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Associations Between Red and Processed Meat Consumption and Risk of Developing Colorectal Cancer: A Comprehensive Meta-Analysis and Systematic Review

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Associations Between Red and Processed Meat Consumption and Risk of Developing Colorectal Cancer: A Comprehensive Meta-Analysis and Systematic Review

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Abstract

Colorectal cancer, a globally prevalent concern, necessitates the investigation of lifestyle factors contributing to its development. Evidence suggested a potential link between colorectal cancer and red/processed meat consumption, prompting a rigorous analysis of relevant studies and utilization of permutation tests for statistical evaluation. This database study explored the impact of red and processed meat consumption patterns on colorectal cancer risk. Leveraging publicly available nutrition reports and relevant studies, the research question posed is: “How does the frequency of consuming red and processed meat influence colorectal cancer risk over a person's lifespan?” It is hypothesized there will be a statistically significant difference in colorectal cancer incidence between those with regular red and processed meat consumption versus minimal consumption. The findings support a significant association between red and processed meat consumption and colorectal cancer risk. The findings emphasize the substantial impact of red and processed meat consumption on colorectal cancer risk, inviting further research to elucidate underlying mechanisms and establish preventative strategies.

Keywords: red meat, processed meat, colorectal cancer, colon cancer, rectal cancer, carcinogenesis, nutrition, cancer prevention

Associations Between Red and Processed Meat Consumption and Risk of Developing Colorectal Cancer: A Comprehensive Meta-Analysis and Systematic Review

Meat Consumption Linked to Colorectal Cancer Incidence

Colorectal cancer is the third most diagnosed cancer worldwide, tallying approximately 1.2 million new cases and 608,000 deaths yearly (Ferlay et al., 2010). As such, it is crucial to identify lifestyle factors that may contribute to the risk of developing this form of cancer as a preventative measure.

Evidence suggested consumption of red and processed meats may increase the chance of developing colorectal cancer. Red meat is defined as any meat that is derived from mammals that are typically red when their meat is uncooked, such as beef, pork, and lamb (The Free Dictionary, n.d.). Meanwhile, processed meat is defined as meat that has been transformed through salting, curing, fermentation, smoking, or other processes to enhance flavor or improve preservation (Cassetty, 2019). This includes bacon, ham, hot dogs, sausage, and deli meats.

The primary aim of this database study is to analyze the nutrition reports of several surveyed volunteers via publicly available studies to answer the research question: “How do patterns of red and processed meat consumption impact one’s risk of developing colorectal cancer throughout the course of their life?”

Permutation Tests

The H_0 (null hypothesis) for this study stated that there is no statistically significant difference between incidence of colorectal cancer in persons who consume a large amount of red and processed meats on a regular basis compared to persons who consume little to no red and processed meat. The H_a (alternate hypothesis) for this study stated that there is a statistically significant difference between incidence of colorectal cancer in persons who consume a large

amount of red and processed meats on a regular basis compared to persons who consume little to no red and processed meat.

The main studies used in this paper include cohorts such as the Nurses' Health Study and the Health Professionals Follow-Up Study (Health Professionals Follow-Up Study, 2022). While these studies can be assumed to be independent and normal, they are not randomly sampled. Thus, they did not meet the requirements to perform various statistical tests such as t-tests or F-tests.

However, "Because randomization rather than random sampling is the norm in biomedical research… exact permutation… tests for differences in location should be preferred" (Ludbrook & Dudley, 1998 p. 127). This statistical test is used throughout the course of this paper to determine whether the null hypothesis is rejected. A permutation test assumed that if the null hypothesis is true and there is no difference in the mean risk ratio of colorectal cancer between persons that consume little to no red/processed meat and persons that eat these types of meats regularly, then shuffling the data points between groups should still result in a similar if not the same mean. Many permutations are performed, and the results are graphed. Lastly, the p-value is found by determining the proportion of the total permutations that generated a result that was as extreme or more extreme than the original value (Ludbrook & Dudley, 1998).

The statistical analysis in this project relies on R software, a programming language designed for data analysis and visualization. RStudio, an open-source integrated development environment for R, enhances the overall efficiency of this statistical analysis. It is used to execute complex calculations such as the permutation tests employed in this study. These tools provided a robust platform for carrying out the time-consuming calculations that expose the intricate relationships within the data set, contributing to a more comprehensive understanding of the experimental outcomes.

Patient Confidentiality and Ethical Standards

The major ethical consideration in this study was protecting the identity of the participants in the various surveys, experiments, and cohorts used. Because they all contained information about the family history, medical records, and other sensitive data pertaining to the participants, releasing the collected raw data publicly would break the convention of confidentiality and therefore sacrifice both ethical standards and the integrity of the research process. For this reason, only processed data that protects the identities of the participants is available for these studies and no raw data will be reported.

