RISK MODELING, DECISION ANALYSIS, AND RISK COMMUNICATION FOR LISTERIOSIS IN CANCER PATIENTS WHO CONSUME FRESH SALAD

By

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ABSTRACT

Listeria monocytogenes is a problematic pathogen for cancer patients, with morbidity and mortality rates higher than those in the general population. The neutropenic diet (ND), which is commonly employed to reduce infection risk by excluding raw foods, including fresh produce, remains a subject of controversy. Correspondingly, produce safety communication strategies are largely unstandardized, with patients and caretakers receiving widely different guidelines and materials depending on their institution. Data-driven food safety diets and communication strategies are needed to improve health and quality of life outcomes in this population.

This dissertation aimed to resolve these issues: by (i) updating a previous listeriosis risk model to improve accuracy and define limitations, (ii) constructing decision models evaluating outcomes for the ND vs. three alternative produce safety diets, and determining parameters that justify the use of the ND, (iii) using quantitative and qualitative data to understand the produce safety beliefs, barriers, motivators, and behaviors of pediatric cancer patient caretakers, and their feedback on communication strategies, and (iv) combining literature and qualitative pediatric cancer patient caretaker data to formulate communication objectives and a resulting produce safety communication strategy prototype.

A previously presented listeriosis risk model for fresh salads was updated to account for tomato contamination from soil, cross-contamination during dump tank washing, and conveyor and waxing surfaces. Main sources of uncertainty and variability and areas lacking data were highlighted, suggesting opportunities for future research. The risk model was then used to build decision models for cancer patients who consume ready-to-eat (RTE) salads. As measured in disability-adjusted life years (DALYs) per person per chemotherapy cycle, outcomes associated with the ND were consistently worse than for alternative, produce-inclusive food safety diets.

Furthermore, when fluctuating uncertain and/or variable parameters were used to compute switchover points, the resulting values were unrealistic (e.g., negative probability), meaning that produce-inclusive food safety diets were the favored intervention for the scenarios examined.

Subsequently, foodborne illness risk management strategies were explored. Quantitative surveys and qualitative interviews were conducted with pediatric cancer patient caretakers to assess their beliefs, barriers, motivators, and behaviors, with respect to produce safety guidelines. While no significant quantitative relationships were observed between demographic variables and produce safety behavior frequencies, qualitative grounded theory coding led to classification of five caretaker archetypes, with commonalities in guidelines received, child's health, food safety behaviors previously enacted, and concerns beyond microbial food safety. The existence of these archetypes underscored the prevalent adoption of the ND and the absence of uniformity in produce safety communication materials. Recommendations for information delivery, timing, and material organization were conceived based on caretaker feedback. These recommendations then were integrated with scientific communication literature to develop objectives conducive to a produce safety communication strategy endorsing safe produce preparation, storage, and dietary inclusion. A novel produce safety communication intervention was prototyped based on corresponding tactics.

Overall, this work quantitatively and qualitatively supports the adoption of produce-inclusive food safety diets, such as those recommended by the U.S. Food and Drug Administration (FDA) and American Cancer Society (ACS), as a replacement for the ND. It also presents a feedback-driven risk communication strategy for imparting this information.

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CHAPTER 1: INTRODUCTION

1.1 The problem

Within the last 20 years, *Listeria monocytogenes* has been recurrently isolated from fresh, ready-to-eat (RTE), and minimally processed produce *(23, 112, 184, 187, 191, 211, 241, 275)* and implicated in numerous outbreaks traced back to contaminated produce *(11, 37, 155, 234)*. Listeriosis outbreaks also caused 65 of 90 deaths in healthcare associated foodborne outbreaks *(25)*, often affecting immunocompromised individuals and prompting discussion on food safety and prophylaxis for susceptible populations *(25, 86, 118, 126, 147, 224, 226, 267)*. While healthy individuals typically develop listeriosis in its noninvasive, self-limiting form, immunocompromised individuals develop invasive listeriosis, which manifests with more severe symptoms, such as meningoencephalitis and septicemia, and a high mortality rate of 20-40% *(4, 38, 41, 68, 105, 112, 233, 237, 269)*. Cancer patients are markedly affected, with higher mortality rates than other immunocompromised groups *(105, 108, 225)*, and disproportionate relative listeriosis risks when compared to healthy individuals younger than 65 years old and individuals with other immunocompromising conditions *(105, 170)*.

Neutropenic diets (NDs), which eliminate the consumption of raw or unpasteurized foods, including RTE salads *(117, 230)*, are a common risk management strategy for foodborne illness in cancer patients, despite reducing intake of crucial micronutrients *(150)*, negatively affecting quality of life *(156, 168)*, and never being proven to reduce rates of infection *(55, 117, 141, 169, 250, 258)*. Therefore, it is crucial to investigate outcomes associated with both the ND and produce-inclusive food safety strategies.

In previous thesis work by this author, *L. monocytogenes* reductions resulting from hyper-hygienic, kitchen-scale produce preparation strategies were assessed, and a quantitative microbial risk assessment (QMRA) was conducted to determine associated listeriosis risk in cancer patients who consume fresh vegetable salads *(94)*. The risk assessment has since been improved to more accurately depict pre- and post-harvest tomato contamination, address key uncertainties, and define future work. However, there remains a research gap for the steps following QMRA – risk management and risk communication. The two most common risk management strategies for food safety in the target population are the ND and the safe food handling (SFH) diet, which is a less restrictive, food-safety-focused diet recommended by the FDA *(169, 230, 253)*. Another approach, surface blanching for the reduction of pathogens on produce surfaces, was explored in the previous work *(99)*.

When risks of listeriosis, ND side effects, compliance rates, and ailment severities are compounded for each strategy, it is unknown which strategy is more favorable, physically, for the patient. Thus, there is demonstrated need for decision models relating each parameter and intervention and their effects on patient health to better protect health during treatment. Due to several recent shifts in cancer care administration, patients and families/caretakers face increased care management responsibilities *(153)*, with the WHO recommending that family members are involved and supported in decision making *(49)*. Therefore, decision models must be designed for use by family members and caretakers.

Results of the decision models will be affected by the perception of food safety interventions, as these directly influence compliance with food safety guidelines. Although a few studies have identified some general patient food safety barriers, motivators, beliefs, and behaviors *(66, 158, 159, 190)*, they are scarce in produce information and do not focus on caretakers/family members, who are responsible for upholding food safety interventions for pediatric patients. Therefore, this study aimed to use quantitative decision models combined with qualitative caretaker experiences to determine an optimal produce safety recommendation for children with cancer and strategies for improving related risk communication interventions.

1.2 Goals and objectives

The overall goal of this study was to improve health outcomes of cancer patients by providing acceptable, data-driven produce safety recommendations to caretakers, and advising improved risk communication interventions. The specific objectives to support this goal were:

1. Develop and analyze decision models comparing three produce safety interventions with the ND across five age groups.
2. Identify pediatric cancer patient caretakers' barriers, motivators, general attitudes, and implemented behaviors regarding produce safety interventions.
3. Evaluate potential disadvantages with current communication strategies and advise improvements.

CHAPTER 2: LITERATURE REVIEW

The following literature review explored how cancer impacts the likelihood of foodborne illness, ND pathology, efficacy, and administration, decision modeling approaches for healthcare, and risk communication strategies for cancer patients.

2.1 Cancer patients and foodborne illness

Cancer treatment compromises several of the body's barriers against enteric infection *(77)*. First and foremost, chemotherapy inhibits the generation of neutrophils, which are an essential constituent of the immune system and the body's inflammatory response *(47)*. Neutrophils ingest microbes through phagocytosis and can also release neutrophil extracellular traps (NETs), conglomerates of DNA and neutrophil proteins, which evoke an immune response to microbes that they capture *(180)*. Due to neutrophil depletion by chemotherapy, many cancer patients have neutropenia, a state of low neutrophil count in which patients are at an increased risk of infection *(47)*.

In healthy individuals, gastric acid and a stomach pH of 1.5 prevents the proliferation of bacteria such as *L. monocytogenes*, but acid-neutralizing drugs that are often included in cancer treatment can cause hypochlorhydria (stomach pH > 4), leaving patients susceptible to listeriosis and other bacterial infections *(18, 19, 43, 118, 151, 244)*. Bactericidal effects can be observed at a stomach pH of less than 4, with possible bacterial overgrowth in hypochlorhydric patients *(19)*. Tennant et al. *(244)* demonstrated that in the hypochlorhydric state, survival rates of four model enteric bacteria (*Yersinia enterocolitica* 8081, *Y. enterocolitica* 8081, *Salmonella enterica* serovar Typhimurium SL1344, and *Citrobacter rodentium* ICC169) were 54-95%, opposed to 0% for all strains at pH 2 (except *Y. enterocolitica* 8081, which had a 37% survival rate) *(244)*.

Additionally, cancer patients often develop gastrointestinal mucositis – inflammation and ulcers throughout the digestive tract – when epithelial cells are killed by cytotoxic therapies and radiation. In general, patients with and without mucositis have been shown to have documented bacterial infection rates of 73% to 36%, respectively *(64)*. These treatments also invoke inflammatory responses and vascular changes that may further disrupt the tissue *(16)*. This disruption of the gastrointestinal mucosal barrier creates a pathway for bacteria to translocate from the digestive system to the bloodstream *(64, 256)*. *L. monocytogenes* is one such "facultative intracellular pathogen," meaning that it has the capacity to translocate easily under such conditions *(263)*.

Finally, due to high mortality rates for bacterial infections in neutropenic patients with cancer, broad-spectrum antibiotics are recommended as the initial course of treatment for generalized fever or suspected infection *(79, 136)*. However, the wide target range of these antimicrobials also leads to the death of endogenous gut bacteria, preventing natural competition and allowing for proliferation of non-host bacteria *(34, 46, 77)*. This dysbiosis in the gastrointestinal tract has been shown to contribute to mucositis and increase the possibility of systemic infection *(165)*.

Due to the aforementioned maladies faced by cancer patients, recent studies have investigated the possibility that they are at an increased risk of listeriosis. In 2011, an analysis of case reports revealed that individuals with cancer were shown to have a relative risk of listeriosis 4.9 times greater than individuals with other underlying conditions *(170)*. Subsequently, Goulet et al. established that patients with chronic lymphocytic leukemia have an incidence of listeriosis 1,000 times greater than members of the population under 65 years old without concurrent conditions *(105)*.

2.2 The Neutropenic Diet

In an attempt to reduce the risk posed by *L. monocytogenes* and other foodborne pathogens, healthcare institutions often place cancer patients on NDs, which exclude higher-risk foods such as fresh produce, deli meat, and cheese *(117, 230)*. These foods are not cooked prior to consumption and therefore pose a higher risk due to foodborne pathogens. However, the ND is controversial, as elaborated upon in the following discussion.

2.2.1 Reduced intake of micronutrients

Maia et al. found that patients on a ND only consumed 62.4% of the recommended daily amount of vitamin C and 81.2% of the daily recommended amount of fiber, respectively *(150)*. However, patients on an unrestricted diet consumed 310% and 92.3% of the recommended amounts of vitamin C and fiber, respectively *(150)*. Cooking fruits and vegetables for inclusion in the ND may not be a viable compromise, as the practice has been shown to significantly reduce vitamin C content by nearly 40% *(83)*.

Adequate fiber intake inhibits constipation by softening and adding volume to the stool. This aids in preventing bacterial overgrowth typical of immunocompromised patients, associated rectal mucosa injury, and therefore the translocation of bacteria out of the gut *(33)*. Consumption of dietary fiber, particularly plant fiber from raw fruits and vegetables, has been shown to reduce bacterial translocation by about half *(52)*. Analogously, Spaeth et al. found that 60% of rats provided a total parenteral nutrition (TPN) diet (28% glucose, 4.5% amino acids) either orally or intravenously experienced bacterial translocation, compared to 0% of rats that were fed normal diets *(232)*. When the TPN diets were supplemented with an oral cellulose pellet, bacterial translocation decreased to 8% and 0% in rats on the oral and intravenous TPN diets, respectively. The intestinal epithelia of mice fed normal and cellulose-supported diets lacked the deformities observed in mice fed TPN diets, suggesting that fiber is crucial in supporting these structures. In a similar study in rabbits, diets containing high levels of soluble fiber led to improved mucosal integrity, whereas low fiber diets resulted in mucosal atrophy *(101)*.

Vitamin C is pivotal to neutrophil function in a variety of ways *(31)*. First, it increases phagocytic motility. Anderson et al. found that supplementing a standard anti-asthma chemoprophylaxis (SAC) treatment with vitamin C significantly improved neutrophil motility *(10)*. Second, vitamin C counteracts anemia, which is common in cancer patients and negatively influences the immune system *(164)*, by increasing absorbance of iron *(146)*. Additionally, oral administration of vitamin C has been shown to significantly increase chemotaxis and phagocytosis in patients with impaired neutrophil function *(144)*. Third, Goldschmidt demonstrated that vitamin C deficiency results in decreased pathogen killing efficacy in neutrophils *(93)*. Finally, vitamin C has been found to protect host structures from damage resulting from excessive development of neutrophil extracellular traps (NETs) during infection *(162)*. NETs catch and kill pathogens but can be overproduced in a systemic infection and facilitate tissue damage, which could then lead to bacterial translocation. In human and mice neutrophils that were either sufficient in or treated with vitamin C, this mechanism was significantly lessened *(162)*. Lastly, increased intake of vitamin C, vitamin E, and β-carotene are associated with fewer treatment delays, fewer days in the hospital, decreased infection rates, and reduced chemotherapy toxicity *(131)*.

Through its stringent restrictions, particularly on fruits and vegetables, the ND curtails consumption of micronutrients that support immune function. However, bacteria that are consumed with these foods may not be the source of harmful infections. In 1999, Österblad et al. compared the antibiotic resistance profiles of Enterobacteriaceae isolated from vegetables and human fecal samples and determined that the two had significantly different antibiotic resistance profiles *(189)*. They concluded that Enterobacteriaceae found on vegetables are likely not the same antibiotic-resistant bacteria that colonize the human digestive tract. This inspired further investigation of the efficacy of dietary elimination of raw produce, such as in the ND, in preventing infection.

2.2.2 Efficacy

In a retrospective study, Heng et al. compared incidence of fever in a group of patients on a ND to a group of patients on a “liberalized” diet (LD), which only excluded raw meat and raw eggs. Eighty-four percent of patients and 65% of patients in the ND and LD groups, respectively, developed febrile neutropenia ($p < 0.05$). These results suggested that the ND is not effective in preventing infection in cancer patients and may actually be harmful *(117)*. Compounding these results, Gupta et al. *(109)* found that 33% of pediatric patients on the ND develop neutropenic enterocolitis (NEC), a severe condition causing diarrhea and intestinal inflammation with high mortality rates, compared to 5% on a standard diet, which followed “standard” food safety steps.

Trifilio et al. also conducted a retrospective study on 726 patients hospitalized for hematopoietic stem cell transplantation (HSCT), a treatment for cancer and other autoimmune disorders *(250)*. Half of the patients (363) were prescribed a ND, and half were prescribed a general diet (GD), in which well-washed fresh fruits and vegetables (minus tomatoes) were permitted. A registered dietician also trained all patients in food safety. Patients on the GD experienced significantly fewer microbiologically confirmed infections. They also experienced significantly fewer incidences of diarrhea and urinary tract infections, which typically are caused by bacteria from the GI tract, than those from the ND.

In a randomized controlled pilot study, van Tiel et al. compared 20 hematological cancer patients who were assigned antibiotic prophylaxis and either a ND or a normal hospital diet *(258)*. There was no significant difference in the number of microbiologically confirmed infections, cytopenic days, or days on antibiotics between the two groups. Another randomized trial conducted by Gardner et al. assigned adult patients with Acute Myeloid Leukemia (AML) to a diet containing only cooked fruits and vegetables, or a diet including fresh fruits and vegetables *(85)*. Twenty-nine percent of patients on the cooked produce diet and 35% of patients on the fresh produce diet developed major infections; this difference was not significant.

In a later randomized pilot study, Lassiter and Schneider found no significant difference in the number of positive blood cultures between 46 HSCT patients assigned either to a ND or unrestricted diet *(141)*. They recommended a diet providing adequate nutrition, as advised by a registered dietician, and adherence to FDA food safety guidelines, as a more effective infection prevention strategy than the ND. Most recently, Moody et al. randomly assigned 149 pediatric oncology patients to diets either following the FDA-recommended food safety guidelines (FSG), or the guidelines and a neutropenic diet (FSG + ND). Percentages of patients developing neutropenic infection in the FSG and FSG + ND diets were 33% and 35%, respectively *(169)*. Therefore, the authors recommended institutional implementation of a diet that follows FSG, as opposed to the ND, which was difficult for children to comply with.

Finally, DeMille et al. educated 23 cancer patients receiving chemotherapy about the ND and monitored their compliance to the diet over 12 weeks using self-reporting questionnaires *(55)*. Four (25%) of the compliant patients and one (14%) of the noncompliant patients were admitted to hospitals for neutropenic infections. Three of the admitted compliant patients and the one noncompliant patient had blood cultures positive for gram-negative bacteria. None of these differences were statistically significant, again recanting the notion that the ND is effective in reducing infection rates.

In existing literature, the ND has not been shown to reduce a cancer patient's risk of developing infections. In fact, in a meta-analysis by Ball et al. *(17)* including many of the aforementioned studies, the infection pooled risk ratio for patients on the ND and unrestricted diets was 1.13. Sonbol et al. conducted a similar study and reported an overall hazard ratio (including fever and major and minor infections) of 1.18 *(230)*. There is a research gap for studies that specifically address the role of the ND in preventing foodborne diseases, as these studies only addressed general infections, the causes of which were much more difficult to attribute to diet. Overall, due to its demonstrated lack of efficacy and drawbacks including decreased quality of life and reduced intake of fiber and vitamin C, it is necessary to question the value of the neutropenic diet in preventing foodborne illness, and the conditions under which it is implemented.

2.2.3 Administration

Institutional definitions of neutropenia and subsequent application of the ND lack standardization and are therefore highly variable between institutions. First, Smith noted that 2.5%, 42%, and 43% of hospitals or physicians defined neutropenia as an absolute neutrophil count (ANC) less than 1,500/mm^3, 1,000/mm^3, and 500/mm^3, respectively *(229)*. In contrast, Braun et al. found ND implementation thresholds were ANCs of 1,500/mm^3, 1,000/mm^3, and 500/mm^3 for 5%, 9%, and 86%, respectively, for respondents that based their use of the ND on ANC *(27)*. These deviating definitions contribute to the sweeping disorganization in diet implementation.

Second, there were inconsistencies in institutional application of the ND. This was initially made evident by Smith and Besser, who sent a survey to members of the Association of Community Cancer Centers (ACCC) *(229)*. One hundred twenty of the 156 respondents (78%) expressed that they modified the diets of neutropenic patients. This is corroborated by French's 2001 survey of ten hospitals that performed pediatric bone marrow transplantations, in which five of the seven respondents (71%) implemented the ND *(80)*, and Carr and Halliday's survey of 573 registered dieticians, where 68% of respondents altered the diets of neutropenic patients *(32)*. More recently, Braun et al. electronically surveyed 1,639 pediatric oncologists, and of the 554 respondents, 57% did implement the ND, and 40% did not *(27)*, demonstrating a clear discrepancy in confidence in the diet's efficacy.

Furthermore, commencement of the ND varies amongst ND-utilizing hospitals. Smith and Bresser documented that not only was a patient's diet restricted once they reached their hospital or physician's definition of neutropenic in 92% of institutions, but 58% of respondents restricted patient diets if they were at risk for neutropenia, 13% restricted diets if neutropenia was anticipated to last more than a week, and 10% restricted diets once cancer treatment began *(229)*. Of the five hospitals that used the ND in French's study *(80)*, two started the ND when patients were admitted for bone marrow transplantation, or related chemotherapy. Two more began the ND on the day of transplant, and the final hospital began the ND when absolute neutrophil count decreased to less than 500 units/mL. Of Braun's respondents, 72%, 14%, and 12% based initiation of the neutropenic diet on ANC, beginning of chemotherapy, and hospital admission, respectively *(27)*. These results reveal disparities in perceived risk posed to cancer patients during various stages of treatment and the capacity of the ND to mitigate such risk. Thorough risk and decision analyses could aid in resolving this research gap.

The types of foods restricted during neutropenia also varied substantially. Smith and Besser reported that fresh and peelable fruits were restricted in 93% and 63% of institutions, respectively, while fresh vegetables were restricted in 98% of institutions *(229)*. Conflictingly, three of the hospitals in French's study simply focused on hyper-hygienic food handling and preparation, while two of the five eliminated the consumption of fresh fruits and vegetables *(80)*. Finally, Braun et al. recorded that 35.6%, 77.6%, and 69.5% of respondents restricted consumption of fresh fruits, fruits that can't be peeled, and raw vegetables, respectively *(27)*. Not only did these results indicate that the composition of NDs is inconsistent across institutions, but the exclusion of fresh fruits and vegetables opposes guidelines established by the FDA in "Food Safety for Older Adults and People with Cancer, Diabetes, HIV/AIDS, Organ Transplants, and Autoimmune Diseases" (SFH guidelines) *(253)*, which suggests that all produce simply be washed or cooked prior to consumption, and proper storage and cross-contamination prophylaxes are followed. Again, this illustrates broad misunderstanding regarding diet-related risk in this population that should be properly examined through risk and decision analyses.

Timing of discontinuation of the ND also differed between institutions. In French's study, two of the five hospitals that responded to the survey ceased the use of the ND once a patient's absolute neutrophil count reached 1,000 units/mL *(80)*. The remaining three hospitals discontinued the ND once transplanted cells engrafted (neutrophil count 1,000 to 1,500 units/mm^3), four to six months after transplantation, and at varying milestones. Braun reported that 82% of respondents suspended the use of the ND when the patients' ANC rose above their threshold for neutropenia, and 17% stopped the diet when the patient was discharged from the hospital *(27)*. Like discrepancies in ND initiation, discrepancies in ND discontinuation highlight a research gap in risk assessment and management for food as a vehicle of infection in cancer patients.

2.2.4 Adherence

It has been reported that 20-80% of cancer patients suffer from malnutrition *(140, 178)*, and that weight loss during cancer treatment negatively impacts survival rates *(59, 178, 259)*. Thus, a nutritionally adequate diet that is appealing to patients is paramount. Compliance to the ND is difficult due to the restrictions of odorless and cold foods, such as fresh fruits and vegetables, salads, yogurt, and ice cream, which may be desirable to patients with chemotherapy-induced nausea, oral mucositis, and altered taste and smell *(117, 141, 168)*. Patients on the ND were significantly less satisfied with the appearance and content of their meals and found diet compliance difficult *(169)*. Additionally, Moody et al. demonstrated that adherence to the ND (92.64 ± 15.32%) was significantly lower than adherence to a diet based on FDA food safety guidelines (99.26 ± 4.8%) *(169)*, and DeMille et al. noted that 30% of the patients who received guidance on the ND were noncompliant *(55)*.

Patients of all ages and their caretakers expressed grievances relating to food not only in terms of nutritional deficit, but also as a predominant quality of life challenge *(156, 168)*. Specifically, adolescents undergoing cancer treatment identified health and normalcy as their biggest hopes *(1)*. Similarly, in a qualitative study, interviews with pediatric oncology patients indicated that two of their four main concerns were loss of a normal childhood and decreased pleasure in food (due to physical effects of treatment and diet restrictions) *(168)*. The same study concluded that restricted diets contribute to social isolation and segregation from peers. It is recommended that care teams consider the food-related stress patients suffer when organizing a treatment plan *(156)*.

While providing no clear outcome benefit, the ND forces the patient into a diet that disrupts their sense of normalcy and is notably difficult to follow. Therefore, it is important to review its efficacy and application in cancer patients.

2.3 Decision models

Modeling difficult decisions can be achieved through the utilization of cost-benefit analysis decision trees, which present all possible decision outcomes and their accompanying probabilities and consequences *(42)*. By calculating the expected value (EV) of each decision, it is possible to choose the most desirable decision.

2.3.1 Metrics

Scholars have utilized several metrics to quantify health outcomes in decision modeling. One of the most widely used (notably, in the World Health Organization Global Burden of Disease studies *(268)*) is Disability-Adjusted Life Years (DALYs). DALYs quantify disease burden by accounting for both disease morbidity and mortality via Years Lived with Disability (YLDs) and Years of Life Lost (YLLs), respectively *(57)*. The metric appraises the disparity between a population's health status and an optimal health condition (zero DALYs) *(92)*. These measures are advisable for comparing burdens of multiple diseases for specific populations and age groups because they encompass disease duration, severity, and remaining life expectancy.

Quality-adjusted life years (QALYs) are a similar metric, but instead recalculate life expectancy based on years of life lived at a certain quality level, represented by a utility value ranging from 0 to 1 *(212)*. This metric is typically used to assess the health benefit gained by choosing a specific intervention. Although QALYs account for illness duration and severity, as well as morbidity (through decreased years lived), they do not consider premature morbidity relative to one's expected life span. This figure is crucial for comparing age groups, or for a population with a shortened life span, as in the present study. As such, this metric is not suitable for this application.

Another type of cost-benefit metric is the Value of Statistical Life (VSL). This metric depicts the amount that individuals are willing to pay for a decreased probability of mortality *(45)*. Unfortunately, the population used as the basis for VSL largely consisted of middle-aged, white, blue-collar men, but risk decisions are likely to vary depending on age and other health conditions *(45)*. For instance, a cancer patient may be more willing to pay for reduced mortality than a healthy individual. Finally, while the VSL is efficient for direct cost comparisons, it only evaluates mortality risks. The ND and listeriosis both have substantial morbidity that must be weighed in decision-making. Therefore, the DALY is the most appropriate cost-benefit metric from literature.

2.3.2 Approaches in healthcare

A decision model for food safety in cancer patients, or for cancer patient caretakers, has never been developed. However, approaches from other health decision models are useful for choosing reliable methodology. One method, based on the construction of decision trees, is to perform a sensitivity analysis to determine the switchover point, or the level of risk where cost-benefit analysis indicates that inaction results in a better outcome than an alternative option *(161)*. This point can be calculated as the point at which the expected values of the action and inaction options are equal. The sensitivity analysis also provides insight into the influence of model input uncertainties on the switchover point *(161)*. This approach is useful for analyses with uncertain risk estimates and inputs, as it does not rely on a risk estimate and quantifies changes in the switchover point based on variation in model inputs. Therefore, it is useful for the current problem, since cancer patients' listeriosis risks and health outcomes are both uncertain and variable.

Another decision modeling approach utilized in healthcare is Markov chain modeling. Markov models simulate disease progression over time through various health states. This approach is notably advantageous for progressive diseases like cancer *(51)*. Designated transition probabilities govern how members of a sample move between health states, which are assigned a utility value representing quality of life *(51)*. QALYs can be calculated by multiplying the utility value and time spent in each state. After simulation, costs and QALYs or quality-adjusted life expectancy (QALE) are reviewed for the targeted alternatives. Unfortunately, this approach may not be applicable for modeling listeriosis as the disease progression time interval is relatively short *(54)*. For this reason, and the added capacity to perform sensitivity analyses on the numerous uncertain variables, the switchover point approach is the most favorable for decision analysis.

2.4 Caretaker and patient produce safety knowledge and beliefs

Most studies described here pertain to cancer patients, not caretakers. However, the assumption is that caretakers of pediatric patients would behave similarly if they themselves had cancer.

2.4.1 Existing information discrepancies

Information provided to immunocompromised populations for home meal preparation is highly variable. In 2017, Evans and Redmond *(65)* found a total of 45 different food safety information sources from the UK's National Health Service chemotherapy providers, indicating that there is not a standard set of food safety guidelines for cancer patients. Of these sources, only 49% noted the importance of handwashing before food preparation, 47% included instructions for thorough heating, and 44% included foods to avoid. In a separate study *(66)*, the same authors found that only 18 of 44 surveyed cancer patients had received information on foods to avoid during their treatment. Only 15 out of 24 cancer patients were told to use a food thermometer. Again, these guidelines vary significantly from each other and FDA SFH guidelines *(253)*. Finally, only 30% of nurses and dieticians caring for immunocompromised patients supplied them with food safety materials as a standard practice *(29)*.

