FACULTY OF BIOSCIENCE ENGINEERING

Foodborne infections and opportunistic pathogens: epidemiological evidence associated with fresh fruit and vegetable consumption

Word count: 32 146

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A dissertation submitted to Ghent University in partial fulfillment of the requirements for the degree of Master of Nutrition and Rural Development

Academic year: 2020 – 2021

UNIVERSITEIT GENT

Acknowledgment

Firstly, I would like to express my gratitude to my promoter Prof. Dr. Ir. Liesbeth Jacxsens for her critical ideal, guidance on the content and writing skill, and tireless reading and revising my thesis. I would also want to thank my tutor Thomas De Bock for his instruction and correcting work for my thesis. Without their dedication, care and encouragement, not only on my thesis but also for the hard time under Covid-19, I would not be able to finish my thesis smoothly. Regular meeting with them made my life well organized.

Secondly, I want to show my appreciation to Prof. Dr. Carl Lachat, who provided me excellent and helpful information about the GRADE system and suggestion on data collection and processing of my thesis. Besides, I would like express further thankfulness for his guidance and help for those two years as the director of the Nutrition and Rural Development program. His rigorous and innovative thinking and idea inspired me to explore the world of nutrition and public health.

I am deeply indebted to the teachers and classmates of all the courses I have participated. It was a wonderful experience to attend lectures given by professors from different areas and work with students with diversity background, which broadening my horizons. Their remote cooperation, support and accompany during the quarantine period made me feel happy and peaceful.

Finally, I would like to express my heartfelt gratitude to my parents, family and friend, who provide me with mental and life support and motivated me throughout the life in Belgium.

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List of abbreviations

CASP	Critical Appraisal Skills Program
CHD	Coronary Heart Disease
CVD	Cardiovascular Disease
DALYs	Disability Adjusted Life Years
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EFSA	European Food Safety Authority
EU	European Union
GBD	Global Burden of Disease
GHG	Greenhouse Gas
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
GRAS	Generally Recognized As Safe
HAIs	Healthcare Associated Infections
HPP	High Pressure Processing
HUS	Haemolytic Uremic Syndrome
MAP	Modified Atmosphere Packaging
NTP-OHAT	National Toxicology Program-Office of Health Assessment and Translation
OR	Odds Ratio
PDI	Plant-based Diet Index
RCT	Randomized Controlled Trials
RH	Relative Humidity
RR	Risk Ratio
SDGs	Sustainable Development Goals
STEC	Shiga-toxin Producing *Escherichia coli*
USDA	United States Department of Agriculture
WHO	World Health Organization
YLDs	Years Lived with a Disability
YLLs	Years of Life Lost Due to Premature Mortality

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Abstract

Background: Healthy diet consists of approximately half a proportion of fruits and vegetables. Healthy dietary pattern has a tremendous influence on human health and environmental sustainability. The benefits of consuming more fruits and vegetables reveal by reducing the risk of diabetes, coronary disease and stroke, as well as reducing greenhouse gas emissions. To preserve the nutritional and sensory value maximally, minimally processed techniques were introduced into the production of fresh fruits and vegetables. Yet, as there is no strict step for microbial inactivation, it is not clear that whether the microorganism existed in minimal-processed products can be a threat to food safety.

Objective and methods: This study aims at determining the relative association of consuming fresh fruits and vegetables with foodborne outbreaks caused by primary (focusing on *Salmonella spp., Escherichia coli, Listeria monocytogenes* and Norovirus) and opportunistic pathogens. Existing published literature from the European region from 2011 to 2020 was obtained from literature database. A meta-analysis was conducted based on the obtained results. Moreover, five quality aspects (risk of bias, imprecision, inconsistency, indirectness and publication bias) of the evidence were be assessed by GRADE (Grading of Recommendations Assessment, Development, and Evaluation), which is a quality appraisal tool used to apply to clinical or nutritional studies.

Results: 25 articles were identified from the database (12 of *Escherichia coli,* 7 of *Salmonella* and 6 of Norovirus). The characteristics of all the identified studies were extracted from 20 studies involved in the meta-analysis. Five studies could not be used, as they did not contain valid data. The overall OR for 13 case-control studies was 16.58 and overall RR of 7 cohort studies was 1.42. Salad and packaged pre-cut leaf vegetables were the most frequent food vehicles of pathogens. The process and criteria of the GRADE system were adjusted and applied. The quality of evidence is relatively low in the aspects of recall bias, large range around confidence interval, insufficient number of control group and publication bias. There was no article about *L. monocytogenes* and opportunistic outbreak was identified by this study.

Conclusion: Fresh fruits and vegetables were considered as the potential food vehicle for *Escherichia coli, Salmonella* and Norovirus that resulted in foodborne outbreak. Interventions targeted at reducing the transmission of pathogens via fresh product are important priorities to reduce the disease burden among the population. Nutrition and food safety are both important part of a sustainable food system. It is necessary to have an integrated evidence appraisal tools for developing related interventions. The possibility of applying GRADE to evaluate food safety study has been proved. Further research needs to be conducted to redesign the assessment criteria in the GRADE system, making it better used in food safety research.

Key words: fresh fruits and vegetables, food vehicle, foodborne outbreak, epidemiological evidence, primary pathogens, opportunistic pathogens

Introduction and research questions

Planetary health diet has been promoted by a handful of countries recently to achieve Sustainable Development Goals (SDGs) (EAT-Lancet Commission, 2019). The main idea of planetary health diet is replacing overconsumption of red meat with consuming more fruits, vegetables, legumes, grains and nuts. Transformation to healthy diet from sustainable food system plays a critical role in nurturing human health, as plant-based foods are an important source of micronutrients, fiber and antioxidants. The shifting diets can avert about 10.8-11.6 million deaths and reduce carbon emissions or preventing deforestation (Willett et al., 2019).

In order to preserve the nutritional value and sensory quality of fruits and vegetables maximally, minimal processing has been widely explored as a potential preservation technique by researchers and applicators. Minimal processing, such as washing (with or without chemical agents), modified atmosphere packaging (MAP) and high-pressure processing (HPP), is a food technology that minimally influences the nutrition and texture of food and gives the food sufficient shelf-life during storage and distribution. However, most of the minimally processed techniques could not meet the requirement of inactivation of microorganisms due to the non-thermal characters.

Plant-based food, especially those are consumed as fresh products, has been considered as a vehicle for transmission of foodborne pathogens. Microorganisms originated from raw food materials are still existed because there is no strict treatment targeting at inactivation of microorganisms during production. The microorganism can be a potential threat to human health and among which, opportunistic pathogens are one of the concerns about food safety problem (Berg et al., 2014). Opportunistic pathogens are microorganisms that are less harmful to healthy people but may be hazardous to people who suffer from immune deficiency or have potential diseases, such as older patients or young children. Study shows that *Enterococci*, one of the most prevalent opportunistic pathogens, can easily cause infection among patients in hospital (Top et al., 2008). Opportunistic pathogens naturally present in soil or vegetation and can be transferred via foods, which differ from zoonosis entomopathogens such as *Salmonella* or Shiga-toxin producing *Escherichia coli* (STEC).

Although scientific evidence about respiratory disease or septicaemia caused by opportunistic pathogens have already been found during the past few years (De Bentzmann et al., 2011; Anzil et al., 2018). It is still unclear that whether those opportunistic pathogens can cause foodborne infections, especially from minimally processed plant-based food. Epidemiological data collections are needed to provide scientific-based evidence for figuring out potential biological hazard in plant-based food.

This master thesis investigates the epidemiological evidence for foodborne diseases caused by primary pathogens and opportunistic pathogens that existed in minimal processing fruits and vegetables. To be more specific, the definition and characteristics of plant-based food, minimally processed techniques, primary and opportunistic pathogens, epidemiological evidence and quality evaluation tool will be discussed in detail. Furthermore, the association between foodborne infection

and fresh fruits and vegetables consumption will be determined. Moreover, assessing each evidence to ascertain whether the evidence is high quality.

Therefore, following research methods will be applied:

- Systematic literature research will be conducted to search for foodborne disease outbreaks caused by primary pathogens (*Salmonella spp., Escherichia coli, Listeria monocytogenes* and Norovirus) and opportunistic pathogens from minimally processed fruits and vegetables, target-infected population are identified as whole population including vulnerable groups (young, old, pregnant, immunosuppressed).
- Evaluating the quality of evidence by GRADE, which used to be applied in the quality assessment of nutritional research, would be an innovation in the thesis (application in a food safety context).

1. Literature review

1.1. Plant-based food

1.1.1. Classification

Plant-based food can be classified in to five groups: fruits, vegetables, legumes, grains and nuts, according to the dietary recommendation by EAT-Lancet Commission (EAT-Lancet Commission, 2019). Plant-based food consist of diverse indigestible compound, such as cellulose, pectin and resist starch, which differ them from animal source food (Fardet, 2017). In addition to fiber, plant-based food is also a good source of protein, lipid, carbohydrate, trace elements and vitamins.

There are many varieties of fruits and vegetables available, that can be consumed by fresh or processed into juice, jams, can food or pickle. To be more specific, fruits usually refer to pulpy seeded tissues that have a sweet (grape, apples, pears, blueberries) or tart (lemons, limes, orange) taste. Vegetables are edible plant parts including stems and stalks (celery), roots (carrots), tubers (potatoes), bulbs (onions), leaves (spinach, lettuce), flowers (artichokes), some fruits (cucumbers, pumpkin, tomatoes) (Pennington et al., 2009). Due to the fast-paced lifestyle in nowadays society, convenience and simplicity are two important factors that consumers will take into consideration when they choose a product. Fresh-cut fruits and vegetables are raw, ready-to-eat products that remain in fresh state and without any thermal treatment or additives (Beaulieu et al., 2002). Consequently, fresh-cut fruits and vegetables can provide customers highly nutritious, convenient and healthful food while still maintaining freshness status, that becoming more and more popular in the marketplace.

1.1.2. Shifting to a healthier diet with more plant-based food

Food is one of the most important elements to maintain human health and environmental sustainability. Unhealthy diet has a greater negative influence on morbidity and mortality compared with unsafe sex, alcohol, drugs or smoking (EAT-Lancet Commission, 2019). Globally, dietary risks were responsible for 188 million (95% UI 156-225) Disability Adjusted Life Years (DALYs) and 7.94 million (6.47-9.76) deaths among adults of ages 25 and older in 2019 (IHME, 2020). Deaths and DALYs caused by low intake of fruits or vegetables were demonstrated in Table 1, respectively. Besides, agricultural and food production sectors were considered as the major source of greenhouse emission, which accounted for 25% of the total amount of the world (Tilman et al., 2015). Actions are needed to avoid the increasing population suffers from malnutrition and preventable diseases, and to provide the next generation a planet with rich resources to lead a better life. It has been proved by lots of studies that changing diet is an efficient way to improve human health and environment, which to be more specified by, doubling the consumption of plant-based food and reducing the excessive consumption less healthy food such as red meat, added sugar or saturated fat (EAT-Lancet Commission, 2019).

Transmission of dietary pattern to a healthier way with diverse plant-based ingredients is necessary to meet the Sustainable Development Goals and the Paris Agreement. According to the latest dietary

guideline designed by United States Department of Agriculture (USDA), plant-based food should account for nearly 75% of the total calorie intake per day (USDA, 2015). Belgium government also has recommendation for Flemish people with consumption 125 g of whole grains, 250 g of vegetables, 300 g of fruits and at least 15 g of nuts per day, as well as one meal with legumes per week (De Backer et al., 2019). Apart from the dietary guideline, food price policies and nutritional education have been implemented by handful of countries to promote the consumption of plant-based food. By reducing 50% of fruits and vegetables price, the percentage of participants who consumed recommended amounts (≥400 g/d) increased from 42.5% at baseline to 61.3% in the Netherland (Waterlander et al., 2013). The increasing consumption of vegetables can also be found among the children who joined school gardening clubs in England. Children ate more vegetables, 120 (95 % CI 111-129) g/d, compared with those that did not, 99.3 (95 % CI 89.9, 109) g/d (Ransley et al., 2012).

Table 1 Deaths and DALYs caused by diet low in fruit or vegetable in 2019 (IHME, 2020).