Experimental Methods and Procedures

Procedures

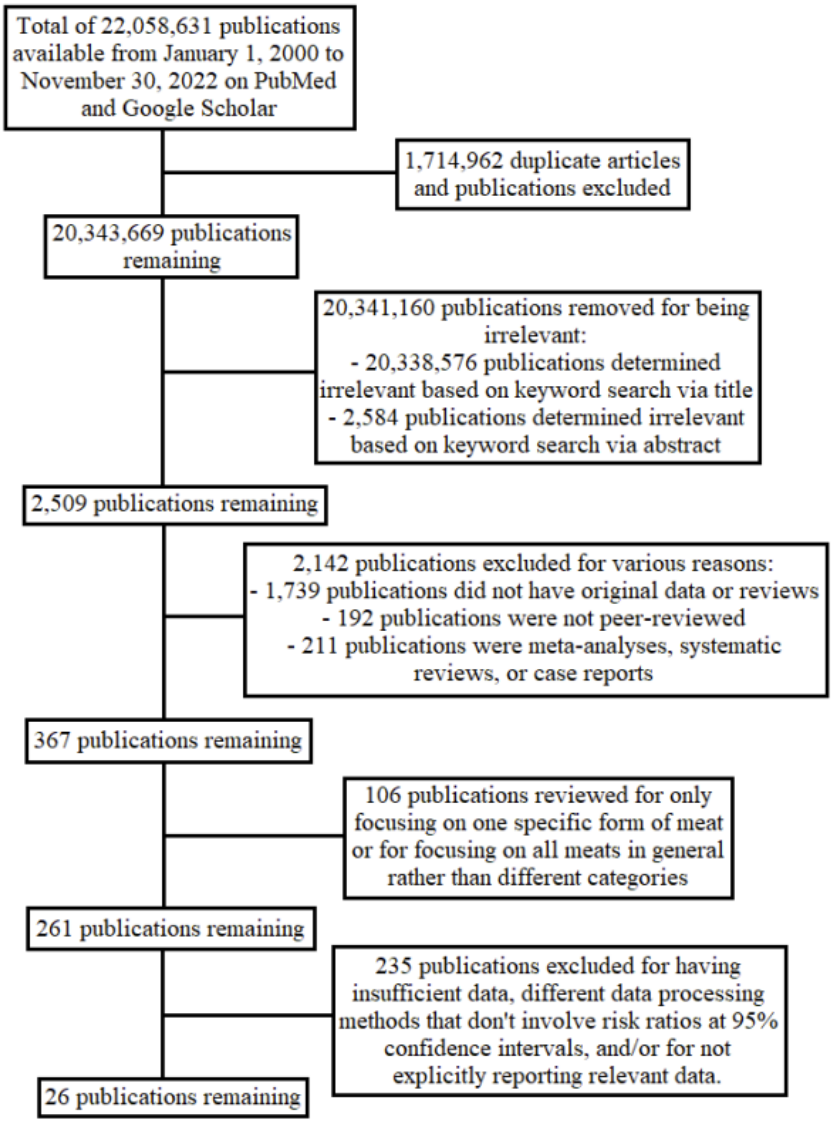
Prior to the start of the data processing, a thorough search was conducted on PubMed and Google Scholar to find peer-reviewed journal articles published after January 1, 2000, that pertain to the research question of interest. There are two reasons to justify why the search is limited only to papers published on or after January 1, 2000:

a) to ensure that all data is recent and up-to-date, and
b) because journal articles published before 2000 are oftentimes hard to unlock via open access, thus making them difficult to use for the purposes of this study.

The choices were narrowed down as shown in Figure 1 below.

Figure 1

Flow diagram depicting method of selection and exclusion to determine which journal articles are to be used for this meta-analysis.



Note. The process of selecting and excluding articles to narrow it down to the most relevant and useful choices was inspired by (Chan, 2011).

After narrowing down the publications to be used in the meta-analysis, multivariate risk ratios for developing colorectal cancer for each of the following three were recorded into a data table:

I. Manipulation #1: A 100 g/day increase in unprocessed red meat consumption.

II. Manipulation #2: A 100 g/day increase in processed meat consumption.

III. Manipulation #3: A 100 g/day increase in all meat consumption.

The multivariate risk ratio calculations—which have already been performed by the publications being used—also consider age, sex, family history, race, smoking, and alcohol consumption. The 95% confidence interval is not used for this portion. Additionally, the multivariate risk ratio for no consumption of the category of meat in each manipulation was assumed to be 1.00. Next, The R software was downloaded and installed from the Comprehensive R Archive Network, and RStudio (an open-source integrated development environment for R) was downloaded and installed from its website.

Once the set-up procedures had been completed, a new file was created called data.csv, which contained two columns:

I. A "score" column which contains the risk ratios propagated from the publications from step #1.
II. A "group" column which assigns each risk ratio to its appropriate group. In the first manipulation, Group 1 refers to a diet consisting of 0 g/day of meat while Group 2 refers to a diet consisting of 100 g/day of unprocessed red meat.

Next in RStudio, the pathway "File > Import Dataset > From text (base)" was followed to upload data.csv into RStudio. The following code, inspired by and altered from (Stevens, 2023), was then inserted into RStudio and the "CTRL+enter" function was used to run the program. The following breaks down each part of the code and what its function is:

Figure 2

This first portion of the code works to locate and read "data.csv" and to assign the dataset in the .csv file to a variable called `data`.

```
# Load the data into R
data <- read.csv("data.csv")
```

Figure 3

This portion of the code creates a `test_statistic` function which will work to calculate the difference between the means of the "score" values for each of the two groups.

```
# Define the test statistic
test_statistic <- function(data, group) {
    mean(data[group == 1]) - mean(data[group == 2])
}
```

Figure 4

This code will calculate the observed test statistic using the `test_statistic` function.

```
# Compute the observed test statistic
observed_statistic <- test_statistic(data$score, data$group)
```

Figure 5

This code will work to generate 1,000 different randomly generated permutations of Groups 1 and 2 and calculate the test statistic for each, storing them in `permutation_stats`.

```
# Generate permutations
num_permutations <- 1000
permutation_stats <- numeric(num_permutations)
for (i in 1:num_permutations) {
    permuted_group <- sample(data$group)
    permutation_stats[i] <- test_statistic(data$score, permuted_group)
}
```

Note. The 1,000 permutations were an arbitrarily chosen yet sufficiently large number to ensure enough permutations are being generated that it can be accurately determined whether or not the difference in means between meat vs. no meat is significant.