Observed discrepancies in specialized diets and food safety protocols indicate a need for the construction of standardized preparation guidelines based on risk analyses for this population. It is most valuable to focus on produce inclusion and preparation habits, as the two dietary elements that neutropenic patients most lack – fiber and vitamin C, could be met with safe inclusion of produce. Constructing these materials based on risk and decision analysis for the target population would provide greatest utility.

2.4.2 Foodborne illness and produce safety knowledge

Produce safety knowledge amongst cancer patients is lacking across multiple categories *(66, 158, 159, 190)*. For instance, although 98% of patients reported understanding the need for proper handwashing, only 79% knew to wash their hands before handling RTE foods, and 50% knew to use hot water, soap, and a clean towel *(66)*. Paden et al. reported that roughly 55% of cancer patients believed that food safety could be determined by appearance and scent, and only 70% scored correctly on storage knowledge *(190)*. Most central to this study, up to 49% of cancer patients knew their condition increased the risk of foodborne illness *(159, 190)*, and knowledge on avoidance of RTE refrigerated foods was lacking *(158)*. Additionally, though Evans and Redmond found that only 9 of 67 surveyed patients knew to avoid unwashed or unpeeled fresh vegetables *(66)*, Paden et al. reported that 90% of patients indicated they wash fresh vegetables *(190)*. The ongoing study will aid in better understanding cancer patients' risk perception of and motivators for following this guideline.

Some patients that did know proper avoidance practices thought the purpose was to prevent cancer reoccurrence or medication interactions, suggesting that true, comprehensive knowledge may be even lower than reported *(66)*. Proper refrigeration, meat thermometer use, handwashing, cross contamination, and risky food avoidance practices may not be initially familiar to cancer patients, as those who were given food safety information exhibited significantly increased knowledge *(66)*. Finally, knowledge was significantly affected by income, enrollment in federal or private food assistance programs, food insecurity, and smoking frequency *(190)*. Interventions should be targeted to such individuals, who face an even higher risk of foodborne illness and focus on the unfamiliar food safety areas described above.

2.4.3 Beliefs and behaviors

Overall, cancer patients believe that food safety behaviors such as washing hands, utensils, and surfaces after contact with raw meat, and rinsing fresh produce are moderately important, with corresponding and high efficacy (> 85% always performing the behavior) in these behaviors. However, despite conveyed knowledge of increased susceptibility to foodborne illness, cancer patients did not believe that they needed to be concerned about food safety *(158)*. For instance, 40-50% of patients surveyed did not believe that avoiding risky foods, like raw sprouts, unpasteurized apple juice, and uncooked hotdogs, is an important food safety behavior *(158, 159, 190)*. Additionally, when certain behaviors (refrigeration and handwashing) were attempted, insufficient food safety knowledge meant that they were performed improperly, and even when patients and caregivers were aware of food safety principles, such as proper storage time and not rinsing raw poultry, these practices were not observed *(66)*.

Patients were reluctant to apply new food safety behaviors that either contradicted their personal preferences or posed an inconvenience *(158, 159)*. Some patients were apprehensive that avoidance guidelines would limit their access to healthy foods *(158)*. However, concerns for one's health, perceived foodborne illness risk, and scientific evidence motivated patients to follow food safety recommendations *(158, 159)*. For some patients, this was bolstered by epidemiological statistics on foodborne illness outbreaks and deaths *(158)*. Prior studies have not deeply explored the food safety beliefs (including susceptibility and severity), barriers, motivators (including cues to action and benefit beliefs), and behaviors of cancer patients' caregivers, of which there are approximately 2.2 million at a given time in the United States *(204)*. Additionally, except for one study that reviewed frequency of produce washing, none investigated these parameters in a context specific to fresh produce handling, storage, and avoidance. This demonstrates a need for the ongoing survey and interview study, along with corresponding communication interventions.

CHAPTER 3: A DECISION MODEL FOR FOOD SAFETY DIETS IN CANCER PATIENTS WHO CONSUME READY-TO-EAT SALAD

It is currently unclear whether the potential benefits of the ND (theoretical listeriosis risk reduction) outweigh the costs (NEC, reduced intake of micronutrients, and lost quality of life). The same is true for less invasive produce safety interventions, which may pose a marginally greater listeriosis risk, but a smaller NEC risk. Therefore, this study aimed to conduct a decision analysis for the ND vs. other proposed food safety interventions, such as surface blanching applicable produce items or the safe food handling (SFH) method recommended by the FDA *(253)*. The switchover point approach was used to compare the ND to three alternative intervention strategies: (i) SFH, (ii) surface blanching, and (iii) no interventions, for five different age groups: (i) 0-4, (ii) 5-14, (iii) 15-44, (iv) 45-59, and (v) 60+. This chapter meets Objective 1 of the dissertation objectives.

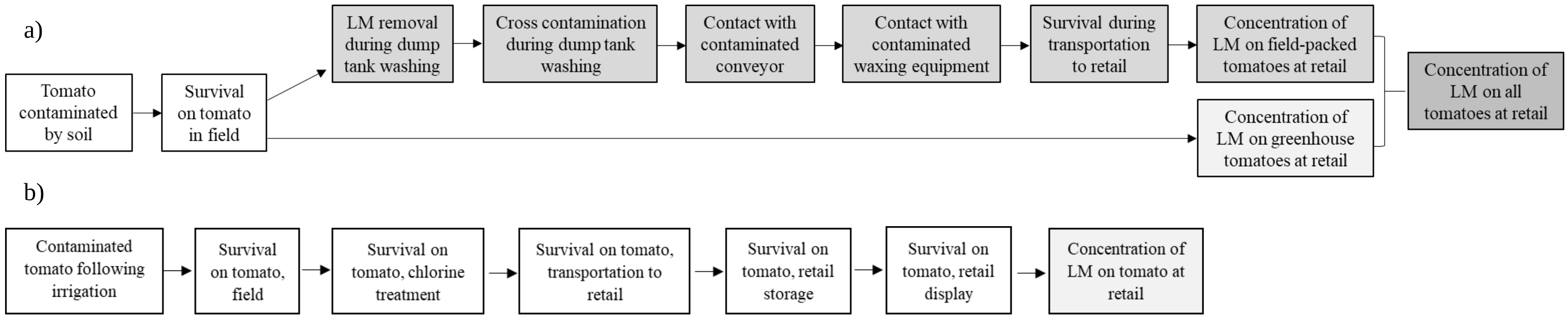
3.1 Previous work

The Master's thesis that was the foundation for this work included a risk model for listeriosis in cancer patients who consume RTE salad, consisting of leafy greens, cucumbers, and tomatoes *(94)*. During the publication review process, several revisions were made that strengthened the manuscript *(98)* and the risk model that was used subsequently in this dissertation. These changes are outlined below.

<u>3.1.1 Tomato exposure scenario</u>

Because retail-level prevalence and contamination data were not available for tomatoes, a contamination scenario was built based upon a previous approach *(247)*, assuming irrigation contamination in the field and subsequent survival through a 200 ppm chlorine wash, transportation to retail stores, retail storage, and retail display. This contamination route was updated to simulate pre-harvest and post-harvest contamination and account for process differences in field-packed vs. greenhouse tomatoes. In the updated model, pre-harvest contamination occurred via contact with contaminated soil. Due to a lack of data, which forced several assumptions, direct contact with contaminated irrigation water was removed as a route of contamination. For field-packed tomatoes, post-harvest contamination routes were expanded to additionally incorporate chlorine dump tank cross-contamination and surface contamination from conveying and waxing. Greenhouse tomatoes were assumed to be packed/sold immediately following field harvest and did not undergo these steps. Retail contamination was then modeled by a distribution containing representative proportions of each tomato type (Figure 1).

Figure 1: Updated tomato contamination route (a) compared to previous (b)



3.1.2 Risk model limitations and future work

Per reviewer comments, "Model limitations" and "Future work" sections were added to the manuscript. First, this section addressed uncertainty and variability in the dose-response parameter *k*, explaining that although inherent variability in host susceptibility, strain virulence, and host-pathogen interactions and uncertainty (due to lacking dose-response feeding data in this population) cannot be eliminated, the current approach synthesized two published calculation methods and characterized variability and uncertainty in *k* to the fullest extent possible. Other limitations, such as lacking field data for kitchen-scale produce preparation methods, use of limit of detection for tomato contamination data, comparison of soil contamination in carrot and tomato fields, use of stagnant growth rates instead of dynamic, home kitchen contamination, and unquantifiable benefits of consuming produce were also discussed.

The "Future work" section highlighted priority areas for future researchers. Notably, this section called for updated dose-response information specific to fresh produce and immunocompromised individuals. Other key areas for future corroboration were tomato contamination throughout processing, *L. monocytogenes* reductions during kitchen-scale produce treatments, and similar risk models for additional pathogens of concern, such as *Salmonella* and STEC O157. Finally, the needs for decision analysis and patient-centered communication strategies, which are examined in this dissertation, were emphasized. Inclusion of these sections allowed for explanation of model weak points and directives for future studies.

3.2 Materials and methods

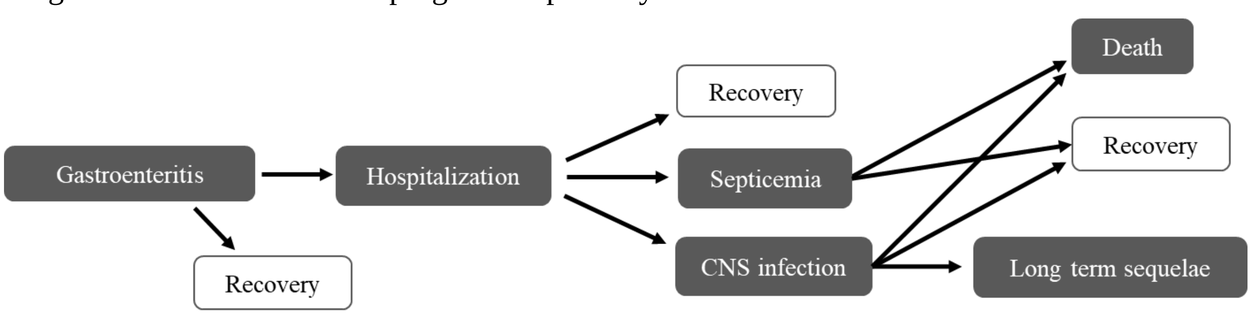
3.2.1 Exposure scenario and interventions

This study's exposure scenario considers cancer patients who consume RTE salad, as prepared by various food safety dietary practices. All types of cancer are considered, though listeriosis risk estimates are conservatively estimated for hematological cancer patients, who have a higher listeriosis risk than other patients *(98, 105, 170)*. Listeriosis risk estimates and corresponding expected DALY calculations were based on the timeframe of one chemotherapy cycle *(98)*. Four food safety interventions were considered: (i) ND (exclusion of all fresh produce), (ii) SFH (following FDA guidelines, notably refrigeration, rinsing, and drying), (iii) surface blanching (following FDA refrigeration guidelines and boiling non-porous produce for 25 s prior to consumption), and (iv) no interventions (following FDA refrigeration but not rinsing guidelines).

3.2.2 Clinical progression pathways

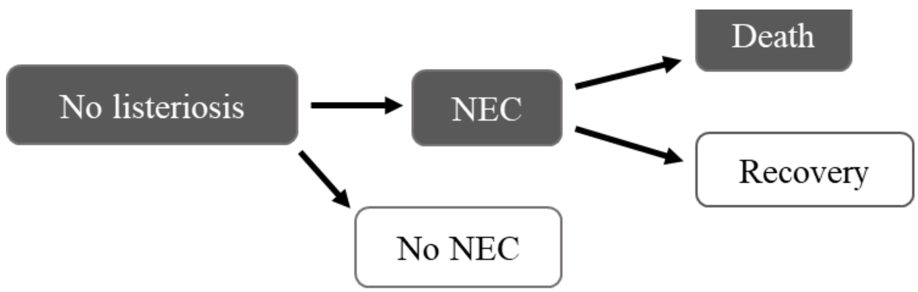
Following the food safety diet decision, there were two potential clinical pathways: (i) listeriosis, and (ii) no listeriosis, with the possibility of NEC. It was assumed that those entering the clinical progression pathway already have been diagnosed with cancer; therefore, the model appraises outcomes due to listeriosis and the chosen food safety diet only. Based on previous listeriosis burden of disease studies *(50, 130, 148)*, five non-perinatal listeriosis health states were considered: (i) self-limiting gastroenteritis (non-hospitalized), (ii) curable gastroenteritis (hospitalized), (iii) central nervous system (CNS) infection, (iv) long-term CNS sequelae, and (v) septicemia (Figure 2), with potential death occurring as a result of septicemia or CNS infection only *(62, 107, 108, 135)*.

Figure 2: Listeriosis clinical progression pathway



Only systemic infections (CNS infection and septicemia) follow hospitalization, as gastroenteritis alone is considered non-invasive listeriosis, described as “mild” and/or “self-limiting” with little to no mortality, only causing death when it progresses into more pervasive infections in immunocompromised individuals, such as cancer patients *(50, 149, 188, 218)*. The clinical progression pathway for no listeriosis consisted of three states: NEC, death, and recovery (Figure 3).

Figure 3: Clinical progression pathway for no listeriosis, with the possibility of neutropenic enterocolitis (NEC)



3.2.3 Model metric and calculations

The metric used to quantify health outcomes for each risk management strategy was DALYs. DALYs account for Years of Life Lost (YLL) and Years Lost to Disability (YLD), representing mortality and morbidity, respectively, both of which are important to the model’s targeted stakeholders, pediatric cancer patient caretakers. Within the YLD calculation (Eq. 1), both duration and severity are considered, which makes the DALY appropriate for comparison of different disease risks. Similarly, the YLL calculation (Eq. 2) can be adjusted to the life expectancy of the multiple target populations (i.e. accounting for age, etc.). It was prudent to use such a metric for comparison in this study because listeriosis outcomes are dominated by mortality (YLL), while NEC outcomes are driven by both morbidity (YLD) and mortality. Hence, use of the DALY ensures a more complete evaluation of this food safety decision.

Conventional DALY formulas summing years lived with disability (YLDs) and years of life lost resulting from untimely death (YLLs) were used with no age weighting or time discounting (Eq. 1-3) *(58)*.

$$YLD = \sum duration\ of\ ailment_i \times disability\ weight_i \qquad 1$$

$$YLL = remaining\ life\ expectancy\ at\ age\ of\ premature\ death \qquad 2$$

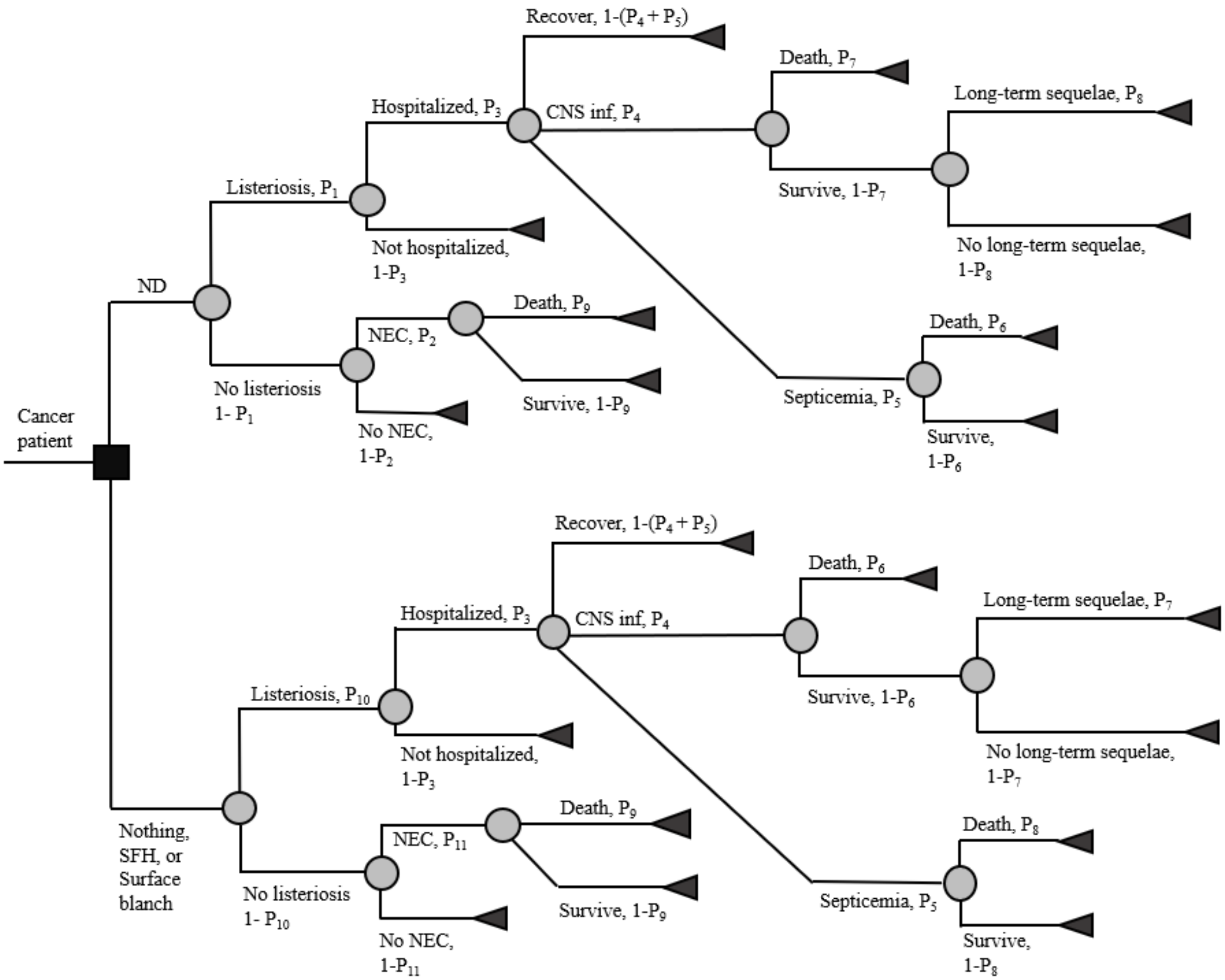
$$DALY = YLD + YLL \qquad 3$$

<u>3.2.4 Decision model and analysis</u>

Each decision model assumes that an individual is presently being treated for cancer. Decision trees were developed for three decisions: (i) ND vs. no interventions, (ii) ND vs. SFH, and (iii) ND vs. surface blanching, for five age groups: (i) 0-4, (ii) 5-14, (iii) 15-44, (iv) 45-59, and (v) 60+, as grouped in the 1990 Global Burden of Disease (GBD) study *(177)*, totaling 15 decision trees. Decision nodes, contrasting the ND with an alternative, were represented as square boxes (Figure 4). Chance nodes appear as circles and denote the probability of an event (outcome) occurring. For example, P_1 and P_{10} represent the probabilities of acquiring listeriosis while on the ND and non-ND intervention, respectively.

The other probabilities are assigned as follows: NEC while on the ND (P_2), NEC while on the alternative food safety diet (P_{11}), death following NEC (P_9), listeriosis requiring hospitalization (P_3), listeriosis with CNS infection (P_4), listeriosis with septicemia (P_5), death following CNS infection (P_7), CNS infection long-term sequelae (P_8), death following septicemia (P_6). Triangles indicate branch terminals.

Figure 4: Example decision model diagram for the neutropenic diet (ND) opposed to no interventions, the safe food handling (SFH) diet, or surface blanching



Expected value equations were coded in R version 4.0.5 (R Core Team, Vienna, Austria) *(197)*. Monte Carlo analysis with 10,000 iterations and a set seed of 123 was used to calculate the expected value (EV) of each intervention based on Equation 4, given outcome DALYs, probabilities associated with each outcome, and uncertainty within each parameter.

$$\boldsymbol{EV}(\boldsymbol{intervention}) = \sum(\boldsymbol{probability} \times \boldsymbol{associated\ DALYs}) \qquad 4$$

Median EVs were then compared to select the intervention strategies with the least DALYs.

As a secondary analysis, sensitivity analyses of each decision tree were then conducted to determine switchover points – the value that justifies one strategy over the other strategy – for the most uncertain parameters.

3.2.5 Model parameterization

A literature search was performed to parametrize the model. Only data concerning acquired (non-perinatal) listeriosis cases were considered. Studies referring to septicemia as sepsis or bacteremia, or CNS infection as meningitis, encephalitis, or meningoencephalitis were included. For disease progression probabilities, data not designating initial condition (e.g., death due to "listeriosis," without designating CNS infection/septicemia) were excluded. Because data specific to cancer patients were lacking, the included studies focused on invasive listeriosis infections regardless of population subgroup.

Input parameter distributions were fit to collected data in R version 4.0.5 (R Core Team, Vienna, Austria), using the function "fitdist" from the package "fitdistrplus" *(53)*. For parameters with ≥ 5 estimates, distributions were fit to data and ranked by the BIC statistic, with the best-ranked distribution chosen. Occasionally, probability distributions included unfeasible values (< 0 or > 1). In such cases, distributions were truncated at 0, 1, or both, following fitting, using an ifelse function. Parameters with < 5 estimates were assumed to follow a uniform distribution between the minimum and maximum estimates. Further calculations were executed in R for greater accessibility to statistical testing and manipulation.

The listeriosis risk distributions for eating a simulated salad consisting of RTE leafy greens, cucumbers, and tomatoes prepared by three strategies: (i) no preparation, (ii) rinsing as recommended by the FDA *(253)* (safe food handling or SFH approach), and (iii) surface blanching (applicable to cucumber and tomato only), were derived from a previous study *(98)*.

Because the ND excludes raw salad ingredients, only noncompliant patients can develop listeriosis from salads. In this case, it was assumed that those noncompliant with the ND were compliant with the FDA food safety guidelines (SFH diet). Therefore, P_1 was equal to the product of ND noncompliance rate, hazard ratios for infection in cancer patients on the ND vs SFH diet, and listeriosis risk on the SFH diet (Eq. 5).

$$P_1 = ND\ noncompliance \times SFH\ risk\ \times ND\ hazard\ ratio \qquad 4$$

A distribution for infection hazard ratios for the ND compared to SFH diet was created using data for general infection, fever, bacteremia, gastroenteritis, and blood stream infections in cancer patients assigned to either diet *(85, 124, 141, 167, 169, 248, 250)*. Data from three studies *(55, 143, 169)* were pooled to create a uniform distribution for patient compliance with the ND. Only one publication *(169)* studied compliance to the SFH diet, which was reported as 99.26 ± 4.8%. For simplicity, it was assumed that compliance to the SFH diet was 100%. As compliance with a surface blanching diet has never been studied, it was assumed to be a uniform distribution from the median of the ND compliance distribution to 1, then adjusted in sensitivity analysis to determine the switchover point.

The disability weight used for both non-hospitalized and hospitalized gastroenteritis listeriosis patients was approximated as the value used by Havelaar et al. *(114)* for *Campylobacter* gastroenteritis patients visiting general practitioners (GP). This type of gastroenteritis - the more serious of the two described and thus more analogous to that faced by cancer patients, was used for both visiting GP and hospitalized patients in a later assessment *(130)*. The distribution for duration of gastroenteritis prior to hospitalization was generated using the minimum and maximum mean times from symptom onset to hospitalization from three studies *(90, 107, 218)*. For probability of progression from gastroenteritis to hospitalization, and all other progressions to new illness states (e.g., septicemia to death, CNS infection to CNS sequelae, etc.), data from multiple sources were pooled into a single distribution.

The duration of hospitalization prior to progression to septicemia, CNS, or recovery was assumed to follow a uniform distribution for the largest range reported, which was for CNS infections, and encompassed the range for septicemia diagnosis *(201)*. Because the range was from symptom onset to specific diagnosis, the duration of illness prior to hospitalization was subtracted to obtain the duration of solely hospitalization. Disability weights for septicemia, CNS infection, and CNS sequelae were previously reported by Maertens de Noordhout et al. *(50)*, who derived these values by combining various states in the 2010 GBD study *(208)*. The durations of septicemia and CNS sequelae were assigned according to Kemmeren et al. *(130)*. A triangular distribution for duration of CNS infection was built using the minimum and median reported by Arslan et al. *(15)*, with the maximum being the point estimate reported by Kemmeren et al. *(130)*. Data for cancer patients' predicted remaining life expectancies (RLEs) based on age at diagnosis, for patients 0 and 1 years from diagnosis *(26)*, were fit to distributions to obtain model RLE estimates. Ages utilized in the present study's age groups were as follows: (i) 17, 22, 27, 32, and 37 for ages 15-44, (ii) 45, 52, and 57 for ages 45-59, and (iii) 62, 67, 72, and 80 for ages 60+. When necessary, distributions were truncated at 0 and the RLE that, when summed with the minimum age in an age range, would equal a total lifespan of 90 years. Given that there were no data for cancer patients under 17, and maximum RLE for 17-year-old cancer patients approached that of the general population, it was assumed that for age groups 0-4 and 5-14, the RLE was a uniform distribution between the minimum and maximum CDC estimates for the ages within the group *(14)*. Because data were reported in increments of five, RLE for 0 and 5, and 5 and 15, were used for the 0-4 and 5-14 age groups, respectively. For all health states, the duration of the previous health state(s) was subtracted from the remaining life expectancy.

For all interventions, it was assumed that salads consisted of RTE greens, cucumbers, and tomatoes refrigerated at 4°C. Probabilities of developing NEC due to the ND and SFH were acquired from Gupta et al.'s pilot study *(109)*. Rates of NEC for surface blanching and no intervention have never been published. In terms of produce inclusion and expected nutrient level, these diets are comparable to the SFH diet. Therefore, they were assumed to have the same rate of NEC as the SFH diet, and sensitivity analyses were later conducted to evaluate this assumption. There is no published disability weight for NEC, so the WHO Global Burden of Disease study's disability weight range for "severe diarrheal disease," acted as the bounds for a uniform distribution *(91)*. Symptoms corresponding with this condition are diarrhea ≥ 3 times a day, severe abdominal pain, nausea, and tiredness, which closely mimic symptoms of NEC *(2, 91)*. Because data were lacking, means and medians were both used to create a distribution for NEC duration. The distribution fit, range, and central tendency were reviewed to validate this assumption. NEC mortality rate differed for children and adults, so two separate distributions were fit to data from studies including patients aged 0 to 25 (corresponding to study age groups 0-4 and 5-14, study indicated pediatric patients) and those older than 19 (corresponding to study age groups 15-44, 45-59, and 60+, study indicated adult population) *(2, 21, 74, 88, 100, 103, 104, 142, 163, 219)*. Studies including both age ranges (e.g., patients aged 5-60) were excluded from these distributions. It was assumed that NEC mortality rate is the same across food safety dietary practices.

3.2.6 Sensitivity analysis

One-way analyses were conducted to understand uncertainty and variability associated with the numerous input parameters within each decision model and how it affects the selection of the risk management strategy. First, Spearman rank correlation coefficients were calculated for all input parameter distributions and corresponding EV (*cor.test* function in R, with method specified as "spearman"). Next, parameters identified as highly influential via Spearman correlations, and particularly uncertain and/or variable parameters, were further examined to determine their switchover point and the likelihood of its occurrence. Parameters deemed particularly uncertain included listeriosis risks resulting from the ND, SFH, surface blanching, and no intervention strategies, the probability of NEC associated with each intervention, compliance rates for SFH and surface blanching, and NEC disability weight, which have only been estimated once previously, or were assumptions *(91, 98, 109)*. Exceptionally variable parameters included parameters with inherent person-to-person variability, such as septicemia, CNS infection, and NEC durations and mortality rates.