	Death (million)		DALYs (million)	
	Diet low in fruit	Diet low in vegetable	Diet low in fruit	Diet low in vegetable
Global	1.05	0.53	27.68	12.95
Eastern Mediterranean Region	0.05	0.06	1.98	1.42
Western Pacific Region	0.29	0.05	7.07	1.05
African Region	0.07	0.06	2.18	1.63
South-East Asia Region	0.36	0.21	10.73	5.77
European Region	0.17	0.08	3.64	1.39
Region of the Americas	0.08	0.08	2.02	1.67

It is obvious that the change of dietary pattern is affecting all aspects of people's lives, especially in level of human health. Plant-based diet has been recognized for its important role in preventing cardiovascular disease (CVD) by significantly reducing the concentrations of total, low-density lipoprotein, high-density lipoprotein, and non-high-density lipoprotein cholesterol in blood (Wang et al., 2015). In a cohort study which aimed at examining the associations of these plant-based diet indices with coronary heart disease (CHD) incidence among more than 200,000 male and female health professionals in the US, plant-based diet index (PDI) was created by assigning positive scores to plant foods and reverse scores to animal foods. The results showed that higher adherence to PDI was independently inversely associated with CHD (Satija et al., 2017). The mechanism of this function can be explained by the lower content of saturated fat and high content of dietary fiber in plant-based food. However, plant-based food which rich in starch and added sugar were associated with a high risk of CHD (Li et al., 2015). Plant-based food is the major source of polyphenols. There are about 200–300 mg polyphenols per 100 g fresh grape or cherry (Pandey et al., 2009). Dietary polyphenols may inhibit α-amylase and α-glucosidase, inhibit glucose absorption in the intestine by sodium-dependent glucose transporter 1, stimulate insulin secretion and reduce hepatic glucose output. In this case, taking plant-based diets become an effective tool for type 2 diabetes prevention and management (Kim, Y et al, 2016; McMacken et al., 2017). Vitamin C is a free radical scavenger, which plays an important role in iron absorption, collagen synthesis and DNA repair in human body

(Lane et al., 2014; Peterkofsky, 1991; Sram et al., 2012). However, humans cannot synthesize Vitamins C so that consuming plant-based food is necessary to meet health needs.

In addition to the health benefits released by plant-based diet, the other part of the society also has positive change. Studies have shown that the increasing consumption of plant-based food is able to ease pressure on resource use and reduce greenhouse gas (GHG) emissions (Springmann et al., 2016; Bajželj et al., 2016). Plant-based food place at the bottom of the food chain. As moving up in the trophic chain, the GHG emission from food production increases several folds. Besides, plant-based food requires less resource input. The production of 1kg soy needs 2.5 m^3 water and 39 g fertilizers, while the production of the same amount of beef needs 20.2 m^3 water and 369 g fertilizers (Sabaté et al., 2015). The economic benefit related to the dietary change can be explained by a lower expenditure of health care and decreasing cost of food production (Springmann et al., 2016).

1.2. Minimal processing

Microbial growth and chemical and/or enzymatic reactions are three major causes of postharvest loss. Fruits and vegetables can be easily contaminated by deteriorative and pathogenic microorganisms that originated from the plant or contaminated during the stage of handling and processing. Besides, endogenous or exogenous enzymes (released by microorganisms) would break down proteins, lipids, carbohydrates, vitamins, and other bioactive compounds into smaller molecules that decrease nutritional and sensory value. In particular, polyphenol oxidase and peroxidase can catalyst enzymatic browning and affect phenolic compounds, resulting in the production of unpleasant colour and flavour. To significantly avoid adverse reactions and inhibit microbial growth, suitable processing techniques are necessary to be applied.

The rising awareness of health and sustainable development resulted in the increasing demand for fresh fruits and vegetables products. However, there are two challenges of producing fresh fruits and vegetables: the first one is maintaining the freshness of products and protecting them from sensory change; the second one is extending the shelf-life and avoiding the problem of nutrition loss and microbiological safety. It is well known that the processing of fruits and vegetables would accelerate the physiological deterioration, biochemical changes and microbial degradation of the products. In order to catering for the consumers' and marketplace's needs, techniques of minimal processing was introduced into the processing of fruits and vegetables products.

Minimal processing is a food production technology, which has minimal influence on the nutritional and sensory quality of food, while also provide food products with sufficient shelf-life during storage and distribution (Ohlsson, 2002). It covers a wide range of techniques that can be applied in stage of processing, packaging, transportation and storage of food products. In addition to the non-thermal minimal processing (such as washing, modified atmosphere packaging, high pressure processing and pulsed electric field), some thermal treatments, like high temperature short time, are also be considered as minimal processing because they have less quality loss compared with the conventional thermal processing technology (Ohlsson, 1996). Most of time, a combination of more than one method, known as hurdle technology, will be applied. Each method has an additive or synergetic effect on microbial inactivation or preventing quality deterioration. During the

production of fresh-cut fruits and vegetables, minimal processing was applied from the beginning—washing to the storage period. Figure 1 shows the process of ready-to-eat fruit, vegetables and root crop. In this thesis, the operation of washing, packaging and storage in fresh-cut production will be discussed in detail.

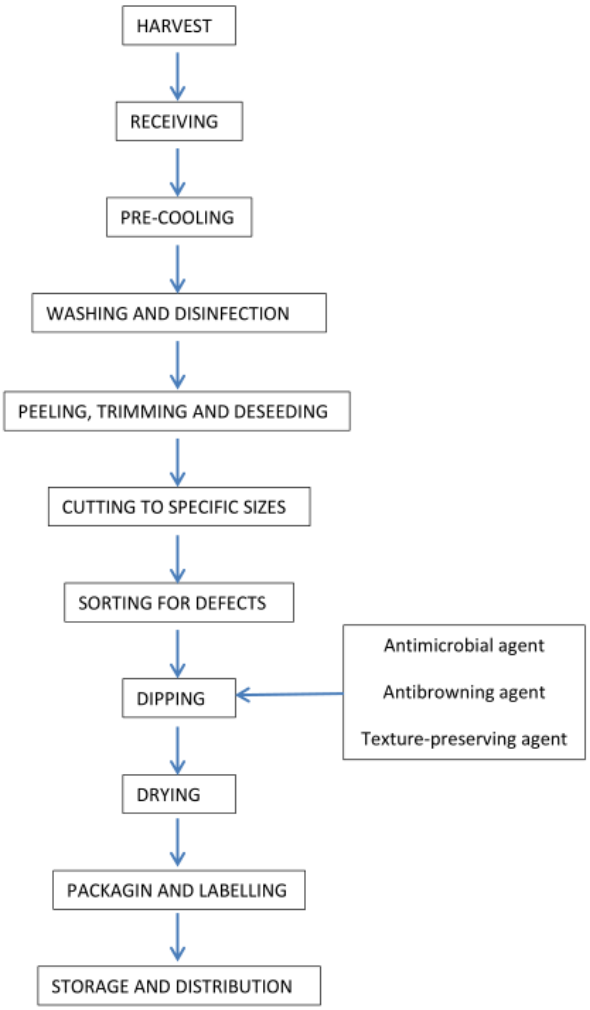

Figure 1 Common ready-to-eat process flow chart for fruits, vegetables and root crops (Jennylynd and Tipvanna, 2010).

1.2.1. Washing

Generally, there are two steps of washing after the fruits and vegetables were harvested from cultivated land. The purpose of pre-washing is to remove soil, plant debris, pesticides as well as microorganisms covered on the surface, and provide a low temperature condition to pre-cool the product, which inhibit the quality deterioration and microbial growth during the subsequent operations (Zagory, 1999). The second washing step usually performed after peeling or shredding to remove microorganisms and tissue fluid, that preventing spoilage and enzymatic browning. The efficacy of washing is associated with the physiochemical properties, such as pH, temperature, organic matter of the washing water, and the type of products (Gil et al., 2009). In practice, large

amount of water is required to achieve the cleaning effect, however, it is not sustainable in the economic and environmental way. Besides, washing water can also be a source of cross-contamination and the vehicles of spreading pathogens between water and products or between different batches of products. In this case, disinfecting and recirculating the washing water are commonly applied. Figure 2 shows an efficient fresh-cut washing operation with the disinfection and recirculation system of washing water. Studies have shown that, after the pre-washing step, there is no significant reduction of the amount of *E. coli* inoculated in iceberg lettuce, while a number of 2 log reduction was observed in the test of aerobic mesophilic bacteria in uncut carrot (Lopez-Galvez et al., 2010; Klaiber et al., 2005). Thus, pre-washing with water is not sufficient to reduce the microbial contamination among fresh fruits and vegetable. Sanitizer needs to be added into the water to improve the cleaning effect (Gil et al., 2009).

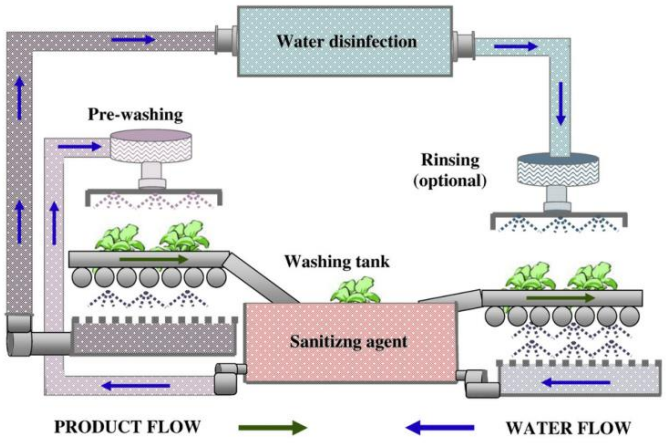

Figure 2 Washing operation with a recirculation system (Gil et al., 2009).

1.2.2. Application of chemical agents

Chemical agents are usually working as antimicrobial and antioxidant during the processing of fruits and vegetables, especially in the second step of washing. Compared with simply dipping in the water, washing in flow or air-bubbling water is more effective (De Corato, 2020). To further reducing microorganism growth and nutrients loss, chemical agents, such as chlorine and related compounds, organic acid or ozone, are added to the washing system. Chemical agents can also be sprayed on the surface of the product or applied as edible coating after the washing steps.

1.2.2.1. Organic acid

Organic acid refers to a wide range of organic chemicals, which contain acidic properties, such as aliphatic and aromatic substances. It has been proved that some organic acids (e.g., Acetic Acid, Citric Acid and Lactic Acid) can be used as antimicrobial against psychrophilic and mesophilic bacteria (In, Y. W et al., 2013; Uyttendaele et al., 2002). Besides, the acetic, oxalic, cinnamic, malic, sorbic, decanoic, propionic, lactic, benzoic, citric, and formic acids were considered as effective antifungal in reducing spoilage of fruits and vegetables (Feliziani et al., 2016). The mechanism of the antimicrobial action by organic acids was described as reduction of environmental pH and disruption of membrane transport and/or permeability, anion accumulation, or a reduction in internal

cellular pH by the dissociation of hydrogen ions from the acids (Beuchat, 2000). Organic acid, which contains only one carboxylic group (–COOH) has less bioactive than the one that contains at least two carboxylic groups (–COOH) (Poli et al., 1979). Study has shown that, with increasing treatment time and concentration of organic acid, the number of *Escherichia coli* O157:H7, *Salmonella typhimurium*, and *Listeria monocytogenes* decreased significantly between fresh apple and lettuce. The antimicrobial activity varied between different organic acids, as about 2 log reduction of *Escherichia coli* O157:H7, *Salmonella typhimurium*, and *Listeria monocytogenes* can be observed in the apple treated with 1% lactic acid for 10min, while acetic acid can only reduce 0.5 log with the same treatment condition (Park et al., 2011). Latic acid also showed excellent ability in controlling contamination caused by microorganism in fresh-cut iceberg lettuce. After treating with 0.5% lactic acid solution for 2 min, the amount of *E. coli* decreased by 2 logs (Akbas, 2007). Temperature can be an influencing factor of antimicrobial ability. Studies showed that washing in warm water (40℃ 5 min) could significantly increase the effectiveness of organic acid washing (Huang, 2011).