Figure 6

This code will work to generate 1,000 different randomly generated permutations of Groups 1 and 2 and calculate the test statistic for each, storing them in `permutation_stats`.

```
# Calculate the p-value
p_value <- mean(abs(permutation_stats) >= abs(observed_statistic))
```

Figure 7

This last portion of the code will print both the observed test statistic and p-value.

```
# Print the results
cat("Observed test statistic:", observed_statistic, "\n")
```

These steps were then repeated for the second manipulation (comparing a diet consisting of 100 g/day of processed meat versus a diet consisting of 0 g/day of meat) and the third manipulation (comparing a diet consisting of 100 g/day of all forms of meat versus a diet consisting of 0 g/day of meat).

Finally, the p-values of each manipulation were compared with each other. If this value is less than the threshold level of significance $\alpha=0.05$, the null hypothesis may be rejected. If it is equal to or greater than the threshold, the null hypothesis fails to be rejected.

Variables

The independent variable in this experiment is the amount of red and/or processed meat eaten, which was reported by people surveyed in various cohorts. The dependent variable is the incidence of colorectal cancer, which is measured using multivariate risk ratios that have already been calculated.

In addition, this experimental design also contains controlled variables as well as confounding variables that may not be controlled but will be monitored (Table 1). These factors may influence the chances of developing certain types of cancer, and thus are important to keep under check.

Table 1

Potentially confounding variables that are unable to be controlled but are able to be monitored throughout the course of the experiment.

Controlled Variable	Why This Variable Should Be Controlled

Biological sex	"Sex difference in cancer incidence is attributed to regulation at the genetic/molecular level and sex hormones such as estrogen. At the genetic/molecular level, gene polymorphism and altered enzymes involving drug metabolism generate differences in cancer incidence between men and women" (Kim, 2018).
Family history of cancer	"It's estimated that between 3 and 10 in every 100 cancers are associated with an inherited faulty gene while the rest of them are caused by other factors such as aging, smoking, being overweight, not exercising regularly, and/or not eating a healthy and balanced diet" (NHS, 2022).
Race	"Black people are at the highest risk for cancer death even though White people have the highest rate of new cancers. This increased mortality risk partly reflects a later stage of disease at diagnosis among Black patients, although Black patients additionally have lower stage-specific survival for most cancer types. There is no solid reason yet as to why there are racial and ethnic patterns of cancer incidence and cancer mortality, but we know that these patterns are present" (Tong, 2022).
Age	"The incidence rates for cancer overall climb steadily as age increases, from fewer than 25 cases per 100,000 people in age groups under age 20, to about 350 per 100,000 people among those aged 45–49, to more than 1,000 per 100,000 people in age groups 60 years and older" (NCI, 2021).
Physical activity	"Exercise has many biological effects on the body, some of which

	have been proposed to explain associations with specific cancers. These include… Lowering the levels of sex hormones, such as estrogen, and growth factors that have been associated with cancer development and progression, preventing high blood levels of insulin, which has been linked to cancer development and progression, reducing inflammation, improving immune system function, altering the metabolism of bile acids [and] decreasing exposure of the gastrointestinal tract to these suspected carcinogens, [and] reducing the time it takes for food to travel through the digestive system, which decreases gastrointestinal tract exposure to possible carcinogens" (National Cancer Institute, 2020).
Weight	"Overweight and obesity can cause changes in the body that help lead to cancer. These changes can include long-lasting inflammation and higher than normal levels of insulin, insulin-like growth factor, and sex hormones" (CDC, 2017).
Height	"Every 10-centimeter increase (about 4 inches) in height was found to be associated with a 14% increased risk of developing colorectal cancer…" (Johns Hopkins Medicine, 2022).
Smoking	"Poisons in cigarette smoke can weaken the body's immune system, making it harder to kill cancer cells. When this happens, cancer cells keep growing without being stopped. Poisons in tobacco smoke can damage or change a cell's DNA" (CDC, 2022). "Inhaling chemicals and toxins into your body invites free radicals

	to damage DNA and mutate healthy cells. Free radicals can cause the development of precancerous polyps in the large intestine, which can become cancerous and eventually cause colon cancer" (Stop Colon Cancer Now, 2023).
Alcohol consumption	"Some epidemiologic studies suggest that even moderate drinking increases the CRC risk. Metabolism of alcohol involves ethanol conversion to its metabolites that could exert carcinogenic effects in the colon" (Rossi, 2018).

Note. These confounding variables were considered during data processing. Each one was one of the prompts on the questionnaires in the cohorts used, and multivariate risk ratios were used that took these factors into account.

Data and Results

Raw Data and Data Processing

Although this report does not have a large amount of raw data as this information was not accessible throughout the course of the study, the following set of data is as close to the raw data as possible via open access.

