutants.

1.2. Problem Statement

The ubiquity and possible health ramifications of PFAS are a major public health issue, especially when it comes to the rate of cancer in the United States. Animal studies show PFAS exposure leads to the development of different types of cancer, indicating a possible carcinogenic risk to humans. Although the exact mechanism and relevance of these findings to human health remain to be established (IARC, 2017), The main problem is the connection between PFAS exposure and cancer development in humans, which remains poorly understood. Due to the extensive use of PFAS in consumer goods and industries and their subsequent appearance in environmental media, there is an imperious need to evaluate the relationship between PFAS exposure and cancer cases. This evaluation is vital to establish the range of public health risks associated with PFAS and to guide the regulatory authorities and public health responses in reducing the exposure and mitigating the possible health implications. Therefore, this study seeks to determine whether PFAS exposure contributes to cancer incidence in the U.S. The finding provides evidence to address public health concerns, which aids in designing health preventive and regulatory measures.

1.3. Research aim and objectives

This research aims to uncover the relationship between major PFAS contaminants and their possible cancer risks in the US. Aside from that, this research will address the independent effects of various PFAS on different cancers and evaluate the role of nutritional intake in modulating cancer risk. From this background, the research objectives for this study are:

1. To analyze the major PFAS contaminants and potential risks in contributing to various types of cancer.

2. To investigate the effect of nutritional intake as a confounding factor on the prevalence of cancer.

1.4. Research Questions

The research questions for this study are:
1. What are the major PFAS contaminants and their potential cancer risks?

2. What is the independent effect of different PFAS contaminants on the prevalence of different types of cancer?

3. What is the effect of nutritional intake as a controlling factor on the prevalence of cancer?

1.5. Significance of the study

This study will be of great importance to many stakeholder groups, such as public health officials, environmental agencies, policymakers, the general public, and the scientific community. The findings may help clarify the relationship between PFAS exposure and cancer risk, which can, in turn, be used to develop public health interventions and regulations addressing the exposure to PFAS in populations. For policymakers and environmental agencies, the study supplies evidence-based knowledge that could serve as a strong basis for enacting stricter environmental standards and cleanup operations with a view to reducing PFAS pollution in water, air, and food sources. Public health officials now have the ability to use the research results to establish special screening allegations and health advisories in PFAS-exposed communities. Furthermore, investigating the modulating actions of the dietary input on cancer prevalence provides suggestions to the public on what dietary adjustments may decrease the risks of the disease brought by PFAS. Thus, the scientific community will extend its understanding of PFAS mechanisms of action and long-term impact after carrying out further studies. Consequently, the study objective is to safeguard the health of the public through participation in the worldwide effort to contain the effects of detrimental contaminants on human health.

1.6. Chapter overview

The study is framed into six key chapters, each of which has been assigned a specific role towards the realization of the objectives of the study. The second chapter is a literature review in which the previous research findings, theoretical constructions, and conceptual models about PFAS contaminants and their possible health implications are presented. After that, the third chapter, which deals with research methodology, tells about the processes of data collection from various databases and the techniques of analysis that are used to examine the data. Chapter four is devoted to the interpretation of the findings, which tries to make the inference possible. Next, chapter five continues the discussion of these results in light of other findings and
incorporates them into the existing framework of knowledge. Furthermore, the sixth chapter summarizes the main findings of the study, bringing out the shortcomings of the present study and discussing the implications of those for future research.
Chapter 2: Literature Review

2.1. Introduction

The study conducts an investigation into the complex connection between PFAS exposure and cancer to clarify the public health issues caused by persistent pollutants. Through analyzing current health data from the environment, this study aims to pinpoint the interaction between PFAS and higher cancer risk in different population groups and travel. Its relevance highlights the need for not only consideration of demographic and geographic differences but also of the possibility of variations in the incidence of PFAS-related cancer in various population categories. The finding should display the policy decision and mitigate risk through protection measures, which is one of the significant requirements in the presence of PFAS exposure. From this background, this chapter presents the analysis of previous research on this particular aspect. Based on these, this chapter first discusses some key terms and then delves into the importance of PFAS. After that, this chapter highlights the role of several PFAS components in cancer. Furthermore, this chapter also presents a theoretical framework and conceptual framework.

2.2. Key terms

The selection of these specific PFAS contaminants might have come from their wide application in industries, their apparent stability towards the environment, the possibility of bioaccumulation, and their known health implications, such as different types of cancers. These aspects hence constitute key components in terms of both the regulations and the health issues.

**PFAS (Per- and Polyfluoroalkyl Substances):** PFAS are human-made chemicals that have been used as raw materials for manufacturing in high-demand applications around the world. They can be found on many surfaces that prevent stickiness in cookware, water-repellent clothing, as well as stain-resistant fabrics, as well as some firefighting foam (Liljestrand, 2022). PFAS are generally considered resistant to degradation in the environment. In human tissue, as they do not break down and can be accumulated over time, results in possible health problems.

**Cancer:** Cancer collectively refers to a wide range of conditions in which cells grow unceasingly and have the capacity to spread to other parts of the body (Maman & Witz, 2018). Due to the ability to evade the usual regulatory mechanisms of the body, it ends up growing beyond normal boundaries and, in many cases, it causes metastasis.
PFBS (Perfluorobutanesulfonic Acid): PFBS is a chemical belonging to the family of PFAS, used as a replacement for more harmful PFAS chemicals in different industries. PFBS poses a lower level of bioaccumulation and toxicity than some of the other PFCs, however, its exposure even at lower levels may still cause health damage (Yue et al., 2020).

PFHpA (Perfluoroheptanoic Acid): PFHpA is a perfluoroalkyl compound that is a part of this unified family of PFAS compounds. Interestingly, it is applied across a number of industries as a surfactant and in a fluoropolymer coating preparation. This contaminant leads to severe health issues in people such as cancer (Weatherly et al., 2023).

PFHxS (Perfluorohexanesulfonic Acid): PFHxS is a human-made chemical, synthesized and belongs to the large PFAS family, which also contains other artificially synthesized chemicals. Some researchers have discovered that this might have led to the rise of health hazards like cancer (Schulz et al., 2020).

PFNA (Perfluorononanoic Acid): PFNA or perfluoronanoic acid consists of a nine-carbon chain and each of the carbons has a fluoroalkyl group binding to it. PFNA is a surfactant and is chemically an artificial fluorinated fatty acid. A correlation has been reported between PFNA and several kinds of cancers (Blake & Fenton, 2020).

PFOA (Perfluorooalkyl Iodide): PFOA is a manufacturing intermediate product in the fluoropolymer production process. Furthermore, PFOA discharge into the environment results in the production of harmful substances that act as toxins for humans, which cause detrimental health effects such as cancer (Bowers et al., 2023).

PFOS (Perfluorooctanesulfonic Acid): PFOS is a perfluorinated alkylated compound. It is used in non-stick and stain-resistant consumer goods, food packaging, and fire-fighting foams. It raises the risk of prostate, kidney, and testicular cancer in men (Deng et al., 2021).