Moreover, organic acid and its various neutral salts and other derivatives have been identified as Generally Recognized As Safe (GRAS) antioxidants, that can be used during the production of fresh fruits and vegetables to prevent browning and oxidative reactions (Bauernfeind et al., 1970). In the case of fresh fruits and vegetables, especially apples and potatoes, tissue discoloration due to browning is the major quality problem that could not be accepted by customers because of the poor appearance. The browning and firmness of sliced potatoes dipped in solutions of various combinations of 4-hexyl resorcinol, N-acetylcysteine and citric acid were analysed under 10℃. Positive results showed that browning as well as soften of slices from potatoes stored 1 month longer were inhibited (Buta et al., 2001). Preventing of browning by organic acid cannot simply explain by the reduction of pH. Organic acid is able to bond with phenolic substrates or polyphenol oxidase to form complexes. As a result, browning is inhibited because of insufficient catalyst (Tsouvaltzis et al., 2017).

Table 2 Summary of the antimicrobial effectiveness of chemical agents.

Articles	Fruits/Vegetables	Sanitizers	Concentrations	Contact times	Effect on pathogen
Organic acid					
Park, S. H et al, 2011	Apple	Lactic acid	1%	10 min	2 logs reduction of *E. coli*
Akbas, M. Y, 2007	Iceberg lettuce	Citric acid	0.50%	2 min	2 logs reduction of *E. coli*
Huang, Y, 2011	Baby spinach	Malic acid	1%	5 min	2.7 logs reduction of *E. coli* O157:H7
Chlorine and related compound					
Lee, S. Y et al, 2004	Lettuce leaves	Chlorine dioxide	0.115mg/L	30 min	5 logs reduction of *Listeria monocytogens*
Han, Y et al, 2004	Strawberries	Chlorine dioxide	4 mg/L	30 min	>5 logs reduction of *Listeria monocytogens*
Kingsley, D. H et al, 2018	Blueberries	Chlorine dioxide	4.16 mg/L	15 min	>2.2 logs reduction
Han, Y et al, 2000	Green pepper	Chlorine dioxide	1.24 mg/L	30 min	6.45 logs reduction of *E. coli* O157:H7
Ozone (O_3)					
Daş, E et al, 2004	Tomato	Gaseous ozone	10 mg/L	20 min	7 logs reduction of *Salmonella enteritidis*
Chuajedton, A et al, 2017	Leaf vegetable	Bubbling ozone water	10 mg/L	30 min	1.2 logs reduction of *E. coli* O157:H7

1.2.2.2. Chlorine and related compound

Chlorine and its related salt compounds, such as sodium hypochlorite (NaClO), have been widely used in washing water to prevent cross-contamination during the processing of fresh products. The disinfection ability of chlorine is associated with the amount of free chlorine iron (mainly hypochlorite), the contact time with the product and pH as well as the temperature of the washing water. The solubility of hypochlorite decreases with increasing pH. It has been proved that at the pH of 6, the solubility of chlorine in water is 97%, while which is only 23% at the pH of 8 (White, 1999). The recommend processing usage of chlorine in fruits and vegetables is 50-200 ppm at the pH of 6-7.5 with at least 5 min (Gonzalez et al., 2004; Rivera, 2005). Lower pH is not applicable due to the corrosion of metallic materials. It is worth noting that the application of chlorine in fresh fruits and vegetables production is forbidden by some European countries, because of the possibility of generating chlorine gas and producing toxin by-products, such as trihalomethanes, haloacetic acids, and chloramines (Van Haute et al., 2013).

Chlorine dioxide (ClO_2) is a yellow to red gas, which has been considered as a useful alternative of chlorine and sodium hypochlorite as it induces fewer potentially carcinogenic compounds by chlorinated reaction products than chlorine (Ramos et al., 2013). It is usually used after wash water to improve the previous sanitization effects. In addition to lower toxicity, chlorine dioxide has better performance in mixing with air, rapid diffusion, and the ability to penetrate permeable surfaces and biofilms compared with chlorine aqueous formulations (Sun et al., 2019). Besides, chlorine dioxide is more effective for inactivating microorganism. Chlorine dioxide can inactivate microorganism through three pathways: damaging the stability of cell membranes; reaction with protein and the inhabitation of protein synthesis; oxidating DNA and RNA (Praeger et al., 2016; Benarde et al., 1967; Buschini et al., 2004). Thus, the efficacy varies between Gram-positive (G+) and Gram-negative (G-) bacteria that Gram-positive (G+) bacteria were more sensitive to chlorine dioxide, while molds and yeast displayed intermediate tolerance (Vandekinderen et al., 2009).

Table 3 shows the effectiveness of ClO_2 for inactivating different pathogens. The ability of microbial inactivation of chlorine dioxide has been tested against foodborne pathogens on lettuce leaves. 4.3, 6.7, and 8.7 mg/20L chlorine dioxide was generated by a dry chemical sachet after 30 min, 1 h, and 3h, respectively. The results showed that a 3.4-log reduction in *E. coli*, a 4.3-log reduction in *Salmonella typhimurium*, and a 5.0-log reduction in *L. monocytogenes* can be observed in lettuce leaves exposure in ClO_2 for 30 min. After 1 h, the reduction of the three pathogens reached 4.4, 5.3 and 5.2 log, respectively. After 3 h, the reductions were 6.9, 5.4, and 5.4 logs, respectively (Lee et al., 2004). ClO_2 can also be applied in the disinfection of perished fruits like blueberries or strawberries. The number of *E. coli* O157:H7 and *L. monocytogenes* in strawberries reduced significantly by more than 5 logs after treating with batch treatment with 4 mg/L ClO_2 for 30 min and continuous treatment with 3 mg/L of ClO_2 for 10 min. Moreover, there were no colour changed and chlorine residuals among the strawberries treated with continuous 3 mg/L ClO_2 for 10 min after storing for 1 week (Han et al., 2004). Efficacy of ClO_2 against the human norovirus surrogate, Tulane virus, was determined through Tulane virus-coated blueberries in a 240 mL treatment chamber. The virus populations were reduced by more than 2.2 logs after 15 min exposure and to

non-detectable levels (more than 3.3 logs reductions) after 180 min exposure (Kingsley et al., 2018). ClO_2 can also be used in the combination of ultrasonic to improve the efficacy of microbial inactivation. Meanwhile, the chlorine residuals decreased with the increasing ultrasonic treatment time (Huang et al., 2006). The concentration of chlorine dioxide is one of the influence factors on the effectiveness of disinfection. Green pepper surface-injured with E. coli O157:H7 experienced a greater microbial reduction of 6.45 logs when treated with 1.24 mg/L ClO_2 for 30 min at 22°C and 95% relative humidity, compared with the reduction of 3.03 log with 0.63 mg/L ClO_2 treatment for 30 min at the same condition (Han et al., 2000).

Table 3 Effectiveness of ClO_2 for microbial inactivation by different treatment.

Articles	Fruits/Vegetables	Treatments	Effects on pathogens
Lee et al., 2004	Lettuce	Up to 0.215 mg/L for 30 min	3.4 log reduction of *E. coli* 4.3 log reduction of *Salmonella typhimurium* 5.0 log reduction of *L. monocytogenes*
		Up to 0.335 mg/L for 30 min	4.4 log reduction of *E. coli* 5.3 log reduction of *Salmonella typhimurium* 5.2 log reduction of *L. monocytogenes*
		Up to 0.435 mg/L for 30 min	6.9 log reduction of *E. coli* 5.4 log reduction of *Salmonella typhimurium* 5.4 log reduction of *L. monocytogenes*
Han et al., 2004	Strawberry	4 mg/L for 30 min followed by 3 mg/L for 10 min	More than 5 log reduction of E. coli and *L. monocytogenes*
Kingsley et al., 2018	Blueberry	Up to 0.6 mg/L for 180 min	More than 3.3 log reduction of Tulane virus (Norovirus surrogate)
Han et al., 2000	Green pepper	1.24 mg/L for 30 min	6.45 log reduction of *E. coli* O157:H7

1.2.2.3. Ozone

Ozone (O_3) is formed by the natural rearrangement of oxygen atoms: when high-energy inputs, the molecular oxygen (O_2) will split into two single oxygen, and then those single oxygen rapidly combine with O_2 to generate O_3. High concentration of ozone has pungent, unpleasant odour, and irritation to the eyes and throat. It is lethal to humans if exposed at concentrations above 4 ppm for a long time. Ozone is extremely soluble in water and quickly degrades to molecular oxygen within 10-20 min so that there are no toxic residuals both in the product or environment (Velez Rivera, 2005). The solubility of ozone influence by several factors like pressure, temperature or pH. It has been proved that ozone has a much higher oxidation ability than chlorine and is effective against a wide range of microorganisms. The mechanism of microbial inactivation by ozone is very complex. Ozone is able to attack different cellular components such as proteins, unsaturated lipids, respiratory enzymes, and nucleic acids in the cytoplasm, and recognize active sites like proteins and peptide-glucans in fungi and bacteria spore coats, and virus capsids (Khadre et al, 2001). Ozone can be applied in aqueous treatment in the washing stage of fruits and vegetables or under gaseous condition. Generally, it can be a low concentration of ozone and exposure for a long time (less than 1.0 µL/L for a few hours daily) to minimize risk for workers, or high concentration for short time

(up to 10 000 µL/L a few hours one day) to inactivate fungal conidia and resistant bacterial spores. During the storage of fresh product, two approaches for gaseous ozone are mainly used: products were stored under continuously low concentrations for many days, or under very high concentration of ozone given briefly once or repeatedly at fixed intervals during storage (Feliziani et al., 2015).

Ozone has been awarded GRAS status by the US Food and Drug Administration (FDA) in 1997 and adopted by EU countries as an environmental-friendly antimicrobial agent in the food industry. It has been proved that gaseous ozone has bactericidal effect on *Salmonella enteritidis.* Tomatoes incubated with high dose (7.0 logs cfu/tomato) and low dose (3.0 logs cfu/tomato) of *Salmonella enteritidis* were treated with 10 mg/L ozone gas for 5-20 min. When the pathogen attachment time was 4 hours, the cells in high-dose incubated group died completely after 20 min exposure. When the pathogen attachment time was 1 hour, 15 min and 5 min treatment is sufficient for the complete cell death in the high dose inoculum group and low dose inoculum group respectively (Daş et al., 2006). The antimicrobial efficacy of ozone in washing water was evaluated on reducing *Escherichia coli* O157:H7 in leaf vegetables. A reduction of 0.8-1.2 logs in the visible *Escherichia coli* O157:H7 cells was observed after treatment of 30 min under 13°C (Chuajedton et al., 2017). Microorganisms have different resistance to gaseous ozone. After treating with 9 ppm gaseous ozone for 6 h, *E. coli* O157, *Salmonella typhimurium* and *L. monocytogenes* reduced 2.89, 2.56 and 3.06 logs, respectively (Alwi, 2014). The microbial inactivation ability of ozone not only determined by the species of microorganisms but also the type of products, initial microbial load levels, physiological state of the bacterial cells and ozone physical states (Miller et al., 2013).

In addition to ensuring microbial safety, ozone also shows an excellent ability of maintaining the physicochemical, sensorial, and nutritional quality of the products and extending shelf-life. After exposure to ozone concentrations ranging between 0.005 (controls) and 1.0 µmol/mol at 13°C, the content of vitamin C, polyphenol and total soluble sugar did not change in the tomato (Tzortzakis et al., 2007). The influence of product colour by ozone treatment was observed during the period of storage. Ozone can inhibit the chlorophyll degrading enzymes and induce antioxidants that can protect chlorophyll. As a result, the yellowing of some leaf vegetables can be significantly prevented within the shelf-life (Forney et al., 2003).

1.2.3. Modified atmosphere packaging (MAP)

Modified atmosphere packaging has been widely used to extend shelf-life of the minimally processed fresh fruits and vegetables. The atmosphere modification in the package can be achieved passively or actively. In the passive package, properly permeable packaging materials will be applied and the desired atmosphere develops naturally as a consequence of the equilibrium of products' respiration and the diffusion of gases through the package. In the active package, gas in the package will be replaced by a special gas mixture associated with a permeable package material (Parry, 2012). The purpose of modifying atmosphere is to provide an optimal environment, in which the products have a lower respiration rate and the microbial growth as well as enzymatic reaction will be inhibited. In general, the recommendation of gas composition is the gas composition of 2-5% CO_2, 2-5% O_2 and the remaining gaseous compounds of N_2. Importantly, physical damage will occur if the CO_2 concentration below the CO_2 tolerance of products, and excessively low O_2

concentration results in anaerobic fermentation and putrefaction, which might cause the formation of acetaldehyde and other off-flavour compounds.