Table 2

Risk ratio score and group dataset for all three manipulations to be used as data.csv (Flood, 2003) (Lin, 2004) (Larsson, 2004) (Norat, 2005) (Berndt, 2006) (Cross, 2010) (Cross, 2007) (Kabat, 2007) (Fung, 2010) (Chao, 2005) (Järvinen, 2001) (Tiemersma, 2002) (English, 2004) (Lee, 2009) (Nothlings, 2009) (Wei, 2003) (Oba, 2006) (Balder, 2006) (Brink, 2005) (Chan, 2011) (Sandhu, 2001).

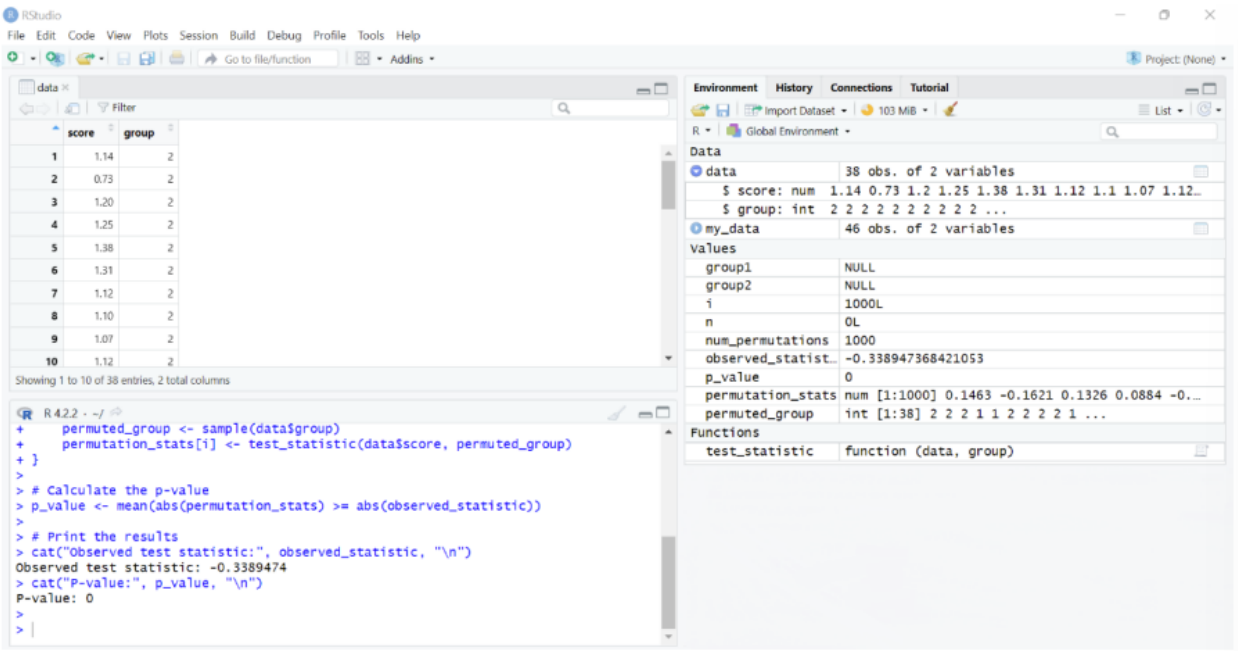
ALL MEATS		RED MEATS		PROCESSED MEATS	
SCORE	GROUP	SCORE	GROUP	SCORE	GROUP
1.14	2	1.37	2	1.17	2
0.73	2	1.69	2	1.61	2
1.2	2	1.19	2	0.56	2
1.25	2	1.23	2	1.13	2
1.38	2	1.21	2	1.15	2
1.31	2	0.8	2	1.21	2
1.12	2	1	2	1.26	2
1.1	2	1.3	2	1.21	2
1.07	2	1	2	1.61	2
1.12	2	1.19	2	1.48	2
1.54	2	1.07	2	1.22	2
1.26	2	1.68	2	1.18	2
0.61	2	1.2	2	1.32	2
1.2	2	0.74	2	1.21	2
1.33	2	0.85	2	1.18	2
1.28	2	1.32	2	3.28	2
1.22	2	1.57	2	1.13	2
4.27	2	0.91	2	1.71	2
1.31	2	0.95	2	0.91	2
1	1	0.98	2	0.8	2
1	1	1.23	2	0.9	2
1	1	0.74	2	1.31	2
1	1	1	1	0.97	2
1	1	1	1	1.1	2
1	1	1	1	1.38	2
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
		1	1	1	1
		1	1	1	1
		1	1	1	1
		1	1	1	1
				1	1
				1	1
				1	1
				1	1
				1	1

Note. All values for score go to hundredths decimal place, even if it is not shown in the table. Group values are only "1" or "2" with no decimas or significant figures.

Processed Data

Figure 8

The RStudio screen after having performed all permutations and having calculated the test statistic and p-value for the "All Meat" manipulation.



Note. This is displayed as an example. The RStudio screen for the other two manipulations was also the same but with their respective values.