While calculating each switchover point, all values besides the parameter in question were held constant at a point estimate (the median of a parameter's respective distribution). Expected DALYs were then calculated and plotted for the ND and intervention in question as a function of the selected parameter, with the point of intersection signifying the switchover point. In some cases, for illustrative purposes, the range of the selected parameter had to be adjusted to include unreasonable values in order to view the switchover point. For instance, RLE ranges had to include negative values to produce alternative intervention values that justified the use of the ND.

3.3 Results

3.3.1 Input distributions

The results of the literature search and fit of input distributions to represent variability and uncertainty in each model parameter used to calculate model expected values are tabulated in

Table 1.

Table 1: Model parameter input distributions

Parameter	Distribution	Source(s)
Listeriosis risk – all scenarios	Previously reported output vectors	*(98)*
Hazard ratio: ND vs. SFH	Laplace: location=1, scale=0.147889, truncated at 0	*(85, 124, 141, 167, 169, 248, 250)*
Gastroenteritis duration (days)	Uniform: min=1, max=2.8	*(90, 107, 218)*
Probability hospitalization	Uniform: min=0.918779, max=0.95	*(89, 225, 245)*
Hospitalization (days)	Difference between uniform: min=0, max=20 and pre-hospital duration	*(201)*
Gastroenteritis disability weight	0.393	*(130)*
Probability CNS infection	Log logistic: shape=3.360269, scale=0.325513, truncated at 1	*(5, 30, 62, 81, 87, 89, 90, 106-108, 122, 123, 135, 139, 171, 186, 203, 218, 225, 227, 260)*
CNS infection duration (days)	Triangle: min=1, likeliest=21, max=182	*(15, 130)*
CNS infection disability weight	0.426	*(50)*
CNS infection mortality rate	Uniform: min=0.031250, max=0.490909)	*(7, 12, 15, 28, 30, 87, 90, 107, 108, 135, 170)*
Probability CNS sequelae	Uniform: min=0.118182, max=0.20	*(7, 12, 28, 30, 107)*
CNS sequelae disability weight	0.292	*(50)*
CNS sequelae duration	Estimated RLE – CNS infection duration	
Probability septicemia	Uniform: min=0.040146, max=0.864967	*(5, 30, 62, 81, 87, 89, 90, 106-108, 123, 135, 139, 171, 203, 218, 225, 227, 260)*
Septicemia duration (days)	Uniform: min=1, max=7	*(130)*
Septicemia disability weight	0.210	*(50)*
Septicemia mortality rate	Uniform: min=0.040146, max=0.739130	*(30, 87, 90, 108, 135, 171)*
Probability NEC, ND	0.3333	*(109)*
Probability NEC, SFH, surface blanch, no intervention	0.0476	*(109)*, and assumptions
NEC disability weight	Uniform: min=0.164, max=0.348	Assumption based on *(91)*
NEC duration (days)	Uniform: min=1.5, max=21.6	*(2, 36, 88, 100, 221, 228, 236)*
NEC mortality rate (adult)	Exponential: rate=3.604231, truncated at 1	*(2, 21, 74, 88, 100, 103, 104, 142, 163, 219)*
NEC mortality rate (child)	Exponential: rate=15.93568)	*(63, 72, 154, 172, 176, 202, 207, 221, 228, 236)*
ND compliance	Uniform: min=0.57143, max=0.92208	*(55, 143, 169)*
SFH compliance	1	Assumption based on *(169)*
Surface blanch compliance	Uniform: min=0.57143, max=1	Assumption
RLE 0-4 (years)	Uniform: min=73.3, max=77.8	*(14)*
RLE 5-14 (years)	Uniform: min=63.4, max=73.3	*(14)*
RLE 15-44 (years)	Weibull: shape=6.269388, scale=53.144223	*(26)*
RLE 45-59 (years)	Logistic: location=22.43124, scale=3.20321, truncated at 0 and 45	*(26)*
RLE 60+ (years)	Weibull: shape=2.382438, scale=12.367824	*(26)*

3.3.2 DALY calculations and distributions

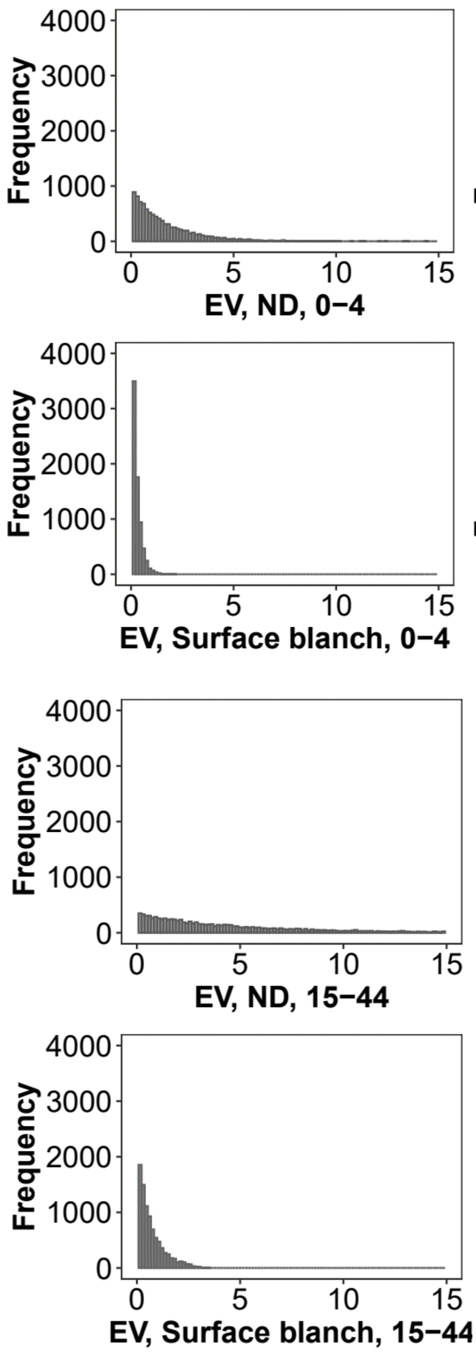
Across all interventions and age ranges, EVs spanned from 1.8E-04 DALYs per person per chemotherapy cycle (SFH and surface blanch, 60+) to 24.5 (ND, 15-44) (Table 2).

Table 2: Expected value in Disability-Adjusted Life Years (DALYs) for each intervention and age group

Intervention	Age	5%	50%	95%
Neutropenic diet	0-4	0.0875	1.0949	4.7000
	5-14	0.0792	0.9920	4.2798
	15-44	0.2222	3.1017	13.6571
	45-59	0.0977	1.3910	6.2722
	60+	0.0409	0.6185	3.1616
SFH	0-4	0.0125	0.1564	0.6712
	5-14	0.0114	0.1417	0.6112
	15-44	0.0317	0.4430	1.9504
	45-59	0.0140	0.1987	0.8958
	60+	0.0058	0.0883	0.4515
Surface blanch	0-4	0.0125	0.1564	0.6712
	5-14	0.0114	0.1417	0.6112
	15-44	0.0317	0.4430	1.9504
	45-59	0.0140	0.1987	0.8958
	60+	0.0058	0.0883	0.4515
No intervention	0-4	0.0127	0.1565	0.6727
	5-14	0.0115	0.1421	0.6121
	15-44	0.0319	0.4431	1.9509
	45-59	0.0140	0.1989	0.8967
	60+	0.0059	0.0883	0.4515

The ND resulted in the highest EVs, with median expected values at each age range up to seven times greater than for all other interventions. SFH and surface blanching EVs were identical at each age group, and no intervention EVs were only slightly (10^{-4} to 10^{-3}) higher. These results suggest that non-ND interventions are favored for all age groups. For each intervention, the lowest and highest EVs occurred in the 60+ and 15-44 age groups, respectively. EV distributions were skewed left for all interventions and age groups, with the ND consistently exhibiting a wider spread, which was attributable to the higher NEC risk on the ND (Figure 5).

Figure 5: Expected (EV) value distributions for age groups 0-4 and 15-44



Expected values for all interventions in the 15-44 age group also displayed a wider spread than those of other age groups.

Most (99.58% to 99.95%) of the intervention EV magnitudes were attributable to EVs of YLLs associated with NEC. EVs of NEC YLDs accounted for a marginal fraction of the total (0.04% – 0.23%), and EVs of listeriosis YLDs and YLLs were a negligible contributor. A sample categorization of median EVs by DALY component and outcome is shown in Table 3.

Table 3: Median expected values categorized by Disability-Adjusted Life Year (DALY) component and outcome, neutropenic diet (ND), ages 15-44

YLD LM ill (%)	YLD LM hosp (%)	YLD sept (%)	YLD CNS inf (%)	YLD CNS sequelae (%)	YLD NEC (%)	YLL sept (%)	YLL CNS inf (%)	YLL NEC (%)
6.22E-13 (~ 0)	2.69E-12 (~ 0)	3.08E-12 (~ 0)	1.01E-11 (~ 0)	2.27E-10 (~ 0)	2.56E-03 (0.08)	1.71E-09 (~ 0)	1.02E-09 (~ 0)	3.10E00 (99.92)

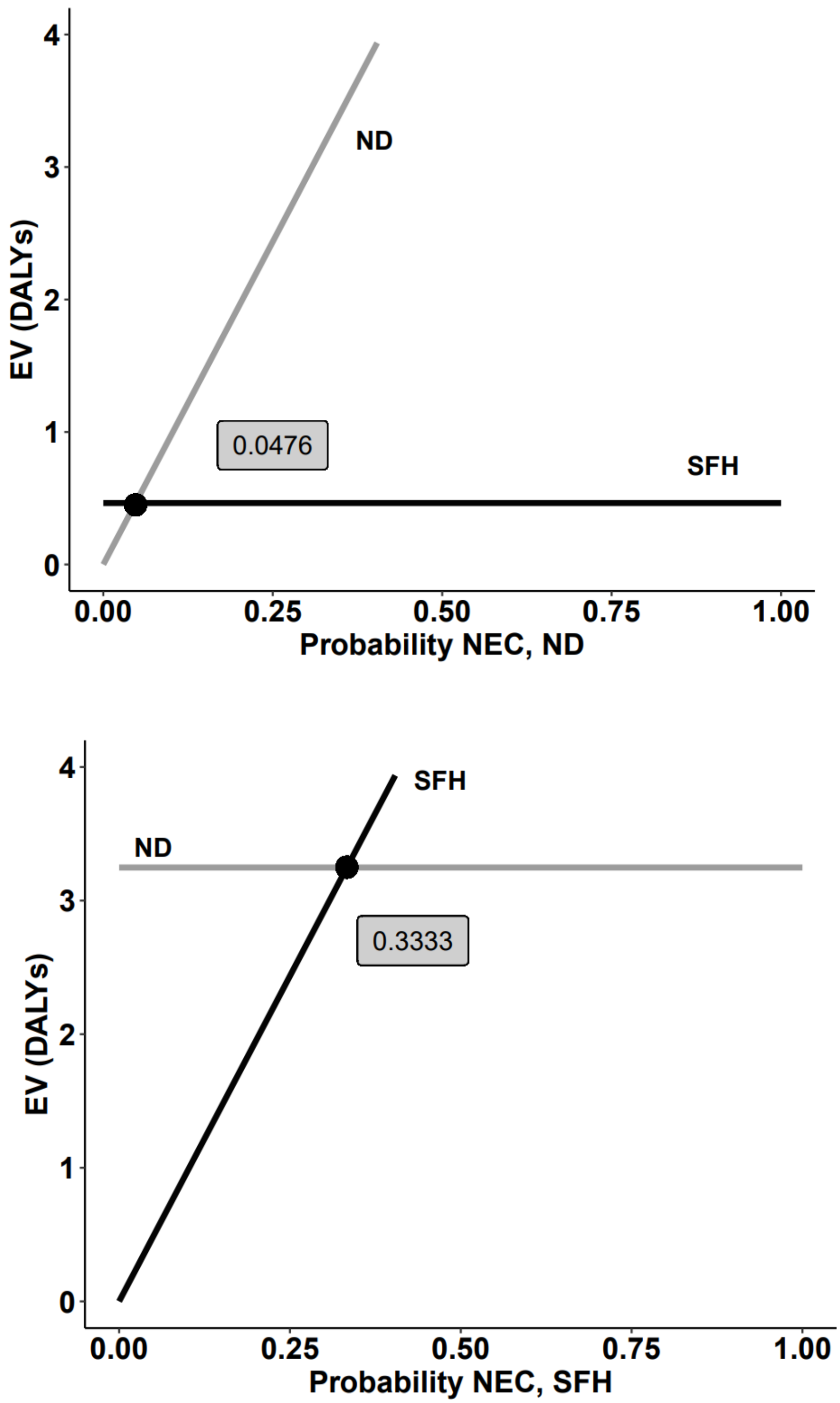
3.3.3 Sensitivity analysis

For all interventions and age groups, the parameter with the highest Spearman correlation coefficient was NEC mortality rate, decreasing with increased age and ranging from 0.90 to ~1 (0.9998). The second-most influential parameter and its relationship strength to an intervention's EV depended on age group. For the 0-4 age group, this was the listeriosis hazard ratio for ND vs. SFH, with a low correlation coefficient (0.02). For all other age groups, RLE had the second-highest correlation coefficient, with value increasing by age: 0.03 (5-14), 0.16 (15-44), 0.22 (45-59), and 0.39 (60+). The absolute values of the remaining parameters' correlation coefficients were ≤ 0.03.

3.3.4 Switchover points

Alternatives to the ND were favored over the ND in all plausible (within reported ranges) scenarios. Under all conditions, the NEC probability switchover points for ND and alternative interventions were 0.0476 and 0.3333, respectively, equating NEC probability on the opposing branch. This reveals that NEC probability must be the same, or greater for the alternative intervention diets to favor use of the ND. Intervention EVs as a function of NEC probabilities, for ND and SFH, ages 15-44, are shown in Figure 6.

Figure 6: Switchover points for neutropenic enterocolitis (NEC) probability for neutropenic diet (ND) and safe food handling diet (SFH), ages 15-44



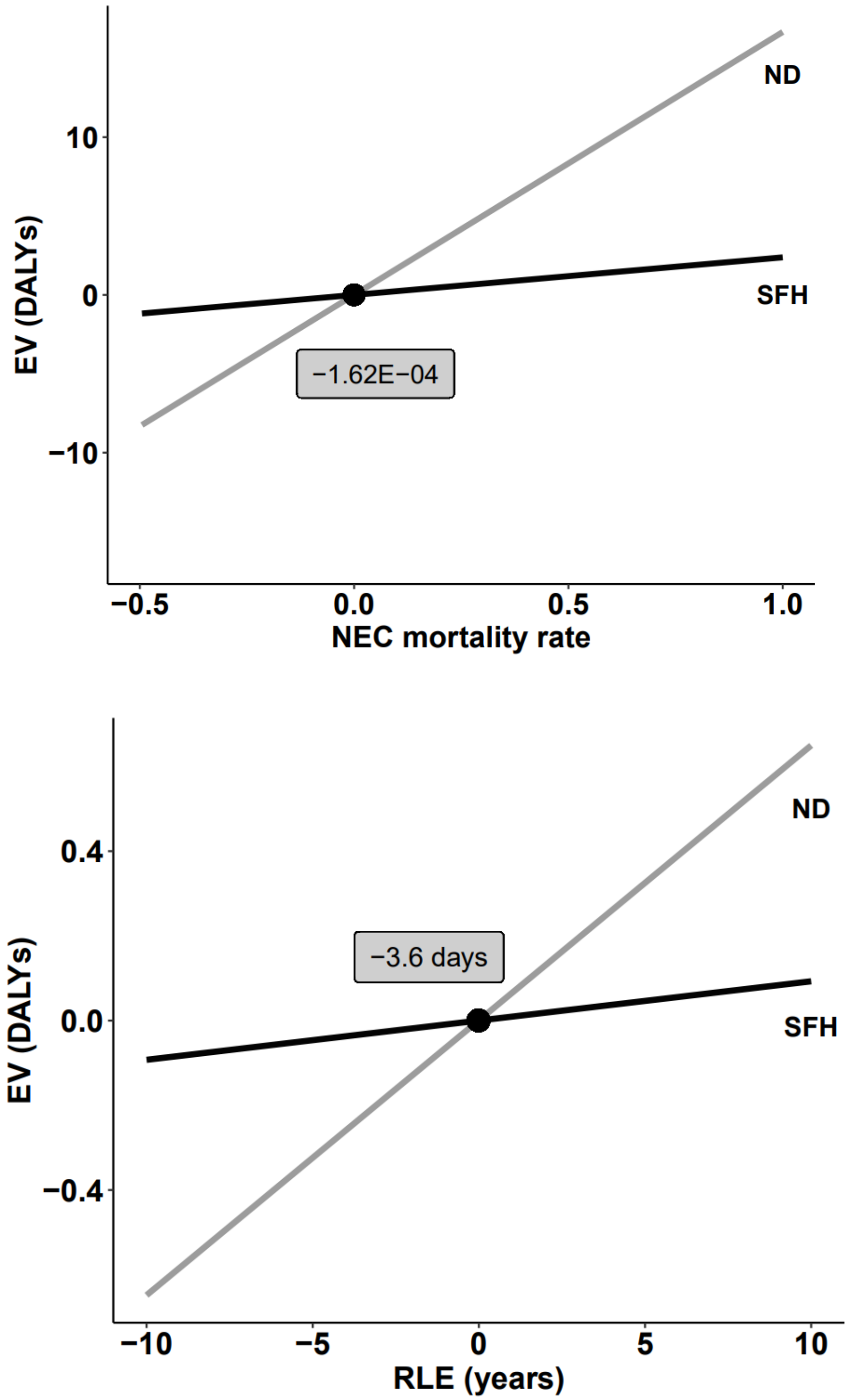
Varying slightly by age group and intervention (SFH, surface blanching, and no intervention), the alternative intervention listeriosis risk switchover points ranged from 02.2E-02 (no intervention, ages 45-59) to 2.8E-01 (SFH, ages 15-44), indicating that the produce-exclusion tenant of the ND is only justified when listeriosis risk associated with an alternative intervention is remarkably high (compared to previous estimates, which range from 8.4E-13 to 2.5E-06) *(60, 98, 251)*. Across interventions, listeriosis risk switchover points were highest for SFH and lowest for no intervention. Within each intervention category, ages 15-44 and 45-59 had the highest and lowest switchover points, respectively (Table 4).

Table 4: Listeriosis risk switchover points for alternative interventions

Intervention	Age	Switchover point
Safe food handling (SFH)	0-4	0.0654
	5-14	0.0633
	15-44	0.2841
	45-59	0.0290
	60+	0.2836
Surface blanch	0-4	0.0568
	5-14	0.0550
	15-44	0.2626
	45-59	0.0250
	60+	0.2620
No intervention	0-4	0.0496
	5-14	0.0480
	15-44	0.2285
	45-59	0.0218
	60+	0.2280

Alternatively, all switchover points for ND listeriosis risk were implausible negative values, ranging from -2.96E-01 to -2.95E-02, characterized by age groups and differing only minutely (on the order of 10^{-6}) between interventions. This signifies that feasible listeriosis risk reductions attributable to produce exclusion on the ND do not justify its use over other interventions. Figure 7 shows EV as a function of NEC adult mortality rate and RLE, respectively.

Figure 7: Neutropenic enterocolitis (NEC) adult mortality rate and relative life expectancy (RLE) switchover points for the neutropenic diet (ND) vs. the safe food handling diet (SFH), ages 15-44



Despite being identified as influential parameters in the sensitivity analysis, and EV increasing dramatically with each parameter, these parameters had implausible (negative) switchover points. All other parameters also had implausible switchover points (e.g., a probability greater than one, an illness duration of many or negative years, etc.). As such, realistic changes in the aforementioned parameters did not influence the preferred dietary intervention.

3.4 Discussion

The present decision model is the first to compare health impacts of listeriosis and intervening food safety diets in cancer patients who consume fresh produce. Previous works calculated DALYs for listeriosis from all foods in the general population *(50, 115, 214)*, which cannot be directly compared with DALYs for the target population. For instance, authors used standard life expectancies for all age groups, which are longer than those expected for adult cancer patients, driving up YLLs. Additionally, cancer patients' increased listeriosis risk is likely to increase expected DALYs beyond that of the general population. Further, no existing studies impute cancer patients' NEC disease burden in DALYs. In this study NEC EVs were high (median DALYs per person per chemotherapy cycle ranged 0.095 to 3.018 per person); however, the present study is specific to cancer patients who are much more susceptible to severe intestinal disease and have a high individual NEC mortality rate (median 18% in adults). Therefore, while this model has provided the first estimates of listeriosis and NEC EVs, more data on burden of disease specific to cancer patients are necessary for validation.

Intervention-specific EVs were highest for the ND and virtually indistinguishable among the other interventions. While any of these interventions may be recommended over the ND, it is prudent to consider ease of administration and diet compliance. Compliance with a surface blanching diet has never been tested, yet it is reasonable to anticipate that administration may be difficult, and adherence viewed as tedious and time-consuming, resulting in subpar compliance rates. Although the no intervention (refrigeration, but no rinsing) diet may technically be the easiest to follow, it contradicts most hospital recommendations, and over 80% of cancer patients report thoroughly washing fruits and vegetables before eating either most or all the time, which hints to an underlying habit or desire to practice this food safety behavior *(190)*. Additionally, this practice is likely to increase foodborne illness risk from other foods. In contrast, the SFH diet is presently recommended by the FDA *(253)*, and current American Cancer Society guidelines closely match *(9)*. SFH guidelines are familiar, simple to follow, and have a published compliance rate nearing 100% *(169)*. For these reasons, the SFH diet is currently recommended, although acceptability and barriers to compliance among cancer patients will require further examination.

The decision model's EVs were overwhelmingly dominated by NEC YLLs. This can be attributed to the differences in risk between NEC (0.3333 for ND and 0.0476 for alternate interventions) and listeriosis (medians ranging from 7.21E-10 to 4.38E-08). When combined with a high NEC mortality rate, this imbalance led to NEC outcomes driving decision making, and listeriosis outcomes having an inconsequential effect on model results. Because alternative food safety diets had a lower NEC risk than NDs, they were always preferred to the ND. Adjusting listeriosis parameters, like probability and duration of CNS or septicemia, within a conceivable range did not change the preferred intervention from alternative diets to the ND. Furthermore, switchover point analysis revealed that for listeriosis outcomes to become quantitatively meaningful, median listeriosis risk on alternative interventions would have to increase to a range of 2.18E-02 to 2.84E-01. When previously reported vegetable-specific listeriosis risks *(60, 78, 210, 251)* were compounded for the duration of a chemotherapy cycle *(8)*, the 95th percentiles ranged from 4.00E-08 to 9.07E-05, which is three to four orders of magnitude lower than the switchover point risk. Additionally, the switchover points for ND listeriosis risk were all negative, indicating that even if a patient perfectly complied with the ND, thereby reducing listeriosis risk from RTE salads to zero, it would not be enough to counteract the ND's increased NEC risk, and EV would still be highest on the model's ND arm. These findings emphasize the improbability of reaching a listeriosis risk that would justify the use of the ND over alternative food safety diets and imply that negative secondary outcomes, such as NEC, should be the main concern for any food safety diet.

The sensitivity analysis determined that NEC mortality rate had a nearly perfect positive relationship with intervention EV (Spearman rank correlation coefficients 0.90 to ~1). This is another manifestation of NEC's dominance in the model, considering NEC mortality rate plays a large role in determining EVs of NEC YLLs. The high correlation coefficient may also reflect the fundamental variability in disease mortality rates, which depend on individual health, age, and treatment options. An attempt was made to mitigate age-related variability using two distinct mortality rates (child and adult). However, many of the adult mortality studies included a large age range (e.g., ages 21-78), and were still intrinsically variable. In the future, public health experts may find it useful to divide this age range to collect more accurate NEC mortality rate data. Nonetheless, despite this variability, NEC mortality rate switchover points did not occur in a feasible range, suggesting that better characterized variability would not change model recommendations.

As the second major component of NEC YLLs, RLE had the second-highest correlation coefficient for all age groups, excluding ages 0-4. Again, this exemplifies the strong influence

NEC outcomes had on model EV. Similar to NEC mortality rate, the high correlation coefficient underscored the inherent variability of cancer patients' life expectancies, which can differ drastically by individual health and lifestyle, cancer type, age at diagnosis, and treatment options. Strategies used to characterize this variability included constructing the RLE distribution based on data for numerous cancer types and diagnosis age, as well as separating models by age group, though fluctuations will also remain. Further, the switchover points for NEC mortality rate were all negative, once again establishing that plausible variations do affect model recommendations.

Lastly, this model included diet compliance rates that were reported in the literature and estimated by assumption *(55, 143, 169)*. If using this decision tool, healthcare workers and families could interchange these compliance rates with their expected or reported compliance. Given the results of the sensitivity and switchover point analyses, this is not likely to change the outcome of the model, but allows for user customization and a more accurate risk assessment.

3.4.1 Model limitations

This study's key finding was that the risk and outcomes of NEC markedly outweighed those of listeriosis, and because the ND had a higher NEC risk than other food safety diets, its use is not justified based on the analyses conducted in this study. It is important to consider that the only available data on diet-based NEC risk were sourced from a pilot study, with 21 children each on ND and "standard diet" (equivalent to SFH diet) arms *(109)*. Even if a full-scale study found a smaller disparity between diet-based NEC risks, the model results would remain the same, because alternative intervention NEC probabilities must be greater than or equal to those of the ND to justify the ND. Therefore, a smaller discrepancy would not change the preferred decision. Nonetheless, collecting more data to better represent diet-based NEC risk is crucial for enhancing model accuracy.

Additionally, this model utilized several assumptions to alleviate literature gaps. Because Gupta et al. *(109)* hypothesized that NEC rates were higher on the ND than the SFH diet due to potential deficiencies stemming from its exclusivity, it was assumed that surface blanch and no intervention diets had equal NEC probability to the SFH diet, which is parallel in terms of produce inclusion. Along with this hypothesis, the effects of dietary fiber and vitamin C on intestinal integrity and colitis have been extensively described in the literature, substantiating the assumption. Al-Qadami et al. reported that gut bacterial fermentation of fiber is needed to generate short-chain fatty acids (SCFAs), which alleviate the gastrointestinal inflammatory response and reduce intestinal mucosa permeability *(3)*. This was exhibited in murine models, where mice with mucositis that were given low and high fiber diets experienced increased and decreased intestinal permeability, respectively *(84)*, and chronic and intermittent dietary fiber deficiency caused colonic mucosa deterioration and subsequent colitis *(56)*. Likewise, proper doses of vitamin C were found to halt intestinal mucosa erosion and stimulate barrier recovery in guinea pigs *(196)*, and assuage enterocolitis symptoms, intestinal cell death, and inflammatory response in mice *(175)*. One concern with the assumed NEC probability for the surface blanch diet may be fiber and vitamin C thermal degradation. Blanching for much longer times (10 min) did not substantially reduce fiber (maximum 15%) *(264)*, and 30-120 s blanches caused small (15-19%) reductions in vitamin C *(220, 242)*. Even if reductions were much greater, as previously stated, small changes in NEC rates would not affect the model's preferred decision; thus, assumptions made in this area are regarded as credible.

Despite model recommendations not fluctuating by age group, the groupings could provide the opportunity to define inherent variability, if selected carefully. Being that model EVs were dictated by NEC YLL, NEC mortality rate and RLE are key indicators for choosing effective age groupings. Model EVs were similar for the two youngest age groups, peaked in the 15-44 age group, and decreased dramatically in the 60+ age group. Age groups 0-4 and 5-14 were analogous since they utilized the same NEC mortality rate and had similar RLE distributions. The 15-44 age group EV spike can be ascribed to the combination of the high adult NEC mortality rate and wide-ranging RLE distribution (range 42 years), which produced artificially high EVs (e.g., a 44-year-old with adult NEC mortality and RLE of 70). This is also why this age grouping's EV distribution was markedly widespread. EVs for those aged 45-59 were decreased in correspondence with the lower, more accurate, RLE. Because RLEs for the 60+ age group were considerably lower than for others, this grouping had the lowest EVs. Based on these inferences, it may be more accurate to have three age groups based on NEC mortality rate and RLE: (i) children and young adults (≤ 30), (ii) adults (31-59), and (iii) older adults (60+).