2.3. Importance and purpose of PFAS

PFAS, a large class of artificially created compounds, have long been used in many industrial and consumer items. PFASs are highly stable against decomposition at either high temperatures or in the presence of chemicals since they bear quite strong links between carbon and fluoride. Thus, they are incredibly difficult to biodegrade in the environment and in living organisms (Cousins et al., 2020). Due to this reason, they are known as "forever chemicals," as they are among the most resistant organic chemicals on earth (Cousins et al., 2020). US residents's biomonitoring tests have demonstrated their exposure to high levels of several PFAS variants
(Rappazzo et al., 2017). People are exposed to eating or touching contaminated things in the environment, such as food, water, and dust, when they use or handle commercial or industrial products. Human contact is likely to occur in many situations, both at work and outside of work. The most common type of pollution in water is related to industrial manufacturing and contamination of groundwater and drinking water. The US Environmental Protection Agency's toxicity database shows the presence of over 8,000 separate types of PFAS (Langenbach & Wilson, 2021). Since these toxic chemicals exert harm on laboratory animals and humans in epidemiology research and cohort working conditions, it can be inferred that they are health hazards (Langenbach & Wilson, 2021). The pervasive occurrence and persistence of PFAS underscore the significance of further tracking and explaining these long-term environmental pollutants.

2.4. Health Effects of PFAS

2.4.1. Evidence of PFAS on Cancer Incidence

The attention of scientists is shifting more towards the possibility that substances related to per- and polyfluoroalkyl substances (PFAS) could be considered carcinogenic agents. The goal of these studies is to discover how PFAS contamination relates to cancer, which is based on the principles involved in the mechanisms that may cause cancer and the types of cancer that may occur. The resultant mechanism of PFAS on cancer risk articulates a complicated relationship between environmental pollutants, long-term exposure, and multifaceted biological processes. Different studies imply PFAS participation in the harmful outcomes, making it clear that there is a relationship between PFAS exposure levels and the rise of cancers in human populations (Seyyedsalehi & Boffetta, 2023). Some of the research has focused on the connection among the liver, kidney, genital tract, and thyroid culture, which are observed in the population with high rates of exposure to PFAS (Li et al., 2022; van Gerwen et al., 2023). Subsequently, renal and testicular cancers have been detected at a higher rate (Bartell & Vieira, 2021; Seyyedsalehi & Boffetta, 2023). Moreover, occupational workers who are exposed to these chemicals in processing plants have revealed the same associations and probably positive dose responses.

Moreover, animal models have been used for the last few years to identify and comprehend the possible biological processes that could explain why PFAS are active in cancer emergence. Studies have shown that PFAS can cause oxidative stress, disrupting hormones and gene expression, which may lead to carcinogenesis (Bonato et al., 2020). Importantly, human population studies reveal that people who are exposed to specific PFAS may develop liver,
pancreatic, or testicular tumors (Steenland & Winquist, 2021). However, these results are also faced with a lot of difficulties, which in turn confuses the proper understanding of the research. Variability in study designs, differences in exposure assessment methods, and the presence of confounding factors can affect associations between PAFS exposure and cancer risk. Moreover, most PFAS compounds, whose structures and properties are different, may not behave synchronously with respect to their carcinogenic properties, therefore making the assessment of the risk difficult. In addition, although epidemiology and laboratory studies have produced substantial evidence of the effects of PFAS on the occurrence of cancer, the application of these findings to human health risk assessment must be done carefully. Therefore, the overall body of evidence from epidemiological and laboratory studies suggests a possible link between exposure to PFAS and increased risks of some types of cancer, such as kidney, testicular, and thyroid cancer. In spite of the problems in study design and exposure assessment, the correspondence of results in different populations and experimental models adds to the need for further research into the carcinogenic effect of PFAS. Establishing the mechanisms by which PFAS may facilitate cancer formation is of great importance for the development of successful public health policies that aim to reduce exposure to these persistent environmental contaminants.

2.4.2. PFAS Exposure and Cancer Incidence

2.4.2.1. Role of PFBS

PFBS, a short-chain PFAS, has been adopted as a safer alternative due to lower bioaccumulation, yet environmental and biotic detections have raised cancer concerns (Steenland et al., 2015). Although it's less accumulative, PFBS may still induce cellular stress and hormonal disruptions implicated in cancer progression (Temkin et al., 2020). While direct links between PFBS and cancer are not established, and its carcinogenic pathways remain undetermined, evidence suggests its potential to affect processes like cell proliferation and DNA repair, which are crucial in cancer pathology (Marinello et al., 2020). Further studies, especially using real-world data on PFBS exposure and subsequent cancer rates, are necessary to understand its health impacts fully (EPA, 2022; Singh & Hsieh, 2021).

2.4.2.2. Role of PFHpA

PFHpA, another compound in the PFAS family, is known for environmental persistence and potential bioaccumulation, similar to longer-chained PFAS compounds. Research into
PFHpA’s carcinogenic effects is scarce, with most studies grouping it with other PFAS chemicals, making it challenging to isolate its individual impact on cancer risk. Despite this, its widespread environmental presence and human ingestion warrant close scrutiny. Epidemiological studies suggest a correlation between PFAS exposure and cancers like kidney, testicular, and thyroid, but disentangling PFHpA’s specific effects remains difficult (Barry et al., 2013; Steenland et al., 2015). PFHpA is believed to influence cancer pathways similar to other PFAS, potentially through hormonal disruption, oxidative stress, and interfering with apoptosis and cell growth signaling. However, the precise role of PFHpA in cancer remains undefined, emphasizing the need for focused epidemiological and mechanistic studies on PFHpA’s interactions with cellular processes in carcinogenesis. Further research is crucial to elucidate the relationship between PFHpA exposure and cancer development.

2.4.2.3. Role of PFNA

PFNA, part of the PFAS group, has emerged as a potential health concern due to its persistence and bioaccumulation, raising questions about its carcinogenicity. Although research is limited compared to other PFAS like PFOA and PFOS, global serum concentration findings suggest widespread exposure to PFNA among populations. Epidemiological studies indicate associations between PFAS exposure and several cancers, including liver and pancreatic in labs, and kidney and testicular in humans (IARC 2017; Barry et al. 2013; Vieira et al. 2013; Steenland & Winquist, 2021). However, the specific relationship between PFNA exposure and cancer risk remains less clear, marking a significant gap in understanding. Further research is necessary to isolate PFNA’s effects, clarify its mechanisms of action, and inform regulations for public health protection.

2.4.2.4. Role of PFHxS

PFHxS, a persistent and bioaccumulative PFAS compound used in various industries, is under scrutiny for its potential role in carcinogenesis, with concerns particularly regarding kidney, testicular, and thyroid cancers (Steenland et al., 2015; Barry et al., 2013). Epidemiological evidence suggests that high PFHxS exposure correlates with an elevated cancer risk (Stevenson et al., 2021). In toxicology, PFHxS’s endocrine disruption, oxidative stress induction, and interference with gene expression and the immune system point to mechanisms that could drive cancer development (Hu et al., 2016; Grandjean et al., 2012). However, research gaps persist due to a lack of long-term studies, especially those reflecting low-level chronic exposure
typical for the general population, and the complexity of mixed substance exposures. Future research should focus on these areas, informing public health measures and regulatory standards to mitigate PFAS-related risks.

2.4.2.5. Role of PFOA

PFOA, a widely used PFAS, is recognized for its environmental persistence and bioaccumulation in human tissues, raising concerns about its role in carcinogenesis, particularly regarding liver, testicular, and kidney cancers. Animal studies indicate that PFOA exposure may lead to hepatic adenomas and carcinomas through the activation of PPARα, a receptor involved in cell proliferation and lipid metabolism, which might promote liver tumorigenesis (Hu et al., 2016). In humans, epidemiological evidence for PFOA’s carcinogenic effects is mixed, with some studies noting associations with testicular cancer, particularly in industrial settings (Temkin et al., 2020), and potential links to kidney cancer. However, inconsistencies arise due to varying study designs, population characteristics, and exposure assessments. PFOA’s tendency to induce oxidative stress and inflammation in kidneys is also noted, contributing to its suspected carcinogenicity. The differences in PFOA metabolism between humans and animals necessitate cautious application of animal study results to humans. Ongoing research is needed to refine exposure assessment techniques, clarify PFOA’s carcinogenic mechanisms, and understand individual susceptibilities to inform effective public health policies and risk management.