Modified atmosphere packaging plays an important role in the storage of fresh fruits and vegetables product. It has been proved that reducing the concentration of oxygen or elevating the concentration of carbon dioxide can significantly delay fruit ripening and retard the composition change. Compared with control group, fresh-cut mango packed in a gas mixture of 10% CO_2, 4% O_2, 86% N_2 resulted in the best maintenance of colour, firmness soluble solid during storage (Martínez-Ferrer et al., 2002). Similar results can be found in the research of the MAP (5% O2 + 5% CO2) fresh-cut tomatoes. For 14 days storage, the lycopene, vitamins C amount in the six cultivars of tomatoes remained stable and there is no significant change of the colour parameters (Odriozola-Serrano et al., 2008). The most suitable concentration of CO_2 and O_2 vary according to the type of product because of the different tolerance of CO_2. Fresh-cut products are more tolerant to high CO_2 concentration than un-cut product that fresh-cut lettuce remained stable under 10-15% of CO_2 while un-cut lettuce cannot tolerance (Rico et al., 2007). Nevertheless, MAP can significantly delay microbial growth. White cabbage was packaged in bags with O_2 permeability of 55 mL-µm/KPa-s-m^2 after treated with lactic acid and then stored for 7 days under 10°C. The air composition inside was modified by CO_2 (100%) or N_2 (100%). Results showed that MAP was effective in maintaining reduced levels of E*scherichia coli* O157:H7, *Salmonella typhimurium*, and *Listeria monocytogenes* on cabbage (Bae et al., 2011). MAP in combination of several natural essential oils has been proved as an effective way to inhibited fungal growth. After treating with eugenol, thymol, menthol or eucalyptol and then packed in MAP (2-3% of CO_2 and 11-12% of O_2), the incidence of quality decay in cherry reduced considerably (Calhan et al., 2013).

1.2.4. Storage condition

Fresh fruits and vegetables are living issues that different chemical reaction, enzymatic reaction as well as microbial growth and proliferation are ongoing and active during the storage period. Storage condition, especially temperature, has a huge impact on the flavour, firmness, taste, nutrients composition and microbial safety of the fresh products. Preserving under a suitable temperature, in combination with proper humidity, can effectively delay sensory quality deterioration due to its effect on reducing respiration rate, moisture loss, ethylene emission and inhibit microorganism growth, which extend the shelf-life of fresh fruits and vegetables (W, C. T, 2010). Generally, storage at a lower temperature results in a longer shelf-life. However, for fresh fruit and vegetable products, temperature should be controlled within the acceptable limit to avoiding colour change, chilling injury and shrivelling (do Nascimento Nunes, 2008).

Appearance is one of the most critical factors that influence the value of fresh product in the marketplace. Study has confirmed that compared with the tomatoes stored under 20 or 30°C, the tomatoes stored under 4°C had less colour index and chroma increment. During the ripening of tomatoes, lycopene will accumulate that increasing the colour index and chroma. The results suggested that storing under low temperature could retard the colour change and ripening of tomatoes (Tadesse et al., 2015). The colour of cranberries showed more darkness and less vividity during the storage, but low temperature was proved to be able to maintain the colour (Nunes et al.,

2003). Other studies have confirmed that low temperature storage can influence the nutritional value of the product. Antioxidant activity, total phenolic content, anthocyanin content of 9 blueberry cultivars were tested at harvest and during the storage (5°C for 3 weeks). Results showed that the antioxidant activity of all cultivars increased significantly, and one of them demonstrated a 29% increment (Connor et al., 2002). Strawberry fruit stored at 10°C or 5°C showed higher antioxidant capacity, total phenolics, and anthocyanins than those stored at 0°C (Shin et al., 2008). In addition, the soluble solids, total sugar and ascorbic acid were investigated to decreasing when the environmental temperature increased (do Nascimento Nunes, 2008).

During the storage of fresh fruits and vegetables, the survival and growth of microorganisms depend on the type of microorganisms, food and the storage temperature, time and relative humidity (RH). *Listeria monocytogenes* were inoculated on fresh lettuce, cucumber and parsley, then storage under 10°C for 7 days, 20°C for 5 days, and 30°C for 24 h, and at 53 and 90% RH. Results show that *Listeria monocytogenes* could not grow on lettuce or parsley, but there was no decline in number. Nevertheless, Listeria monocytogenes can grow in cucumber under all three temperatures and the amount of which increased 1.5 logs cfu/cm2 at the humidity of 90% (Likotrafiti et al., 2013). *Listeria monocytogenes* was found to have higher growth potential than *Salmonella* in 8 different ready-to-eat salads stored at 7°C. However, both *L. monocytogenes* and *Salmonella* were inhibited in grated carrot and a more significant effect was found against *L. monocytogenes* (Sant'Ana et al., 2012). The growth potential of *L. monocytogenes* tested by another study showed that a number of 2.3 logs cfu and 2.8 logs cfu increment were observed under the storage condition of 23°C for 5 h and 4°C for 21 days. Low temperature can retard the *L. monocytogenes* growth, but they can survive in frozen condition (-18°C for 120 days) (Bardsley et al., 2019). *Escherichia coli* O157:H7 was inoculated in fresh-cut escarole, carrot and pineapple with the initial concentration of 4.3, 4.5 and 4.9 logs cfu/g. After storing at 25°C for three days, the amount of which in fresh-cut escarole reached 6.3 logs cfu/g, while there was no considerable change of the number of *E. coli* O157:H7 in carrot and pineapple. Besides, under the storage condition of 5°C for 8 days, the amount of *E. coli* O157:H7 with the same initial concentration in fresh-cut escarole, carrot and pineapple decreased significantly (Abadias et al., 2012). Temperature control is critical for commercial fresh fruits and vegetables, the products should be placed at low temperature in the whole supply chain to ensure safety.

1.3. Microbiology hazard in the minimally processed fruits and vegetables

Foodborne disease has been considered as a serious threat to public health and impeded the socio-economic development worldwide. Foodborne disease is defined as disease commonly transmitted through ingested food, it comprises a broad group of illnesses, caused by microbial pathogens, parasites, chemical contaminants or biotoxins (WHO, 2008). Table 4 shows the global diseases burden of four pathogens. In 2010, about 600 million people suffered from foodborne illness and microbial pathogens accounted for more than 99% of the infectious agents, in particular norovirus (120 million), *E. coli* (111 million), *Salmonella typhi* (7.6 million) (WHO, 2015). The implicated food vehicles were mainly animal-based food. However, an increasing number of foodborne outbreaks can be traced back to the consumption of fresh fruits and vegetables recently (Yeni et al., 2015). This trend may explain by the rising consumption of fruits and vegetables, improved surveillance, global or centralized distribution chains, and a higher portion of vulnerable people

within the population (Warriner, 2005).

Table 4 Median global number of foodborne illnesses, deaths and Disability Adjusted Life Years (DALYs), percentage of foodborne deaths aged lower than 14 years old and higher than 65 years old with 95% uncertainty intervals, 2010 (WHO, 2015).

Hazard	Illnesses (million)	Deaths (million)	DALYs (million)	Deaths aged lower than 14 years old	Deaths aged higher than 65 years old
Norovirus	124.80 (70.31-251.35)	0.03 (0.02-0.08)	2.50 (1.20-5.55)	50%	10%
Listeria monocytogenes	0.01 (0.006-0.09)	0.003 (0.001-0.02)	0.12 (0.05-0.75)	6%	58%
Salmonella spp.	88.01 (34.71-234.20)	0.12 (0.025-0.22)	5.81 (1.98-13.73)	/	/
Escherichia coli	111.48 (60.64-217.24)	0.07 (0.03-0.10)	5.01 (2.77-8.36)	51.60%	10%

Figure 3 shows the pathway of pathogens transmitted from environment to human. Fruits and vegetables can be contaminated by pathogens from seeds, water, soil or insects during the preharvest stage, and during the postharvest stage through cross-contamination (water, equipment, handlers) (Adams, 2007). Although there are natural defence mechanisms, for instance, wax cover, low pH or rich in polyphenols, fruits and vegetables are suitable habits for pathogens to grow and multiplicate, as they full of nutrients and have natural openings (stomata, lenticels) (Lattanzio et al., 2006; Yeni et al., 2015). Most of the fruits and vegetables are consumed raw or without heating treatment to inactivate microorganisms, that they were recognized as a vehicle for transmission of human pathogens.

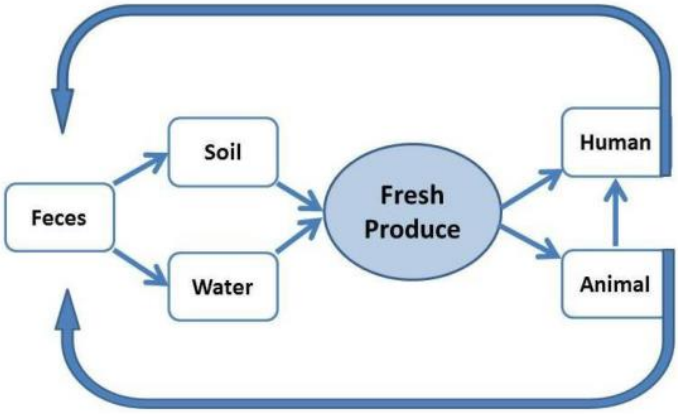

Figure 3 Potential pathways of pathogens transmission to humans via fresh produts (Zhu et al., 2017).

1.3.1 Primary pathogens

1.3.1.1. *Salmonella spp.*

Salmonella enterica (*S. enterica*) is a Gram-negative facultative intracellular anaerobe, which has been identified by over 2 500 serovars (Ochman, 1994). The serovars were distinguished by two different surface antigens: O antigen with the variation in the exposed part of the lipopolysaccharide and H antigen variation in flagellin (Lan et al., 2009). *S. enterica* can cause diseases in both human and animals, the infection typically results in four syndromes: fever, enterocolitis or diarrhoea, bacteraemia and chronic asymptomatic carriage. In humans, serovars Typhi, Paratyphi and Sendai are responsible for enteric fever, while most serovars cause enterocolitis or diarrhoea (Fierer, 2001). *S.* Typhi is one of the most common foodborne illness causes all around the world, accounting for 7.6 million cases and 52 000 deaths in 2010 (WHO, 2015). For many years, salmonellosis associated with serovar *Typhi* is the major health concerns globally. However, more attention needs to be paid to non-typhoidal *S. enterica*, as it accounted for 59,000 deaths in 2010 (Lan et al., 2009; WHO, 2015). More than half of *Salmonella* outbreaks were caused by *S. enteritidis* in 2018, while typhoid and paratyphoid fevers are relatively rare in the European Union/European Economic Area (EU/EEA) (EFSA, 2019). In 2017, 29 countries in the EU/EEA reported a total of 1 098 cases and 90% of which were travel related. About 68% of the cases associated the infection of *S.* Typhi, while the others were caused by *S.* Paratyphi (ECDC, 2020).

Salmonella is able to contaminate plant host through soil and then colonize in the nodule-like structures and rhizosphere of the plant (Hernández-Reyes, 2013). The colonization efficiency depends on the cultivar of plant and serovar of *Salmonella* (Klerks et al., 2007). Other contamination routes can be through fecal, water, insects, animals or human. The European commission has established the limitation of *Salmonella* in products placed on the market during their shelf-life (absence in 25 g food samples) and collected the information of the prevalence among different food products annually (European Commission, 2005). In 2018, 4 490 units of vegetable sample from the European region were tested and 0.6% of them showed *Salmonella* positive, while 2 out of 1 575 units of fruit sample was *Salmonella* positive (EFSA, 2019). The prevalence of *Salmonella* in unpacked or packed vegetable retail establishments was estimated by 0.9% with 95% CI: 0.5-1.2% and which for fruit was 0.54% with 95% CI: 0.55-4.60% (Silva et al., 2017). The infection of *Salmonella* in human mainly through fecal-oral transmission or the intake of contaminated products. The infection dose is determined by the physiological characters, healthy status of the host and type of food stuffs (Fatica, 2011). In European region, 91 857 cases and 1 581 outbreaks related to the infection of *Salmonella* in 2018. Among the strong-evidence outbreaks, 0.7% of them were proved to transmit through vegetable and juices and other their products (EFSA, 2019). Ready-to-eat salads contained cucumber was considered as a potential vehicle of a multi-country outbreak of *S. agona.* 122 cases were reported by 5 European Union countries in 2017 and 25 cases were reported between 2014 and 2016 (EFSA, 2018). In another multi-country outbreak, *S. strathcona* was proved to infect 53 people through contaminated datterino tomatoes in 2011 (Müller et al., 2011). 82 cases were confirmed in an outbreak of monophasic *S. typhimurium* in Sweden between 28 August and 29 October in 2019. Small tomatoes were considered as the source of outbreak in case-control study (adjusted odds ratio (OR): 10.8, 95% CI: 4.15-112.68, $p<0.001$) (Colombe et al., 2019).