It was not possible to quantify some effects of the ND for use in this model. Previous works documented negative mental health and quality of life effects in cancer patients assigned to restrictive diets *(156, 168)*. Unfortunately, these effects have never been clearly defined, and there are no data regarding their prevalence on ND and alternative intervention diets. Additionally, given that the ND provides inadequate fiber and vitamin C compared to the SFH diet *(150)*, it is possible that it may lead to deficiencies in compliant patients *(166)*. Nutritional deficiencies during cancer treatment can worsen cancer prognoses, quality of life, and cause treatment complications *(113)*. Including DALYs associated with these effects could drive the ND EVs even higher, making justification even more unlikely.

For simplicity, this model considered two pathways: (i) listeriosis, and (ii) no listeriosis, with the probability of NEC. However, there is a very small probability (6.85E-11 to 1.05E-10) that both disease states (listeriosis and NEC) could occur simultaneously. In this case, the combined disability weight would likely increase in correspondence with the presumed more severe form of illness, and duration would likely lengthen. Despite this, the combined outcome would not be expected to influence model results, given the event's low likelihood.

Finally, this model is applicable to listeriosis and the consumption of RTE salad products only, but the ND eliminates the consumption of all fresh produce, as well as other high-risk foods, such as deli meat and unpasteurized cheese, to minimize risk from multiple pathogens, including nontyphoidal *Salmonella* and Shiga toxin (Stx)-producing *E. coli* (STEC) O157:H7. Produce, represented here by a model RTE salad, was the target restriction, given reported nutrition, quality of life, and compliance issues *(150, 156, 168, 169)*. Ideally, the model could be expanded to include other produce types to better depict patient outcomes. Listeriosis was chosen as the model's focus, given that it primarily affects the immunocompromised (e.g., cancer patients) and has the highest mortality rate of the three pathogens *(213)*. Because *Salmonella* and *E. coli* O157:H7 also carry substantial burden of disease *(214)*, incorporating risk assessments for these pathogens, in addition to *L. monocytogenes*, in a variety of produce would broaden the decision tool. However, because median listeriosis risk would have to increase to 2.18E-028 to 2.84E-01 to justify the ND, it is unlikely that including risk from *Salmonella* and *E. coli* O157:H7, as well as other produce types would sway the decision.

Finally, human decision making, especially during cancer treatment, is affected by a myriad of variables, given the vast range of experiences with treatment and life circumstances. Further, current risk-informed educational materials are incongruous and vary from institution to institution *(27, 32, 80, 229)*. For the information presented in this study to translate to patients, strategic, streamlined communication interventions must be considered.

3.5 Conclusions

The model presented in this study is the first to quantify cancer patients' health outcomes associated with the controversial neutropenic diet and less invasive alternatives. Due to the predominant effects of NEC, which was more prevalent on the ND, for fresh produce, the three ND alternatives were preferred over the ND in all age groups. Of the three, the SFH diet is recommended due to its high compliance rates and ease of implementation, though future work should evaluate acceptability and compliance barriers for cancer patients. Estimated listeriosis EVs were comparable to previous reports, but the lack of NEC disease burden data made full model validation difficult. More data are needed to ensure accuracy in this area. Switchover point analysis revealed that for all parameters but diet-based NEC risk, there were no plausible scenarios favoring ND use. Further investigation is needed to ensure this parameter's accuracy, as current data are from a pilot study. Overall, this study provides quantitative evidence supporting the adoption of produce-inclusive food safety diets and discontinuation of the ND during cancer treatment.

CHAPTER 4: PRODUCE SAFETY BEHAVIORS, MOTIVATORS, BARRIERS, AND BELIEFS IN PEDIATRIC CANCER PATIENT CARETAKERS

The decision model from Chapter 3 revealed that potential negative outcomes associated with neutropenic enterocolitis (NEC) far outweigh negative risks associated with listeriosis when rinsing and refrigerating fresh produce according to U.S. Food and Drug Administration (FDA) guidelines *(253),* concluding that the restrictive ND is rarely justified. Despite this, many hospitals still employ the ND, and provided produce safety information varies widely, leading to inadequate caretaker produce safety knowledge and guideline adherence. There is a clear need for improved methods for communicating produce safety guidelines; however, to ensure a strategic approach, factors contributing to cancer patients' food safety behavior adoption must also be better understood. Therefore, this chapter investigates the food safety beliefs, barriers, motivators, and behaviors of cancer patients' caregivers to satisfy Objective 2 of the dissertation. Results and recommendations from this study advance understanding of drivers of produce safety behaviors in cancer patient caretakers and support future endeavors to improve communication strategy interventions.

4.1 Materials and methods

All methods employed in this study were approved by the Institutional Review Boards of Michigan State University, Sparrow Hospital (Lansing, MI), and UnityPoint Health (Des Moines, IA).

<u>4.1.1 Study design</u>

The present work consisted of two segments: (i) a 10-minute quantitative online Qualtrics survey (Qualtrics, Provo, UT) (Appendix D), and (ii) a 30-minute, semi-structured, qualitative interview. The interviews utilized a third-party online platform that provided audio data as well as rough dialogue transcripts. Because previous works reported links between food safety practices and numerous demographic factors *(6, 138, 190, 193)*, quantitative survey independent variables were included to capture participant age, relation to the cancer patient, child's age at diagnosis, time since diagnosis, and number of days out of the last 30 the participant smoked cigarettes. Additionally, multiple choice questions were used to address gender, race, education level, household income, marital status, number of people living in the household, number of children under 18 living in the household, number of children over 18 living in the household, and food assistance programs used. Other independent variables included perceived child vulnerability, measured using a modified, 7-item version of the Child Vulnerability Scale (CVS) *(76)*, and household food security, ascertained using the U.S. Household Food Security Survey Module *(252)*. The modified CVS measure had a maximum score of 28 points, as opposed to the original 32, due to the removal of one item, "In general my child seems less healthy than other children". When scored proportionally to the original scale, scores of 9 or greater indicated high perceived vulnerability.

The dependent variable, total food safety score, was the reported frequency of 15 produce safety behaviors grouped into four different categories, measured via a 5-point Likert-scale ranging from "never" to "always". The survey contained a mixture of positive (e.g., rinsing fresh produce under running water) and negative (e.g., serving bruised/damaged fresh produce) behaviors. To preclude bias, reverse wording was only used in one instance, to depict a negative behavior *(231)*. For positive behaviors, scores ranging from 0 to 4 were ascribed according to responses of "never," rarely," "sometimes," "most of the time," and "always," respectfully. Scoring was reversed for negative behaviors. Individual behavior scores were summed to give the total food safety score. Behaviors were chosen for study inclusion based on endorsement by experts in cancer and food safety (Table 5).

Table 5: Produce safety guidelines included in quantitative survey

Behavior category	Produce safety behavior	Source
Storage and handwashing	Wash hands before handling fresh produce	*(9, 253)*
	Refrigerate fresh produce	*(9, 253)*
	Follow "use-by" dates on packaging	*(9)*
Produce preparation	Rinse fresh produce under running tap water	*(9, 253)*
	Rinse bagged/mixed salads	*(9, 253)*
	Dry rinsed fresh produce with a clean cloth or paper towel	*(254)*
	Peel fresh produce that can be peeled	*(160)*
"High risk" food avoidance	Avoid bruised/damaged produce	*(253)*
	Avoid non-thick-skinned fresh produce	*(255)*
	Avoid fresh produce pre-cut at the grocery store	*(9)*
	Avoid fresh produce at restaurants	*(9)*
	Avoid fresh produce from self-serve/bulk containers	*(9)*
	Avoid fresh produce from the school cafeteria	*(9)*
Cross-contamination	Wash cutting boards and utensils with hot, soapy, water in between using them for raw meat/poultry/fish and fresh produce	*(9, 253)*
	Use separate cutting boards for raw meat/poultry/seafood and fresh produce, or wash with hot, soapy water in between uses	*(9, 253)*

Willing participants (recruitment described in next section) completed an informed consent form detailing each study strand prior to beginning the survey. The goal of the quantitative study strand was to describe demographically the pediatric cancer patient caretaker population and determine the effects of the aforementioned independent variables on enactment of various produce safety behaviors. Participants completing the quantitative survey were given the option to complete the qualitative interview. Qualitative interview questions were semi-structured and anchored in grounded theory *(133)*. The interviewer's script included topics regarding experience with provided food safety information and its communication, with designated probes (Table 6).

Table 6: Question topics and probes utilized in qualitative interview

Question	Probes
Experiences with provided food safety information	Person providing information Independent research Choosing reliable information Inpatient vs. outpatient Information familiarity Timing Format
How to make decisions on what is safe for child to eat	What influences decisions Who influences decisions Responsibilities influence decisions Difficulty of decisions
Implementing new food safety behaviors	Altered view of child's safety Impacts on daily life
Helpful aspects of communication process	Photos/tables The way information was explained Individual explaining information
"Missing" or difficult to understand aspects of communication process	Barriers
Topics not included in the interview that are salient	-

Questions were expanded via probes or omitted depending on individual applicability. The ultimate goal of the qualitative study strand was to identify pediatric cancer patient caretakers' motivators, barriers, and beliefs for understanding and following produce safety guidelines, in order to recommend guideline communication improvements for use by healthcare staff.

Quantitative and qualitative data were mixed to better comprehend which produce safety guidelines were followed and the rationale behind decision-making. Both data strands were collected simultaneously, with results interfaced during interpretation. As such, this study followed a mixed methods convergent parallel design *(48, 137)*, steered by three research questions:

1) Do sociodemographic factors and perceived child vulnerability affect frequency of caretakers' produce safety behaviors (quantitative strand)?
2) How do specific contexts, beliefs, and intervention characteristics affect caretakers'

produce safety behaviors (qualitative strand)?

3) Do interviews with pediatric cancer patient caretakers explain relationships identified by question 1, or lack thereof (parallel convergence)?

4.1.2 Recruitment

Study inclusion criteria were being an adult (age 18 or older) caretaker of a pediatric (age 18 or younger) cancer patient who had undergone treatment within the past two years. Eligible participants also had to be from the United States or a country with similar food safety standards. Participants were recruited by consecutive convenience sample *(145)*, both in-person and online. Participants recruited in-person were contacted by collaborating healthcare workers with backgrounds in pediatric nursing while the participants' children were receiving treatment at either Sparrow Hospital (Lansing, Michigan), or Blank Children's Hospital at UnityPoint Health (Des Moines, Iowa). Healthcare workers disseminated study flyers with QR codes linking to full study information and informed consent documentation during routine appointments. Due to unprecedented workloads for said healthcare workers, some participants from Sparrow Hospital were approached by a trained study team member. Participants received a $10 e-gift card of their choice for completing the survey, and an additional $25 e-gift card for also completing the interview.

Participants were also recruited online using targeted Facebook advertisements (campaigns) and posts in pediatric cancer support Facebook groups. The campaign was built using Facebook Ad Manager and run through a Facebook page entitled "Food Safety for Pediatric Cancer Patients – MSU Study" for 36 days. The campaign's lifetime budget was $500, with daily costs optimized to maximize landing page (survey) views. This was determined by Facebook's Meta using machine learning and predicted engagement rates. Audience members were targeted based on age (18-65), demographics (parents), location (United States), interests (motherhood/fatherhood, childcare, etc.), field of study (pediatrics, cancer, or oncology), and job title (oncology RN or oncology nurse). Field of study and job title criteria were included to attempt to reach healthcare workers and initiate the IRB approval process for their hospital. Daily reach (the number of times the campaign was seen) was estimated to be between 2,100 and 6,100, with 5 to 25 clicks on the survey link.

Support groups were identified through Facebook's "group search" feature, using the terms, "pediatric cancer," "cancer caretaker," or specific types of pediatric cancer, such as "neuroblastoma" and "Hodgkin lymphoma," as well as "families" and "support". Per ethical recommendations, groups were only joined and IRB-approved recruitment flyer posted if group rules allowed research recruitment *(128)*. If necessary, group administrator approval of the recruitment flyer was obtained. Two months following the initial post, a second and final post was made in all joined groups. Finally, we contacted a childhood cancer collaboration network comprising parents, advocates, healthcare professionals, non-profit organizations, and corporations. They agreed to publish the study recruitment language in their weekly online newsletter for a duration of three weeks.

4.1.3 Quantitative strand analysis

Three shortened, pilot surveys were conducted with three participants. Given the short pilot survey duration (< 5 minutes), the CVS measure and Likert-scale produce safety behavior questions were added, along with minor word changes. Soon after deploying the pilot survey, many survey responses were found to be "bots" or duplicates. Qualtrics collects reCAPTCHA (Google, Mountainview, CA) and RelevantID (Imperium, Shelton, CT) data designed to detect duplicate and fraudulent responses and failing reCAPTCHA scores. Responses meeting these programs' duplicate/fraudulent criteria were removed. Responses with redundant IP addresses, duplicate or suspicious email addresses, survey time of less than two minutes, unvarying Likert-scale answers, or incongruous answers (e.g. annual income > $100,000 but uses food stamps) that were not flagged by these programs were manually removed *(270)*. Midway through data collection, an attention-check was added, as well as a statement in the informed-consent document stating suspicious and/or bot responses would not be compensated *(270)*.

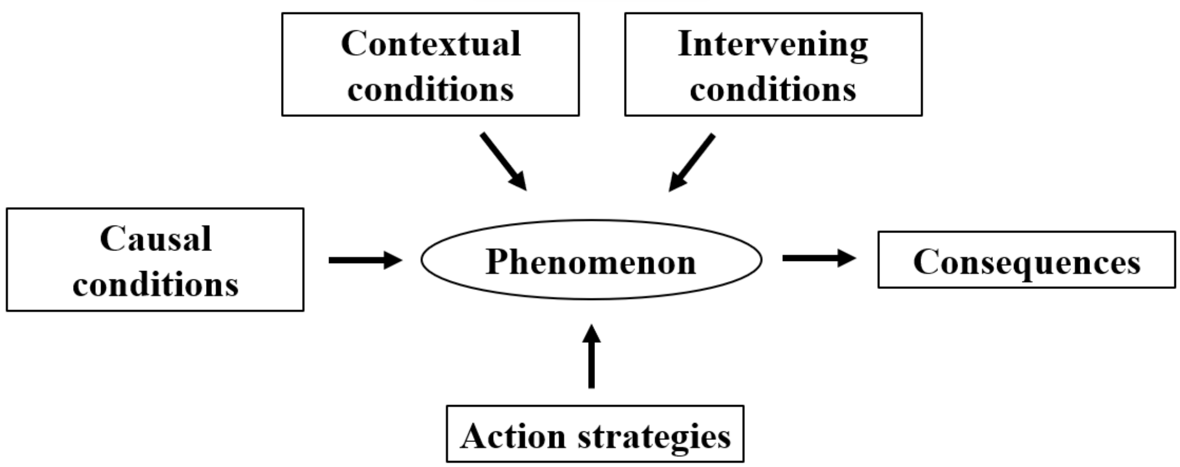
A total of 33 surveys were accepted, based on the above criteria. Quantitative analyses were performed in R version 4.0.5 *(197)*. Independent variables were audited for sufficient variation (most popular response comprising < 60% of total responses). Ineligible variables were not considered for further analysis. The answer "don't know/prefer not to answer" was chosen by two participants for income, and one to four participants for food safety behavior questions, with 14 total occurrences. Given the small total sample size (n = 33), these responses were replaced with the median of that question's remaining responses. Due to the small sample size, distributions violating the normal assumption, diverse data types (continuous, ordinal, categorical), and occasional outliers, descriptive statistics and a permutation test were used to characterize the sample and evaluate independence between the total produce safety score and independent variables *(102, 119, 120)*. Bivariate Spearman correlations and corresponding *p*-values for numeric independent variables and the total food safety score were calculated using the cor() and rcorr() functions in R.

The permutation test was conducted using the "coin" package in R with 10,000 iterations and blocking based on education level (Appendix E) *(120)*. In order to avoid inflating the likelihood of a Type 1 error, only the total food safety score was evaluated as a dependent variable, as opposed to each category's food safety score *(198)*.

4.1.4 Qualitative strand analysis

Qualitative interviews were conducted over Zoom, which automatically generated an initial verbatim transcript. One member of the research team performed a quality assurance step by reviewing these initial transcripts to correct automated transcription errors, redact personal information, and employ intelligent verbatim transcription *(157)*. Next, two researchers began to independently code following an abridged version of the paradigm model for grounded theory coding, typically including open, axial, and selective coding *(75, 235, 261)* (Figure 8).

Figure 8: Paradigm model, as employed in current study



Open coding and axial coding were combined, as the study's target domain was known; therefore, the study did not lend itself to a full-scale grounded theory analysis. During open/axial coding, co-coders read each response line-by-line and assigned each item into a subcategory based on its meaning. Subcategories were then sorted into one of the paradigm model categories: causal conditions, phenomenon, contextual conditions, intervening conditions, action strategies, and consequences, which were then defined in the present study context (Table 7) *(133, 235)*.

Table 7: Study-specific definitions for paradigm model categories

Paradigm category	Definition
Causal conditions	Perceptions/conditions/beliefs that influence a caretaker's produce safety decision
Phenomenon	Actions taken/not taken regarding produce-specific food safety guidelines
Contextual conditions	"Background" or socioeconomic conditions that allow the phenomenon to happen
Intervening conditions	"Outside" conditions and information that facilitate the phenomenon
Action strategies	Descriptors of produce safety strategies encountered by participant
Consequence	Confidence in produce safety decision and impacts on child's health

Following the first pass through the first 10 (of 19 total) transcripts, a third researcher with a qualitative research background was given four randomly selected sample transcripts to validate the range of subcategories and their category placement.

Next, the two original co-coders individually performed a second line-by-line pass of the first 10 transcripts, establishing concepts within each subcategory and which participants expressed them. Initial codebook inter-rater reliability was then calculated by determining whether concepts and their supporting participants matched. If there were any inconsistencies in concept names or supporting participants, coders were considered to disagree. Coders then provided evidential participant quotes to substantiate their codes and disagreements were resolved through discussion and consensus. The resulting codebook, with 100% inter-rater reliability, was utilized for the remaining 9 transcripts, with the addition of several emerging concepts. Second pass inter-rater reliability, for all 19 transcripts, was established via the same methods.

In a third and final coding pass, selective coding was implemented to construct an analytic theory, or "core category" *(133),* depicting the contexts, causal and intervening conditions, and strategies that lead to the central phenomenon concepts. This led to revision of categories and subcategories from open and axial coding, which were confirmed via consensus, for a final inter-rater reliability rating of 100%.

4.1.5 Integrating quantitative and qualitative data

Following individual strand analysis, results were merged via explanatory unidirectional framework *(174)*, with qualitative core category concepts explaining quantitative findings. Results were reported using a contiguous approach (strand results described in the same work, but different sections) *(71)*.

4.2 Results

4.2.1 Participant demographics

Thirty-three and 19 participants completed the quantitative survey and qualitative interview, respectively. Thirty-two participants were from the United States and one participant, who completed both the survey and interview, was from Singapore. The overwhelming majority of participants were mothers (31/33), married (29/33), white (29/33), had obtained an associate degree or beyond (30/33), had high food security (26/33) and had not smoked in the last 30 days (31/33) (Table 8).

Table 8: Participant demographic attributes (*n* = 33)

Attribute	Response	*n* (%)
Relation to patient	Mother	31 (94)
	Father	2 (6)
Highest level of education	≤ High school	3 (9)
	≤ Associate degree or trade school	5 (15)
	≤ Bachelor's degree	15 (45)
	≤ Graduate or professional degree	10 (30)
Household annual income	$30,000 - $39,999	1 (3)
	$40,000 - $49,999	2 (6)
	$50,000 - $59,999	0 (0)
	$60,000 - $69,999	1 (3)
	$70,000 - $79,999	2 (6)
	$80,000 - $89,999	4 (12)
	$90,000 - $99,999	2 (6)
	$100,000 +	19 (58)
	Did not respond	2 (6)
Marital status	Married	29 (88)
	Single	3 (9)
	Divorced/widowed	1 (3)
Race	White	29 (88)
	Asian	2 (6)
	Hispanic	1 (3)
	American Indian or Alaskan Native	1 (3)
Children under 18 in household	1	8 (24)
	2	12 (36)
	3	11 (33)
	4	2 (6)
Children over 18 in household	0	30 (91)
	1	2 (6)
	2	1 (3)
Smoked in past 30 days	Yes	2 (6)
	No	30 (91)
	Did not respond	1 (3)
Food assistance program	None	33 (100)
Food security status	High	26 (79)
	Marginal	5 (15)
	Low	2 (6)

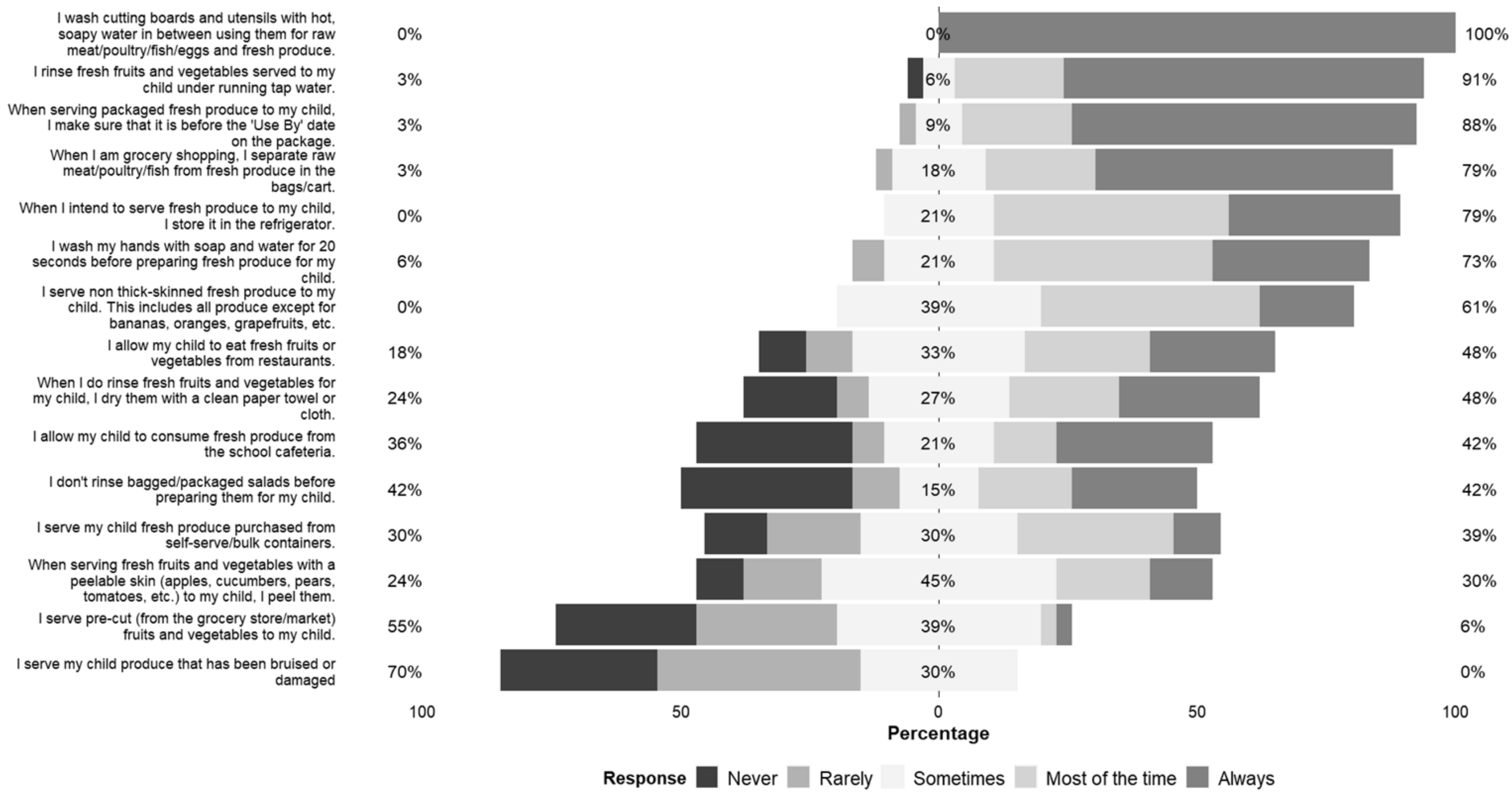
Participant ages ranged from 27 to 50, with a median of 41. Child's age at diagnosis spanned between two months and 17 years, though the median age at diagnosis was 4 years. The median time since diagnosis was 1 year and three months, with a minimum of three months and a maximum of nine years and six months. CVS scores ranged from 0 to 25 out of a maximum 28.

The median CVS score was 14, with 23/33 participants scoring in the high perceived vulnerability range.

4.2.2 Produce safety behavior frequencies

All participants reported always washing cutting boards with hot, soapy water in between uses for raw meat/poultry/fish and fresh produce (Figure 9).

Figure 9: Caretaker produce safety behavior frequencies. Left and right percentages are the proportion of negative and affirmative responses, respectively



The majority of respondents answered “always” for rinsing produce with running tap water, separating fresh produce from raw meat/poultry/fish in the grocery cart, and following “Use By” dates on packaged produce. Further, many participants answered “most of the time” or “always” for storing fresh produce in the refrigerator, washing hands with soap and water before preparing fresh produce, and serving produce other than those with a thick skin (bananas, oranges, etc.). Frequencies for consuming produce from the school cafeteria, rinsing bagged salad, serving produce from self-serve/bulk containers, and peeling applicable produce were evenly distributed across response options. For serving pre-cut grocery store and bruised/damaged produce, most participants answered “Never” or “Rarely”.

4.2.3 Quantitative analysis

Participant age and CVS score were significantly positively and negatively correlated, respectively, to child’s age at diagnosis (Table 9).

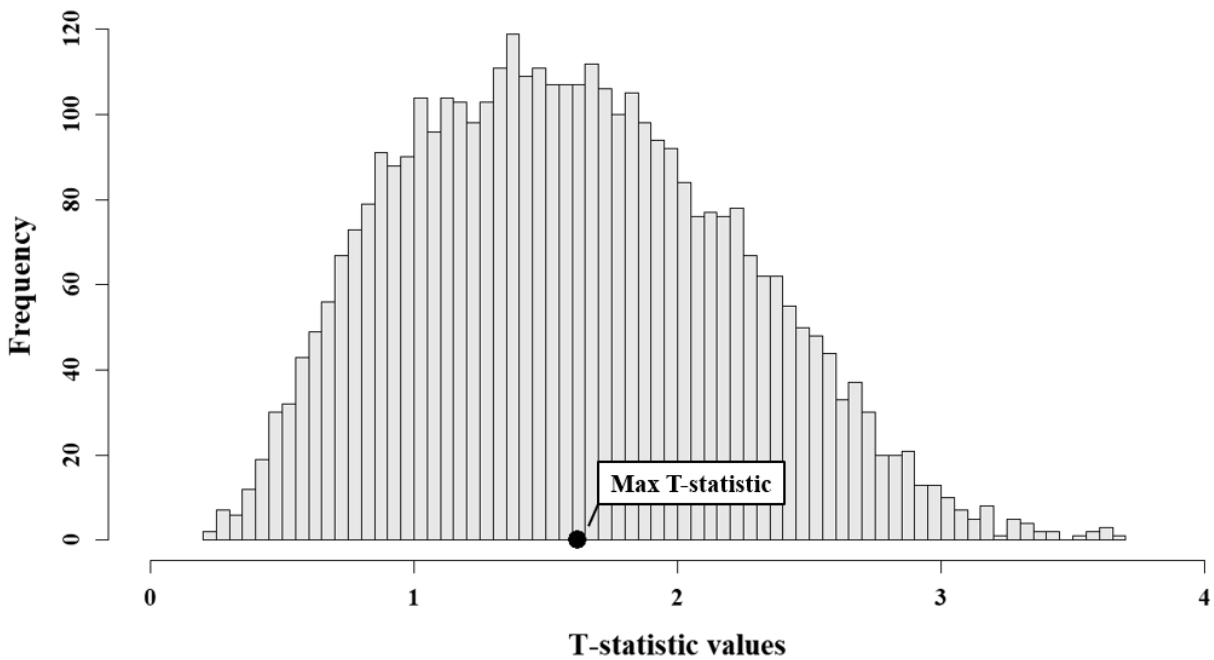
Table 9: Independent and dependent variable Spearman rank bivariate correlation matrix

Variable	Age	Child’s age at diagnosis	Time since diagnosis	Children in household	CVS score	Education
Child’s age at diagnosis	**0.63**					
Time since diagnosis	0.12	-0.23				
Children in household	-0.10	0.11	-0.10			
CVS score	-0.36	**-0.42**	0.24	-0.03		
Education	0.08	0.14	0.21	0.29	0.07	
Total produce safety score	0.11	-0.13	-0.18	-0.24	0.08	-0.08

*__Bolded__ items indicate $p \leq 0.05$

The permutation test indicated no significant effects of the model independent variables on the total food safety score, with maximum t-statistic of 1.62 and $p = 0.41$ (95% confidence interval 0.39 to 0.42) (Figure 10). As such, further analyses were not conducted.