2.4.2.6. Role of PFOS

PFOS is a synthetic substance widely used in various industrial products for its unique wetting properties, leading to its pervasive environmental presence and human exposure through water and food sources, including fish, with a significant bioaccumulation rate of 5.4 years (De Silva et al., 2021). It is associated with adverse health effects on the liver, development, immune, and reproductive systems. Studies suggest PFOS may act as an endocrine disruptor with estrogentic properties, raising concerns about its role in hormone-related cancers like breast cancer. The compound’s interaction with estrogen receptors and its influence on estrogen-dependent transcriptional activation have been linked to breast cancer risk (Pierozan & Karlsson, 2018). Epidemiological evidence, including a study among Greenland Inuit people, found high serum PFOS levels correlated with increased breast cancer incidence (Hurley et al., 2018). Laboratory research using models like the MCF-10A human breast cell line has shown
that PFOS can expedite cell division and alter key cell cycle regulators such as CDK4, p27, p21, and p53, which are crucial for tumor suppression (Qu et al., 2021; De Silva et al., 2021). PFOS's estrogenic properties and ability to disrupt cell functions highlight the urgency of updating public policies to reduce exposure and mitigate its carcinogenic potential.

2.5. Theoretical Framework

2.5.1. Risk Perception and Communication Theory

Risk communication is a two-way flow of information that takes place among interested parties, from a government agency to the public. Information about risks is conveyed to enhance individuals' knowledge, activism, and attention and to look for solutions to the problem (Sjöberg, 2020). Moreover, this theory has gained more relevance when PFAS and their link to cancer are investigated, especially in the field of environmental health research. The significance of PFAS exposure lies in an intricate mixture of sources and many different types of molecules, which all lead to the health implications of this exposure. Such communication on PFAS creates the need for clear, transparent, and engaging dissemination, which should encourage public involvement and actions. Considering risk perception and communication theory, necessary information about probable dangers should be communicated to all interested parties in an open, straight, and interesting manner. This becomes especially important when the risks, such as PFAS contamination, are complicated and varied. These substances, which are ubiquitously used in industrial and consumer products, have been evidence for several health issues, including cancer. However, the characteristics of these compounds, their long residence time in the environment, and the subtlety of their influence on human health are not readily grasped by the public at large. Therefore, this theory, when used for the study of PFAS and cancer, should help in the development of measures that not only help the public understand the risks but also those that have a dialogue with them, encourage their involvement in the risk mitigation efforts, and empower them to make the right decisions concerning their health.

For the sake of assessing the primary PFAS pollutants and their potential relationship with cancer, it is necessary to simplify the scientific results in such a way that non-experts can comprehend and utilize them. This translates into an attempt to quantify the severity of various forms of cancer caused by different PFAS pollutants that spread widely in the environment and persist for long periods of time. Successful communication is key to building a bridge between scientific knowledge and public understanding to help citizens understand the relevance of the
research findings to their own lives and to a safer society. Furthermore, when evaluating the separate contribution of every type of PFAS to cancer prevalence and the role of diet as a modulating factor, Risk Perception and Communication Theory advocate the need to deliver such a message within the framework of the personal experiences and apprehensions of the potential target group. It entails informing how a person’s activities and choices, such as dietary regimes, contribute to the risk of developing cancer through PFAS exposure. Based on the theory of communication, it not only informs but also initiates a discussion among people whereby they can provide feedback, ask questions, and participate in the discussion, which eventually helps them to understand the preventive measures deeper. As a result, risk perception and communication theory are the prerequisites for effective transmission of the delicate issues related to PFAS exposure and cancer. There is an existing idea that promotes such communication strategies, which do not only inform but also engage the listeners, persuade them to take action, and provide solutions and recommendations. Therefore, awareness empowers the population by equipping them with the knowledge that helps them safeguard their lives and health when facing environmental risk factors.

### 2.6. Conceptual Framework

![Conceptual Framework](Source: Self-generated).

**Figure 1:** Theoretical Framework (Source: Self-generated).
The conceptual model provides an opportunity to get a better understanding of the relationships between the impacts of some non-organic substances and types of cancer (Fig. 1). It reveals the association between the presence of specific PFAS in the blood and the prevalence of seven specific types of cancer. This group of cancers encompasses thyroid, kidney, renal, bladder, non-Hodgkin's lymphoma, prostate, breast, and ovarian cancer. They are directly affected by the presence and concentration of PFAS contaminants. Here, PFAS refers to six different compounds, namely: perfluorobutanesulfonic acid (PFBS), Perfluoroheptanoic acid (PFHpA), perfluorohexanesulfonic acid (PFHxS), perfluorononanoic acid (PFNA), perfluorooctanoic acid (PFOA), and perfluorooctanesulfonic acid (PFOS). These pollutants are viewed as independent variables that could possibly increase the rate of this kind of malignancy.

The model wisely does not only analyze the source of PFAS by exposure but also includes malnutrition as a confounding factor. Here, the consumption of fruits and vegetables, as a primary factor, is assessed to determine whether it may affect the cancer risk or can alter it. The research delegates that the connection between chemical exposure and cancer is multi-layered and can be changed by a diet since diet may alter the body's reaction to them. Through the adjustment of fruit and vegetable intake, researchers will distinguish the effect of PFAS exposure on cancer development from the impact of nutritional factors. This holistic method gives more insight into the interpretation of data.

2.7. Summary

After a thorough literature review on PFAS (per- and polyfluoroalkyl substances) exposure-cancer incidence, some important findings were identified. Specifically, findings show a link between exposure to some PFAS compounds, such as PFOA, PFOS, and, to some extent, PFNA, and the occurrence of different types of cancers, for example, kidney, testicular, and liver cancers. Although some PFAS chemicals are phased out, their existence as legacy and ongoing pollutants remains one of the major concerns for public health at large. The research into the influence of PFAS on cancer incidence is a fast-evolving area with a growing number of epidemiological investigations, which add to the mosaic of possible health consequences. Nevertheless, this stage of investigation also reveals large differences in study designs, populations considered, and the types of PFAS that were examined, resulting in dissimilar findings across different studies. The variability in exposure levels, an additional component that makes generalizations about PFAS as carcinogens even more difficult, is another example of the complexity of this problem.
Taking into account the present research status, it can be seen that although a lot of progress has been made in terms of knowing what PFAS exposure might cause health effects, there are still a number of gaps in the field. The significance of enough investigation cannot be overemphasized so as to make the links between PFAS intake and cancer cases more transparent. Future research should emphasize prospective studies with rigorous exposure assessment methods, cover the occurrence of lower doses and compound PFAS exposures, and elaborate on the mechanisms by which PFAS might lead to cancer development. Such actions are central to building public health practices on top of PFAS exposure risks and preserving people's safety from future troubles.
Chapter 3: Methodology

3.1. Introduction

The information regarding the different levels of PFAS contaminants present in different states and the information regarding cancer-specific prevalence rates in different states that were observed from 2014 to 2020 by the governing bodies and consensus were used in this research. Apart from these exposure and outcome factors, a control variable is also included in this study to control nutrition factors within different populations. In terms of nutrition factors, fruit and vegetable intake-related state-wise national data has been collected.