1.3.1.2. *Listeria monocytogenes*

Listeria monocytogenes (*L. monocytogenes*) is a Gram-positive and facultative intracellular bacterium, which can be found in agricultural environment, such as soil, water or manure, and presents in lots of food categories. It is able to survive in the salt concentration of up to 14% and grow at the temperature range from 1 to 45°C. Besides, *L. monocytogenes* is relatively resistance to heat and lower pH. Listeriosis caused by *L. monocytogenes* is a rare but serious disease. Nearly 95% of human listeriosis was caused by *L. monocytogenes* strains belonging to serotypes 1/2a, 1/2b and 4b (Graves et al., 2007). Syndromes of listeriosis can be mild as gastroenteritis or severe as septicaemia, encephalitis, meningitis, abortions and stillbirths (Zhu et al., 2017). *L. monocytogenes* was first recognized as a foodborne pathogen in the 1980s and has caused several foodborne outbreaks since it was discovered. In 2010, *L. monocytogenes* resulted in 23 150 illness and more than 60% of which was identified as foodborne illness. The number of 3 175 foodborne deaths and 118 340 foodborne DALYs were also reported by WHO in 2010 (de Noordhout et al., 2014; WHO, 2015). The incidence of listeriosis in high-income countries was quite low but the mortality rate was relatively higher. 2 549 cases of foodborne Listeriosis were confirmed with an EU notification rate of 0.47 cases per 100,000 populations by EFSA in 2018. The case fatality was high (15.6%, while that for salmonellosis was only 0.19% in 2018), which makes listeriosis one of the most serious food-borne diseases in EU (EFSA, 2019).

L. monocytogenes is widely present in the natural environment. This bacterium has a strong life cycle adaptation capability that it lives a saprophytic life in the soil but change into a pathogen when it enters human or animal cells (Freitag, 2009). Besides, the ability of persists and multiplies in the low temperature make it different from other pathogens, which pose a threat to refrigerated fruit and vegetable products. The limitation of *L. monocytogenes* in ready-to-eat products placed on the market during their shelf-life is 100 cfu/g (European Commission, 2005). 16 member states in EU conducted investigations of *L. monocytogenes* on 1,257 units of ready-to-eat fruits and vegetables. The overall occurrence was of 1.8%. For ready-to-eat salads, 1.5% of the units tested were reported as positive (EFSA, 2019). The occurrence rate of *L. monocytogenes* in fruits and vegetables from European retails were estimated as 1.91% and 3.4% correspondingly (Silva et al., 2017). Fruit and vegetable products have been considered as an important vehicle of listeriosis recently years. The category ‘vegetables and juices and other products’ therefore was the food vehicle causing the higher number of strong evidence foodborne outbreak (two) in 2018 (EFSA, 2019). It has been proved that frozen corns are the source of *L. monocytogenes* (serogroup IVb, multi-locus type 6) outbreaks that 47 cases and 9 deaths have been reported by ECDC since 2015. Other frozen vegetables may also be the potential source of *L. monocytogenes* outbreaks, however there is still lack of evidence (EFSA, 2018).

1.3.1.3. *Escherichia coli*

Escherichia coli (*E. coli*) is a Gram-negative, facultatively anaerobic, chemo-organotrophic, non–spore-forming, rod-shaped bacterium. *E. coli* strains are distinguished by O-antigen in the lipopolysaccharide on the outer envelope of the cell, the flagella H-antigen, and the capsular K-antigen. Similar to *Salmonella*, the serovars identification of *E. coli* base on the O antigen (more

than 185 groups) and H antigen (53 groups) (Smith, 2017). Most of *E. coli* strains are harmless, while others can cause intestinal diseases extraintestinal infections, such as urinary tract infections and neonatal sepsis (Johnson, 2002; Vila et al., 2016). Shiga toxin-producing *E. coli* (STEC) is an intestinal pathogenic *E. coli* and often associated with nonspecific diarrhoea, haemorrhagic colitis, and the haemolytic uremic syndrome (HUS) in human body (Griffin et al., 1995; Karmali et al., 1985). In 2010 *E. coli* resulted in more than 110 million foodborne illness worldwide. Enteropathogenic *E. coli* (EPEC) and enterotoxigenic *E. coli* (ETEC) accounted for 37,000 and 26,000 foodborne deaths respectively (WHO, 2015). In 2018 the number of foodborne illness caused by STEC increasing rapidly and 8 161 cases were confirmed (39% higher than which in 2017) in EU (EFSA, 2019). The proportions of the top-one serotypes reported in food in 2018 were: O157 (0.12% of the 20 424 samples tested and 4.95% of the positive samples), followed by O103 (0.06% of the samples tested and 2.47% of the positive samples) (EFSA, 2019).

E. coli exists in human and warm-blooded animal gut and is able to adherence in the epithelial cell of human intestine (Table 5). Pathogenic *E. coli* have evolved mechanisms for attaching on the surface of raw vegetables that several *E. coli* foodborne outbreaks were associated with fresh vegetables, especially sprouts and green leafy vegetables (Luna-Guevara, 2019). European commission has implemented limitation of *E. coli* in pre-cut fruits and vegetables, the acceptable amount is less than 1000 cfu/g and the satisfactory amount is less than 100 cfu/g (European Commission, 2005). Vegetable commodities were tested by 8 member states of EU, one out of 2 117 samples showed *E. coli* positive, and the isolate was a STEC O179:H8 possessing the *stx2f* gene. The prevalence of STEC in vegetable and fruit from European retail establishments were estimated by 1.9% and 4.7% (Silva, et al., 2017). STEC was identified with 48 food-borne outbreaks and one of them caused by consumption of vegetables with strong-evidence (EFSA, 2019). In 2011, one of the largest reported outbreaks of HUS and bloody diarrhoea caused by STEC O104:H4 occurred in 14 EU countries. The source of outbreak was identified as sprout consumed raw. This outbreak resulted in 877 cases of HUS with 32 deaths and 3 043 cases of enterohaemorrhagic *Escherichia coli* (EHEC) with 16 deaths that created anxiety among the public and even panic within regions of the EU. (Foley et al., 2013). STEC serotype O157:H7 caused an outbreak by contaminated leaf-mix salad in England. One year later, new cases were identified sharing the same outbreak strain (Mikhail, 2018).

Table 5 Pathotypes of *Escherichia coli* and associated illness (Smith, 2017).

E. coli pathotypes	Symptoms
Intestinal Pathogenic *E. coli*	
Enteroinvasive *E. coli* (EIEC)	Acute dysenteric diarrhoea
Diffusely adherent *E. coli* (DAEC)	Watery diarrhoea in children
Enteropathogenic *E. coli* (EPEC)	Acute and/or persistent diarrhoea
Enteroaggregative *E. coli* (EAEC)	Persistent watery diarrhoea
Enterotoxigenic *E. coli* (ETEC)	Acute watery diarrhoea
Shiga toxin–producing *E. coli* (STEC)	
A. O157:H7 STEC	Diarrhoea, haemorrhagic colitis, HUS
B. Non-O157 STEC	
C. Enteroaggregative *E. coli* (STEAEC)	

	Adherent invasive *E. coli* (AIEC)	Diarrhoea, inflammatory bowel diseases
	Non-intestinal Pathogenic *E. coli*	
	Extraintestinal pathogenic *E. coli* (ExPEC)	
A.	Uropathogenic *E. coli* (UPEC)	Urinary tract infections
B.	Neonatal meningitis *E. coli* (NMEC)	Gram-negative–associated meningitis in new-borns
C.	Sepsis-associated *E. coli* (SEPEC)	Sepsis
D.	Avian pathogenic *E. coli* (APEC)	Colibacillosis in fowls

1.3.1.4. Norovirus

Norovirus is an RNA virus of the family *Caliciviridae*, are classified into five genogroups: GI-GV, among which three cause gastrointestinal illness in humans: GI, GII, and GIV (Bitler et al., 2013). It was described as "winter-vomiting disease" or "stomach-flu", because it has seasonal predilection and spread fast in human with syndrome of vomiting (Robilotti, 2015). Human norovirus has different genotypes with as much as a 2.8% difference between strains of an individual virus (Zheng et al., 2006). Norovirus can infect humans in two ways. The first one is consuming contaminated foodstuff that has infected by norovirus. In this case, water can also be a contaminated and spread agent. The other one is transmitting between humans directly. Noroviruses are highly contagious and 10-100 viral particles may be sufficient to infect an individual (Ohe, 2013). Patients infected by Norovirus can be asymptomatic or have the symptom of vomiting, diarrhoea or more sever as leukocytosis and thrombocytopenia (Robilotti, 2015). Norovirus is the leading cause of foodborne illness worldwide, which resulted in 120 million cases and 35 000 deaths globally in 2010 (WHO, 2015). In 2018, Norovirus and other caliciviruses caused 8 507 foodborne illnesses and 219 hospitalizations in EU. A considerable increasing in the number of norovirus outbreak can be observed in France (+119; +219% more than 2017) and in Spain (+37; +336% than 2017) (EFSA, 2019). Norovirus had an important influence on the public healthy in EU, as it was responsible for a larger number of illness and several large size outbreaks.

Contamination of Norovirus in fresh fruits and vegetables occurs during the stage of processing by sewage drained from areas where seafood is farmed or from contaminated irrigation water. It may also be contaminated directly through the hands of infected handlers (El-Senousy et al., 2013; Le Guyader et al., 2008). 2018, 10% of strong-evidence foodborne outbreaks associated with the consumption of fruit and vegetable were caused by Norovirus in the EU (EFSA, 2019). A norovirus outbreak was reported with 74 illnesses in November 2013. Identified food was raspberries served in mousse at the meeting hold at a conference centre but contamination from food handler could not be excluded (Einöder-Moreno, 2016). A Sweden office-based company reported a number of gastroenteritis in 2015. 8 illness cases were defined as employees worked in the company with symptom of vomiting and diarrhoea and their fecal samples were collected to analysis. All 8 fecal samples tested positive for GII norovirus, which was also detected in coleslaw collected from the in-house restaurant (Sharma, 2020). A large size of outbreak with over 1,000 customers and staff reported gastroenteritis after eating at all 23 branches of a restaurant group was reported in the United Kingdom. The potential norovirus source was chipotle chili imported from outside EU (Morgan et al., 2019).

1.3.2. Opportunistic pathogens

1.3.2.1. Characteristics

Opportunistic pathogens are usually harmless to healthy people but could be dangerous to immunocompromised persons. Some of them are also zoonotic and exploit numerous other hosts (e.g., *Bacillus anthracis* and rabies virus). These opportunistic pathogens can emerge from among the ranks of normally commensal symbionts or from the environmental microorganisms (Brown, et al., 2012). Although these opportunists belong to different phylum, for instance, *Firmicutes* (*Staphylococcus, Enterococcus*) and *Gammaproteobacteria* (*Proteus, Serratia, Pseudomonas, Escherichia, Enterobacter,*), they have common characters: copiotrophs, cultivable, antagonistic towards other microorganisms, highly competitive and versatile in their nutrition, hypermutators, resistant against antibiotics and toxins, and forming biofilms (Berg et al., 2014). The common characters are acquired through horizontal gene transfer and are strain-specific, which means that new strains of pathogens will emerge constantly in the future, and the virulence keeps evolving to adapt the environmental change (Sydnor, 2011; Brown et al., 2012). The mechanism of opportunistic pathogens by interacting with hosts includes invasion, competition for colonization sites and nutrients, competition for minerals, development of antibodies resistance and establishment of virulence (Berg et al., 2005).