Figure 10: Permutation test distribution



4.2.4 Qualitative analysis: Open and axial coding

Nineteen participants completed the qualitative interview. Theoretic saturation was reached, considering the addition of no new subcategories or concepts for the final participant, and only two new concepts for the second-to-last participant. The final codebook contained 165 unique codes, capturing a rich range of experiences (Table 10). Notably, due to the semi-structure interview format, a participant not mentioning a particular concept does not mean that they did not experience it; it simply may not have materialized in their particular interview. For instance, eight participants stated that their household food preparers employ strong washing practices. This does not mean that the other participants do not; they just did not state so in their interview.

Table 10: Open and axial coding results from qualitative interviews

Paradigm category	Subcategory	Concept	*n*
Causal conditions	Barriers	Cutting out food is challenging for the child	7
		Caretaker desires to improve child's quality of life by serving requested food when child is willing to eat	6
		Lacking time to research or implement guidelines	6
		Not enough information given	6
		Food safety took a back seat to other precautions (general infections, COVID, etc.)	5
		Parent's desire to serve child healthy foods (that are restricted)	4
		Lack of support for food-related tasks	2
		Cost of food not previously purchased	2
		Information lost between multiple hospitals	2
		Challenges related to relearning to eat	1
		Meal preparation for school becomes difficult	1
		COVID made it difficult to access food	1
		Child fed restricted food by hospital	1
	Motivators	Desire to protect child during vulnerable state	6
		No barriers to following guidelines	5
		Fear of infection or hospital admission	3
		Trust in information source (healthcare team, website, etc.)	3
		Recommended foods more budget-friendly than fresh produce/going out to eat	2
		Child adheres to new guidelines	2
	Child influences food safety decisions	Tastes for certain foods makes following guidelines either easier (cooked produce) or more difficult (restricted produce, like strawberries)	11
		Childhood pickiness makes following guidelines difficult	3
	Child's health during treatment drives behavior	Nutrition and eating main concern, not food safety	6
		Child's counts during treatment increase (low counts) or decrease (normal counts) motivation to follow guidelines	4
		Poor prognosis meant quality of life was main priority, not food safety	1
	Trust in food preparation drives behavior	Food where preparation is unknown is unsafe, and vice versa	4
		Low trust in food available to many people for a long time (e.g., buffet, cafeteria)	2
		Low trust in canned foods	1
		High trust in produce from farmers markets	1
	Perceived guideline rationality guides behavior	Understanding immunocompromised state improves guideline acceptance	6
		Understanding guideline purpose improves guideline acceptance	5
		Not understanding guideline purpose decreases acceptance and adherence	3
		Perceive guidelines as similar to previous pregnancy guidelines	2
		Conflation of "food safety" and perceived "healthy" foods	2

Table 10 (cont'd)

Paradigm category	Subcategory	Concept	*n*
Phenomenon	Food safety behaviors enacted as a result of child's condition	Wash produce thoroughly	11
		Peel fresh produce	5
		No berries	4
		Time limit for cooked leftovers	4
		Purposeful inclusion of fresh produce	4
		Follow all guidelines from healthcare team	3
		Canned produce	3
		Restrict food with uncertain preparation (friends/restaurants)	3
		Wash and peel bananas	3
		No salad bars	2
		Specialized antimicrobial produce spray	2
		No bruised/damaged produce	1
		Cooked produce	1
		Cooking area cleanliness	1
		Spray produce with vinegar	1
		Proper refrigeration	1
		Use disposable utensils	1
		Wash produce in salt water	1
	Food safety behaviors relaxed over time	Nothing bad has happened	5
		Only implement guidelines when counts low	3
		Did not find scientific support for specialized spray	1
	Food safety guidelines not followed	Berries eaten	2
		Leftovers eaten outside of time limit	1
		Produce not peeled	1

Table 10 (cont'd)

Paradigm category	Subcategory	Concept	*n*
Contextual conditions	Socioeconomic factors	Career in relevant field (nursing, dietician, nutrition, cook, etc.)	5
		Hospital area (rural, metropolitan, etc.)	2
		Food security	2
		Single mother	1
		Live-in helper for assistance	1
		Child attends private school	1
	Child-related factors	Multiple children	5
		Child's age (4 and under)	4
		Tube-fed	3
		Child's age (teen)	2
		Child's age (middle school)	1
		Child's age (elementary school)	1
Intervening conditions	Family practices	General food safety practices already in place	11
		Strong washing habits	8
		Guidelines not followed by caretaker/other family members	4
		Family members other than participant prepping food	2
		No buffets	1
		All organic produce	1
	Sought out formal information sources	Hospital/cancer center websites	2
		Medical journals/published research	2
		National cancer organization	2
		Friend that is dietician	2
		Friend that is nurse	1
		Local cancer services	1
		Government agency	1
		Personal dietitian/nutritionist	1
		Libraries	1
	Sought out informal information sources	Facebook groups	2
		Pinterest	1
		Natural health sites/blogs	1
		Personal experiences	1
		Friends in restaurant business	1
		Family members	1
		Acupuncturist	1
		Naturopath	1

Table 10 (cont'd)

Paradigm category	Subcategory	Concept	*n*
Action strategies	Produce safety guidelines given	Wash produce thoroughly	8
		Nutrition information given in lieu of food safety due to nutrition concerns	8
		Peel produce before consumption	7
		Do not consume berries	5
		Time limit for consuming leftovers	3
		Some wiggle room/grace with guidelines	3
		No fresh produce from restaurants	2
		No produce that interacts with chemo	2
		Only utilize guidelines when counts are low	2
		Maintain thorough handwashing	2
		Sanitize cooking area	2
		Wash fresh produce with vinegar	2
		Follow guidelines from medical/scientific organization (e.g., ACA)	2
		No salad bars	1
		No pre-packaged salads	1
		Properly refrigerate fresh produce	1
		Do not dry fresh produce after washing	1
		Consume fresh produce	1
		Wash produce in salt water	1
		Use disposable utensils	1
	Provided produce safety materials	Family received large binder or hard copy information	13
		No pictures or tables in materials	8
		Hard copy preferred – family could review at home	7
		Visual organization (bold, bullet points, tables, etc.) more effective for understanding than text alone	6
		Materials perceived as comprehensive	5
		More credibility for scientific/medical/government publications	5
		Families received personalized information	4
		Large binder perceived as useful handbook	3
		Mostly verbal information	3
		Lists of food to eat/avoid when neutropenic/not neutropenic helpful	3
		Less credibility if paid/funded	2
		Too much information in large binder	1
		Included additional credible resources	1
		Family appreciated receiving food safety equipment	1

Table 10 (cont'd)

Paradigm category	Subcategory	Concept	*n*
Action strategies	Healthcare team	Nurse/nurse practitioner	10
		Dietitian/nutritionist	10
		Doctor/physician	9
		Healthcare team availability for family questions improved perception	7
		Healthcare team perceived as credible, qualified	6
		Reviewing with healthcare team multiple times enhanced knowledge	5
		Healthcare team perceived negatively (unable to answer questions, condescending, glazing over, etc.)	5
		Nurse email/phone lines available at all times	4
		Guidelines only provided when asked for	4
		Healthcare worker tailored approach to individual family needs	3
		Healthcare team perceived as empathetic	3
		Outcome uncertainties not clearly communicated	2
		Oncologist perceived as too busy for food safety information	2
		Collaboration within healthcare team	2
		Healthcare team understaffed	2
		Social worker/in-home healthcare worker/other	2
		Healthcare workers providing information early on were perceived as open, forthcoming	1
		Specialized (pediatric oncology) nurses perceived as more credible than non-specialized	1
		Met with other family members who prepare child's food	1
	Information timing	Important to receive information at beginning, even if overwhelming	9
		Extensive information received at the beginning of cancer journey can be overwhelming	5
		Family received information at the beginning, then tapered off	3
		Follow through throughout treatment is helpful	3
		Difficulty remembering information from early days	2
		Spreading out information sessions over initial week is helpful	1
		Information should not be given until transition to home-based care	1

Table 10 (cont'd)

Paradigm category	Subcategory	Concept	*n*
Action strategies	Communication improvement suggestions	Designated food safety/nutrition healthcare team member (dietitian/nutritionist)	8
		Cancer cookbook for safe, child-friendly meals	2
		Revisit and consider recommendations over time and with age	2
		Information system for families	2
		Condense information	2
		Flowchart for when guidelines are important to follow	1
		Minimize food restrictions	1
		Inpatient menus include safe food options that are appealing to children	1
		Provide nutritional replacements for restricted foods	1
		Dietician/nutrition support at beginning of treatment	1
		Utilize table for food safety information	1
		Large children's oncology organization distribute reference guide	1
		Provide financial resources for food assistance	1

4.2.4.1 Action strategies

The most common produce safety guidelines given were thorough washing, peeling produce prior to consumption, and restriction of berries. Five families were instructed to only consume fresh produce that could be peeled. Eight families were given limited (4/8), or no (4/8) food safety information, as their healthcare team prioritized nutrition. Thirteen participants mentioned receiving a large "cancer binder," or other hard copy information, with seven caretakers preferring this format, and one caretaker displeased with the amount and relevancy of information:

- "It's my handy dandy cancer handbook. If I have any questions, this is where I can go to first".
- "And then again, having that written information was crucial, for when I came home and needed to review it, or review it with family members or others. That that was helpful".
- "We asked that if there was anything that she should or shouldn't be eating, or anything she should avoid or anything we should focus on, and they said, 'No; the name of the game is calories. She just needs calories'".
- "I think that giving people this big binder, with information that you may or may not need, is helpful for some people that want all that information. But for me, if it was like, 'Hey, you need to make sure you're cleaning off your vegetables,' and if there was a one-page sheet that said, 'Do this, this, and this, because this is very important,' that would have been a lot more helpful than giving me a book".

Five participants explicitly stated that they perceived materials they received to be comprehensive. Information from scientific, medical, or government sources was viewed as credible, as opposed to materials that were clearly paid or funded. Participants articulated that visual organization strategies, such as colored pages, bulleted lists, and “do’s vs. don’ts” tables were most effective for summarizing produce safety information, although eight participants noted that their materials did not include pictures or tables:

- “The way that the food was broken down in the categories of foods to avoid while neutropenic, and then foods that can be eaten when they’re not neutropenic…I thought it was great and easy to understand”.
- “There were tabs, but it was all color coded. So, all the food stuff is in bright orange. And so just having an easy way to find that, because you're not going to remember it all”.

Five participants expressed that receiving produce safety information alongside the barrage of new cancer diagnosis information is overwhelming, though nine caretakers indicated that this timing is necessary for those cooking at home. One participant, whose child was inpatient upon diagnosis, explained that the information was not an immediate priority and could have been postponed until commencement of home-based care:

- “It was a lot of information thrown at you at once and it's very overwhelming”.
- “I think that since we received this right at the time of diagnosis, that was very helpful, because then we were aware immediately of the different concerns and things that could impact my child's health and safety”.
- “But no, I don't think it was a great time, because there's a lot of other information you’re trying to absorb that has more far reaching implications - treatment choices and that type of thing, especially because the first week we were inpatient, and we weren't really doing any food handling for her”.

Healthcare teams disseminating produce safety information consisted of physicians, nurse practitioners, nurses, dietitians, nutritionists, social workers, and home-health aides. Six participants explicitly described their care team as credible or qualified, and others communicated a positive perception of healthcare teams that were available for questions (in-person or via 24/7 phone/email), were empathetic towards one's child, or adapted their communication approach to meet a family's needs. Additionally, because of the initial bombardment of information, reviewing food safety information with the team was crucial for understanding:

- "You knew that they were looking at our daughter as if she were their own".
- "I was the type of parent that wanted to really know it all, and our oncologist recognized that, and was really good and wasn't annoyed by it, and he would give me handouts."
- "I had two different people review it on the same day, and then again they hit on it a couple other times. I feel like I had a pretty good understanding of what they were recommending for him."

In contrast, two participants were also dissatisfied with outcome uncertainties, such as the possible need for a feeding tube, not being presented. Healthcare teams were also perceived negatively when they were unable to answer participants' questions, were difficult to reach, or participants felt they spoke condescendingly:

- "You know, feeling like they thought I was an idiot or something half the time, because of the way they talked to me about stuff".

Participants shared many ideas for improving their hospital's produce safety communication strategy, among them, the team including a designated food safety/dietitian contact, a cancer cookbook for safe, child-oriented meals, a coordinated information system for families, and to revisit food safety recommendations with age:

- “It would have been helpful to have a dietitian meet with us and kind of talk through, ‘Here's your food safety,’ in regards to being able to ask questions like, ‘Well, if I can't have berries then what's a good replacement?’”.
- “She gave us all these guidelines, but it would have been good to come up with recommendations of, “this might be a good lunch. This is a good dinner option that doesn't have any of this...”.

4.2.4.2 Phenomenon

Participants recounted enacting food safety behaviors, reducing vigilance over time, and noncompliance to provided guidelines. The most-reported behavior was thorough washing of fresh produce, followed by peeling, avoiding berries, reducing leftover storage time, and purposeful dietary inclusion of fresh produce. Caution diminished with time if nothing bad (foodborne illness or generalized infection) happened to the child, or absolute neutrophil count (ANC) increased. One participant stopped using an advertised antimicrobial produce spray after finding it had no scientific support. Avoiding berries, peeling, and strict leftover time limits were guidelines reportedly broken by participants:

- “So, I aired on the side of caution of saying, you know, “We're gonna wash these fruits and vegetables. We're going to peel them”.
- “Now that I know that his counts and everything are fine. I don't double wash food anymore”.
- “But if he specifically said, “I really want strawberries,” then I would buy them”.

4.2.4.3 Causal conditions

One of the driving factors for caretaker behavior was their child’s health during treatment. When children tolerated treatment well and had high counts, food safety vigilance was decreased. On the other hand, low counts motivated caretakers to comply with food safety guidelines. Six participants explained that nutrition and eating in general was their or their healthcare team's main objective, as malnutrition was an imminent risk. Lastly, one participant was guided to allow their child to eat an unrestricted diet, due to a poor prognosis:

- "I feel like some of those restrictions are unnecessary when his counts have been so good, we could relax on those, and we have".
- "The only time I was concerned is when his blood counts were super low".
- "We just wanted her to eat anything. We tried anything."
- "We were so worried about holding back and not letting her experience things because we were told it was such a limited time".

Furthermore, caretakers faced numerous barriers when implementing food safety guidelines. First, eliminating certain foods, as in restrictive NDs, was challenging for their child, and many caretakers also disclosed wanting to allow their child a restricted, healthy item, particularly during treatment when the child was having difficulty eating. Multiple participants felt that they did not have enough information to make an informed produce safety decision, and others lacked time to research and/or implement the guidelines. For some families, preventing COVID-19, nosocomial, or port infections took top priority over food safety. Two participants also missed out on food safety information, as their treatment was split between multiple hospitals, and others expressed lacking support for their new food safety tasks, and an added financial burden for food they hadn't purchased previously (e.g., smaller portions to limit storage time):

- "It seems like as soon as you tell somebody that this is off the table that's what they want".

- “I wasn't going to not give her fruits, if that's what she wanted to eat at the time. Her eating habits have been very up and down, so if there's something that she's really liking and it's healthy, I'm going to give it to her”.
- “But we weren't actually given any explicit instructions by the oncology team”.
- “Washing everything was very time consuming”.
- “I think we were so worried about, not a foodborne illness, but something else that she would catch because she had a port during that time”.
- “I did feel like I lacked support in that aspect because I was then trying to keep track of what she was getting by tube feed, plus what she was taking orally”.

Conversely, some caretakers identified the desire to protect their child during a vulnerable time, facing no systemic barriers in following the guidelines, complete trust in their information source, fear of hospital admission, lower cost of recommended foods, and their child’s willingness to adhere to the recommendations as factors that motivated them to follow food safety guidelines. Examples of such statements include:

- “Well, you become exceptionally protective, and I will admit that”.
- “Overall, I don't think that the guidelines are difficult to maintain”.
- “No, I follow the guidelines they provided 110% because I don't want to go to where she's admitted unforeseen”.

Participants also reported instances of their child influencing their ability to comply with produce safety guidelines. For instance, it was difficult to comply with food restrictions when a child craved the restricted food, and easy when the child disliked the food:

- “I had one day that sticks out, I was picking raspberries of the neighbors, and I look over and she's just cramming them in her mouth *(laughs)*”.

- “My daughter doesn’t love raw vegetables anyway, so that’s not a terrible thing for us; we just have to cook her food”.

Similarly, caretakers of “picky eaters” faced additional struggles when trying to comply with both guidelines, and their child’s preferences:

- “…and my daughter's already a picky eater, so it made it worse for me at the time”.

Another factor impacting food safety behavior adoption was perceived guideline rationality. Overall, understanding their child’s immunocompromised status, or rationale behind a guideline led to greater acceptance, whereas a lack of understanding decreased caretaker acceptance. Some participants also recalled the food safety guidelines they were given during pregnancy and were able to appreciate the premise of their child’s guidelines. Lastly, two participants conflated the rationale behind the produce safety guidelines (foodborne pathogen risk) with chemical and nutritional food safety risks:

- “I did like that the information that was given also had reasons why some of the things were in place, because I know for me personally, it's easier to follow rules when I know why they are that way”.
- “I think it doesn't make sense, because the banana is inside the skin, but we have to wash it, and then we give it to her”.
- “When I got home, though, we did switch to a lot of organic produce items, and grass-fed chicken and what not”.
- “Well, for example, when his blood counts were low, I looked up what fruits can he eat to boost his white blood cell count the most”.

Finally, trust in a food item’s preparation influenced food safety decisions. Caretakers had lower trust in foods that had unknown preparation, or that were accessible to many people, and greater in trust in foods they knew the preparation of:

- "…but if I'm going to a friend's house and they're having a group of people over, and they have food that they've just prepared and it's out, that is something that I would be more comfortable with. I know who prepared it, I know how long it's been out, I know when it was prepared.".
- "To me…buffet, no. It's not just the food at that point; it's all the people going and touching things and coughing on it".

4.2.4.4 Contextual conditions

There were several socioeconomic factors that facilitated phenomena. Five participants specified that they had previous food safety knowledge from a related career, such as nursing or the culinary industry. Rural or distant hospital locations also hindered resource access and utilization. A wide range of food security circumstances were depicted, encompassing unrestricted access to safe food, private schools with small cafeterias presumed to be safe, access to farmers markets, rural locations, and food assistance. Availability of domestic support was also compelling, with participants reporting situations ranging from a single mother lacking any support to a family employing a live-in helper for domestic tasks:

- "Being that I'm a family nurse practitioner, I'm generally giving guidance to families on how to feed their kids".
- "And I really didn't want to make another trip. So yeah, we would typically just try to schedule everything we could in one day".
- "I'm a single mother, so I can't get these extra added…I can feed my daughter what I can afford".

4.2.4.5 Intervening conditions

Family practices employed prior to a child's diagnosis altered the transpiration of phenomena. The majority of participants stated that they had pre-existing strong washing practices and/or general food safety precautions (e.g., proper refrigeration, avoiding cross contamination, etc.). Four caretakers added that they only utilize the recommended produce safety guidelines for their child with cancer and prepare meals separately for themselves and other family members. Two participants noted that other individuals, such as grandparents or domestic helpers assist in food preparation:

- "I always rinse off the berries and stuff and wash lettuce. It's what I've always done".
- "The guidelines of washing the banana, for example, before eating, my child follows it, but I don't".
- "It was difficult if someone else was watching her, like a grandma, or a friend, because it was a lot of having to tell them, "Hey, you really have to be careful with this," so it was difficult to rely on others because I can't expect them to remember all that information".

Several caretakers sought out information beyond that provided by their healthcare teams. Such information was gleaned from both formal (medical/scientific journals, national cancer organizations, cancer center websites, friends working as nurses, etc.) and informal (acupuncturist, blogs, Pinterest, Facebook groups, etc.) sources:

- "I generally only listen to published papers in mediated peer reviewed sources. So, if I'm able to find something that's on NIH, or something that has been published by a credible scientific source…".
- "I listen to a lot of blogs, follow a lot of natural health sites".

4.2.5 Qualitative analysis: Selective coding

Following selective coding, key phenomena archetypes emerged, sharing aspects of causal, contextual, and intervening conditions, and action strategies (Table 11).

Table 11: Selective coding results

Archetype	Description	Definition	Shared characteristics	*n*
1	Enacting FDA/ACS* recommendations or similar	Participant increased vigilance with hand and produce washing, hygiene, use-by dates, leftovers, kitchen sanitization, proper refrigeration, and preventing cross contamination	Produce safety materials perceived as comprehensive, important to receive information early on, appreciated hard copy, visual information, understood guideline rationale	2
2	Above and beyond FDA/ACS recommendations	Participant enacted behaviors from (1) plus produce restriction, vinegar sprays, saltwater washes, disposable utensils, etc.	Restrictive guidelines provided by healthcare team, (only peelable fruits, no berries), additional washing procedures, child's taste for restricted foods was a barrier, important to receive information early on	8
3	Nutrition focus	Participant behaviors are centered around treating or preventing their child's malnutrition	Child in danger of malnutrition, tube-fed child, healthcare team provides nutrition information in lieu of food safety guidelines	5
4	Seeking information beyond microbial food safety	Participant concerns and behaviors are directed towards chemical hazards and using food/nutrition to fight/prevent cancer	Dissatisfaction with healthcare team, desire for dietitian/nutritionist team member, desire for holistic/natural approach, feel not enough information was given, strong washing practices already in place	2
5	Participant discontinues new produce safety habit	Participant enacted new guideline(s), then discontinued and returned to typical behaviors	Strong washing habits and general food safety practices already in place, implemented new guideline for a short time, then discontinued	2

Because participants recounted many experiential aspects in the same interview, the archetypes were not mutually exclusive, as some behaviors and communication strategies fell under numerous themes.

The first archetype consisted of participants who were provided, and began to enact, produce safety guidelines similar to those recommended by the FDA and/or American Cancer Society (ACS). These include directives such as thoroughly washing produce, proper refrigeration, no cross-contamination with raw meat/poultry/fish, but do not exclude fresh produce, except for raw sprouts and produce from bulk containers or buffets *(9, 253)*. Two individuals fit this descriptor, with both reporting washing produce thoroughly and generally improved food safety vigilance, and feeling informed about the new guidelines:

- "Yes, I think some of it is just basic food safety. I think there were some that were a little more specific, or maybe a little more careful in handling of different fruits and vegetables. But most of it felt like, 'just be really extra vigilant in washing what you have'".
- "Probably washing everything that they eat, because we do a lot of raw stuff. So I remember being like, 'gotta wash'".
- "I thought it was pretty clear and comprehensive"

The second archetype, consisting of those who were instructed to follow guidelines beyond those of the FDA and ACS, was the largest. These participants received the same guidelines as archetype 1, plus additional instructions to restrict certain produce perceived as more risky (non-peelable produce, berries, etc.), use only disposable utensils, or wash produce with solutions other than water (vinegar, soap, or saltwater). Many of these participants noted time and their child's desire for restricted foods as barriers to following the guidelines, and agreed that information is important to receive early on:

- "So that's what they recommended to me when I was serving our food, to serve throw away plates, throw away cups, everything".
- "Yeah, there were definitely certain things that she couldn't eat - anything, any vegetable or fruit that couldn't be peeled, she couldn't eat it"

- “I had a spray bottle with vinegar at the sink, and everybody just knew, and it said, ‘for REDACTED’s fruits and vegetables’”.
- “You can't peel a strawberry, and I feel like explaining the ‘why’ or explaining what was the concern with it was helpful for me to then be able to try to explain when my daughter is throwing a fit because she wants some strawberries, why we can't do it, even though she really still didn’t understand at 5 years old; she just wanted some strawberries”.

Participants categorized into the third archetype received limited food safety information, as nutrition, or quality of life in the case of a poor prognosis, was the healthcare team’s primary focus. Instead, caretakers were encouraged to increase their child’s caloric intake by any means possible. Three of five of these participants’ children had a feeding tube for a period. These caretakers reported few barriers to following their nutrition instructions:

- “I don't think anything relative to food safety per se…she was two when she was diagnosed, so they were so worried she was going to lose all kinds of weight because she was sedated for radiation. So, it was more about making sure that we gave her enough - like we put butter on everything”.
- “But honestly, the focus mainly was on tastebuds changing and being able to get more of a high caloric diet as opposed to the safety aspect of things”.
- “At the time, when we were talking about trying to get her to eat again, we were kind of open ended in that, the doctors felt like if there was a desire to eat, we were going to try to make sure that she was able to eat”.
- “Anything she could eat, yeah, and they never really said anything about what not to eat, because we were just happy if she was eating because she lost 40 pounds within two months. That's why she got the feeding tube”.

The fourth archetype was composed of two participants who had strong washing practices or adhered to standard good safety guidelines prior to their child's diagnosis, but were presently searching for information beyond microbial food safety, such as chemical hazards, organic practices, and using food or nutrition to treat and prevent cancer. They both shared that lacking information was a barrier to their decision making. Both individuals felt that their healthcare team did not address their concerns with these issues when discussing food safety, were dissatisfied, and turned to alternative sources for information:

- "I have been not having great experiences with doctors lately. But you ask them a question, and if it doesn't relate to something that they're doing right now, they don't know".
- "That kind of thing, for instance, reading about not drinking sugar is just a big deal, and that really hit me on making changes there".
- "They told me that having a pediatric cancer was not because of food choices. And so, they told me that he should just eat whatever he wants except raw food. But when I did my own research, I did it for two reasons - how to prevent Hodgkins in the future. And basically it was to stay away from any lunch meat, sausages, be more of a plant based diet…I was also looking up, 'how do I increase his blood counts using food?'"
- "I don't think the oncologists really care about the nutritional side. They don't think that nutrition had anything to do with this cancer".

The fifth and final archetype was composed of two participants who attested to previously enacting general food safety practices (as recommended by the FDA/ACS), and did not permanently adopt new, more restrictive guidelines, such as peels or washing with specialized sprays. Caretakers either discontinued a new guideline because their child was doing well with treatment, or because they did not find scientific support for said guideline (specialized produce spray), expressing belief that their typical food safety practices were adequate:

- "But my son has been very healthy, thankfully, throughout the entire treatment, and so we have kind of an adopted a 'you can have whatever you want' policy for him, so he is eating all of the things he's not supposed to be eating as far as the precautions at this point".
- "My wife and I both practice general, common sense food safety, food handling techniques. I have worked in restaurants before and in professional food service settings. So, I take from that ServeSafe knowledge".
- "No; we started at the beginning using a REDACTED spray at the recommendation of a family member. After research that I did, I thought that was maybe more marketing than anything else. So, we just carefully wash and rinse herbs, and scrub harder rind produce - limes, lemons, oranges".