3.2. Data Source and Collection Process and Data Measures

Secondary observational data was collected for this research. The secondary observational data collection from authentic sources enabled this study to have a more reliable, valid, and credible dataset for a large population without investing a significant amount of time and money (Vallejo-Yagüe et al., 2021). The online government and authentic agency-based publications of data inventories and databases have been used for the data collection process of this research.

The government website www.epa.gov was used to collect state-wise PFAS contamination records, cancer incidence rates, and nutrition levels. For PFAS contamination records in the UCMR3 dataset, they were collected from The Third Unregulated Contaminant Monitoring Rule (UCMR 3): Data Inventory (Epa.gov, 2017). The United States Environmental Protection Agency published the data inventory, where the data sampling was done from 2013 to 2017. The sampling data for six PFAS contaminants were collected, namely PFBS, PFHpA, PFHxS, PFNA, PFOA, and PFOS, from 2014 to 2016, and there are other types of contamination records that were also done from 2013 to 2017 (Epa.gov, 2018). The measure of contamination was milligrams per liter.

The nutrition-related data was collected from data publications done by the Behavioral Risk Factor Surveillance System (BRFSS). The data was available on the Centers for Disease Control and Prevention website (CDC.gov, 2022). Sampling for nutritional and behavioral databases was done from 2016 to 2020. The dataset includes crude and demographic-specific lifestyles, healthy behaviors, and food intake practices of people. The location of the sampling was recorded in the database, and the measure of nutritional intake was malnutrition of fruits and vegetables. People were asked whether they take at least one fruit and at least one vegetable in their meals each day (CDC, 2023). The percentage of people who said “no” was recorded in
that dataset, and therefore the measure is the percentage of fruit malnutrition and the percentage of vegetable malnutrition.

The data regarding cancer is collected from the National Program of Cancer Registries (NPCR), where the dataset includes the state-wise incident rate of cancer (health.gov, 2022). The data was published in the CDC database under the State Cancer Profile sub-division. The dataset included records that were collected from 2016 to 2020. The measure of cancer prevalence was the age-adjusted incident rate per 100,000 persons, which is based on the average incident rate of the dataset from 2016 to 2020 (Statecancerprofiles.cancer.gov., 2023). A total of 8 datasets were collected from this source, of which 7 were about 7 different types of cancer, namely thyroid, kidney, renal, bladder, non-Hodgkin’s lymphoma, prostate, breast, and ovary. A single dataset was collected that is based on the crude presentation of cancer incidence rates, considering all types of cancer.

3.3. Sensitivity and Reliability Test

Cronbach’s alpha reliability analysis has been done within the variables, including exposure (PFAS) variables, control variables (nutrition), and the outcome variable (cancer incidence rate), that are used to develop the predictive models.
Figure 2: Reliability Analysis Considering Final Variables for Predictive Model Development

Figure 2 indicates that the raw alpha of this dataset is 0.65, whereas the standardized alpha is 0.86. Considering 0.65 as the threshold for accepting a model, it can be said that the collected data and accumulated datasets have an acceptable level of reliability. From the list of reliability of resultant reliability, if an item is dropped, it can be seen that deletion of any variable cannot improve the reliability of the reliability alpha value more than 0.66. Therefore, the deletion of any item is not needed, and the dataset can be considered acceptably reliable for predictive modeling and inferential analysis.

3.4. Data Handling and Processing

The data handling process of this research includes the processes of storing, capturing, cleaning, preprocessing, and managing multiple datasets that were collected from different authentic sources. The purpose of the data handling process of this research was to develop location-centered data where cancer incidence rate, PFAS contamination, and malnutrition can be collectively handled for data analysis. The unit of analysis is the contamination amounts, which were float values close to zero, which was an existing mg/l measure, and therefore it was multiplied by 1000 to make it the measure of microgram per liter to have more comprehensible values. The crude contamination results from 2014 to 2016 were taken for final analysis. The CDC-BRFSS Nutrition dataset was based on sampling from 2016 to 2020, and the average of these years is taken as the final consideration of nutritional intake. The CDC, NCI, and SCP cancer datasets include the age-adjusted incident rate per 100,000 persons from 2016 to 2020. The data processing has been done to have state-level data where each record represents each state.

The following analysis aims to construct multiple regression models for the incidence rate of different cancers to find the effect of PFAS contaminants while controlling the role of nutritional intake in individuals. It is assumed that diet and PFAS exposure are the same across time and don’t vary within individuals. After cleaning the contamination data, cancer-specific data, and nutrition data, it has been found that in the State-Wise PFAS contamination dataset, records from only 17 states can be found where contamination of PFAS has occurred at more than the Minimum Reading Limit. After joining all datasets, only records of 15 states in the USA have been found. The analysis has been done on the 15 state-based data, considering the regional contamination level of six PFAS components. Two control variables for nutrition include malnutrition of fruit and malnutrition of vegetables. It is measured by considering the
percentage of people in each state who do not consume at least one fruit or one vegetable per day.

The data cleaning and processing were done using the R scripting language on the R-studio platform. The data handling method is aimed at developing a data frame that can contain state-specific PFAS contamination levels, state-specific incidence rates of cancer, and state-specific nutritional data. The panel dataset was not developed in this study; instead, year-adjusted records are made by taking the average of the data from 2014 to 2016 to have crude data on exposure and outcome factors.

In the data cleaning process, no data imputation method is used, whereas records with missing values were expelled from the dataset. It has been found that in the contamination dataset, the PFAS records were taken from 2014 to 2016, and therefore only these records with six types of PFAS contaminants were extracted from the dataset. Therefore, the dataset was reframed to present state-specific records. After that, the summation of the PFAS contamination amount from 2014 to 2016 was calculated and stored in an attribute for each location.

From the BRFSS dataset, only those records were extracted that included the responses for fruit and vegetable intake. Then only those records were extracted, where data were presented at a crude level without having any specific cluster based on demographic backgrounds such as age, sex, ethnicity, and others. Then Sampling year, location, and fruit and vegetable intake attributes were further extracted. The dataset includes records from 2016 to 2020 to have a crude estimation of long-term contamination and its crude outcomes. Therefore, the yearly average of malnutrition percentage has been calculated to form a cleaned dataset for only year-adjusted fruit malnutrition and vegetable malnutrition data. Calculating the average instead of excluding missing data and avoiding presenting the dataset in a panel dataset format with amputated data made the handling process less complex and made the data more reliable (Jäger, Allhorn, & Bießmann, 2021). The 8 datasets of cancers were based on location-wise records of incidence rates. Finally, for each of these 8 cancer databases, the nutrition dataset and the PFAS dataset were joined by using location as the joining condition attribute. Then, the study has eight separate datasets that include state-specific data about the contamination amount of six different PFAS contaminants: fruit malnutrition, vegetable malnutrition, and the prevalence rate of specific cancers.
3.5. Data Analysis Process

In this quantitative research, statistical data analysis methods have been considered, considering both the graphical and tabular presentation of data and their interpretations. This research employs both descriptive and inferential data analysis methods (Stapor & Stapor, 2020). The descriptive data analysis research has been used to examine the existing exposure levels of different groups of the population to the different PFAS contaminants and the current levels of cancer incident rates in different groups. It also helps to examine the nutritional intake or malnutrition level in different populations. For descriptive statistics, mean, standard deviation, maximum, minimum, and quartiles are used. The normality analysis has been done through kurtosis and skewness results in descriptive statistics.