Globally, about 15 to 20% of the total population shows a higher possibility of pathogen infection (Lund et al., 2011). Elderly people are one of the vulnerable groups as their immune system is gradually deteriorating and some of them also suffer from chronic diseases. In the United Kingdom, people older than 65 accounts for 16% of the population, and the number is increasing because of demographic change. Elderly people are the group most likely to die after infection with *L. monocytogenes* and STEC O157 (WHO, 2010; Gould et al., 2009). Immunocompromised persons, including those treated with chemotherapy or radiation therapy, recipients of transplants taking immunosuppressive drugs, persons with leukemia, persons with diseases of the immune system, AIDS patients, are also in the vulnerable groups. Tuberculosis, *Pneumocystis jiroveci pneumonia*, candida infection, *cytomegalovirus* infection were the most common opportunistic infections and resulted in a longer period of hospitalization in AIDS patients in China (Pang et al., 2018). *L. monocytogenes* is the most important foodborne pathogen to pregnant women, which may cause foetal loss, stillbirth, or birth of a severely infected infant. Neonate would have the symptoms of bacteraemia, respiratory distress, fever, and neurologic abnormalities if the infection occurs transplacentally (Smith, 1999). Infants are more sensitive to the spores of *Clostridium botulinum*, which results in severe nerve underdevelopment (Lund, 2011). Opportunistic pathogens cause substantial number of health-care-associated infections (HAIs), as the number of immunocompromised persons in health care centre is relatively high. It has been proved that HAIs resulted in 1.7 million illnesses and nearly 99 000 deaths per year in the US (Klevens et al., 2007). It is interesting to notice that the incidence of opportunistic infection can be influenced by the socioeconomic status as well as racial of the susceptive people (Colugnati et al., 2007; Vincent et al., 2014).

1.3.2.2. Opportunistic pathogens associated with plant and pant-based foods

Plant roots can release diverse substances, such as organic acid, sugar, amino acid or vitamins, which are suitable for microorganism's growth (Neumann, 2007). Rhizosphere is a layer of soil, surrounding and influencing by roots. A handful of studies have proved that the biomass in rhizosphere is higher than the other part of planted soil, which makes rhizosphere one of the complex ecosystems on earth (Raaijmakers et al., 2009; Hinsinger et al., 2009). Microorganisms existed in rhizosphere are able to invade hosts and reach different parts of the plant, including leaves, fruits and seeds. Many genera of the microorganisms, including *Stenotrophomonas, Staphylococcus, Herbaspirillum, Ralstonia, Burkholderia, Enterobacter, Ochrobactrum* and *Pseudomonas* were found in rhizosphere, some of them benefit for the growth and development of plants. They are antagonistic bacteria and recognized as nitrogen-fixing bacteria, mycorrhizal fungi, plant growth-promoting rhizobacteria, bio-control microorganisms (Mendes, R et al, 2013). On the other hand, those microorganisms are able to degrade environmental pollutants like xylene or benzene (Lee et al., 2002). However, human pathogens were discovered among the ecosystem and can colonize in the human body, as plant and human hosts share similar or the same recognition and invasion sites (Berg et al., 2005). It has been reported that *B. cereus* or *Proteus vulgari,* which can induce skin, wound, and urinary tract infections can be found in rhizosphere environments (Berg et al., 2005). In this case, plant-based foods can be a potential source of foodborne outbreaks caused by opportunistic pathogens.

Study shows that opportunistic pathogens took up to 1.7% of the total bacterial community with the dominancy of *Pantoea agglomerans* and *Stenotrophomonas maltophilia*, which would have ambivalent interaction with plant and human (Berg et al., 2014). *Pantoea agglomerans* has been proved as a risk factor for occupational disease and cause pneumonia that can be a life threatening to young children (Büyükcam et al., 2018). *Stenotrophomonas maltophilia* would cause bloody-stream infection and pneumonia among immunosuppressed patients that results in high morbidity (Looney et al., 2009). Besides, *Klebsiella pneumoniae* and *Enterococcus casseliflavus* were also very common in plant-based foods, as each of them accounted for 10% of total microorganisms isolated from fresh fruits and vegetable samples. Compared with fruits, vegetables are more likely to be contaminated as they are closer to soil (Al-Kharousi et al., 2016). Similarly, *Klebsiella pneumoniae* and *Enterococcus casseliflavus* have been found as the cause of infection including pneumonia, urinary tract infections, and bloodstream infections (Martin & Bachman, 2018). *Serratia marcescens* and *Citrobacter freundii* belong to the family of *Enterobacteriaceae*. *Serratia marcescens* has been reported as a common pathogen isolating from grapes and leaf vegetables (Barata et al., 2012). It is associated with a wide range of serious infections, including pneumonia and endocarditis in community settings and hospitals (Jones, 2010). *Citrobacter freundii* is able to produce heat-stable toxin and Shiga-like toxin, which has been implicated in the infection of urinary and respiratory tracts, central nervous system, as well as intra-abdominal and bloodstream infections (Kanamori et al., 2011; Guarino et al., 1989). Studies proved that *Citrobacter freundii* has been isolated from a variety of vegetables such as prepacked mix salad, carrot and cucumber (Uzeh et al., 2009).

1.4. Epidemiology and epidemiological evidence

Epidemiology studies the occurrence and distribution of health-related events, states and processes in specified populations, including the study of the determinants influencing such processes, and the application of this knowledge to control relevant health problems (Porta, M, 2014). The theory of epidemiology developed alongside the change patterns of risk factors of population morbidity and mortality. The scope of epidemiology has been enlarged to the area of investigating the risk factors associated with lifestyle changes, socioeconomics, and macro factors such as climate change (Santosa et al., 2014; Kirch, 2008). Epidemiological studies include both descriptive and analytical studies. In descriptive studies, impacts of health-related states are described across one or more variables, such as over time and place, while analytical studies quantify the relationships between identifiable factors and health-related states (EFSA, 2020). Analytical studies can be subdivided into experimental and non-experimental studies (observational studies), which largely avoid the extrapolations across species and levels of exposure that are required for the use of data from animal experiments (WHO, 2000). To be more specific, experimental studies include randomized controlled trials (RCT) and crossover studies; observational studies include case-control study, cross-sectional study and cohort study (Coggon et al., 2009). Generally, experimental studies are methodologically superior to observational studies, as they provide better control on selection bias and blinding (Hannan, 2008; Mariani & Pego-Fernandes, 2014).

Epidemiological studies provide evidence for the history of disease, assessing the preventive and therapeutic methods and developing health care system and planning (Gordis & Gold, 1984; Kirch, 2008). To comprehensively measure the epidemiological evidence at the global level, the terms of Global Burden of Disease (GBD) were developed by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington. GBD provides a tool to quantify health loss from hundreds of diseases, injuries, and risk factors, that researchers and policy makers are able to implement evidence-based health intervention and improve the health system. The burden of specified disease and condition is estimated by Disability Adjusted Life Years (DALYs). DALYs is defined as the sum of the years of life lost due to premature mortality (YLLs) and the years lived with a disability (YLDs) due to prevalent cases of the disease or health status in a population (WHO, 2013). The YLLs for a cause are estimated as the number of cause-specific deaths multiplied by a loss function specifying the years lost for deaths as a function of the age at which death occurs. YLDs are determined by the prevalence of each non-fatal condition weighted for the severity of the condition (WHO, 2013). DALYs are also used to evaluate health benefits in the denominator of cost-effectiveness ratios (Culyer, 2014). Figure 4 shows the change of leading causes of DALYs. In 2019, cardiovascular disease was considered as the most important cause of DALYs, while it was ranked in third place in 1990. A neoplasm has become an important cause of DALYs, increasing from 7th place in 1990 to 2nd place in 2019.

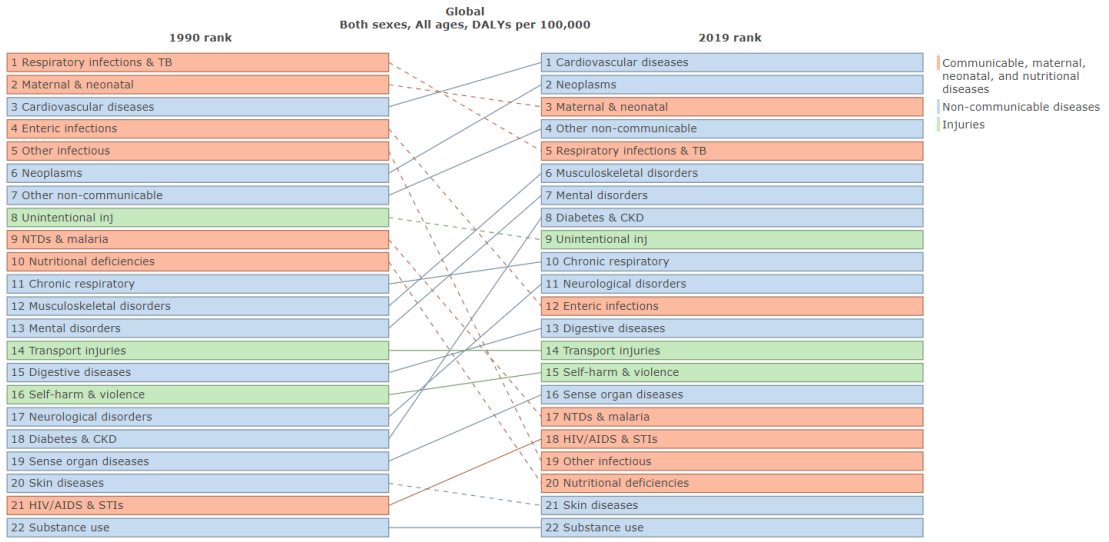

Figure 4 Cause of DALYs per 100 000 people at global level, changing from 1990 to 2019 (IHME, 2019).

In terms of food safety, the purpose of epidemiology studies is figuring out the risk factors, understanding the interaction pathway between identified factors and human beings, and the relative importance of those factors in foodborne infection (Potter & Tauxe, 1997). Furthermore, epidemiology data can be used to establish surveillance systems and outbreak management strategies within the food chain (CMSF, 2006). A golden standard epidemiological evidence should be developed from analytic studies which illustrate a strong link between the particular food item and foodborne illness, and most of the cases associated with the outbreak reported the consumption of this food item with the exposure period (Health Canada, 2011).

1.5. Tools of evaluating evidence

Quality of evidence plays an important role to guide future research and inform practice. The quality of evidence reflects the confidence that the reported estimates of effect are adequate to support a specific recommendation. High quality evidence can ensure that the conclusion is accurate, reliable and applicable. Integrating evidence from food safety epidemiological studies should be able to serve three needs: firstly, hazard assessment, the strength of association between evidence and the assessment of causality; secondly, quantitative description of exposure-response relationship; thirdly, better evaluate potential bias by including multiple studies (EFSA, 2020). Generally, in a risk assessment study or meta-analysis, the information sources for evidence retrieval, study design and context or population characteristics are numerous and various, resulting in the generation of bias in a different way. Besides, as the volume of available evidence increasing constantly, the accumulation of evidence with different designs and outcomes would also decrease the consistency between each evidence (Diefenbach et al., 2016). In this case, it is necessary to develop an appraisal instrument to meet the practical need for standardizing the process and criteria for evidence evaluation.

Some researchers, risk assessment organizations and governmental bodies have put their effort on developing critical evaluation tools, however, there was no agreement on a well-established tool which can be considered as the gold standard. The evaluation tools are developed for different purposes and contexts: for evaluating the quality of a single study; for assessing the risk of bias in systematic review; for quantifying the weight of evidence (EFSA, 2020). Most of the tools assess the inclusion criteria of participants and the methods used to measure the study variables and source of bias, a limited number of them included the conflict the interest (Sanderson et al., 2007).