Table 3

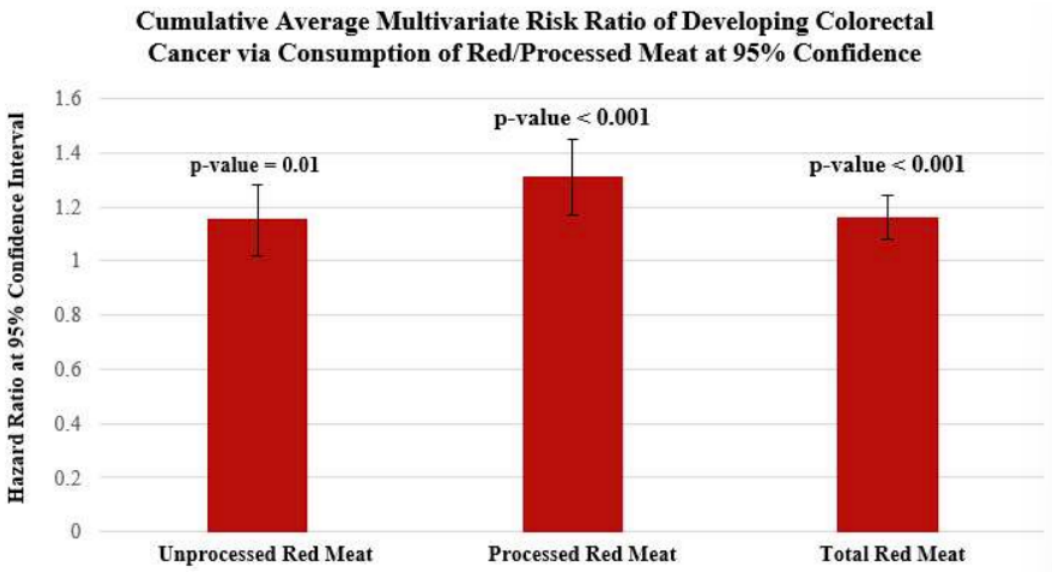
Observed test statistics and p-values for all three manipulations as calculated by RStudio using the process demonstrated in Figure 8.

	RED MEAT	**PROCESSED MEAT**	**ALL MEAT**
TEST STATISTIC	-0.15	-0.28	-0.34
P-VALUE	0.013	<0.001	<0.001

Note. The p-values displayed each have an uncertainty of ±0.005 due to the 95% confidence interval that the raw data was taken from. Each data point in the table is limited to a maximum of two significant figures or limited to the thousandth decimal place (whichever comes first). The p-value as displayed in RStudio for the Processed Meat and All Meat manipulations was 0 because the program cannot accurately report values smaller than 0.001 and instead rounds down. Therefore, the conservative estimate for these two values is <0.001. This emphasizes the fact that our p-value is not zero but is still a very small number.

Figure 9

Since all three p-values calculated using RStudio are very close together, this is the cumulative average of multivariate risk ratios for each of the three manipulations.



Note. The error bars are based on the 95% confidence interval for the MVRR and the cumulative averages for each manipulation are calculated using an increase of 100 g/day of each type of meat.

Evaluation

Discussion

Based on the evidence present in this paper, we can reject the null hypothesis stating that there is no statistically significant difference between incidence of colorectal cancer in persons who consume a large amount of red and processed meats on a regular basis compared to persons who consume little to no red and processed meats. Table 3 reports p-values for all three manipulations—unprocessed red meat, processed meat, and all meat. These p-values represent the probability as a percent of getting data this extreme or more extreme simply by chance. Because the threshold level of significance was $\alpha=0.05$, it is required to obtain p-values less than 0.05 to reject the null hypothesis. With the p-values of 0.013, <0.001, and <0.001, it is reasonable to reject the null hypothesis and accept the alternate hypothesis stating there is a

statistically significant difference between the incidence of colorectal cancer in persons who consume a large amount of red and processed meats on a regular basis compared to persons who consume little to no red and processed meat. However, the fact that there is a correlation between consumption of red/processed meat and risk ratio of developing colorectal cancer does not mean it is okay to assume causation yet. These two variables could have a correlative relationship, meaning that they are proportional, but one does not necessarily cause change in the other.

The results from this experiment match those available in other scientific contexts. In 2015, the World Health Organization's (WHO) International Agency for Research on Cancer (IARC) classifies processed meat as a Group 1 carcinogen, meaning that it is a substance that has been proven to cause cancer in humans (International Agency for Research on Cancer, 2015). Additionally, red meat has been classified as a Group 2A carcinogen, meaning that it is a substance that is probably carcinogenic to humans (International Agency for Research on Cancer, 2015). This means the WHO determined that the relationship between processed meat and colorectal cancer rate is not simply a relationship of correlation (which may still be due to chance or due to an invisible third party), but that the consumption of processed meat directly increases the risk of developing colorectal cancer. As red meat is a Group 2A carcinogen, the WHO is not yet certain whether this is a relationship of causation or simply correlation.

One possible reason that could link red meat to directly causing an increased ratio is its heme iron content. “Red meat is a rich source of heme iron. Intakes of heme iron and red meat have consistently been shown to be positively associated with body iron status. Iron is a prooxidant that may increase colon cancer risk by enhancing the production of free oxygen radicals. In addition, iron appears to be essential for the proliferation of tumor cells” (Larsson, 2004). Another possibility is that “high red meat consumption might increase the risk of colon cancer by enhancing the endogenous formation of NOCs [as in, N-nitroso compounds], most of

which are known carcinogens. Human experimental studies have demonstrated that consumption of red meat, but not of white meat, significantly increases in a dose-dependent manner fecal levels of NOCs" (Larsson, 2004).

In 2021, Marios Giannakis, M.D., Ph.D., of the Dana-Farber Cancer Institute and Harvard Medical School co-led a study in Cancer Discovery that discovered alkylating mutational signatures associated with the consumption of red and processed meats. This discovery incriminates diet in terms of the development of certain types of cancer including colorectal, testicular, and breast carcinoma because alkylating damage leads to cancer-causing mutations in certain protein-coding genes. Red meat consumption was positively associated with an increase in alkylation signatures caused by N-nitroso compounds in tumor tissue from patients with colon cancer. This was true for both processed and unprocessed red meat. There was no difference between men and women after adjusting for differences in red meat intake (Harvard Medical School, 2021).