In terms of inferential analysis, the correlation analysis has been done within six types of PFAS contaminants: fruit malnutrition and vegetable malnutrition, in order to identify associations within different independent predictors of the models of incidence rate prediction. In correlation, both the coefficients of each pair and the visual scattered plot for each pair are present in a single matrix for dynamic understanding and visualization. It helped to examine the prevalence of one or more contaminants being present together in a water body, which could lead to further evaluation of the collective contamination of multiple PFAS contaminants. The correlation between nutritional variables helped to evaluate the behavioral pattern of fruit and vegetable intake.

In order to develop a predictive model, a linear regression model has been used. The predictive models for seven different types of cancer, namely thyroid, kidney, renal, bladder, non-Hodgkin’s lymphoma, prostate, breast, and ovarian, have been developed independently considering the independent presence of six PFAS contaminants: PFBS, PFHpA, PFHxS,
PFNA, PFOA, and PFOS. Fruit malnutrition and vegetable malnutrition were also included in the models. The effect size of exposure and control factors was analyzed considering the coefficients of each independent variable, and the predictability of the model was tested using R-square and adjusted R-square values. The significance level of different predictors was analyzed, considering a 95% confidence interval where alpha is 0.05 and a 90% confidence interval where alpha is 0.1.

Four diagnosis plots that were used to evaluate the robustness of the model are the residual vs. fitted plot, the normal Q-Q plot of residual, the scale-location plot, and the residual vs. leverage plot.

3.6. Summary

This research is aimed at testifying the relationship between different PFAS containment exposures and the prevalence of cancers using hypotheses that were developed from existing pieces of literature, and the deductive research approach has been chosen for this. In terms of the structure of this research, this study has used an explanatory study design that is aimed at finding the relationship between PFAS exposure and cancer-related outcomes. In terms of the tool and strategic selection of this study, it is based on an observational study design while using secondary data.

The data on PFAS contamination was collected from the UCMR3 data inventory published on the Epa.gov website. A total of six PFAS contaminants were collected, namely PFBS, PFHpA, PFHxS, PFNA, PFOA, and PFOS, from 2014 to 2016. The data is measured in micrograms per liter. Fruit and vegetable malnutrition data was collected from the BRFSS dataset. It is measured in the percentage of people who do not consume 1 fruit or 1 vegetable at least a day. The cancer data was collected from the NPCR data inventory, where data from 2016 to 2020 was stored with the measure of the prevalence of cancer per 10,000 people. A total of 8 datasets were collected regarding cancer, where 1 dataset was about crude cancer prevalence and 7 datasets were about 7 different types of cancer, namely thyroid, kidney, renal, bladder, non-Hodgkin’s lymphoma, prostate, breast, and ovary. Using CSV files and R-studio-driven data cleaning, data handling and data analysis processes were done. There are a total of eight separate datasets that include state-specific data about the contamination amount of six different PFAS contaminants, fruit malnutrition, vegetable malnutrition, and the prevalence rate of specific cancers. The descriptive, correlation, and regression analysis methods were used in this study. In regression analysis, the model diagnosis test has been done using a
residual vs. fitted plot, a normal Q-Q plot of residuals, a scale-location plot, and a residual vs. leverage plot. For inferential analysis, both 95% CI ($\alpha = 0.05$) and 90% CI ($\alpha = 0.1$) were considered. The Cronbach alpha reliability was tested to ensure reliability, and data credibility, validity, and authenticity were ensured through data collection, data processing, and data analysis methods.
Chapter 4: Findings

4.1 Descriptive Statistics

As per the descriptive statistics of contamination in Figure 4.1.1, the highest contamination can be found in PFOS, where the mean water contamination from 2014 to 2016 per state was 375 micrograms per liter. The contamination of PFOS within the first and third quartiles ranges from 0 to 729 micrograms per liter, which highlights a significant level of contamination. For PFHxS, the mean water contamination from 2014 to 2016 per state was 129 micrograms per liter, whereas it mostly ranged from 0 micrograms to 272 micrograms and had a maximum contamination of 965 micrograms per liter. The third highest contamination can be found in PFOA, where the average water contamination is 129 micrograms per liter, which mostly ranges from 0 to 142.695 micrograms per liter and has a maximum level up to 1071 micrograms per liter. The contamination level of other contaminants is comparatively lower, whereas, for PFHpA, the contamination per state from 2014 to 2016 was 40.87 micrograms per liter, which ranges from 0 to 264 micrograms per liter. The contamination levels of PFNA and PFBA are negligible. The average fruit malnutrition in each state of the US is 38.39%, which indicates 38.39% of people in each state do not consume at least 1 fruit per day. It can range from 34% to 41% in different states. The average vegetable malnutrition is 19.54%, which implies 19.54% of people in the USA for each state do not consume at least 1 vegetable per day, which is better than fruit consumption. The skewness and kurtosis values indicated that most of the variables have a moderate to low-level normal distribution of data.
The results show that the average contamination of PFBS at the state-specific level is almost 0. The data indicates that PFHpA contamination is highest in Massachusetts (264 micrograms per liter), followed by New York and Minnesota. Massachusetts also has the highest level of PFHxS contamination (965 micrograms per liter), the highest level of PFNA contamination and PFOS contamination (1695 micrograms per liter), and the highest level of PFOS contamination (1695 micrograms per liter). Minnesota also has a high level of PFHxS contamination (365 micrograms per liter), PFOA contamination (1071.9 micrograms per liter), and the second highest level of PFOS contamination (1283.2 micrograms per liter). Therefore, Massachusetts, Minnesota, New York, and Ohio are the major areas of PFAS contamination. The highest level of fruit malnutrition can be found in Mississippi and Louisiana, where 46.9% and 46.1 percent of people do not eat at least one fruit every day. The highest vegetable malnutrition rate has been found in Louisiana, where 24.75% of people do not eat at least one vegetable every day.

4.2. Correlation Analysis

The following correlation has been found between exposure variables (PFAS contamination amount) and control variables (fruit and vegetable malnutrition). The purpose of this correlation is to understand associations within different independent predictors of the models of incidence rate prediction.
As per the correlation in Figure 5, there are moderate to high-level correlations ($r = 0.2$ to $0.95$) within the different PFAS contamination components. It indicates that in water bodies where a single component of PFAS contaminants is found, the risk of other PFAS contaminants being present in that water body is high. The association between PFOA, PFHxS, and PFHpA being present in a natural water body or water storage body is very high. However, moderately negative correlations are found between the level of contamination of PFOS and all other PFOA contaminants ($r = -0.47$). It indicates that in a water body where the presence of PFOS contamination is higher, the risk of having PFOA contamination will be lower, and the opposite can be true as well. A low to moderate negative correlation has been found between PFAS contamination and fruit malnutrition ($r = -0.36$ to $-0.47$). It indicates that states where the PFAS contamination is high in the water bodies have lower levels of malnutrition in terms of the regular fruit intake of adults. A moderately positive correlation has been found between fruit malnutrition and vegetable malnutrition ($r = 0.46$). Is it possible that higher PFAS levels in those that have low malnutrition are due to PFAS contamination in the fruit and vegetables?
4.5 Model Development and Testing

4.5.1 Model for All Cancer Data

In the following section, a linear regression model has been developed considering the joint dataset for the crude incidence rate projected for all types of cancers. For each regression model, starting with the regression model of all cancer types, the model diagnosis was done after the model development.