1.5.1. GRADE

Some evaluation instruments have been applied by researchers and systematic reviewers, and among which, GRADE is the most widely used method. GRADE is an assessment system, which provides a transparent and comprehensive process of rating the quality of evidence and grading the strength of recommendations in systematic reviews, health technology assessments, and clinical practice guidelines addressing alternative management options (Guyatt et al., 2011). Quality assessment is based on data and information reported in primary studies that have to then be explained in the full-text section of the article (Dreier, 2013). GRADE is superior to other appraisal tools because the quality of evidence is assessed for each outcome and it upgrades the quality of observational study if they meet certain criteria. Besides, it separates quality of evidence and strength of final recommendation, which means that the balance of desirable and undesirable effects, cost-effectiveness and value & preference would also be taken into consideration when making the recommendation (Goldet, 2013; Andrews et al., 2013).

The evaluation by GRADE includes three steps:

1) Defining the question and collecting evidence.
2) Rating evidence quality (randomized controlled trials are assigned a priori ranking of “high” and “low” observational studies).
3) Grading recommendations.

For systematic reviewers and health technology assessments, the end points of GRADE process are restricted to summary of evidence: the quality rating for each outcome and the estimate of effect (Guyatt et al., 2011). Figure 5 shows the reasons to rate down the quality of evidence. Besides, there are three reasons to rating up the quality: large effect of the outcome, dose-response relationship between the intervention and outcome, plausible confounders or biases that would decrease an apparent treatment effect (Guyatt et al., 2011). So far, most of the experience of applying GRADE is from evaluation of preventive and therapeutic interventions and addressing clinical questions. There is a very limited application in the area of public health and health system, especially in the evaluation of epidemiological evidence associated with foodborne infection caused by pathogens. Applying GRADE in the area of food safety should be creative but challenging, as the evidence is mostly obtained from observational studies.

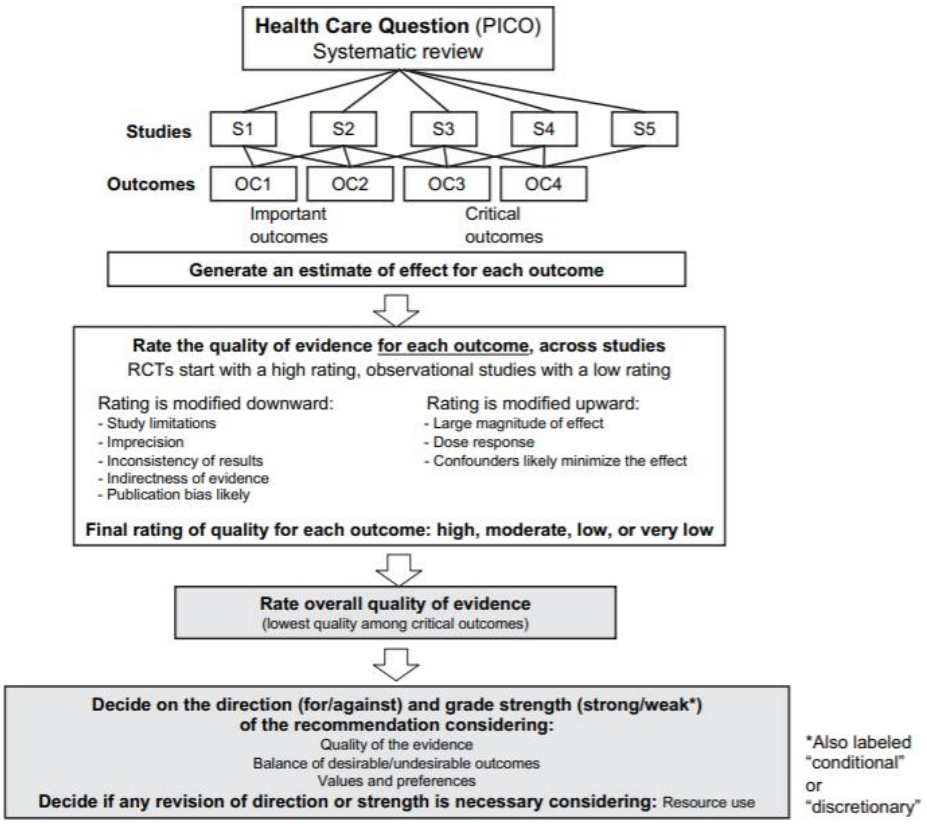

Figure 5 Schematic view of GRADE's process for developing recommendations (Guyatt et al., 2011).

1.5.2. Other methods

In addition to GRADE, there are various appraisal tools which were developed in different structures: checklists for different study design (Critical Appraisal Skills Program, CASP); scale with a list of criteria and scores attached, including an overall score or summary (Jadad score, Newcastle-Ottawa score); tools for risk of bias assessment (Cochrane RoB; National Toxicology Program-Office of Health Assessment and Translation, NTP-OHAT). Table 7 shows the characteristics of appraisal tools mentioned above (Jadad et al., 1996; Peterson, 2011; Higgins et al., 2011; U.S. National Toxicology Program, 2019; Critical Appraisal Skills Program, 2018).

For applying the CASP, Newcastle-Ottawa Scale, NTP-OHAT and Cochrane RoB to evaluate for different study designs, different checklists (scales) were developed. Table 6 compared the criteria included in each tool (criteria was generated based on the content of the 6 identified appraisal tools mention above). All of those tools assess various aspects of trial quality, including study design, blinding and randomization. It can be observed from the table that no health technology assessments single tools can cover all the 11 dimensions: GRADE rates 9 of them, Cochrane RoB and NTP-OHAT rate 8 and 7 of them, respectively. Most of the current tools tend to apply the checklist or scale with binary responses resulting in the inadequate evaluation (Berger & Alperson, 2009). Tools like NTP-OHAT and Cochrane RoB elaborate the response option into 4 or 5 degrees, which is superior to the other as they grade the evidence in detail to fit into different studies. CASP is the only tool that includes the cost-effectiveness and possibility of reinforcement among all those 6

tools. The current tools were developed to assess the studies in health-related area and have also been applied in the EFSA scientific risk assessment since 2015 (EFSA, 2020).

Table 6 Dimensions of trial quality measured by different assessment tools.

Dimension	CASP	Jadad Score	Newcastle-Ottawa Scale	Cochrane RoB	NTP-OHAT	GRADE
Randomization	√	√	√	√	√	√
Blinding	√	√	√	√	√	√
Allocation concealment				√	√	√
Measurement of exposure	√		√		√	√
Measurement of outcome			√	√	√	√
Withdrawals and dropouts		√	√	√		√
Selection report	√			√	√	√
Statistical methods	√			√		√
Confounding and modifying variables				√	√	√
Cost-effectiveness	√					
Reinforcement	√					

Table 7 The content characteristics, scoring systems and covered fields of 5 appraisal tools.

Evaluation tools	Developer	Contents	Structures	Applications
CASP	CASP UK - OAP Ltd	Three perspectives: validity of study design, methodology, results and relevance	11 "Yes or No" questions to be answered; an appraisal summary should be given	Health intervention (All kind of study design)
Jadad Score	Alejandro R. Jadad	Three key methodological Feature: randomization; Blinding; Withdrawals and dropouts	Simple methods with 5 items to assess; final score range from 0-5	Systematic review in medical fields; randomized controlled trials
Newcastle-Ottawa Scale	Collaboration between the University of Newcastle, Australia, and the University of Ottawa, Canada	Three broad perspectives: (1) the selection of the study groups; (2) the comparability of the groups; (3) and the ascertainment of either the exposure or outcome of interest	Quick methods with 8 items to assess; stars are awarded to each item.	Nonrandomized studies, including case-control and cohort studies
Cochrane RoB	Centre for Evidence-Based Medicine Odense (CEBMO) and Cochrane Denmark	Five domains: (1) bias arising from the randomization process; (2) bias due to deviations from intended interventions; (3) bias due to missing outcome data; (4) bias in measurement of the outcome; (5) bias in selection of the reported result.	22 Risk-of-bias questions or domains; evaluating fixed set of domains of bias, focusing on different aspects of trial design, conduct and reporting	Health (randomized trials; crossover trials)
NTP-OHAT	U.S. National Toxicology Program	Evaluating individual study risk of bias (indirectness, timing and other factors) or internal validity	11 Risk-of-bias questions or domains; Questions are grouped under 6 types of bias (selection, confounding, performance, attrition/exclusion, detection, and selective reporting)	Human and animal studies (all kind of study design)

2. Methods

2.1. Data extraction

Study searches were conducted from 1 October 2020, in the following database: PubMed, EMBASE, Scopus, Web of Science. Also, searched in the European Food Safety Authority (EFSA) Journal and Eurosurveillance Journal. The search keyword included: "Europe" AND "foodborne outbreak" AND "*Escherichia coli*" OR "*Salmonella*" OR "*Listeria monocytogenes*" OR "Norovirus" OR "opportunistic pathogens", published date limited to the years "2011 to 2020". Search keywords were adapted to each database. For initial relevance screening, title and abstracts were screened with the inclusion criteria: outbreak within the timeline of 2011 to 2020; caused by *Escherichia coli*, *Salmonella*, *Listeria monocytogenes* or Norovirus; within the area of Europe; food vehicles were identified as fresh fruits or vegetables (including dishes as salad, sauce contained fresh fruit and vegetable ingredients). Further screening was conducted through reading the full articles. In addition to those above, the inclusion criteria were: reported data should belong to a primary research, rather than review; epidemiological information should be described; food source investigation should be reported. Duplicated articles were excluded after advanced screening.

Data were extracted for the following variables: country, outbreak time frame, number of cases and hospitalizes or hemolytic uremic syndrome, population group. Information for food exposure study was extracted: study type, study methods, food source, cases definition, control definition, case exposure window, control exposure window, food source (Odds Ratio or Risk Ratio) and case lab test.

2.2. Evaluation of evidence by GRADE

Evaluation of evidence will be processed after extracting data from each study. Table 8 shows the traffic light system for rating the quality of evidence. Criteria were developed based on the guideline of GRADE and have been adjusted to fit into the situation of evaluating evidence as observational study. The traffic light system was applied to rank studies into tiers, as most of the identified studies could not entirely satisfy the criteria. Generally, the green colour indicated the study satisfies the specified criteria entirely, which results in high quality of evidence. Yellow and orange colour show that study partly satisfies the criteria. While the red colour demonstrates that the study fails to meet the criteria and possibly decreases the quality of evidence. The traffic light system is applied to evaluate the dimension of risk of bias, imprecision and indirectness. Detailed information about each criteria is described as follow:

1) Risk of bias: In an observational study investigating foodborne infection, the potential risk of bias can be found in failing to develop and apply appropriate eligibility criteria to choose control group in case-control study, and do not choose the unexposed group in cohort study. Evidence will be ranked in green level if the exposed and unexposed people were selected from the same population in cohort study. Incomplete follow-up (low response rate) is the other limitation. Response rate is defined as the percentage of cases that participated in the food exposure study.

2) Imprecision: As to the precision of the evidence, examination of 95% confidence intervals is considered as the optimal primary method. The ratio of cases and controls also contributes to the imprecision of evidence. In cohort study, the ratio of exposed and unexposed people is fixed and ranked as red level. Generally, researchers appreciate direct evidence as the target population, intervention and outcome, which is highly associated with what the researchers interested in. In the study of foodborne infection, indirectness may come from one of the four ways: population, exposure, comparator and outcome.
3) Indirectness: GRADE also suggests rating down the quality for large inconsistency. Criteria used to evaluate the inconsistency (heterogeneity) include similarity of point estimate, overlap of the confidence intervals and statistic test of I^2. It is worth noting that the quality would not be rated up if the evaluation results show consistent.
4) Publication bias: Publication bias is a common reason for low quality of evidence. Studies with positive outcome are more likely to be published. Moreover, if the data search performed earlier, that only a few relative studies are available, the negative results may be overestimated. Funnel plot can be used to describe the publication bias of the study. Funnel plots are used to show the magnitude of the treatment effect of individual studies (OR or RR) is plotted against either the sample size or precision of the studies (standard error) may be used to detect publication biases. Figure 6 shows an example of symmetrical inverted funnel plot. A symmetrical funnel plot represents that the studies with different sizes and results are likely to be inclusive, whereas an asymmetrical plot suggests that small, negative, or neutral studies have been omitted. The dashed vertical line implies the overall pooled estimate of the effect of the included studies.
5) Inconsistency: Forest plot will be used to describe the inconsistency of the evidence. Forest plots (blobbograms) are used to illustrate the differences between studies and provide an overall estimate of the results. Figure 7 shows an example of the forest plot. The *x*-axis represents the relative benefit of each individual study. The squares represent the point estimate (OR or RR) of each study and the width of the horizontal lines through them indicates the 95% confidence interval of this estimate. The size of the squares shows the weight of each study contributing to the overall result. Finally, the diamond at the bottom represents the point estimate of the overall result.