4.2.6 Combining quantitative and qualitative results

As previously stated, quantitative and qualitative data were combined following individual analysis via convergent parallel design. Grounded theory coding, particularly the selective coding phase, provided insight into the non-significant relationships in the quantitative data strand. The identified archetypes suggested that produce safety behaviors were dependent upon various motivators and barriers, including materials received, child's health, food safety behaviors previously enacted, and concerns beyond microbial food safety. These hidden variables' absence from the quantitative survey explains the lack of any relationship between independent variables and produce safety scores. To investigate this relationship more accurately, future quantitative works should include measures for hidden variables identified in the qualitative strand of this study. Lastly, given the small overall sample sizes (33 and 19 for quantitative and qualitative strands, respectively), and small archetype sizes (minimum two participants), it was not statistically sound to conduct further quantitative analyses blocked by archetype.

The majority of caretakers responded affirmatively to performing produce safety behaviors currently recommended for the general population by the FDA, with the exception of drying rinsed produce with a clean cloth or paper towel. Responses became more mixed and negative for behaviors recommended specifically to cancer patients, such as avoiding pre-cut fresh produce, fresh produce from bulk containers, restaurant, the school cafeteria, washing bagged salad, and peeling fresh produce. Given the results from the qualitative study strand, the likeliest explanations may be caretakers not receiving these guidelines due to nutritional concerns, the caretakers' desire to serve their child healthy and/or requested foods, lacking time to implement the additional guidelines, and concerns for other issues being more top-of-mind. Despite the qualitative strand revealing that five caretakers were told to restrict the behavior, no respondents answered "never" or "rarely" for serving non-thick-skinned produce (all produce except for bananas, oranges, and grapefruits), a behavior that is restricted by certain cancer centers but not the FDA or ACS. This suggests that, in addition to the barriers above, overly restrictive guidelines contribute to noncompliance.

4.3 Discussion

This study provided, for the first time, a quantitative and qualitative account of produce safety beliefs and behaviors in pediatric cancer patient caretakers. Previous works focused quantitatively on behaviors, attitudes, acquisition habits, and broad education needs of patients *(66, 158, 159, 190)*, but did not include or investigate caretaker beliefs and behaviors for produce-specific guidelines during cancer treatment.

4.3.1 Quantitative results

While the hidden variables uncovered in the qualitative analysis likely led to the independence of the independent and dependent variables, there were significant correlations between a few independent variables. Caretaker age was positively correlated with child's age at diagnosis, which is intuitive (e.g., an older parent may have an older child, and the converse), and has been reported previously *(44)*. Alternatively, CVS score was negatively correlated with child's age at diagnosis (e.g., younger children were perceived as more vulnerable). This finding is novel, though it has been hypothesized previously *(246)*. Nevertheless, CVS scores reliably predict acute health behaviors, and not preventative behaviors, which may further explain the lack of relationship with produce safety scores. Therefore, this information would be best used for acute conditions, such as malnutrition or present foodborne illness.

4.3.2 Guidelines provided and self-reported produce safety behaviors

Nine of 19 participants (47%) received restrictive produce safety guidelines typical of the ND, which is comparable to Braun's 2014 survey of ND use, which found that 36 to 78% of pediatric oncologists restrict the consumption of fresh fruits and vegetables, berries, and produce that cannot be peeled *(27)*. This is notable, as following the 2014 study, numerous professional oncology organizations, such as the American Society of Clinical Oncology (ASCO) and Infectious Diseases Society of America (IDSA), published guidelines opposing ND use *(243)*. Contrarily, eight participants first received nutrition-focused information to either treat or prevent weight loss and malnutrition, with four receiving general food safety information later. This dichotomy in hospital food safety prioritization is best illustrated by one participant seeking treatment at two hospitals; one hospital gave nutrition information to treat their child's weight loss, and one restricted consumption of non-peelable produce during neutropenia. Overall, these results imply that updated produce safety guidelines have not been implemented in many hospitals, and that standardization could result in improved care through consistent messaging and therefore reduced barriers to compliance.

Self-reported produce safety behavior frequencies were analogous to those previously described. Affirmative responses for rinsing fresh produce, washing cutting boards and utensils with hot water and soap after contact with raw items, and handwashing prior to food preparation, were selected by 73%, 91%, and 100% of caretakers in the present study, respectively, compared to 90%, 87-88%, and 89-95% in previous works *(66, 158, 159, 190)*. Considering that these studies included minimal caretakers, and even fewer caretakers of children, the similarities indicate that pediatric caretakers may not exhibit different behaviors from cancer patients themselves, or adult caregivers.

4.3.3 Produce safety barriers, motivators, and beliefs

Caretakers' main barriers for following restrictive guidelines were potential quality of life and nutrition issues for their child, and time constraints, whereas main motivators for compliance were materials received, their inclination to protect their child during a vulnerable time, and to avoid infection/hospital admission. McGrath and Moody found similar sentiments relating to children's displeasure with food restrictions and caretakers' desires to help their loved ones eat a healthy diet *(156, 168)*. Another common barrier to adopting food safety guidelines was the greater urgency to protect against COVID-19 or port infections. Several study participants' children underwent chemotherapy during the 2020-2021 pandemic, and it is natural and anticipated that these concerns overshadowed food safety during that time.

The five identified archetypes revealed shared motivators for produce safety behaviors.

Perceived child's susceptibility was a key motivator for archetypes 1 and 2, with low counts, known immunocompromised status, fear of hospitalization, and comparison of immune system health to that during pregnancy all improving guideline acceptance and adherence. Normal blood counts and/or the absence of foodborne illness issues led some caretakers to relax guidelines. Caretakers matching archetype 3 communicated that the increased susceptibility to and severity of malnutrition promoted guideline adherence. Despite this discernible trend in perceived susceptibility and behavior, CVS score did not significantly influence produce safety score. Again, it can be surmised that this may be due to the quantitative survey primarily testing produce safety behaviors recommended to the general public, as opposed to restrictive behaviors uncovered in interviews, and excluding the hidden variables uncovered in qualitative analyses. Future work in this area should include such behaviors to better understand this relationship.

The type of guidelines received by the caretaker was also a determining factor in caretaker behavior. Archetype 1 caretakers likely did not enact restrictive guidelines because they were not provided them, whereas archetype 2 caretakers were. Archetype 3 caretakers were mainly provided nutrition information; this, combined with their child's health during treatment, guided behavior. Caretakers matching archetype 4 were provided limited information, and sought guidance elsewhere, implementing behaviors beyond those of microbial food safety. Lastly, archetype 5 caretakers received guidelines exceeding FDA/ACS guidelines, which were implemented initially. Standardizing guidelines may reduce the present variability in behaviors.

Finally, consistent with previous literature *(20, 215, 257)*, participant self-efficacy played a role in guideline cooperation, with five participants expressing that they found no barriers to implementing the recommended food safety behaviors, or that the behaviors were easy to implement. These participants all adhered to two or more recommended food safety guidelines.

Further, four of these five participants, including both archetype 5 participants, reported previously performing some level of food safety behavior in their home and were confident in their abilities to perform these behaviors. Therefore, although the archetype 5 caretakers received restrictive, new, produce safety information, they may have persisted in prior behaviors because of existing self-efficacy. Inversely, one participant self-described as a single mother lacking support and knowledge for food safety tasks disclosed difficulty observing recommended guidelines. These findings suggest that self-efficacy should be an objective for updated produce safety communication tactics.

4.3.4 Recommendations for produce safety communication

The first step in adequate produce safety communication is ensuring the guidelines themselves are sound. Previous decision modeling demonstrated that the ND is seldom warranted *(96)*; yet, produce-restrictive guidelines were reported by many participants, with the most disclosed study barrier being the difficulty of excluding foods for their children. As such, this work's primary recommendation is to rescind the use of the ND in favor of standardized use of data-driven, produce-inclusive alternatives, such as the FDA or ACS guidelines.

This study identified five archetypes of caretaker produce safety behaviors. Across most archetypes, perceived guideline rationality, hard copy materials with visual organization, receiving information early in treatment, access to healthcare workers for questions, and the desire to protect their child improved acceptance of or adherence to guidelines. However, despite the efficacy of and strong preference for visual organization among participants, almost half of the participants did not receive materials that included images and tables. These aspects should be incorporated into future produce safety communication strategies, with the condition that inpatient families receive the information once they are responsible for meal preparation, per one study participant.

Aside from those associated with unnecessary produce restriction, which may be resolved by utilizing appropriate guidelines, shared barriers included intervention cost, insufficient information, and time constraints for researching and implementing guidelines. Insufficient information and limited time to research can be addressed by including additional resources participants deemed credible (government organizations, cancer centers, or peer-reviewed sources). Perceived intervention cost and limited time to implement guidelines may be managed with self-efficacy interventions, which have been shown effective for food safety behaviors *(20, 257)*. Participants proposed an intervention in the form of a cookbook tailored for children with cancer. This cookbook could feature cost-effective, quick recipes, accompanied by relevant produce safety guidelines at every stage, aimed at fostering self-efficacy. One hospital also gave families thermal bento boxes to maintain the temperature of foods brought to the hospital. Interventions such as these ensure that caretakers feel confident in their abilities to serve produce safely and should be considered for widespread use.

Another broadly suggested improvement was having a designated dietitian/nutritionist healthcare team member. This would be particularly advantageous for those resembling archetypes 3 and 4, as they described a need for nutritional information beyond what a doctor could provide. Moreover, only one participant received explicit guidance emphasizing the nutritional benefits of increased fresh produce intake. Several such benefits have been published *(33, 52, 131)*, and given that participants were motivated by guideline rationale and the desires to protect their child and serve healthy foods, a dietitian/nutritionist team member sharing these benefits should become a central aspect of future communications.

4.3.5 Recruitment notes

Caretaker strain is a well-documented challenge for cancer patient/caretaker recruitment *(110, 116, 199)*. This study was no exception; the quantitative study strand was challenged by inefficient recruitment, resulting in an insufficient number of participants to conduct regression analysis and the burden arising from an overwhelming influx of bot and counterfeit responses. Recruitment was conducted via on-site approach by researchers and/or healthcare workers, Facebook advertisements and support group posts, and cancer collaboration network newsletters, with Facebook advertisements and cancer collaboration network newsletters yielding zero participants. Low yield has been previously reported for similar methods to the latter two *(240)*. Facebook advertisements further encumbered researchers by generating thousands of bot and counterfeit responses. Unless the desired study population can be better targeted beyond a broad age range and parent demographic, this approach is not recommended for future researchers.

On-site and Facebook support group recruitment were more prosperous, though time consuming recruitment strategies. Sygna et al. reached a similar conclusion for on-site recruitment of cancer patients and their caretakers *(240)*, though noting greater success with opt-out (potential participants must deny involvement, as opposed to actively joining the study) strategies. Opt-in strategies, as employed in this study, led to a relatively homogenous sample in terms of gender, marital status, race, education, and food security. This under-recruitment pattern aligns with that reported by Trevena et al. following opt-in recruitment *(249)*. Therefore, while this study further contributes to the growing body of works successfully using Facebook support groups to recruit hard-to-reach populations *(13, 239)*, it is recommended that opt-out recruitment strategies are utilized when feasible.

4.3.6 Limitations

This study was primarily limited by its small, demographically similar sample size, which prevented the use of more sophisticated quantitative analyses, such as regression, and decreased generalizability of results. The unvaried sample population predominantly comprised educated, middle and upper class, food-secure mothers, which is not representative of the Midwest or United States. Use of food assistance programs and food insecurity have been linked to food safety knowledge, and may play a role in produce safety frequencies *(190)*. Additionally, including these perspectives in qualitative analyses could expand understanding of produce safety motivators, barriers, and beliefs, and better guide communication improvements. Although saturation was reached, a greater qualitative strand sample size would be desirable to maximize archetype bin size and allow for further statistical comparison between qualitative and quantitative study strands. Currently, the smallest archetypes consist of two participants, which is not enough to make robust conclusions. Thus, recommended recruitment strategies should be used to increase qualitative and quantitative strand sample size and scope, and corroborate present findings.

Because grounded theory, as utilized in this study, is an inductive method (developing broad conclusions from specific data), conclusions may not be generalizable to food safety scenarios and populations other than cancer patients/caretakers and fresh produce. Nevertheless, sharing these findings is imperative, as such work has never been completed for this population, who lack standardized, data-driven resources. Finally, present intervention recommendations require prototyping and efficacy testing by trained scientific communicators prior to implementation. This verification is essential, considering the small sample sizes in this study.

4.3.7 Positionality

This study's first author conducted all interviews, performed all transcriptions, and led each round of qualitative analysis, with secondary investigation and verification being provided by the second author and third-party codebook reviewer. These secondary analyses confirmed that findings and conclusions were consistent with raw data. Nevertheless, in this statement of positionality, the first author recognizes that their education and experience in food safety and engineering research may affect qualitative data analysis and conclusions. Stating this possible bias source maintains integrity of the research process.

4.4 Conclusions

This study is the first to consider, quantitatively and qualitatively, the barriers, motivators, and beliefs regarding produce safety behaviors in the target population. Frequencies of FDA/ACS recommended produce safety behaviors were determined and were not significantly related to demographic characteristics or CVS scores. Grounded theory coding led to the categorization of five caretaker archetypes, grouped by commonalities in child's health/perceived susceptibility, guidelines provided, and self-efficacy. The largest archetype employed overly restrictive ND behaviors, which were associated with many barriers. The existence of archetypes highlighted the need for standardized, produce-inclusive guidelines and communication strategies, for which this study provided feedback-based recommendations. Further validation of study findings is needed with a larger, more representative population, and future work should entail prototyping and evaluation of proposed communication strategy recommendations. Ultimately, this work presents information necessary for modernization of this aspect of cancer treatment, and improved outcomes for patients and caregivers.

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CHAPTER 5: A PROTOTYPED COMMUNICATION INTERVENTION FOR PRODUCE SAFETY IN CANCER PATIENTS

Because the Health Belief Model, which asserts that health behaviors are guided by an individual's perception of susceptibility, issue severity, behavior barriers and benefits, cues to action, and self-efficacy *(39)*, has been useful in predicting food safety behaviors and advising interventions *(111, 158, 215, 262)*, it was combined with discoveries from the qualitative interview study to guide development of a produce safety communication intervention prototype for pediatric cancer patient caretakers. Note that while the communication objectives and prototype described here are expected to be effective and appreciated by pediatric cancer patient caretakers, testing and analysis by trained scientific communicators is needed for verification.

5.1 Communication objectives

Establishing communication objectives is the first step to developing strategic interventions *(22)*. Given the results of the decision model and produce safety behavior and belief studies, the goal of this intervention is for pediatric cancer patient caretakers to de-adopt the ND, and to instead focus on safe food handling with produce inclusion. Literature and present results suggest that the objectives outlined below will be effective in supporting communicators in reaching this goal *(22)*.

<u>5.1.1 Trustworthiness beliefs</u>

Having a trustworthy healthcare provider can serve as a cue to action within the Health Belief Model framework *(24)*. Communicator trustworthiness can also impact perceived outcome severity, which is crucial for communicating risks associated with foodborne illness and a diet lacking in nutrients *(209)*. As such, one goal of this intervention is to increase perceived trustworthiness of intervention communicators. Perceived competence, willingness to listen, and empathy can all impact whether an audience trusts a communicator. Specifically, perceived competence affects perceived persuasiveness; perceived willingness to listen improves perceived decision legitimacy; and conveying empathy reduces an audience's desire to impede a communicator *(22)*. In this case, the individual carrying out the intervention must successfully embody these traits to adequately function as a cue to action for the target behavior. These beliefs must be considered in the administration of the proposed intervention.

5.1.1.1 Willingness to listen/perceived openness

Cancer patient caretakers have frequently remarked that they prefer to receive information from a healthcare provider who they perceive as willing to listen *(132, 134, 153, 173)*. For instance, Kirk et al. interviewed patient/family dyads who identified "giving time," to listen to patients and answer questions, as a key aspect of patient/provider communication *(134)*. Likewise, Zachariae et al. reported that patients rated importance of "attentiveness" (measured by items such as "The physician gave me the opportunity to ask questions") highly, with attentiveness significantly predicting patient satisfaction for both personal contact and handling of medical aspects *(274)*. Schmid-Büchi et al. also found that when asked about unmet psychosocial needs, relatives of cancer patients express the need for healthcare professionals to listen to them, and the need to be included in treatment choices *(216)*. Similarly, Kimberlin et al. reported that caretakers who felt they did not have a voice in decision-making experienced a sense of hopelessness *(132)*.

These ideas were empirically observed in this study's pediatric cancer caretaker interviews. Caretakers who described their healthcare team answering questions, or providing them with requested materials had positive perceptions of the healthcare team and ultimately described greater satisfaction with the produce safety strategy, whereas caretakers who felt outcome uncertainties were not openly communicated, or who felt brushed off when they tried to ask questions (such as archetype 4 caretakers) reported negative experiences with their healthcare team.

5.1.1.2 Benevolence/empathy

Benevolence, caring, or empathy, are personal characteristics highly conducive to patient/caretaker satisfaction and effective communication *(274)*. Zachariae et al. indicated that, in addition to attentiveness, affective empathy (as rated by items indicating understanding of patient feelings) was linked to higher patient satisfaction and decreased emotional distress *(274)*. In the present study, participants that perceived healthcare workers as empathetic (e.g., wishing the best for their child or treating the caretaker's child as their own) depicted greater trust in their healthcare team. Patients and caregivers reported feeling dismay and becoming withdrawn or switching providers when they perceived communication to lack empathy *(35, 132)*. These behaviors diminished trust in healthcare providers *(153)*. On the other hand, providers that displayed their personality were perceived as down-to-Earth and easy to communicate with; in fact, patients seemed to appreciate interactions with such providers *(132)*.

5.1.1.3 Competence/ability

Competence, or ability of the healthcare team to provide quality care, is of utmost importance to cancer patients and caretakers. On a scale of 1 - 5, with 5 representing "extremely important," caretakers of cancer patients rated the need "Be assured that best possible care is being given" the highest or second-highest of all considered needs, at 4.91 - 4.97 *(152, 185)*. In qualitative interviews, one participant recounted trusting specialized pediatric nurses more than general nurses, and numerous participants suggested that produce safety information would be better communicated by specialists, such as dietitians or nutritionists.

Patients and caretakers in several studies reported that the use of medical jargon was confusing to them *(35, 132, 134)*. This can pose a problem, as in advisory forums, medical professionals who frequently use jargon are perceived as higher in expertise, but lower in benevolence, integrity, audience accommodation, and overall credibility *(276)*. Participants in qualitative interviews echoed this idea, noting that visual organization instead of "giant medical words" made materials easier to interact with.

5.1.2 Self-efficacy beliefs

As indicated within the Health Belief Model framework, self-efficacy beliefs play a role in chosen health behaviors *(39, 223)*. A meta-analysis reviewing experimental studies (participants assigned to either a control or attitude/norm/self-efficacy intervention with measured behavior change) found this to be supported, with 109 interventions having an overall Cohen's *d* of 0.65 *(223)*. Compellingly, self-efficacy interventions for encouraging behaviors had a greater effect size than self-efficacy interventions discouraging behaviors. Therefore, it may be beneficial for self-efficacy interventions in the present study to emphasize capability to perform improved food safety recommendations, such as rinsing, peeling, and/or flash boiling raw produce, and proper storage techniques, and inclusion of nutrient-dense, fresh produce, as opposed to dissuading caretakers from the ND. This was effective experimentally, with participants who did not perceive barriers to the produce safety behaviors frequently reporting adopting them. Effect sizes were also larger for "disease management" and "infrequent prevention" behaviors than for "frequent prevention" behaviors (d = 0.7, 0.68, and 0.41, respectively). Unfortunately, food safety behaviors are recurrent, so a smaller behavioral effect is expected, unless self-efficacy interventions successfully frame produce safety behaviors as being part of cancer management.

In a more recent study specific to safe food handling practices (clean, chill, cook, and separate – the same practices recommended by the FDA *(253)*), van Rijen et al. employed a behavioral intervention involving participants action planning, goal setting, and committing to a goal *(257)*. Not only did this significantly increase perceived and actual self-efficacy (as measured by perceived time and knowledge to perform clean, chill, cook, and separate behaviors), but there was a direct effect for self-efficacy and food safety behaviors, which was amplified when the behavioral intervention was specific to food safety. In a meta-analysis, Young et al. also found that self-efficacy beliefs, as measured by confidence in ability to execute a behavior, perceived skills, and perceived control over home food safety, were consistently strongly correlated to food safety behaviors, except for adequate cooking *(272)*, a variable behavior hypothesized to be dominated by personal tastes. This was unique compared to other psychosocial variables, and as such, self-efficacy will be a large focus of the proposed intervention. This will not only reaffirm those already confident in their produce safety abilities, but will assist those who, like some participants, expressed lacking support for food-related tasks.

Finally, improving a caretaker's self-efficacy beliefs can benefit both the caretaker and the child. In a study on parent caregivers and their 3 to 12 year-old children undergoing cancer treatment, Peterson et al. found that increased caregiver self-efficacy for explaining procedures to their child, and overall self-efficacy, were significantly correlated to reduced caregiver distress and increased child cooperation during procedures *(195)*. While the food safety diets considered presently are not necessarily "procedures," this sentiment may be inclusive for a variety of unfamiliar protocols.

5.1.3 Sharing knowledge

As previously discussed, cancer patients and their caretakers have insufficient food safety knowledge of home food safety practices *(66, 158, 159, 190)*. The current literature suggests that imparting food safety knowledge is likely to increase the occurrence of various food safety behaviors *(272)*. In a meta-analysis on determinants of safe food handling, Young et al. found that knowledge of home safe food handling practices and common foodborne pathogens significantly predicts cross-contamination avoidance and personal hygiene *(272)*, two food safety behaviors recommended for cancer patients *(253)*. However, the relationship did not hold for all food safety behaviors, such as adequate cooking and time-temperature control *(272)*. As such, it is not recommended that communication interventions focus only on boosting knowledge. Fortunately, combining this approach with increasing perceived risk is evidently more effective, as those with compromised health status are more likely to seek food safety knowledge and adopt corresponding behaviors *(273)*. Again, this concept was illustrated empirically in the qualitative interviews; caretakers who learned that their child was susceptible to foodborne illness or nutritional issues described adopting new behaviors.

Regrettably, there seems to be an optimism bias (one's tendency to overestimate their probability of having a positive outcome *(222)*) related to home cooking. This can lead to decreased diligence performing food safety behaviors *(182)*. Cancer patients state high levels of food safety knowledge (grouped in the categories of general food safety, cross-contamination, food preparation, food storage, and clean-up), despite self-reported home cooking knowledge and behaviors being misaligned with FDA standards *(190)*. For example, although 91% of study participants report knowing how to keep food safe at home, 60% thought that wiping a cutting board used to cut raw meat with a wet sponge was enough to prevent cross-contamination, and 54% incorrectly answered that hamburger color could be used to ascertain if the meat is fully cooked. Additionally, Fein et al. reported that survey participants were twice as likely to believe it is "very common" to get sick from eating at a restaurant, as opposed to food from one's home

(70), despite the opposite being true, with up to 50% of cases estimated to originate in consumer homes *(200)*. This, combined with similar results from Nesbitt et al. *(181)*, and Evans et al. *(67)* suggest that unless the optimism bias is addressed, shared knowledge in this space may not have large effects on behavior. Provided food safety materials and those sharing them should emphasize often disregarded standards, like the recommended time for washing hands, and ensure that caretakers understand these steps.

5.1.4 Communicating risks

Perceived risk, comprising perceived severity and perceived susceptibility, has been shown to significantly affect food safety behaviors, such as hazardous food avoidance and safe food handling/preparation *(40, 111)*. In an investigation on food safety behaviors at tailgate events, Hanson et al. determined that perceived severity of foodborne illness is significantly associated with sanitation and cross-contamination behaviors *(111)*. This sentiment was shared by Yeung and Morris, who invoked the example of Mad Cow Disease (a foodborne illness with severe consequences but very low occurrence) to highlight the imbalanced influence outcome severity holds over food safety risk perception, compared to susceptibility *(271)*. This is analogous to the present scenario; overly restrictive guidelines are utilized and adhered to due to fear of severe foodborne illness, despite its low occurrence. Communication interventions should therefore leverage this dissertation's produce safety diet decision model, which demonstrates that compared to NEC, the likelihood of severe listeriosis is too low to justify use of restrictive diets.

On the other hand, Fischer et al. found that while individuals were amenable to adopting behaviors to reduce foodborne illness risk, their diligence was guided by the behavior's practicality and effect on food taste *(73)*. Even so, participants contended that they would be inclined to take extra care when preparing food for a vulnerable/high-risk group, demonstrating that susceptibility plays a role in food safety behavior when preparing food for others, as a caretaker may. This was corroborated in the qualitative interviews, where participants reported that understanding their child's increased risk of foodborne illness led them to enact produce safety behaviors. Those who believed their child was susceptible to malnutrition also took steps to prevent it. Correspondingly, in a review, Young and Waddell determined that a role preparing food for a dependent in a high-risk group is a strong facilitator of food safety behaviors *(273)*. However, the optimism bias present when cooking in one's own home leads to decreased risk perceptions and neglect of food safety behaviors *(70, 273)*, with consumers believing their own probability of illness is low and outcomes may not be severe. Evans et al. determined that increasing individuals' risk perception for their current unsatisfactory food safety habits can increase food safety thoroughness *(67)*. Therefore, it is necessary for caretaker communication materials to emphasize risks associated with lapses in expected behaviors, along with their child's increased foodborne illness susceptibility and the severe consequences of infections like listeriosis.

5.1.5 Communicating benefits

Produce-inclusive food safety diets, such as the FDA's recommended diet, which encourages overall safe food handling (SFH) *(253)*, have several physiological benefits, as described in Section 2.2.1 Reduced intake of micronutrients). Briefly, benefits that are pivotal to communicate are reduced bacterial overgrowth *(33)* and bacterial translocation *(52)*, and decreased treatment delays, infections, days in the hospital, and treatment toxicity *(131)*. A produce-inclusive safe diet also has quality of life benefits. Adolescents undergoing cancer treatment identified health and normalcy as their biggest hopes *(1)*. Moody et al. found that children believe that maintaining a normal childhood and pleasure in food are important to them, and that unrestricted diets could aid in social and peer integration *(168)*. A produce-inclusive food safety diet would allow children with cancer to maintain as "normal" of a diet as possible, while upholding these benefits. Finally, fresh fruits and vegetables, because of their cold and odorless qualities, are often desired by patients suffering from chemotherapy-induced nausea and altered taste and smell *(117, 168)*. Berries, which are frequently restricted on NDs, were highly requested by caretaker's children in the present study. Therefore, aside from specific nutritional benefits, raw produce can also act as a welcome and reliable source of sustenance during treatment. These benefits were missing from most produce safety materials received by caretakers in this study and must be highlighted in proposed interventions.

5.2 Tactics for communicating with caretakers

5.2.1 Reported barriers

Caretakers of pediatric cancer patients face numerous emotional and financial impacts that must be considered throughout communication. First, negative emotions associated with diagnosis and treatment, such as anxiety, shock, uncertainty, and fear, can intensify, with 40-50% of parents of diagnosed children matching diagnostic standards for Acute Stress Disorder *(127, 194)*. As in the present study, these feelings can be overwhelming at the beginning of treatment, when families are bombarded with decisions and information. Financially, diagnosis often led to employment disruptions, decreased income, perceived financial burden, and reduced competitiveness in a caretaker's profession *(205)*. These effects are exacerbated for caretakers of a young child, a child with hematological cancer, or low socioeconomic status *(205)*. Caretaker and patient stress can be compounded by food and eating issues *(156, 168, 265)*, with caregivers feeling accountable for a patient's nutrition *(265)*. Similarly, one common barrier in the present study was caretaker disconcertment when their children with low appetites (caused by cancer treatment) requested a restricted food *(97)*. Lastly, cancer patient focus groups reported that barriers to adopting food safety behaviors were personal preference (such as for raw sprouts), not knowing which foods are dangerous (e.g., which dairy products were made with unpasteurized milk), not knowing why certain foods are dangerous, fear of missing out on healthy foods, and inconvenience*(158)*. Again, this was seen in the present interview study; many caretakers allowed their children to consume restricted produce or felt that following the guidelines was inconvenient at times.