![Regression Model for All Types of Cancer (Source – Self-generated).](image)

As per Figure 6, no significant effect has been found by any of the PFAS contaminants on the cancer prevalence. The p values of the ANOVA (F = 0.6552) indicate that the model is not significant. Only a 39.58% variance in the total incidence rate per 100,000 people of all types of cancers can be predicted by the contamination (R-square = 0.3958), whereas the residual of this model is very high. Therefore, levels of PFAS contamination and malnutrition are considerable predictors of the overall cancer rate in the US.
In Figure 7, the residual vs. fitted plot shows that most of the data distributions are on the same side of the zero-residual line, and in the scale location plots, a trend in data-point distribution can be found. It indicates that the model has heteroscedasticity. The Q-Q plot indicates that the residuals are mostly normally distributed. The Cook’s Plot showed that the number of outliers within this model is high. Therefore, the model for all cancer types is not robust.
4.4.1 Model for Thyroid Cancer Data

According to Figure 8, there is no evidence of a relationship between PFAS contaminants and the prevalence of thyroid cancer. The ANOVA (F = 1.168, p = 0.42) results indicated that the model is not significant. Only a 7.76% variance in the total incidence rate per 100,000 people of thyroid cancer can be predicted by the contamination, whereas the residual of this model is very high (adj-R-square = 0.0766). Therefore, the level of PFAS contamination and malnutrition are not predictors of the thyroid cancer rate in the US.
In Figure 9, the residual vs. fitted plot shows that the distributions are equally distributed on both sides of the zero-residual line, and in the scale location plots, no prominent trend in data-point distribution can be found. It indicates that the model is homoscedastic. However, the Q-Q plot shows that the residual points do not follow the normal distribution. The Cook’s Plot showed that the number of outlets within this model is very high. Therefore, the model for thyroid cancer is not robust.
4.4.2 Model for Kidney Renal Cancer Data

As per the model, the malnutrition of fruit percentage is only related to the prevalence of kidney and renal cancer, and no PFAS contaminants are related to the prevalence of kidney and renal cancer. Therefore, the PFAS contamination is not significant for this model. It indicates that the fruit intake of a population can only be used for predicting kidney and renal cancer, whereas exposure to PFAS contaminants is not independently related to the prevalence of kidney and renal cancer. A 73.52% variance in the total incidence rate per 100,000 people of kidney and renal cancers can be predicted by the model (adj-R-square = 0.7352). The ANOVA (F = 6.554, p < 0.05) results indicated that the model is not significant (Fig. 10.).
As per Figure 11, the residual vs. fitted plot shows that the data points are not equally distributed on both sides of the zero-residual line. In the scale location plot, a trend in data-point distribution can be found. It indicates that the regression model is heteroscedastic. However, the Q-Q plot shows that the residual points moderately follow the normal distribution. The Cook’s Plot showed that the number of outlets within this model is very low, and the points are scattered across the graph. Therefore, the model for kidney and renal cancer is marginally robust; however, further improvement of the model is required.
4.5.4 Model for Bladder Cancer Data

According to Figure 12, a marginally significant predictor is found, which is malnutrition of vegetable percentage ($p < 0.1$). Therefore, the PFAS contamination is not significant for this model. A 30.28% variance in the incidence rate per 100,000 people of bladder cancer can be predicted by the model (adj-R-square = 0.3028). The ANOVA results ($F = 1.869$, $p = 0.21$) indicated that the model is not significant.
As per Figure 13, the residual vs. fitted plot shows that the data points are equally distributed on both sides of the zero-residual line. However, in the scale location plot, a trend in data-point distribution can be found. It indicates that the regression model can be heteroscedastic. However, the Q-Q plot shows that the residual points follow the normal distribution appropriately. The Cook’s Plot showed that the number of outlets within this model is moderate, and the points are scattered across the graph. Therefore, the robustness of the model for bladder cancer is undetermined, whereas further improvement of the model can be done to increase its robustness.

Figure 13. Diagnosis Plots of Regression Model Results for Bladder Cancer (Source – Self-generated).
4.5.5 Model for Non-Hodgkin's Lymphoma Cancer Data

According to Figure 14, the ANOVA (F = 1.227, p = 0.39) results indicated that the predictive model for non-Hodgkin’s lymphoma is not significant. Only a 10.13% variance in the total incidence rate per 100,000 people of non-Hodgkin’s lymphoma can be predicted by the contamination (adj-R-square = 0.1013), whereas the residual of this model is very high. Therefore, the level of PFAS contamination and malnutrition are not the predictors of non-Hodgkin’s lymphoma in the US.
Figure 15. Diagnosis of Regression Model Results for Non-Hodgkin’s Lymphoma (Source – Self-generated).

As per Figure 4.5.4.1, the residual vs. fitted plot shows that the data points are not equally distributed on both sides of the zero-residual line. In the scale location plot and the residual vs. fitted plot, a trend in data-point distribution can be found. It indicates that the regression model is heteroscedastic. However, the Q-Q plot shows that the residual points moderately follow the normal distribution. The Cook’s Plot showed that the number of outlets within this model is moderate, and the point’s distribution also forms a trend. Therefore, the model for non-Hodgkin’s lymphoma is not robust.
4.5.6 Model for Prostate Cancer Data

According to Figure 16, the ANOVA (F = 0.3219, p = 0.92) results showed that the predictive model for prostate cancer is very insignificant. Only a 24.35% variance in the total incidence rate per 100,000 people of prostate cancer can be predicted by the contamination (R-square = 0.2435), whereas the residual of this model is very high. Therefore, the level of PFAS contamination and malnutrition cannot predict the incidence of prostate cancer in the US.
According to Figure 17, the level of PFAS contamination and malnutrition cannot predict the incidence of prostate cancer in the US. The ANOVA (F = 0.3219, p = 0.92) results showed that the predictive model for prostate cancer is very insignificant. Only a 24.35% variance in the total incidence rate per 100,000 people of prostate cancer can be predicted by the contamination (R-square = 0.2435), whereas the residual of this model is very high.
4.5.7 Model for Breast Cancer Data

As per the model in Figure 18, With 90% confidence, the contamination level of PFHxS (B = 0.0732, p < 0.1) can be considered a marginally significant predictor of breast cancer. Contamination of PFOS (B = 0.0449, p <0.1) is also found as a marginally significant predictor of breast cancer at a 90% confidence level. PFOA contamination (B = 0.0338, p <0.1) is a third marginally significant independent predictor of breast cancer. However, no effect of control variables such as fruit malnutrition and vegetable malnutrition can be found on the incidence rate of breast cancer. A 65.42% variance in the total incidence rate per 100,000 people of breast cancer can be predicted by the model (R-square = 0.6542). The ANOVA (F = 1.89, p < 0.2097) results indicated that the model is not significant. However, from the coefficients, it can be seen that there are some marginally significant independent predictors.
As per Figure 19, the residual vs. fitted plot indicated that the data points are equally distributed on both sides of the zero-residual line. In the scale location plot, no trend in the data point distribution can be found. It indicated that the regression model is not heteroscedastic. Besides, the Q-Q plot shows that the residual points follow the normal distribution. The Cook’s Plot indicates that the number of outlets within this model is very low and the point’s distribution is scattered, which has no trend. Therefore, the model for breast cancer is robust. The model can be further refined by considering sub-region-specific data across the US to increase the predictability of the model.
4.5.8 Model for Ovary Cancer Data

According to Figure 20, the contamination level of PFHxS (B = 0.0106, p < 0.05) is the most significant predictor of ovarian cancer, with a large effect size. Contamination of PFOS (B = 0.0059, p <0.05) is also found to be a highly significant predictor of ovary cancer. PFOA contamination (B = 0.00316, p <0.05) is a third strongly significant independent predictor of breast cancer. The contamination of PFNA (B = 0.0456, p <0.1) is a marginally significant predictor with a large effect size. Both fruit malnutrition and vegetable malnutrition are significant predictors of this model, whereas fruit malnutrition is the most significant predictor of ovarian cancer. A 93.4% variance in the total incidence rate per 100,000 people of ovarian cancer can be predicted by the model (R-square = 0.934). The ANOVA (F = 14.15, p < 0.05) results indicated that the model is highly significant. However, as per the coefficients, there are some highly significant independent predictors in this model.