As for solely processed meats, some studies have suggested that preservatives such as nitrates and nitrites that are added to processed meats can produce compounds that damage DNA. Other studies have investigated how chemicals that are formed when red meat is cooked at high temperatures, such as in grilling, cause the accumulation of mutations that lead to cancer (DellaValle, 2013).

Although the true reason why processed meat causes an increase in risk of developing colorectal cancer is unknown, these hypotheses have been published in peer-reviewed and supported scientific contexts. Additionally, it may remain a mystery for several more years whether the link between red meat consumption and colorectal cancer risk is truly a relationship of causation or a coincidental correlation between the two. Even looking at the data collected in this investigation, the 95% confidence interval error bars for Unprocessed Red Meat in the bar

chart in Figure 9 are much larger than those of the other two manipulations, even stretching down to about 1.00 MVRR. Regardless of the p-value of 0.01, this creates a grey area where it is hard to tell whether this value is truly significant.

Strengths and Weaknesses

The topic of interest in this experiment had a large amount of existing scientific research to back up the claims and provide background information. Additionally, the questionnaires had very accurate responses from participants because the Nurses' Health Study and Health Professionals Follow-Up Study both surveyed people working in the health field as they would be able to report their nutrition, family history, and other factors more accurately (Nurses' Health Study, 2022).

Because this experiment only had access to processed data from published works instead of the raw data directly from the cohorts served as a limitation during the data processing components. It is difficult to accurately process data and determine uncertainties when the raw data is unavailable. The process of sorting through publications was also very tedious and time-consuming, and it is possible that some articles that could have worked in this investigation were omitted on accident on account of human error while reviewing said publications.

Extensions and Further Experiments

A potential extension to this investigation could include studies into the impacts of white meat such as poultry and fish as well. The same processes could be done with these types of meats to determine whether there is a statistically significant difference in colorectal cancer risk ratio when comparing a white meat only with no red/processed meat diet to a vegetarian diet with no meat whatsoever.

Further manipulations can also be done to eliminate all animal products, including milk, honey, eggs, and animal by-products such as gelatin. As the Nurses' Health Study and Health Professionals Follow-Up Study had full nutrition reports in the questionnaires, this would be possible to do using the same cohorts. It would be interesting to see what meat and other animal products cause a statistically significant change in one's risk of developing colorectal cancer.

References

Alcohol and cancer risk fact sheet. *National Cancer Institute*. (2021, July 14). Retrieved February 8, 2023, from https://www.cancer.gov/about-cancer/causes-prevention/risk/alcohol/alcohol-fact-sheet/.

Balder, H. F., Vogel, J., Jansen, M. C. J. F., Weijenberg, M. P., van den Brandt, P. A., Westenbrink, S., van der Meer, R., & Goldbohm, R. A. (2006). Heme and chlorophyll intake and risk of colorectal cancer in the Netherlands Cohort Study. *Cancer Epidemiology, Biomarkers & Prevention*, 15(4), 717–725. https://doi.org/10.1158/1055-9965.epi-05-0772.

Berndt, S. I., Platz, E. A., Fallin, M. D., Thuita, L. W., Hoffman, S. C., & Helzlsouer, K. J. (2006). Genetic variation in the nucleotide excision repair pathway and colorectal cancer risk. *Cancer Epidemiology, Biomarkers & Prevention*, 15(11), 2263–2269. https://doi.org/10.1158/1055-9965.epi-06-0449.

Bernstein, A. M., Song, M., Zhang, X., Pan, A., Wang, M., Fuchs, C. S., Le, N., Chan, A. T., Willett, W. C., Ogino, S., Giovannucci, E. L., & Wu, K. (2015). Processed and unprocessed red meat and risk of colorectal cancer: Analysis by tumor location and modification by Time. *PLOS ONE*, 10(8). https://doi.org/10.1371/journal.pone.0135959.

Brink, M., Weijenberg, M. P., de Goeij, A. F., Roemen, G. M., Lentjes, M. H., de Bruïne, A. P., Goldbohm, R. A., & van den Brandt, P. A. (2005). Meat consumption and K-ras mutations in sporadic colon and rectal cancer in the Netherlands Cohort Study. *British Journal of Cancer*, 92(7), 1310–1320. https://doi.org/10.1038/sj.bjc.6602491.

Cassetty, S. (2019, June 30). What exactly is a processed meat? and how much is safe to eat? *NBCNews.com*. Retrieved August 08, 2023, from

https://www.nbcnews.com/better/lifestyle/what-exactly-processed-meat-how-much-safe-eat-ncna1023401.

Centers for Disease Control and Prevention. (2017, October 3). Cancer and Obesity. *Centers for Disease Control and Prevention*. Retrieved February 15, 2023, from https://www.cdc.gov/vitalsigns/obesity-cancer/index.html/.

Centers for Disease Control and Prevention. (2022, May 5). Smoking and Cancer. *Centers for Disease Control and Prevention*. Retrieved September 16, 2023, from https://www.cdc.gov/tobacco/campaign/tips/diseases/cancer.html.

Chan, D. S., Lau, R., Aune, D., Vieira, R., Greenwood, D. C., Kampman, E., & Norat, T. (2011). Red and processed meat and colorectal cancer incidence: Meta-analysis of Prospective Studies. *PLOS ONE*, 6(6). https://doi.org/10.1371/journal.pone.0020456.