To meet the aforementioned communication objectives, it is crucial to address these barriers in the proposed intervention. For example, the intervention should highlight the ease and simplicity of food safety behaviors, most of which are likely already performed. It could also be useful to state the low cost of food safety technology, such as refrigerator thermostats and meat thermometers, or even provide these items, as one caretaker reported their hospital doing. Additionally, although caretakers stated that information received early on can be overwhelming, many agreed that the produce safety information is needed at this point, but that having hard copy materials available for later review is key.

5.2.2 Tactics praised by caretakers

In previous qualitative studies, caretakers and family members expressed that more information would help them understand how to aid in treatment and contribute to decision-making, and that they do not always have access to such information *(61, 153, 173, 206)*. Specifically, treatment information, including options, side effects (such as what to expect of the patient at home), and prognosis was highly sought-after *(153, 173)*. This could be facilitated through certain tactics; for instance, relatives were grateful when healthcare workers asked them if the rendered aid was useful, and if they needed more support or education *(266)*. As suggested in the current study, provided materials could also include additional credible information sources.

Healthcare workers were perceived by relatives and caretakers as willing to listen when they incorporated time for questions and answers, and did not rush *(134)*. Patients and caretakers perceived providers as caring or empathetic when they showed their personality, for example by making jokes, and also through physical gestures such as handholding, or sitting with the patient *(132, 134)*. In terms of competence beliefs, patients primarily trusted physicians, nurses, and dieticians with providing food safety information, but also viewed healthcare workers with an "appropriate" or "scientific" background as credible *(158, 159)*. Likewise, in the current study, most healthcare workers were perceived as credible, but many caretakers specifically requested the aid of a dietitian or nutritionist. Video and written materials were also deemed acceptable, provided the authors had notable scientific or professional credentials *(159)*. Because food safety training varies across healthcare professions *(29)*, it is important to ensure that involved employees are informed on current practices. It is also advantageous to use language similar to that of the audience, as accommodative language increases perceived communicator credibility *(276)*. Using careful judgement is consequential for this tactic; in qualitative interviews, one caretaker felt disrespected when providers spoke to them "like they thought I was an idiot". Alternatively, providers who recognized caretaker needs and tailored their approach to meet them were highly regarded.

As long as they were not esoteric, written communications (pamphlets, brochures, and fact sheets) and websites were favored by patients *(158)*. Aspects of materials that patients found appealing included a title specific to cancer patients, guides for dining out, picnics, and cold storage, tables with substitutions for risky foods, and having all necessary food safety information in one document *(158)*. These aspects were praised in the present study, as well as color-coded pages. Additionally, patients shared that foodborne illness and death data increased their risk perception *(158)*. These findings should be considered when developing targeted intervention strategies for this group.

Although most patients in previous studies did not receive food safety information until they were neutropenic, they preferred to receive it promptly after diagnosis, and in their treatment clinic or facility *(158, 159)*. However, patients who attended a "fast-track" type clinic (diagnosis and 4-6 consultations in one day) only remembered 43% of lifestyle recommendations; this was significantly associated with anxiety observed following the consultations *(183)*. Similar studies tracking retention rates after long consultations also found low retention rates (as low as 20.5%) for information provided immediately after diagnosis *(82, 125)*, and emphasize the need to minimize information unloaded at diagnosis *(69)*, due to the shock reaction from patients. Thus, literature suggests it is crucial for communication interventions to reduce anxiety and optimize retention, possibly by categorizing food safety information or discussing it on a separate date *(125)*. However, many participants in current qualitative interviews desired to receive the information earlier. This approach may need to be combined with retention-optimizing tactics, like follow-up appointments or hard copy information for reviewing. Overall, there is a reliable body of work on general communication with cancer patients that, combined with the ongoing study targeted towards caretakers and food safety, can help guide communication intervention improvements.

5.3 Communication intervention prototype: Explained

Generally, the behavioral goal this intervention focuses on is adequate produce safety with dietary inclusion of fresh produce (rejection of the ND). Specifically, this means encouraging the produce-applicable behaviors listed in the table below, as encouraged by the FDA and ACS, and divided into comprehensible categories by The Partnership for Food Safety Education (Table 12) *(192)*. Note that many of these behaviors are recommended for everyone, regardless of immune status, and should be somewhat familiar.

Table 12: Produce safety guidelines for intervention prototype

Behavior category	Produce safety behavior	Source
Select	Avoid bruised/damaged/expired produce	*(253)*
	Avoid pre-cut, bulk, and self-serve produce	*(9)*
Clean	Wash hands with soap and water for 20 s before handling fresh produce	*(9, 253)*
	Rinse fresh produce under running tap water; scrubbing firm-skinned produce with clean brush, even if skin will not be eaten	*(9, 253)*
	Dry rinsed produce with clean paper towel or cloth	*(254)*
Separate	Use separate cutting boards for raw meat/poultry/seafood and fresh produce, or wash with hot, soapy water in between uses	*(9, 253)*
	Separate raw poultry/meat/fish from fresh produce in grocery carts/bags	*(253)*
	Wash plates that previously touched raw meat/poultry/seafood/eggs, with hot water and soap before using for fresh produce	*(253)*
Chill	Keep refrigerator at 40°F or below	*(9, 253)*
	Refrigerate fresh produce within 2 hours	*(9, 253)*

Aligning with the Health Belief Model, the key objectives for meeting this goal are to instill the following beliefs: 1) Food safety communicators are empathetic, willing to listen, and competent (relevant cue to action), 2) Caretakers have self-efficacy, in terms of time, skills, and resources, to perform key food safety behaviors (self-efficacy and barriers), 3) Not implementing the behaviors increases the risk of foodborne illness, such as listeriosis, which can be severe, and excluding produce can increase risk of neutropenic enterocolitis, which can be severe (susceptibility and severity), 4) Implementing the advised behaviors is beneficial by increasing intake of micronutrients that support digestion and the immune system, and helps maintain normalcy and quality of life (benefits). This will be done through the use of a produce-safety guidebook distributed and explained by a nurse/dietician/nutritionist familiar to the caretaker. Specific tactics that will be used to facilitate this intervention are described in detail below.

5.3.1 Source tactics

As indicated in the literature review and qualitative interviews, physicians, nurses, and dieticians, and nutritionists are seen as the most credible sources for food safety information *(158, 159)*. However, because ability to explain nutritional benefits of consuming produce and having availability for questions and answers are critical for trustworthiness beliefs, and considering requests from caretakers, dieticians would be the optimal candidate for this. Specifically, in our qualitative interviews with caretakers, caretakers expressed preferring pediatric nurses and dieticians for food safety and nutrition information, as they had more "boots on the ground" experience with what small oddities are considered normal or urgent, and were more familiar with their children *(95)*. Therefore, the ideal information source would be pediatric dieticians; however, given hospital staffing shortages, all dietitian specialties, or pediatric oncology nurses will suffice. Finally, having a "scientific" source made written materials appear more credible to patients and caretakers in both the literature and current qualitative interviews, so sources like the CDC and FDA are cited in provided materials *(159)*. This will help ensure that caretakers view this intervention as a trustworthy cue to action.

5.3.2 Behavior tactics

When dieticians present the material, they should be aware of several behaviors that are likely to increase perceptions of benevolence, willingness to listen, and competence. First, when speaking with caretakers and patients, communicators should try to show their personality, and discern when supportive physical touch, such as a hug or handholding, may be appropriate. These behaviors can increase perceptions of caring *(132, 134)*. Additionally, communicators should not behave in a rushed manner. Medical professionals who sit, as opposed to standing when communicating with patients/caregivers, are perceived as spending more time at the bedside, while those who stand are perceived as rushing *(238)*. Sitting when speaking with a patient/caregiver can also boost patient/caregiver perceived understanding and overall perception of the interaction *(238)*. Therefore, to boost credibility and strengthen the cue to action, dieticians sharing the information are instructed to sit with the patient while they correspond. To ensure that caregivers feel that the communicator is willing to listen, the communicator is also advised to allow time for caregiver questions and concerns, and specifically ask if the given information is helpful and if more support is needed *(266)*. Also, to promote empathy and overall credibility perceptions, communicators should strive to mirror the language used by caretakers, avoiding medical jargon *(276)*.

5.3.3 Content and styling tactics

The sections below refer to the prototype produce safety guidebook, available in Appendix F.

5.3.3.1 Cover page

The guidebook cover page features a bright, lively color scheme of green, blue-green, and white. Because it has been shown to elicit pleasant emotions such as comfort, relaxation, and calmness, and has the most positive perception of all principle hues, green was utilized as the main color on the guidebook cover page *(129)*. Likewise, blue-green can evoke similar emotions, and also happiness *(129)*. The tagline reads, “Simple steps to prevent foodborne illness while maintaining nutrition”. The use of the word “simple” is intended to instill self-efficacy, while the focus on maintaining nutrition addresses an immediate concern of many pediatric cancer patient caretakers – getting their child to eat enough nutrients *(265)*.

Because the use of images increases likelihood to read communication materials and can also enhance recall, many stock images are used throughout the guide *(121)*. The images used are intended to make safe food preparation seem approachable and straightforward, with an overall positive affect. It is important that images/photos included in the guide do not evoke negative emotions, which can decrease enactment of the target behavior, especially since morbidity/mortality rates are used later in the guidebook to increase risk perception *(121)*. The cover page presents a large photo of a mother and child preparing food together. They appear relaxed and content; it is expected that this will conjure positive emotions, like comfort and hope, and cultivate self-efficacy (e.g., "Look how easy this is"). Finally, the MSU logo is used to establish credibility by confirming a "scientific" source. The tactics utilized on this page support the self-efficacy and cue to action (source credibility) tenants of the Health Belief Model.

5.3.3.2 Why is food safety extra important for you?

This section began with facts on foodborne illness, hospitalization, and death rates in the general population, then explains that many of these cases occur in individuals who have a compromised immune system, which is the case for cancer patients. These facts were chosen because foodborne illness/death statistics were shown to increase risk perception (both susceptibility and severity) in patients *(158)*. Additionally, the CDC was cited to further establish competence. The second text block on this page details the science behind why cancer patients have an increased foodborne illness risk, given that many cancer patients and caretakers are not aware that they face this risk. The materials approach risk perception from several angles, citing both personal health/illness and treatment delays as risks of foodborne illness. This may also help caretakers, such as those categorized as archetype 4, understand the importance of microbial food safety during cancer treatment. Because overwhelming an audience with risk information can lead to fear and an undesired avoidance response, the last message on the page suggests, in a hopeful tone, that eating safe, healthy foods can support the immune system *(22, 179)*. The intent of this was to implore the viewer to continue to read the materials.

The images shown on this page were chosen to maintain attention and highlight key points. For instance, the first photo, a boy holding his stomach, emphasizes the consequences of foodborne disease. The second photo, two individuals pointing at a food chart, with a mango nearby, underscores the important role fruits and vegetables can play in maintaining a healthy diet and supporting the immune system during cancer treatment. The tactics utilized on this page supported the susceptibility, severity, cue to action, and benefits tenants of the Health Belief Model.

5.3.3.3 You can keep nutritious foods safe!

The title of this section was selected to instill self-efficacy, in terms of skill and perceived behavioral control, in the reader. Yes, they can serve nutritious, safe food! The first portion of this page specifies some ways in which produce may become contaminated, then reminds the reader that if they follow the recommended food safety behaviors, their child will be far less susceptible to foodborne illness. This focus on minimizing already low susceptibility helps correct the inflated food safety risk perception based mainly on severity. The next heading reads, “The Good News,” switching to a hopeful tone regarding the ease of food safety behaviors. Additionally, self-efficacy is instilled with the phrases “You can still serve your child fresh produce,” and “a few simple steps,” to empower readers to engage in the suggested behaviors. Finally, a nod to the American Cancer Society adds credibility.

Next, four food safety steps are described, each with two to three corresponding behaviors and explanations for their utility. Again, the goal of sharing these explanations is so that caretakers are informed on how produce becomes contaminated and can adjust their own practices. As found in this work’s qualitative interviews, caretakers were more accepting of guidelines when they understood background rationale. For the “Select” safety step, consisting of three different behaviors, two images (one “good” and one “bad” in terms of following each food safety behavior) are used with the text “this not that” to illustrate what applying each behavior looks like. Green and orange text is used to insinuate good and bad practices, respectively. Caretakers in the present study found similar visual organization tactics useful and preferable to paragraph format. The “Clean” food safety step includes a flow chart with images depicting each step of the cleaning process (handwashing, rinsing produce, drying produce, and eating produce). These images help impart knowledge on how this process should occur, and the inclusion of a child happily eating fresh produce may provoke positive affect.

The “Separate” step includes three target behaviors, and three diagrams of proper/improper refrigerator layouts. Green checkmarks and the thumbs-up emoji depict correct behaviors, while a red “X” symbol and thumbs down indicate incorrect behaviors. Similar to the smiley face used as good feedback in energy efficient household electric bills, it was hypothesized that the green check and red “X” would mimic norms and lead to increased behavior adoption *(217)*. The “Chill” step includes images portraying timely refrigeration of cut produce, as well as a green “Helpful Hint” with accompanying thermometer photo. This box aims to promote self-efficacy by underscoring the low price and widespread availability of refrigerator thermometers. Lastly, this page contains a “Food Safety Recipe” for a kid-friendly food, tacos. The recipe includes food safety instructions for each of the four discussed areas, for instance, “Rinse lettuce and tomato under running water”. By following the recipe, or even reading it carefully, viewers will hypothetically develop self-efficacy for adjusting their own recipes to the recommended food safety guidelines. This feature was requested by two caretakers in my qualitative interviews.

Finally, the page “How will these practices affect your child” shares benefits and risks associated with following/not following the food safety guidelines. Similar to the “Select” section, the benefits section is headed in green, and the risks section is headed in orange, to evoke positive and negative affect. Several types of benefits are listed, from quality of life, to reduced risk of foodborne illness, intestinal effects, and treatment delays. Listed risks range from severe foodborne illness, with mortality rate listed, delayed treatment, medical/missed work costs, and decreased nutrient intake. This frames the issue from multiple perspectives so that the reader is more likely to connect with the materials. The bottom half of the page includes resources for more information, such as the CDC foodborne illness outbreak list, giving readers the means to keep up to date on ongoing food safety issues. Lastly, a photo of a child cooking with a smile instills hope and overall positive affect. The tactics utilized on these pages support the self-efficacy, susceptibility, severity, cue to action, barriers, and benefits tenants of the Health Belief Model.

5.3.4 Timing tactics

In the qualitative interviews with caretakers in the present study, a common theme was a desire for produce safety knowledge as early as possible, unless the caretaker's child would be inpatient. However, long consultations or combining multiple specialist visits increases anxiety and leads to reduced knowledge retention *(69, 82, 125, 183)*. Therefore, in order to increase the saliency of this cue to action, I propose that the food safety information consultation occurs at an appointment (with one of the child's assigned dieticians/nurses) within the first few weeks of diagnosis, if the caretaker's child will be outpatient. In any case, hard copy materials should be provided at this meeting so that caretakers can review concepts they may not remember. At this time, the dietician/nurse can read over the materials with the caretaker (which should take ~15 min) and answer any immediate questions.

5.3.5 Channel tactics

Because literature reports caretakers preferred simply phrased written materials *(158)*, and the interviews in the present study revealed a preference for hard copy, visually organized information, the channel chosen for this intervention is a physical, printed, guide, with typed information and photos. The guide is sized to fit into a binder or folder, which many recently interviewed caretakers described using to organize treatment information and refer back to when needed. Readability was guaranteed to be under a ninth-grade level using the Flesch-Kincaid Grade Level score from an online readability analyzer. This helped to keep jargon to a minimum, which may improve perceptions of communicator warmth, integrity, and accommodation *(276)*. Again, these choices were intended to maximize the saliency of the guidebook as a cue to action.

5.4 Conclusions

This chapter summarized scientific communication literature germane to food safety and cancer patients and their caretakers. These data were combined with revelations from qualitative interviews with pediatric cancer patient caretakers to construct feedback-driven recommendations for an improved produce safety communication strategy, focused on safe produce handing and inclusion. Building upon these concepts led to formulations of key communication objectives for the present strategy prototype. Source, behavior, content and styling, timing, and channel tactics were utilized to develop a prototype that met these objectives. Ultimately, this work resulted in a novel produce safety communication strategy that is hypothesized to improve the caretaker decision making experiences and compliance to produce safety behaviors. Future efficacy testing is needed to confirm this hypothesis.

CHAPTER 6: CONCLUSIONS

This dissertation described: (i) improvements made to an existing listeriosis risk model for cancer patients who consume RTE salad, (ii) fabrication of 15 decision models weighing the ND against three alternative produce safety diets, for five age groups, (iii) identification of parameter values justifying the use of the ND, (iv) establishment of pediatric cancer patient caretakers' salient beliefs, barriers, and motivators for produce safety behaviors, and (v) application of previous literature and pediatric cancer patient caretaker feedback to create an improved produce safety communication intervention prototype.

Chapter 3 chronicled changes made to the listeriosis risk model from the master's thesis preceding this dissertation. Most notably, the tomato contamination route was updated to include contamination from soil, cross-contamination during dump tank washing, and conveyor and waxing surfaces. A "model limitations" section was also added to address main sources of uncertainty and variability and areas lacking data, and a new "future work" section highlighted the need for population-specific dose-response data, decision modeling, and risk management strategies. This led to the decision models also produced in Chapter 3, which quantified health effects of the ND for the first time. Across all age groups and alternative produce safety diets (SFH, surface blanching, and no intervention), the ND resulted in greater DALYs, primarily due to higher rates of NEC on this diet. Moreover, when uncertain and/or variable parameters were adjusted to calculate switchover points, switchover point values were implausible (e.g., negative years). These findings signified that produce-inclusive food safety diets are preferred over the ND in all plausible scenarios.

In Chapter 5, a mixed-methods quantitative survey and qualitative interview study was conducted to determine pediatric cancer patient caretaker beliefs, barriers, and motivators to produce safety behaviors. Sample sizes were too small for a full regression analysis, but a permutation test revealed no significant relationships between demographic variables and FDA/ACS-recommended produce safety behaviors. Grounded theory coding facilitated categorization of five caretaker archetypes, motivated by guidelines received, child's health, food safety behaviors previously enacted, and concerns beyond microbial food safety. These archetypes accentuated widespread use of the ND and lack of standardization in produce safety communication materials. The study also yielded caretaker suggestions for updated communication strategies, including information channels, timing, and material organization. Employing these suggestions, existing literature, and decision model results, Chapter 6 devised communication objectives for a prototype produce safety communication strategy focused on hygienic preparation, storage, and produce inclusion for the target population. Various tactics were aligned with these objectives to design the novel communication intervention prototype, which is included in this work.

The outcomes outlined in this dissertation provide both quantitative and qualitative evidence to dispute the highly prevalent application of the ND, in favor of produce-inclusive food safety diets. The enhanced produce safety communication intervention prototype supplies future researchers with a basis for clinical implementation testing. These results will contribute to standardization, quality of life, and health outcome improvements of this aspect of cancer treatment.

CHAPTER 7: FUTURE WORK

The studies presented in this dissertation offer numerous possibilities for further development in future projects. First, given the substantial uncertainty and variability associated with listeriosis dose-response parameter *k*, the listeriosis risk model may be further refined by the incorporation of population-specific dose-response data. Although this characterization is unlikely to alter decision model outcomes, it would advance the field of risk assessment by providing an accurate dose-response model for this vulnerable population.

Furthermore, considering the sizable impact of NEC probability on decision model outcomes, it is pivotal to confirm that there is a marked difference NEC probability between SFH diets and NDs, as indicated in Gupta's pilot study *(109)*. Similarly, there are currently no data on rates of nutritional deficits, or quantified quality of life effects in those prescribed the ND and other produce safety diets. If there is a significant difference, as current literature hypothesizes *(150, 156, 159, 168)*, including these conditions would increase model validity. These studies should be conducted on a full clinical scale, in cancer patients or other immunocompromised individuals to maintain applicability. Additionally, the risk and decision models were built specifically for listeriosis and RTE salads. However, *Salmonella* and *E. coli* O157:H7 also carry a high disease burden *(213, 214)*, and foodborne pathogens survive on produce types other than RTE salad. Therefore, the reliability of this tool could be improved with the inclusion of these pathogens and food vectors.

Another avenue for continuation of this work is applying recruitment notes (5.3.5) to recruit a larger sample for quantitative and qualitative testing of pediatric cancer patient caretakers' produce safety beliefs, barriers, motivators, and behaviors. A larger sample would allow for logistic regression in quantitative analysis, as originally intended, and enable quantitative comparison between qualitative archetypes. An expanded sample may also be more representative of Midwest or United States populations. Additionally, it was hypothesized that current quantitative analyses did not reveal relationships that were apparent in qualitative interviews because excessively restrictive behaviors were not included in the quantitative survey. Therefore, future quantitative surveys in this area should include behaviors such as avoiding fresh produce, avoiding fresh produce that cannot be peeled, peeling fresh produce, and using specialized sprays/washes.

Lastly, one outcome of this dissertation was a prototyped produce safety communication intervention. This strategy should be clinically validated, with a large, representative sample of pediatric cancer patient caretakers, prior to implementation. It must be confirmed that the materials and strategy meet their goals of encouraging safe produce habits and inclusion, fostering self-efficacy and trustworthiness in providers, and communicating risks of foodborne illness and benefits of produce inclusion. There are also opportunities for advancement in terms of technology and telehealth; the materials depicted here may be made available on virtual and accessible platforms. These suggestions will widen the impact of work detailed in this dissertation and better serve the target population of cancer patients and their caretakers.

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APPENDIX A: DECISION MODEL DISTRIBUTIONS R CODE

```
#for loop for all distributions
set.seed(123)

##create objects for for loop initially
compliance_ND <- runif(10000, 0.57143, 0.92208) #compliance to ND
compliance_boil <- runif(10000, 0.7461142, 1) #compliance to boiling  #lower end is median of
compliance to ND
list_in_canc_patient <- runif(10000, min = 0.228, max = 0.34) #percent of listeriosis cases in
cancer patients
dur_LMillness_years <- runif(10000, min = 1/365, max = 2.8/365) #LM illness prior to
hospitalization
percentLMhospitalized <- runif(10000, min = 0.918779, max = 0.95)
dur_sym_to_isolation_years <- runif(10000, min = 0/365, max = 20/365)
percentsept <- runif(10000, min = 0.040146, max = 0.864967) #note: original dist was truncated
@ 0 with a negative min. Unable to truncate in R, therefore this dist is slightly different
dur_sept_years <- runif(10000, min = 1/365, max = 7/365) #year
percentCNS_seq <- runif(10000, 0.118182, 0.20)
severityNEC <- runif(10000, 0.164, 0.348)
library(flexsurv)
percentCNSinf <- rllogis(10000, shape = 3.360269, scale = 0.325513)
library(ExtDist)
hazrat_NDvSFH <- rLaplace(10000, mu = 1, b = 0.147889)
mortalityrate_NEC_child <- rexp(10000, rate = 15.93568)
mortalityrate_NEC_adult <- rexp(n = 10000, rate = 3.604231)
mortalityrate_CNS <- runif(10000, min = 0.031250, max = 0.490909)
library(triangle)
dur_CNS_years <- rtriangle(10000, 1/365, 182/365, 21/365) #years
mortalityrate_sept <- runif(10000, 0.040146, 0.739130)
dur_NEC_years<- runif(10000, min = 0.004110, max = 0.059178)

##for loop, base values
for (i in 1:10000) {
  compliance_ND[i] <- runif(1, 0.57143, 0.92208)
  compliance_boil[i] <- runif(1, 0.7461142, 1)  #lower end is median of compliance to ND
  list_in_canc_patient[i] <- runif(1, min = 0.228, max = 0.34) #percent of listeriosis cases in
cancer patients
  dur_LMillness_years[i] <- runif(1, min = 1/365, max = 2.8/365) #LM illness prior to
hospitalization
  percentLMhospitalized[i] <- runif(1, min = 0.918779, max = 0.95)
  dur_sym_to_isolation_years[i] <- runif(1, min = 0/365, max = 20/365)
  percentsept[i] <- runif(1, min = 0.040146, max = 0.864967)
  percentCNS_seq[i] <- runif(1, 0.118182, 0.20)
  severityNEC[i] <- runif(1, 0.164, 0.348)
  percentCNSinf[i] <- rllogis(1,  shape = 3.360269, scale = 0.325513)
```

```
  hazrat_NDvSFH[i] <- rLaplace(1, mu = 1, b = 0.147889)
  mortalityrate_NEC_child[i] <- rexp(1, rate = 15.93568)
  mortalityrate_NEC_adult[i] <- rexp(n = 1,  rate = 3.604231) #note parameter given in @risk is
inverse rate
  mortalityrate_CNS[i] <- runif(1, min = 0.031250, max = 0.490909)
  dur_CNS_years[i] <- rtriangle(1, 1/365, 182/365, 21/365) #days
  mortalityrate_sept[i] <- runif(1, min=0.040146, max=0.739130)
  dur_NEC_years[i] <- runif(1, min = 0.004110, max = 0.059178)

}

mortalityrate_NEC_adult <- as.numeric(mortalityrate_NEC_adult)

##create objects for life expectancy for loop

###life expectancy, no effects
RLE_0_4 <- runif(10000, 73.3, 77.8)
RLE_5_14 <- runif(10000, 63.4, 73.3)
library(crch)
RLE_45_59 <- rlogis(10000, location = 22.43124, scale = 3.20321)
RLE_15_44 <- rweibull(10000, shape = 6.269388, scale = 53.144223)
RLE_60 <- rweibull(10000, shape = 2.382438, scale = 12.367824)


##for loop, life expectancy, years
for (i in 1:10000){
  ###life expectancy, no effects
  RLE_0_4[i] <- runif(1, 73.3, 77.8)
  RLE_5_14[i] <- runif(1, 63.4, 73.3)
  RLE_45_59[i] <- rlogis(1, location = 22.43124, scale = 3.20321)
  RLE_15_44[i] <- rweibull(1, shape = 6.269388, scale = 53.144223)
  RLE_60[i] <- rweibull(1, shape = 2.382438, scale = 12.367824)
}

#truncate distributions
percentCNSinf <- ifelse(percentCNSinf > 1, 1, percentCNSinf)
mortalityrate_NEC_adult <- ifelse(mortalityrate_NEC_adult > 1, 1, mortalityrate_NEC_adult)
hazrat_NDvSFH <- ifelse(hazrat_NDvSFH < 0, 0, hazrat_NDvSFH)
RLE_45_59 <- ifelse(RLE_45_59 < 0, 0 , RLE_45_59)
RLE_45_59 <- ifelse(RLE_45_59 > 45, 45 , RLE_45_59)
```