Figure 20. Regression Model Results for Ovary Cancer (Source – Self-generated).
Figure 21. Diagnosis of Regression Model Results for Ovary Cancer (Source – Self-generated).

As per Figure 21, the residual vs. fitted plot indicated that the data points are equally distributed on both sides of the zero-residual line, whereas in the location plot, no trend in data-point distribution can be found. It indicated that the regression model is not heteroscedastic. Besides, as per the Q-Q plot, residual points follow the normal distribution. Cook’s Plot indicated that there are no outliers and the point distribution is scattered, which has no trend. Henceforth, the model for ovarian cancer is robust.
Chapter 5: Data Analysis

5.1. Introduction

The chapter is built on thorough research that was done on the results of the recent study. The chapter has highlighted the significant role of key PFAS contaminants, such as their environmental persistence and buildup in the organism, as a causal factor in cancer.

The obtained results, which allowed for the identification of environmental carcinogens, also had certain limitations. Since the data from the cross-sectional setup was limited in drawing causal inferences, more long-term studies are needed that can confidently show the PFAS influence on cancer development. Furthermore, the study's concern about waterborne contaminants does not reflect other modes of exposure. This leads to the conclusion that a broad environmental assessment is needed to comprehensively understand the role of PFAS in increasing cancer risk. Furthermore, the correlation analysis revealed the existence of complicated interactions between PFAS contamination and undernourishment, especially with the consumption of vegetables and fruits. States with higher PFAS contamination tended to have lower levels of malnutrition. This finding reflects socio-economic factors or public health interventions that target diet improvement in areas known for environmental pollution. The association between higher PFAS pollution and reduced malnutrition rates introduces socio-economic and public health elements to the environmental exposure discourse. This result indicated that particular dietary methods seem to be preferable in regions that are contaminated with PFAS. In this context, Naja et al. (2019) suggested that if people eat better, it might stop cancer cases from getting worse. It highlights the need for integrated health measures that address environmental pollution and dietary inadequacies.

While PFAS contamination and an unhealthy diet are apparent causes of higher cancer rates, these factors are different for different cancer types. Moreover, the models for kidney cancer and, to a lesser extent, for breast and ovarian cancer suggested that PFAS exposure was not quite crucial. However, one important limitation of this research is its usage of aggregate information that could hide individuals' variations in exposure and dietary practices. Furthermore, the design of the study does not allow researchers to determine the relationship between PFAS exposure, malnutrition, and cancer frequency. Thus, the association between environmental contaminants, health, and nutrition reveals the need for creating a complex approach to public health policies on cancer prevention. Therefore, the study reveals the risks of key PFAS contaminants and the complicated relationship between environmental and
nutritional factors in cancer progression. These findings advocate for the continued examination of PFAS exposure's role in health outcomes, emphasizing the importance of integrated research that encompasses both environmental science and nutritional epidemiology.

5.2. Effect of different PFAS contaminants on the prevalence of different cancer types

The assessment of the correlation between PFAS exposure and cancer incidence reveals varied impacts on different cancer types. For thyroid, prostate, and non-Hodgkin's lymphoma cancers, the findings suggest that PFAS contamination levels are not predictive indicators of incidence rates. These findings pointed towards a negligible or non-significant impact of these contaminants on the prevalence of these cancers. Therefore, though this current study showed a non-significant impact of PFAS contaminants on these three types of cancers, several studies showed a positive impact of PFAS on these three cancers. However, van Gerwen et al. (2023) have shown a significant correlation between PFAS exposure to linear perfluorooctanesulfonic acid (n-PFOS) and a heightened rate of thyroid cancer. It specifically illuminates the critical risk of papillary thyroid cancer linked to such chemical exposures. Contrary to this view, Imir et al. (2021) have proposed that PFAS may finally increase the risk of prostate cancer progression by interacting with PPARα, β/δ, and γ receptors. Through this interaction, PFAS toxicity and the initiation of its prostate cancer-related mechanism are revealed. Besides, Liljestrand (2022) has found out that PFOA is also a potent carcinogen for non-Hodgkin lymphoma cancers. Therefore, PFAS triggers thyroid, prostate, and non-Hodgkin’s lymphoma cancers that need to be elucidated in extensive studies.

In another regard, cases of breast, ovarian, and bladder cancer demonstrated that some PFAS compounds became marginally significant predictors. In the breast cancer case, certain PFAS compounds, including PFHxS, PFOS, and PFOA, were indicated as marginally significant predictors that may show some impact. The ovarian cancer association is also stronger with PFAS exposure, whereby PFOA, PFOA, and PFHxS were determined to be the major predictors. In addition to that, PFNA was also observed to be a slightly significant predictor of ovarian cancer. Similarly, Li et al. (2022) found that exposure to PFAS chemicals is an established risk factor for breast cancer in women from China, Europe, and America. Furthermore, the research done by Rickard et al. (2022a) stated that exposure to PFAS and PFAS mixtures at sub-cytotoxic concentrations could also increase the survival fraction of ovarian cancer cells. This indicates that PFAS has the potential to disrupt regular ovarian
function. After analyzing all cancer types, it could be deduced that PFAS contamination showed more pronounced contamination on the incidence of ovarian cancer compared to other types. However, in the case of kidney and bladder cancers, the evidence does not support a significant role for PFAS exposure. However, Shearer et al. (2021) showed that individuals who are employed in a PFAS-producing chemical plant and are exposed to elevated levels of PFOA have been found to have a greater incidence and mortality of kidney cancer. Similarly, Messmer et al. (2022) showed that PFAS may increase the risk of bladder cancer beyond the average risk in the United States.

Moreover, out of 7 cancers, the prominent role of PFAS contamination has been shown in ovary and breast cancer. It implies that females, more than males, might have an increased susceptibility to particular cancers seen in people once PFAS contamination occurs. By identifying different genders with distinct risks of PFAS contamination, researchers emphasize the necessity of continuing research in this area (Crowder, 2019). In this regard, Rickard et al. (2022b) found out that breast and ovarian cancer in women is due to PFAS, which can create problems for reproductive tissues either directly or indirectly through endocrine system disruption. Consequently, PFAS interferes with women's reproductive function. A key limitation in the findings has been identified in such cases where PFAS did not show any significant effects. This limitation arose from the non-robustness of the models for prostate, non-Hodgkin’s lymphoma, and thyroid cancers; undetermined robustness for bladder cancer; and only marginal robustness for kidney and renal cancer. Thus, addressing the robustness and improving these models in future studies might help find stronger links between PFAS exposure and cancer.

5.3. Effect of malnutrition on the prevalence of different types of cancer

The investigation into the interplay between nutrient aspects and the prevalence of various types of cancers reveals a multifaceted perspective. It highlights that while PFAS contamination is a concern, nutritional deficiencies also play an important factor in causing cancer. This study revealed that fruit and vegetable malnutrition has been shown to contribute to cancer as much as PFAS. In the case of kidney and renal cancers, the model revealed that fruit malnutrition was a major factor in cancer development. Besides chemical pollutants, dietary practices play a significant role in cancer risk. This result suggests that confronting malnutrition can be as important as detoxifying environmental pollutants when cancer prevention strategies are implemented. It seems that malnutritional disorders, particularly in
fruits and vegetables, might amplify the consequences of PFAS on cancer growth and development. PFAS such as PFHxS, PFOS, and PFOA were marginally predictive only for ovarian and breast cancers, while the absence of significant predictors in other models reveals that the role of factors beyond PFAS exposure, including nutritional deficiencies, in the incidence of cancer cannot be excluded. The complicated link demonstrates the need for a complete approach to cancer prevention strategies where environment and diet are considered essential components. In the case of cancers like thyroid, bladder, and non-Hodgkin’s lymphoma, where PFAS do not have an important role as predictors, attention shifts towards the more comprehensive environmental context and nutrition, hinting at the complexity of the disease aetiology. Even more complex models, like breast and ovarian cancer ones, in which PFAS exposure is significantly related to incidence rates, show the importance of nutrition as a factor.