Chao, A. (2005). Meat Consumption and risk of colorectal cancer. *JAMA*, 293(2), 172. https://doi.org/10.1001/jama.293.2.172.

Cross, A. J., Ferrucci, L. M., Risch, A., Graubard, B. I., Ward, M. H., Park, Y., Hollenbeck, A. R., Schatzkin, A., & Sinha, R. (2010). A large prospective study of meat consumption and colorectal cancer risk: An investigation of potential mechanisms underlying this association. *Cancer Research*, 70(6), 2406–2414. https://doi.org/10.1158/0008-5472.can-09-3929.

Cross, A. J., Leitzmann, M. F., Gail, M. H., Hollenbeck, A. R., Schatzkin, A., & Sinha, R. (2007). A prospective study of red and processed meat intake in relation to cancer risk. *PLOS Medicine*, 4(12). https://doi.org/10.1371/journal.pmed.0040325.

DellaValle, C. T., Xiao, Q., Yang, G., Shu, X.-O., Aschebrook-Kilfoy, B., Zheng, W., Lan Li, H., Ji, B.- T., Rothman, N., Chow, W.-H., Gao, Y.-T., & Ward, M. H. (2013). Dietary nitrate

and nitrite intake and risk of colorectal cancer in the Shanghai Women's Health Study. *International Journal of Cancer*, 134(12), 2917–2926. https://doi.org/10.1002/ijc.28612.

English, D. R., MacInnis, R. J., Hodge, A. M., Hopper, J. L., Haydon, A. M., & Giles, G. G. (2004). Red Meat, chicken, and fish consumption and risk of colorectal cancer. *Cancer Epidemiology, Biomarkers & Prevention*, 13(9), 1509–1514. https://doi.org/10.1158/1055-9965.1509.13.9.

Farlex. (n.d.). Red Meat. *The Free Dictionary*. Retrieved November 18, 2023, from https://www.thefreedictionary.com/red+meat.

Ferlay, J., Shin, H.-R., Bray, F., Forman, D., Mathers, C., & Parkin, D. M. (2010). Estimates of worldwide burden of cancer in 2008: Globocan 2008. *International Journal of Cancer*, 127(12), 2893–2917. https://doi.org/10.1002/ijc.25516.

Flood, A. (2003). Meat, fat, and their subtypes as risk factors for colorectal cancer in a prospective cohort of women. *American Journal of Epidemiology*, 158(1), 59–68. https://doi.org/10.1093/aje/kwg099.

Fung, T. T., Hu, F. B., Wu, K., Chiuve, S. E., Fuchs, C. S., & Giovannucci, E. (2010). The Mediterranean and dietary approaches to stop hypertension (DASH) diets and colorectal cancer. *The American Journal of Clinical Nutrition*, 92(6), 1429–1435. https://doi.org/10.3945/ajcn.2010.29242.

Harvard Medical School. (2021, June 17). Red meat consumption may promote DNA damage-associated mutations in patients with colorectal cancer. *Dana-Farber Cancer Institute*. Retrieved February 8, 2023, from https://www.dana-farber.org/newsroom/news-releases/2021/red-meat-consumption-may-promote-dna-damage-associated-mutations-in-patients-with-colorectal-cancer/.

Health Professionals Follow-Up Study. Harvard T.H. *Chan School of Public Health*. (n.d.). Retrieved December 28, 2022, from https://www.hsph.harvard.edu/hpfs/.

International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 114. Red and Processed Meats. Lyon, *France: IARC*; 2015 Available from: http://monographs.iarc.fr/ENG/Monographs/vol114/mono114.pdf.

Järvinen, R., Knekt, P., Hakulinen, T., Rissanen, H., & Heliövaara, M. (2001). Dietary fat, cholesterol and colorectal cancer in a prospective study. *British Journal of Cancer*, 85(3), 357 – 361. https://doi.org/10.1054/bjoc.2001.1906.

Kabat, G. C., Miller, A. B., Jain, M., & Rohan, T. E. (2007). A cohort study of dietary iron and heme iron intake and risk of colorectal cancer in women. *British Journal of Cancer*, 97(1), 118–122. https://doi.org/10.1038/sj.bjc.6603837.

Kim, H.-I., Lim, H., & Moon, A. (2018). Sex differences in cancer: Epidemiology, genetics and therapy. *Biomolecules & Therapeutics*, 26(4), 335–342. https://doi.org/10.4062/biomolther.2018.103.

Larsson, S. C., Rafter, J., Holmberg, L., Bergkvist, L., & Wolk, A. (2004). Red meat consumption and risk of cancers of the proximal colon, distal colon and rectum: The Swedish mammography cohort. *International Journal of Cancer*, 113(5), 829–834. https://doi.org/10.1002/ijc.20658.

Lee, S.-A., Shu, X.-O., Li, H., Yang, G., Cai, H., Wen, W., Ji, B.-T., Gao, J., Gao, Y.-T., & Zheng, W. (2009). Adolescent and adult soy food intake and breast cancer risk: Results from the Shanghai Women's Health Study. *The American Journal of Clinical Nutrition*, 89(6), 1920–1926. https://doi.org/10.3945/ajcn.2008.27361.

Lin, J. (2004). Dietary fat and fatty acids and risk of colorectal cancer in women. *American Journal of Epidemiology*, 160(10), 1011–1022. https://doi.org/10.1093/aje/kwh319.