APPENDIX B: SAMPLE EV CALCULATION R CODE

```
#Calculating EV 0-4, ND

set.seed(123)

EV_CNSsequelae_0_4 <- percentCNS_seq*(YLD_CNS_sequelae_0_4)
EV_recoverCNS_0_4 <- 0
EV_surviveCNS_0_4 <- (1-mortalityrate_CNS)*(EV_CNSsequelae_0_4 +
EV_recoverCNS_0_4)
EV_deathCNS_0_4 <- mortalityrate_CNS*YLL_CNS_0_4
EV_CNSoutcome_0_4 <- EV_deathCNS_0_4 + EV_surviveCNS_0_4 #note: this does not
include YLDs from CNS. those are included in LM hosp

EV_survivesept_0_4 <- 0
EV_deathsept_0_4 <- mortalityrate_sept*YLL_sept_0_4
EV_septoutcome_0_4 <- EV_deathsept_0_4 + (1-mortalityrate_sept)*EV_survivesept_0_4
#note YLD included in LM hosp

EV_recoverLMhosp <- (1-percentsept-percentCNSinf)*0
EV_CNSinf_0_4 <- (percentCNSinf*YLD_CNS) + (percentCNSinf*EV_CNSoutcome_0_4)
EV_septinf_0_4 <- (percentsept*YLD_sept) + (percentsept*EV_septoutcome_0_4)
EV_LMhosp_0_4 <- EV_recoverLMhosp + EV_CNSinf_0_4 + EV_septinf_0_4 #note YLD for
hospitalization included in illness

EV_LMill_0_4 <- (percentLMhospitalized*EV_LMhosp_0_4) +
(percentLMhospitalized*YLD_LMhosp) + (1 - percentLMhospitalized)*0 #0 DALYs when one
is recovered without hosp

EV_list_ND_0_4 <- (riskLM_ND*YLD_LMillness) + riskLM_ND*EV_LMill_0_4

EV_NEC_0_4 <- percent_NEC_ND*YLD_NEC + (1 - percent_NEC_ND)*0 +
percent_NEC_ND*mortalityrate_NEC_child*YLL_NEC_0_4
EV_nolist_ND_0_4 <- (1 - riskLM_ND)*EV_NEC_0_4

EV_ND_0_4 <-  EV_list_ND_0_4 + EV_nolist_ND_0_4
median(EV_ND_0_4) #Note: very similar to Monte Carlo values in Precision Tree
quantile(EV_ND_0_4, probs = 0.95)
quantile(EV_ND_0_4, probs = 0.05)
min(EV_ND_0_4)
max(EV_ND_0_4)

#calculating yll and yld

totalYLD_ND_0_4 <- riskLM_ND*YLD_LMillness +
riskLM_ND*percentLMhospitalized*YLD_LMhosp +
```

```
riskLM_ND*percentLMhospitalized*percentsept*YLD_sept +
riskLM_ND*percentLMhospitalized*percentCNSinf*YLD_CNS +
riskLM_ND*percentLMhospitalized*percentCNSinf*percentCNS_seq*(YLD_CNS_sequelae_0
_4) + (1 - riskLM_ND)*percent_NEC_ND*YLD_NEC
perc_YLD_NEC_ND_0_4 <- ((1 -
riskLM_ND)*percent_NEC_ND*YLD_NEC)/totalYLD_ND_0_4

YLL_sept_ND_0_4 <-
riskLM_ND*percentLMhospitalized*percentsept*mortalityrate_sept*YLL_sept_0_4
YLL_CNS_ND_0_4 <-
riskLM_ND*percentLMhospitalized*percentCNSinf*mortalityrate_CNS*YLL_CNS_0_4
YLL_NEC_ND_0_4 <- (1 -
riskLM_ND)*percent_NEC_ND*mortalityrate_NEC_child*YLL_NEC_0_4
totalYLL_ND_0_4 <- YLL_sept_ND_0_4 + YLL_CNS_ND_0_4 + YLL_NEC_ND_0_4

YLL_YLD_dataframe_ND_0_4 <- data.frame(totalYLD = median(totalYLD_ND_0_4),
totalYLL = median(totalYLL_ND_0_4), YLL_sept = median(YLL_sept_ND_0_4), YLL_CNS =
median(YLL_CNS_ND_0_4), YLL_NEC = median(YLL_NEC_ND_0_4))

YLL_YLD_dataframe_ND_0_4
perc_EV_YLDNEC_ND_0_4 <- ((1 -
riskLM_ND)*percent_NEC_ND*YLD_NEC)/EV_ND_0_4
median(perc_EV_YLDNEC_ND_0_4)
```

APPENDIX C: SAMPLE SWITCHOVER POINT CALCULATION R CODE

```
#Switchover point analysis, duration LM hospitalization, ND v SFH, ages 15-44

##dur lm hosp, years switchover vector
switchover_durLMhosp_SFH_15_44 <- seq(from =  0, to = 1*10^10, length.out = 100)

###sub in values, ND arm
##no list arm stays same point estimate

switchover_YLD_LMhosp_durLMhosp_SFH_15_44 <-
switchover_durLMhosp_SFH_15_44*df_pointestimate$severityLMhosp
switchover_EV_LMill_durLMhosp_SFH_15_44 <-
(df_pointestimate$percentLMhospitalized*EV_LMhosp_15_44_PE) +
(df_pointestimate$percentLMhospitalized*switchover_YLD_LMhosp_durLMhosp_SFH_15_44
) + (1 - df_pointestimate$percentLMhospitalized)*0 #0 DALYs when one is recovered without
hosp
switchover_EV_list_ND_durLMhosp_SFH_15_44 <- (riskLM_ND_PE*YLD_LMillness_PE) +
riskLM_ND_PE*switchover_EV_LMill_durLMhosp_SFH_15_44
switchover_EV_ND_durLMhosp_SFH_15_44 <-
switchover_EV_list_ND_durLMhosp_SFH_15_44 + EV_nolist_15_44_PE

###sub in values, SFH arm
##no list arm stays same, point estimate
switchover_EV_list_SFH_15_44 <- (riskLM_SFH_comp_PE*YLD_LMillness_PE) +
riskLM_SFH_comp_PE*switchover_EV_LMill_durLMhosp_SFH_15_44
switchover_EV_SFH_durLMhosp_SFH_15_44 <- switchover_EV_list_SFH_15_44 +
EV_nolist_SFH_15_44_PE

###create data frame
df_switchover_durLMhosp_SFH_15_44 <- data.frame(switchover_durLMhosp_SFH_15_44,
switchover_EV_ND_durLMhosp_SFH_15_44, switchover_EV_SFH_durLMhosp_SFH_15_44)

##calculate switchover point
switchoverpoint_x_durLMhosp_SFH_15_44 <-
approxfun(df_switchover_durLMhosp_SFH_15_44$switchover_EV_SFH_durLMhosp_SFH_15
_44 - df_switchover_durLMhosp_SFH_15_44$switchover_EV_ND_durLMhosp_SFH_15_44,
df_switchover_durLMhosp_SFH_15_44$switchover_durLMhosp_SFH_15_44, rule=2)

library(ggplot2)

colors_switchover_durLMhosp_SFH_15_44 <- c("SFH" = "darkslategray", "ND" =
"darkgoldenrod2")

durLMhosp_switchover_plot_SFH_15_44 <- ggplot(df_switchover_durLMhosp_SFH_15_44,
aes(x = switchover_durLMhosp_SFH_15_44)) + geom_line(aes(y =
```

```
switchover_EV_ND_durLMhosp_SFH_15_44, color = "ND"), size = 1.5) + geom_line(aes(y =
switchover_EV_SFH_durLMhosp_SFH_15_44, color = "SFH"), size = 1.5) + labs(x = "Duration
LM hospitalization", y = "Expected DALYs", color = NULL) +  xlim(0, 1*10^10)  +
scale_color_manual(values = colors_switchover_durLMhosp_SFH_15_44) + geom_point(aes(x
= switchoverpoint_x_durLMhosp_SFH_15_44(0), y = 4.1, fill = "black"), size = 5) + guides(fill
= "none") + theme(panel.grid.major = element_blank(), panel.grid.minor = element_blank(),
panel.background = element_blank(), axis.line = element_line(colour = "black"), axis.text.x =
element_text(face="bold"), axis.text.y = element_text(face="bold"), axis.title.x =
element_text(face="bold"), axis.title.y = element_text(face="bold")) + geom_label(label =
"6.91E09", x = 7.5*10^9, y = 2.5, label.padding = unit(0.55, "lines"), label.size = 0.35, color =
"black", fill = "#69b3a2")
durLMhosp_switchover_plot_SFH_15_44

# Print plots to a pdf file
pdf("switchover_durLMhosp_15_44_SFH.pdf", width = 7, height = 5)
print(durLMhosp_switchover_plot_SFH_15_44)     # Plot 1 --> in the first page of PDF
dev.off()
```

APPENDIX D: QUANTITATIVE SURVEY

I certify that I am 18 years old or older

- ○ Yes (1)
- ○ No (2)

I certify that I acted as the caretaker for a pediatric (younger than 18 years old) cancer patient within the past two years

- ○ Yes (1)
- ○ No (2)

Research Participant Information and Consent Form

Study Title: Produce safety communication, attitudes, barriers, and motivators for pediatric cancer patient caretakers

Researcher and Title: Carly Gomez, Michigan State University Biosystems Engineering Ph.D. student

Department and Institution: Michigan State University

Contact Information: Email: gomezca2@msu.edu Phone: 248-766-0517
Sponsor: Dr. Bradley Marks, Ph.D., PE, Principal Investigator

BRIEF SUMMARY

You are being asked to participate in a research study. Researchers are required to provide a consent form to inform you about the research study, to convey that participation is voluntary, to explain risks and benefits of participation including why you might or might not want to participate, and to empower you to make an informed decision. You should feel free to discuss and ask the researchers any questions you may have.

You are being asked to participate in a research study examining your attitudes, barriers, and motivators for following food safety information (food preparation, storage, avoidance, handwashing, and cross-contamination) provided during your child's cancer treatment, as well as your experience with how the material was communicated to you. Your participation in this study will consist of an online survey taking about 20 minutes. In the survey, you will be asked to answer questions about yourself and your family, such as your age, gender, race, relationship to child, time since child's diagnosis, income, and food availability.

The most likely risks of participating in this study are:

-Some questions may be personal. You can choose "prefer not to answer" or quit the survey at

any time.
-Breach of confidentiality: There is a chance your data could be seen by someone who shouldn't have access to it.

We're minimizing this risk in the following ways:

-Directly identifying information (name, address, email address, etc.) will not be collected.
-Names will be replaced with participant ID numbers during data analysis.
-Raw data will be stored in a password-protected document on MSU's secure Sharepoint

You will not directly benefit from your participation in this study. However, your participation in this study may contribute to the understanding of how to help pediatric cancer patient caretakers make food safety decisions and how to better communicate food safety information.

Participation in this study is completely voluntary and refusal to participate will not affect your care.

PURPOSE OF RESEARCH
The purpose of this research study is to understand what factors may contribute to pediatric cancer patient caretaker use of different precautions when preparing fruits and vegetables for their child(ren) during cancer treatment, and how to effectively communicate food safety guidelines. We hope to use this information to create improved food safety recommendations and communication efforts for pediatric cancer patient caretakers.

WHAT YOU WILL BE ASKED TO DO
You will be asked to complete a 20-minute electronic survey, with mostly multiple choice and some fill-in-the-blank questions. You will be asked about various demographics (ex. Age, race, education level, income, marital status, etc.), and food availability in your household.

You can complete the survey one time anonymously from your own device. You are free to answer "Don't know/prefer not to answer" for questions you would prefer not to answer.

The survey link will be provided to you via email after you complete the informed consent document.

PRIVACY AND CONFIDENTIALITY
Contact information for participants will be stored in a password-protected document on MSU's secure Sharepoint. No directly identifying information (name, address, email address, etc.) will be collected in the survey. Raw data (multiple choice answers) will be rewritten in code in a password-protected document on MSU's secure Sharepoint so that individuals cannot be identified from their combinations of answers. This deidentified data will be stored indefinitely for use in future research.

YOUR RIGHTS TO PARTICIPATE, SAY NO, OR WITHDRAW
You have the right to say no to participate in the research. You can stop at any time after it has already started. There will be no consequences if you stop, and you will not be criticized. You

will not lose any benefits that you normally receive. Participation or lack of will not influence your relationship with your care team, or the quality of care you are provided.

COSTS AND COMPENSATION FOR BEING IN THE STUDY
You will receive a $10 gift card of your choice for completing the survey.

CONTACT INFORMATION
If you have concerns or questions about this study, such as scientific issues, how to do any part of it, or to report an injury, please contact the researcher Carly Gomez via methods below:

Email address: gomezca2@msu.edu

Phone number: 248-766-0517

Mailing address: 524 S. Shaw Lane, East Lansing MI 48824

If you have questions or concerns about your role and rights as a research participant, would like to obtain information or offer input, or would like to register a complaint about this study, you may contact, anonymously if you wish, the Michigan State University's Human Research Protection Program at 517-355-2180, Fax 517-432-4503, or e-mail irb@msu.edu or regular mail at 4000 Collins Rd, Suite 136, Lansing, MI 48910.

DOCUMENTATION OF INFORMED CONSENT.

Checking the "I consent" box below means that you voluntarily agree to participate in this research study.

○ I consent

○ I do not consent

What is your age?
____

What is your relation to the pediatric cancer patient?
____

What was the child in question's age at the time of diagnosis?

○ Type below ____

○ Don't know/prefer not to answer

How long, in years and months, has it been since diagnosis? Example format: 1 year, 3 months

- ○ Type below ____
- ○ Don't know/prefer not to answer

What is your gender?

- ○ Male
- ○ Female
- ○ Other ____
- ○ Prefer not to answer

What is the highest level of education that you have completed?

- ○ < High school
- ○ High school or equivalent
- ○ Associate's degree or trade school
- ○ Part of bachelor's degree
- ○ Bachelor's degree
- ○ Part of graduate school or professional degree
- ○ Graduate school or professional degree
- ○ Don't know/prefer not to answer

What is your household's annual income?

- ○ $0 - $9,999
- ○ $10,000 - $19,999
- ○ $20,000 - $29,999
- ○ $30,000- $39,999
- ○ $40,000 - $49,999
- ○ $50,000 - $59,999
- ○ $60,000 - $69,999

- ◯ $70,000 - $79,999
- ◯ $80,000 - $89,999
- ◯ $90,000 - $99,999
- ◯ $100,000 +
- ◯ Don't know/prefer not to answer

What is your marital status?

- ◯ Single
- ◯ Married
- ◯ Divorced/Widowed
- ◯ Other ____
- ◯ Prefer not to answer

What is your race?

- ◯ American Indian or Alaskan Native
- ◯ Asian
- ◯ Black or African American
- ◯ White
- ◯ Other ____
- ◯ Don't know/prefer not to answer

How many people live in your household?

- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6+
- ◯ Prefer not to answer

How many children under age 18 live in your household?

- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5+
- ◯ Prefer not to answer

How many adult children live in your household?

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5+

Do you use a food assistance program, and if so, which one?

- ◯ SNAP/food stamps
- ◯ WIC
- ◯ None
- ◯ Other ____
- ◯ Prefer not to answer

During the past 30 days, on how many days did you smoke cigarettes?

- ◯ Enter number of days ____
- ◯ Prefer not to answer

Please indicate the level to which you agree or disagree with the following statements about how you perceive your child.

	Strongly agree	Somewhat agree	Neither agree nor disagree	Somewhat disagree	Strongly disagree	Prefer not to answer
I often think about calling the doctor about my child.	○	○	○	○	○	○
When there is something going around, my child will catch it.	○	○	○	○	○	○
I often keep my child indoors because of health reasons.	○	○	○	○	○	○
Sometimes I get concerned my child doesn't look as healthy as s/he should.	○	○	○	○	○	○
I get concerned about circles under my child's eyes.	○	○	○	○	○	○
My child gets more colds than other children I know.	○	○	○	○	○	○
I often check my child at night to make sure s/he is okay.	○	○	○	○	○	○

The statements below have been made by people about their food situation. For these statements, please indicate whether the statement was often true, sometimes true, or never true for your household in the last 12 months - that is since last (month name).

	Always true	Sometimes true	Never true	Don't know/prefer not to answer
"We worried whether our food would run out before we got money to buy more."	◯	◯	◯	◯
"The food that we bought just didn't last, and we didn't have money to get more."	◯	◯	◯	◯
"We couldn't afford to eat balanced meals."	◯	◯	◯	◯

In the last 12 months, since last (name of current month), did you or other adults in your household ever cut the size of your meals or skip meals because there wasn't enough money for food?

◯ Yes

◯ No

◯ Don't know/prefer not to answer

*QUESTION ONLY DISPLAYED IF AFFIRMATIVE RESPONSE TO ONE OR MORE PREVIOUS QUESTIONS
How often did this happen—almost every month, some months but not every month, or in only 1 or 2 months?

◯ Almost every month

◯ Some months but not every month

◯ Only 1 or 2 months

*QUESTION ONLY DISPLAYED IF AFFIRMATIVE RESPONSE TO ONE OR MORE PREVIOUS QUESTIONS
In the last 12 months, did you ever eat less than you felt you should because there wasn't enough money for food?

- Yes
- No
- Don't know/prefer not to answer

*QUESTION ONLY DISPLAYED IF AFFIRMATIVE RESPONSE TO ONE OR MORE PREVIOUS QUESTIONS
In the last 12 months, were you ever hungry but didn't eat because there wasn't enough money for food?

- Yes
- No
- Don't know/prefer not to answer

*QUESTION ONLY DISPLAYED IF AFFIRMATIVE RESPONSE TO ONE OR MORE PREVIOUS QUESTIONS
In the last 12 months, did you lose weight because there wasn't enough money for food?

- Yes
- No
- Don't know/prefer not to answer

*QUESTION ONLY DISPLAYED IF AFFIRMATIVE RESPONSE TO ONE OR MORE PREVIOUS QUESTIONS
In the last 12 months, did you or other adults in your household ever not eat for a whole day because there wasn't enough money for food?

- Yes
- No
- Don't know/prefer not to answer

*QUESTION ONLY DISPLAYED IF AFFIRMATIVE RESPONSE TO ONE OR MORE PREVIOUS QUESTIONS
How often did this happen - almost every month, some months but not every month, or in only 1 or 2 months?

- ◯ Almost every month
- ◯ Some months but not every month
- ◯ Only 1 or 2 months
- ◯ Don't know/prefer not to answer

The statements below have been made by people about the food situation of their children. For these statements, please tell me whether the statement was OFTEN true, SOMETIMES true, or NEVER true in the last 12 months for your child/children living in the household who are under 18 years old.

	Always true	Sometimes true	Never true	Don't know/prefer not to answer
"We relied on only a few kinds of low-cost food to feed the children because we were running out of money to buy food."	◯	◯	◯	◯
"We couldn't feed the children a balanced meal, because we couldn't afford that."	◯	◯	◯	◯
"The children were not eating enough because we just couldn't afford enough food."	◯	◯	◯	◯

*QUESTION ONLY DISPLAYED IF AFFIRMATIVE RESPONSE TO PREVIOUS QUESTION
In the last 12 months, since (current month) of last year, did you ever cut the size of any of your children's meals because there wasn't enough money for food?

- ◯ Yes
- ◯ No
- ◯ Don't know/prefer not to answer

*QUESTION ONLY DISPLAYED IF AFFIRMATIVE RESPONSE TO ONE OR MORE PREVIOUS QUESTIONS
In the last 12 months, did any of the children ever skip meals because there wasn't enough money for food?

- Yes
- No
- Don't know/prefer not to answer

*QUESTION ONLY DISPLAYED IF AFFIRMATIVE RESPONSE TO ONE OR MORE PREVIOUS QUESTIONS
How often did this happen - almost every month, some months but not every month, or only 1 or 2 months?

- Almost every month
- Some months but not every month
- Only 1 or 2 months
- Don't know or prefer not to answer

*QUESTION ONLY DISPLAYED IF AFFIRMATIVE RESPONSE TO ONE OR MORE PREVIOUS QUESTIONS
In the last 12 months, were the children ever hungry but you just couldn't afford more food?

- Yes
- No
- Don't know/prefer not to answer

*QUESTION ONLY DISPLAYED IF AFFIRMATIVE RESPONSE TO ONE OR MORE PREVIOUS QUESTIONS
In the last 12 months, did any of the children ever not eat for a whole day because there wasn't enough money for food?

- Yes
- No
- Don't know/prefer not to answer

The following questions ask you to consider how often you perform certain food safety behaviors when cooking for your child. There are no wrong answers.
How often do you perform the following behaviors for foods served to your child?

Figure 11: Produce safety behavior frequency chart from quantitative survey

	Never	Rarely	Sometimes	Most of the time	Always	Don't know/prefer not to answer
I rinse fresh fruits and vegetables served to my child under running tap water.	○	○	○	○	○	○
When I do rinse fresh fruits and vegetables for my child, I dry them with a clean paper towel or cloth.	○	○	○	○	○	○
I serve my child produce that has been bruised or damaged.	○	○	○	○	○	○
When serving fresh fruits and vegetables with a peelable skin (apples, cucumbers, pears, tomatoes, etc.) to my child, I peel them.	○	○	○	○	○	○
I serve non-thick skinned fresh produce to my child. This includes all produce except for bananas, oranges, grapefruits, etc.	○	○	○	○	○	○
I don't rinse bagged/packaged salads before preparing them for my child.	○	○	○	○	○	○
I serve pre-cut (from the grocery store/market) fruits and vegetables to my child.	○	○	○	○	○	○
When I intend to serve fresh produce to my child, I store it in the refrigerator.	○	○	○	○	○	○
I allow my child to eat fresh fruits or vegetables from restaurants.	○	○	○	○	○	○
I serve my child fresh produce from self-serve/bulk containers.	○	○	○	○	○	○
I wash my hands with soap and water for 20 seconds before preparing fresh produce for my child.	○	○	○	○	○	○
When serving packaged fresh produce to my child, I make sure that it is before the "Use By" date on the package.	○	○	○	○	○	○
When I am grocery shopping, I separate raw meat/poultry/fish from fresh produce in the bags/cart.	○	○	○	○	○	○

APPENDIX E: PERMUTATION TEST R CODE

```
library(readr)
library(coin)
library(dplyr)

df <- read_csv("C:/Users/carly/OneDrive - Michigan State
University/Dissertation/Communication/Quantitative analysis/Carly_data.csv")

hist(df$total_fs_score, main="Total Food Safety Distribution",
    col='dodgerblue', breaks=20, xlab='Food Safety Total Score', xlim=c(25,58))

df$edu <- as.factor(df$edu) #Change education variable to factor

#conduct permutation test with 10,00 iterations
test <- independence_test(total_fs_score ~ age + age_at_diag + time_since_diag +
                CVS + children_in_household | edu,
                data = df,
                distribution = approximate(nresample = 10000))
print(test)

#standardized coefficients
statistic(test, type = "standardized")

#variance covariance matrix
covariance(test)

#p value + its confidence interval based on an observed test statistic c
# and its conditional null distribution
pvalue(test)

#Permutation distribution containing 99:999% of the probability mass

windowsFonts(times = windowsFont("Times New Roman"))
par(family = "times", font = 2, font.lab = 2, font.axis = 2, cex.axis = 1.2, cex.lab = 1.5)
hist(support(test),col='lavender', main = '', breaks=50, xlab='T-statistic values', xlim=c(0,4))
points(1.62, 0, pch = 19, col = "black", cex = 2)  # pch is the point shape, and col is the point
color

# Print plots to a pdf file
pdf("permutationdistribution2.pdf", width = 7, height = 5)
print(hist(support(test),col='dodgerblue', main = '', breaks=50, xlab='T-statistic', xlim=c(0,4)))
dev.off()
```

APPENDIX F: PROTOTYPE PRODUCE SAFETY GUIDEBOOK

Figure 12: Produce safety guidebook prototype

Figure 12 (cont'd)

Why is food safety *extra* important for you?

The Facts

- The U.S. Centers for Disease Control and Prevention (CDC) estimates that 1 in 6 Americans will become sick with food-borne illness each year
- This leads to 128,000 hospitalizations and 3,000 deaths
- Many of those with severe outcomes have a weakened immune system

Cancer patients' immune systems often become weak during treatment. This makes it hard for the immune system to fight germs in food, raising the chance of serious foodborne illness.

Cancer Patients and Their Immune Systems

When healthy, the immune system can fight off most foodborne bacteria. If a cancer patient eats contaminated food, they are more likely to get severely sick, need to be hospitalized, or even die. Also, minor infections may slow cancer treatment.

Nutritious and safe food supports the immune system. It is important for your child to eat enough calories, vitamins, and minerals to stay strong during treatment.

Your child's immune system keeps them healthy by protecting their body from disease-causing germs. Cancer treatment such as chemotherapy or radiation, can weaken the immune system in the following ways:

- Reducing levels of infection fighting white blood cells
- Damaging mucous membranes that keep germs from entering the body
- Offsetting acid in the stomach, which normally kills germs
- Causing death of natural "good" bacteria that compete with germs

2

Figure 12 (cont'd)

You *can* keep nutritious foods safe!

Fresh Produce - The Facts

- Produce is grown in or around soil, where contact with bacteria may contaminate it
- Produce can also contact germs during processing or when cut or stored at home
- When produce is eaten fresh, without cooking, bacteria survive and may be consumed
- Properly selecting, cleaning, separating, and chilling your produce dramatically reduces your child's risk of getting sick

The Good News

You can still serve your child fresh produce. In fact, it's recommended by the American Cancer Society! All you need to do is follow a few simple steps to make your fresh produce more safe.

1 SELECT

- Choose produce that is not bruised or damaged
  - ➡ Damaged areas can hold bacteria
- Do not purchase pre-cut produce; instead, cut whole produce yourself
  - ➡ Pre-cut produce can be contaminated by unclean utensils and hands
- Do not purchase produce from a salad bar or buffet
  - ➡ Many people may contact this produce
  - ➡ This produce may have been left out at an improper temperature

THIS not THAT

THIS not THAT

THIS not THAT

3

Figure 12 (cont'd)

4 CHILL

- Refrigerate cut produce within 2 hours
  - Bacteria transferred to the produce during cutting reproduces quickly at higher temperatures

- Maintain a refrigerator temperature of 40°F or less
  - This will help slow the growth of dangerous bacteria

HELPFUL HINT!

Refrigerator thermometers, like the one pictured, are available online and at hardware stores for less than $5! They can be placed in your fridge to ensure it's the correct temperature.

Putting it All Together—A Food Safety Recipe

Taco Night!

Serves 4

Ingredients:

- 1 lb lean ground beef, chicken, or protein alternative
- 1 packet taco seasoning
- 1 package taco shells
- 1 cup shredded cheese of your choice
- 4-8 pieces lettuce
- 1 tomato
- 4 green onions
- Salsa of your choice

Instructions:

1. Wash hands with soap and water
2. Thoroughly brown the protein in stovetop skillet over medium heat
3. Add taco seasoning according to packet directions. Turn heat down to low
4. Wash hands with soap and water
5. Rinse lettuce, tomato, and green onions under running water
8. Dry vegetables with a paper towel. Slice on designated produce cutting board
9. Assemble tacos, using clean utensils to pick up the fresh produce, and enjoy
10. Refrigerate any leftovers ASAP

Any recipe can be modified into a food safety recipe! Try it out with your family's favorites!

5

4

Figure 12 (cont'd)

How will these practices affect your child?

Following Food Safety Guidelines - the Risks and Benefits

Benefits of following guidelines

- Maintain a normal diet safely—your child can still eat produce!
  - Normalcy = higher quality of life
  - Produce is a great, low-odor food option for when your child is nauseous
- Adequate fiber intake = reduced risk of severe intestinal disorders
- Adequate vitamin C intake = fewer treatment delays, reduced treatment toxicity

Risks of not following guidelines

- Severe foodborne illness
  - Bacteria such as *Listeria* and *E. coli* can cause severe illness, lifelong impairments, or even death.
  - Delayed treatment
  - Costly treatment
  - Missed school/work
- Avoiding produce
  - Decreased nutrient intake
  - Poor intestinal health makes infection more likely

We hope you found these produce safety tips useful! For more information, check out the sources below!

Foodborne illness outbreaks - CDC
https://www.cdc.gov/foodsafety/outbreaks/index.html

Safe food handling and preparation - FDA
https://www.fsis.usda.gov/food-safety/safe-food-handling-and-preparation

Nutrition for people with cancer - American Cancer Society
https://www.cancer.org/treatment/survivorship-during-and-after-treatment/coping/nutrition.html