Additionally, the results are in accordance with the research of Yahia et al. (2019), which demonstrated that dietary patterns rich in fruits and vegetables were negatively associated with the risk of cancer. This phenomenon indicates that a healthy diet plays a role in cancer prevention. This coincides with a kidney and renal cancer study that showed that malnutrition is a critical baseline predictor. The recommendation is that tackling the problem of malnutrition should be on the frontlines of PFAS mitigation while promoting healthy diets and integrating dietary habits into health strategies. Moreover, the studies of Logan and Bourassa (2018) showed that higher consumption of fresh vegetables and fruits contributed to the incidence of cancer. Their findings established that nutritional components, particularly the intake of the products of the soil such as fruit and vegetables, affect mainly cancer development where there is an exposure to PFAS. Similarly, Bahrami's (2023) research showed that some dietary patterns could have a preventive effect on breast and prostate cancer. This research, focused on whole grain, fruit, and vegetable diets, demonstrated that nutritional therapy can be utilized to reduce the risk of cancer.

These findings highlight the importance of diet in risk reduction and suggest that dietary treatments may help reduce environmental contamination, including PFAS. These findings emphasize that nutrition and the environment should be considered in cancer prevention efforts. This comprehensive perspective posits the need for integrated health solutions and the implementation of multifaceted approaches to cancer prevention. Thus, it also suggests that improved diets and proper PFAS disposal can reduce cancer risk.
5.4. Summary

Thus, this chapter discusses the complicated association between exposure to PFAS, malnutrition, and cancer incidence. It indicates that these environmental and dietary factors may have played the leading role in the formation of cancer. In this regard, many hazardous chemicals, such as PFOS, PFHxS, and PFOA, were found in water sources in the USA. These substances stay inside the body for a protracted period and accumulate, which results in the development of cancer. It was revealed that not only PFAS exposure but also fruit and vegetable shortages have a great influence on the development of cancer. This points out the need to take environmental and nutritional deficiencies into account when developing comprehensive cancer prevention policies.

The outcomes emphasize that all cancers are not equally affected by PFAS exposure, specifically kidney, renal, breast, and ovarian cancers. Interestingly, a higher degree of PFAS contamination is associated with a lower prevalence of malnutrition. Such an observation indicates the possibility for mutually beneficial synergy between socio-economic and public health strategies in areas that experience environmental pollution. Notwithstanding that the study managed to highlight possible waterborne environmental carcinogens, it acknowledges its cross-sectional nature and emphasis on water-borne carcinogens as a drawback, which calls for further comprehensive research. Thus, the chapter favors a comprehensive public health approach, having to deal with the complex relationships between diet, environmental pollutants, and cancer risk.
Chapter 6: Conclusion

6.1. Introduction

This sixth chapter is the conclusion of the study. It reveals the crucial outcomes concerning the PFAS exposure background, dietary deficiencies, and the confirmation of cancer cases, highlighting the multifaceted consequences of these pollutants. In addition, the paper identifies the limitations experienced during the research process. In addition, future research directions are outlined, which are aimed at guiding future interventions and a better understanding.

6.2. Key findings

The investigation has reported that PFOS, PFHxS, and PFOA are the most prevalent PFAS contaminants in the USA. Hence, their abundance in the environment combined with their persistence and bioaccumulation traits uncover potential risks to human health. These contaminants are traced to the greater public health issue that accompanies their long-term effects. Investigations into PFAS exposure and different cancers show that the PFAS effect is not shown in all cancer types. Particularly, PFAS concentration and thyroid, prostate, and non-Hogkin's lymphoma incidence are not found to be correlated. There is a higher association with breast and ovarian cancers, implying that PFAS exposure may be more pronounced in these types of cancers because they affect mainly the female reproductive organs or functions of hormonal glands.

Alongside this, the paper analyzes the role of dietary factors in the PFAS presence in the development of cancer. It emphasizes that nutritional imperfections, particularly the shortage of fruits and vegetables, which provide vitamins and minerals essential to people, are among the main cancer risks. The health-affecting impact of PFAS on the kidneys and renal cancers is related to this deficit, which is determined by the fact that proper dietary intake could lower some cancer risks associated with PFAS exposure. The findings further demonstrate that although PFAS and malnutrition are predictors of various types of cancer, their relative importance varies among different types, and the data does not firmly establish causality due to its cross-sectional design. This shows a multilevel connection between the toxicity of the environment and cancer development. Hence, the research demonstrates that it is essential to employ integrated public health programs that deal with both environmental and dietary factors to come up with the most effective cancer prevention programs. Further research is needed to understand these complex relationships between PFAS exposure, malnutrition, and cancer risk,
which will support an anti-cancer strategy that addresses chemical contaminants and nutritional health.

6.3. Limitation of this study

The crucial limitation of this study is the cross-sectional design, which renders it difficult to determine the long-term health risks like cancer that are exposed to the person over a lengthy period of time. However, the main problem is that the PFAS levels recorded during the study are not a good indicator of the exposure levels from 10–20 years earlier, which is a concern. Such an assumption is problematic, as cancer associated with PFAS exposure can have a long enough dormancy period and manifest after many years. The persistence of PFAS as environmental pollutants means that their concentration in ecosystems and human populations changes considerably in the long run because of changes in manufacturing patterns, regulatory measures, and environmental degradation. Consequently, ignoring the normal PFAS levels during the years involved in malignancies' development may not be a faithful indicator of exposure history.

On the other hand, the restriction of methodology creates a limitation on the ability to draw firm conclusions regarding the causal relationship between PFAS exposure and cancer incidence. The use of current exposure data to extrapolate historical PFAS exposure levels might not actually reveal the real health effects of PFAS. Without considering the varying PFAS levels throughout the duration of the study, the conclusions may be taken with skepticism, especially when it comes to policy development and individual risk evaluation.

6.4. Recommendation for Future Research

The main problem with the cross-sectional approach to the study of PFAS exposure and cancer risk in the current study should be given preference to the implementation of longitudinal studies. Such studies are important, as they trace the extent of exposure as well as the health outcomes over the long years during which there is a probability of developing cancer. The use of longitudinal research would create an opportunity for a more accurate investigation of the nature through which PFAS exposure leads to cancer; changes in an individual's exposure level and their health impacts over time could also be analyzed. Apart from that, fusing historical environmental data relating to PFAS concentrations into the models would possibly increase awareness of earlier exposure levels. Researchers should try to find old historical records and environmental samples that can be used in the investigation of PFAS contamination at various
environmental sites. This method will help to accurately record the duration of exposure, the key parameter here for understanding the long-term effects of these chemicals. By paying attention to the weaknesses of these study designs and taking steps to deal with them, future research will eventually be able to conclusively establish the link between PFAS exposure and cancer. Thus, the diversification datasets could enhance better-informed decision-making in health campaigns and policy formulations for PFAS risk management.
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