Ludbrook, J., & Dudley, H. (1998). Why permutation tests are superior to T and F tests in biomedical research. *The American Statistician*, 52(2), 127. https://doi.org/10.2307/2685470.

Mayo Clinic Staff. (2022, October 8). Colon cancer. *Mayo Clinic*. Retrieved January 21, 2023, from https://www.mayoclinic.org/diseases-conditions/colon-cancer/symptoms-causes/syc-20353669.

NHS. (2022, July 19). Am I more at risk if my relatives have cancer? *NHS choices*. Retrieved December 29, 2022, from https://www.nhs.uk/common-health-questions/lifestyle/am-i-more-at-risk-if-my-relatives-have-cancer/.

Norat, T., Bingham, S., Ferrari, P., Slimani, N., Jenab, M., Mazuir, M., Overvad, K., Olsen, A., Tjønneland, A., Clavel, F., Boutron-Ruault, M.-C., Kesse, E., Boeing, H., Bergmann, M. M., Nieters, A., Linseisen, J., Trichopoulou, A., Trichopoulos, D., Tountas, Y., … Riboli, E. (2005). Meat, fish, and colorectal cancer risk: The European Prospective Investigation Into Cancer and Nutrition. *JNCI: Journal of the National Cancer Institute*, 97(12), 906–916. https://doi.org/10.1093/jnci/dji164.

Nöthlings Ute, Yamamoto, J. F., Wilkens, L. R., Murphy, S. P., Park, S.-Y., Henderson, B. E., Kolonel, L. N., & Le Marchand Loïc. (2009). Meat and heterocyclic amine intake, smoking, nat1 and nat2 polymorphisms, and colorectal cancer risk in the multiethnic cohort study. *Cancer Epidemiology, Biomarkers & Prevention*, 18(7), 2098–2106. https://doi.org/10.1158/1055-9965.epi-08-1218.

Nurses' Health Study. (2022, August 26). Retrieved December 28, 2022, from https://nurseshealthstudy.org/.

Oba, S., Shimizu, N., Nagata, C., Shimizu, H., Kametani, M., Takeyama, N., Ohnuma, T., & Matsushita, S. (2006). The relationship between the consumption of meat, fat, and coffee and the risk of colon cancer: A prospective study in Japan. *Cancer Letters*, 244(2), 260–267. https://doi.org/10.1016/j.canlet.2005.12.037.

Physical activity and cancer fact sheet. *National Cancer Institute*. (2020, February 10). Retrieved February 2, 2023, from https://www.cancer.gov/about-cancer/causes-prevention/risk/obesity/physical-activity-fact-sheet/.

Red Meat, processed meat and cancer. *Cancer Council NSW*. (2021, January 8). Retrieved January 15, 2023, from https://www.cancercouncil.com.au/1in3cancers/lifestyle-choices-and-cancer/red-meat-processed-meat-and-cancer/.

Risk factors: Age. *National Cancer Institute*. (2021, March 5). Retrieved January 19, 2023, from https://www.cancer.gov/about-cancer/causes-prevention/risk/age/.

Rossi, M., Jahanzaib Anwar, M., Usman, A., Keshavarzian, A., & Bishehsari, F. (2018). Colorectal cancer and alcohol consumption—populations to molecules. *Cancers (Basel)*, *10*(2), 38. https://doi.org/10.3390/cancers10020038.

Sandhu MS, White IR, McPherson K. Systematic review of the prospective cohort studies on meat consumption and colorectal cancer risk: a meta-analytical approach. *Cancer Epidemiol Biomarkers Prev*. 2001 May;10(5):439-46. PMID: 11352852.

Smoking and Colon Cancer. Risk Factors | Smoking | *Stop Colon Cancer Now*. (n.d.). Retrieved September 16, 2023, from https://www.stopcoloncancernow.com/colon-cancer-facts/risk-factors/smoking-and-colon-cancer.

Stevens, S. (n.d.). Using R: Chapter 8 Hypothesis Testing - One Sample. *Introduction to Statistics, Think & Do*. Retrieved January 28, 2023, from https://cosmosweb.champlain.edu/people/stevens/WebTech/R/Chapter-8-R.pdf.

Study: Taller adults may be at increased risk for colorectal cancer. *Johns Hopkins Medicine Newsroom*. (2022, March 3). Retrieved February 14, 2023, from https://www.hopkinsmedicine.org/news/newsroom/news-releases/study-taller-adults-may-be-at-increased-risk-for-colorectal-cancer/.

Tiemersma, E. W., Kampman, E., Bas Bueno de Mesquita, H., Bunschoten, A., van Schothorst, E. M., Kok, F. J., & Kromhout, D. (2002). *Cancer Causes and Control*, 13(4), 383–393. https://doi.org/10.1023/a:1015236701054.

Tong, M., Hill, L., & Artiga, S. (2022, February 3). Racial disparities in cancer outcomes, screening, and treatment. *Kaiser Family Foundation*. Retrieved February 1, 2023, from https://www.kff.org/racial-equity-and-health-policy/issue-brief/racial-disparities-in-cancer-outcomes-screening-and-treatment.

Wei, E. K., Giovannucci, E., Wu, K., Rosner, B., Fuchs, C. S., Willett, W. C., & Colditz, G. A. (2003). Comparison of risk factors for colon and rectal cancer. *International Journal of Cance*r, 108(3), 433–442. https://doi.org/10.1002/ijc.11540.