To evaluate the Risk of bias, imprecision and indirectness, relative information (population, exposure, comparator and outcome (PECO) of the food exposure study provided in each article, inclusion criteria of case and control group, study method, study design, response rate of invited participant and the estimated OR or RR and CI) will be extracted from the identified article. Forest plot and funnel plot will be made based on the number of cases and control people through RevMan 5.0 (The Cochrane Collaboration). The data used in forest and funnel plots was the most significant OR or RR associated with specified food vehicles reported by identified studies.

Table 8 Quality dimension and items for rating quality of evidence.

Dimension	Criteria in Dimension		
Risk of bias	Failure to develop and apply appropriate eligibility criteria (age, sex, region, time lag≤2 weeks) Selection from same population in cohort study	number of inclusion criteria	4
			3
			2
			≤1
	Differences in measurement of exposure	study methods	same method
			different method
			not report
	Recall bias	study methods	interview
			telephone questionaire
			online questionaire
		study type	cohort
			case-case
			case-control or other
	Incomplete follow-up (reponse rate)		reponse rate≥75%
			reponse rate≥50%
			reponse rate<50% or not report
Imprecision	Wide were the CI around the effect estimate		0.75-1.25OR(RR)
			0.5-1.5OR(RR)
			wider or not report
	Number of control: case		≈3:1
			≈2:1
			≈1:1 or fixed
Indirectness	Population (no lab confirmed/negative case)	number of points included	≤1
	Exposure (no test or food sample(s) neagtive)		2
	Comparator missing		3
	Outcome (low association (<50%) between true case and food)		4

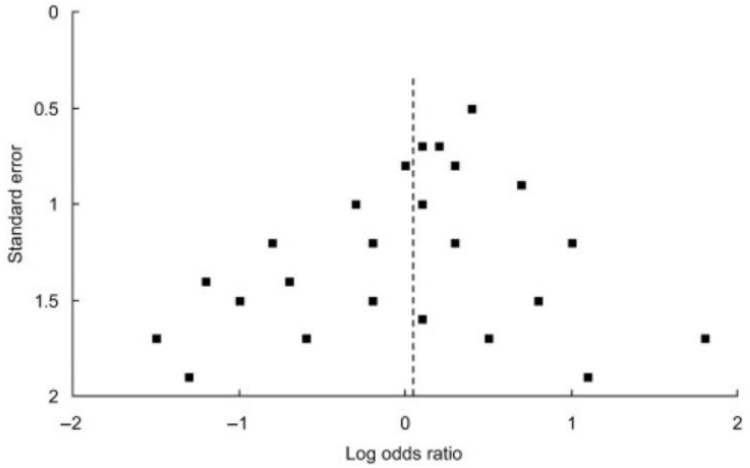

Figure 6 Example of funnel plot (Lalkhen et al., 2008).

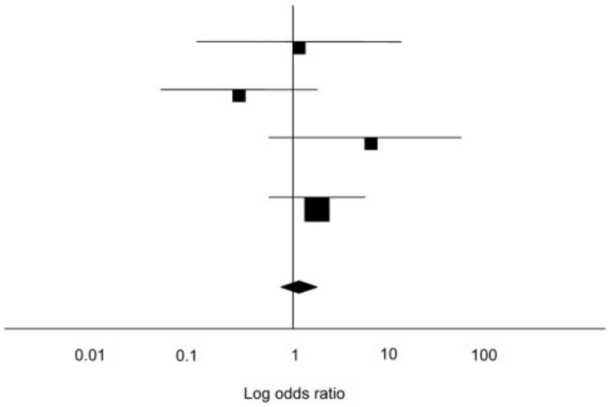

Figure 7 Example of forest plot (Lalkhen et al., 2008).

3. Results

From a total of 3 805 identified articles, 77 were retrained after screening for relevance. The excluded articles could not meet the following criteria: outbreak reported within Europe; outbreak caused by target pathogens (*Escherichia coli, Salmonella,* Norovirus, *Listeria monocytogenes*); the potential food vehicles were fresh fruits and vegetables; outbreak within the time period of the years 2011 to 2020; a report of specified outbreak rather than systematic review. After advanced screening, 25 articles were selected, among which 12 were research associated with outbreaks caused by *Escherichia coli*, 7 studies investigated the outbreak of *Salmonella* infections, 6 reported the outbreaks caused by Norovirus. A total of 52 articles were excluded as they were duplicates (14 articles), full text could not be accessed (8 articles) and insufficient or irrelevant information (30 articles). No article about *Listeria monocytogenes* outbreak met the inclusion criteria and identified from the database in this study. Articles about outbreaks caused by opportunistic pathogens were not identified.

3.1. Description of the identified studies

3.1.1. *Escherichia coli*

Characteristics of 12 eligible studies of *E. coli* outbreaks were provided in Table 9. The outbreak time frame ranged from the years 2011 to 2017, 4 out of 12 (33%) were reported in 2016. Six investigations were conducted in United Kingdom (Great Britain). The others were found in German, France, Italy, Romania, Finland and Sweden. The serotypes of *E. coli* varied between each outbreak and two of the outbreaks were associated with *E. coli* O157:H7. One study did not report the number of infected cases and the number of HUS was reported by three studies. The infected population of 5 outbreaks (42%) individuals of all age with different genders (general) and one was found among children. For the rest 6 outbreaks, the infected population narrowed down into event settings (venue, street food festival or conference) or in the restaurants or canteen. Women were reported as the majority group (over 50%) in the seven outbreaks (58%) and three outbreaks only focused on adults.

For the food exposure study reported by each article (Table 10 & 11), 6 out of 12 (50%) investigated through case-control study, while three reported the result of cohort studies and two reported case-case study. Only one investigation published as a report that did not include the information of case or control selection. In all studies, exposures were ascertained through questionnaire (telephone or online). In one study, information was collected by interviewed the parents or guardians of cases, as the outbreak cases were young children who could not answer the questionnaire themselves. One study did not provide adequate description of control definition. Five studies reported that over 50% of identified cases responded to the food exposure study. For the exposure window, six studies accessed the same exposure window for cases (exposed) and control (unexposed) groups, while the other studies did not provide adequate description. In 10 studies (83%), cases were confirmed by lab test and one of them reported negative. Information of laboratory investigation for the cases did not provide in three studies. Food samples were tested and reported positive in two studies, the serotypes were found to be identical to the pathogens isolated from the cases. 5 studies reported that no food sample was collected and tested, while food test results were negative in three studies. Food

vehicles associated with each outbreak were illustrated in Table 12, OR or RR were calculated in 11 studies. Salad (prepacked or served in buffet) was the category most frequently implicated in 4 out of 12 studies. The most extensive outbreak with 166 cases (2 deaths and 9 HUS) was reported in United Kingdom in 2016, and salads served in one catering premises were detected as the source (OR=8.30; 95% CI: 1.96–35.15).

3.1.2. *Salmonella spp.*

As shown in Table 13, information of 7 outbreaks was collected. The outbreak time frame ranged the years 2011 to 2019 in different countries within Europe. In 2013, outbreak caused by *S. agona* phage type 40 was reported in England and resulted in a total of 592 cases and about 2 cases were sent to hospital. Among the 7 studies, all of them included individuals of all ages with different genders (general) and 4 of them reported that women are the majority group in the population. Cases from one outbreak were identified that attended the same street food festival, while cases from the other outbreaks were people of all ages with different genders (general).

To investigate the type of fruits or vegetables associated with the illness (Table 14 & 15), case-control was conducted in 6 out of 7 research studies and one cohort study. In four of the studies, controls were chosen from the national pool or Danish Civil Registration System. In the two case-case studies, controls were defined as *Salmonella* cases that were confirmed to be caused by other serovars. One study did not report the match criteria of control. Cases and controls were required to answer the questionnaire through web-based and telephone interview. All studies assessed the case exposure window during the incubation period prior to disease onset. As for the exposure window for control, two assessed the period prior to interview while two case-case studies investigated the same incubation time for control. One of the studies did not provide the information about controls' exposure window and one is ambiguous. Lab tests for food samples were conducted in 6 studies, 4 of them confirmed that food samples were tested positive. Three studies indicated that all the cases were confirmed by lab tested. Table 16 shows the food vehicles of the 7 studies. Tomatoes were reported as the food vehicles in two studies (with OR 33.95 and 10.8, respectively). Sprout or salad was also being proved as the source of infection in two studies (with OR 31.95 and 14.3). The largest outbreak, which caused more than 500 illnesses, was associated with the consumption of Coconut chutney (OR 33.95) in a street food festival in England.

Table 9 The origins, periods, associated serotypes of the pathogens, number of cases and patient groups of 12 *E. coli* outbreaks (ordered by time frame).

Authors	Countries	Outbreak time frame	Pathogens	No. of cases (death)	No. of HUS	Outbreak population
Buchholz et al., 2011	Germany	5.2011	*E. coli* O104:H4	Unknown	Unknown	General
King et al., 2012	France	08.06.2011-23.06.2011	*E. coli* STEC O104:H4	24	7	Adults (aged>15 years) present at the buffet (75% female)
Launders et al., 2013	United Kingdom	9.2013	*E. coli* O157 PT 2 *stx2*	19	0	General (65% female)
Peron et al., 2014	Italy	14.04.2012	*E. coli* O96:H19	109	Unknown	Employees of the city of Milan Fire Brigade (15% female)
Escher et al., 2014	Romania	2.2016	*E. coli* O26	15 (3)	15	Children
Newitt et al., 2016	United Kingdom	06. 2014	*E. coli* O96:H19	157	Unknown	Consumers of a takeaway restaurant (44% female)
Sinclair et al., 2016	Great Britain	25.09.2014-30.10.2014	*E. coli* PT8 Stx1	102	0	General>18 (65% female)
Mikhail et al., 2017	England	8.2015-09.2015	*E. coli* O157:H7	47	0	General (69% female)
Gobin et al., 2017	United Kingdom	31.05.2016-29.07.2016	*E. coli* O157:H7	165(66)	9	General age>18 (76% female)
Gardiner et al., 2018	United Kingdom	7.2016	*E coli* O157 PT34	24	Unknown	People who ate at Venue A or Venue B during the exposure reference period (75% female)
Kinnula et al., 2018	Finland	19.08.2016-22.09.2016	*E. coli* ONT:H11	237	0	People who had participated in one of the events that the catering company had served between 19 and 21 of August 2016
Lagerqvist et al.,2020	Sweden	11.2017	*E. coli* O96:H19	83	Unknown	Venue visitors and employees (67% female)

Table 10 Relative information of study types, methods, exposure window and lab tests the food exposure investigations extracted from the studies of 12 *E. coli* outbreaks.

Authors	Food exposure study						
	Study types	Study methods	No. of cases (exposed); no. of controls (unexposed)	Exposure window case	Exposure window control	Results of the food example lab test	Results of the case lab test
Buchholz et al., 2011	Case-control	Interview	24; 80	14 days before the onset of illness	14 days before the interview	No food sample was tested	No case was tested
King et al., 2012	Retrospective cohort	Standardized questionnaire and telephone interviews	28; 53	During the buffet	During the buffet	All samples were negative	10 cases were confirmed with *E. coli* O104
Launders et al., 2013	Case-case	Interviewed by telephone using the case–case study questionnaire	11; 11	During the buffet	Unknown	Unknown	Unknown
Peron et al., 2014	Self-report	Parents or guardians of the cases were interviewed with a questionnaire	8	10 days before onset of illness	Unknown	Unknown	5 out of 8 were confirmed
Escher et al., 2014	Case-control	Semi-structured questionnaire	103; 37	Between 9 and 14 April 2012	Between 9 and 14 April 2012	All samples were negative	59 cases were tested all negative
Newitt et al., 2016	Case-control	Questionnaire and telephone interviews	108; 28	14 days before the onset of illness	Unknown	1 sample was positive	19 cases were confirmed

Sinclair et al., 2016	Case-control	Standardized exposure questionnaire (receipt or loyalty card were provides)	36; 85	Unknown	Unknown	No sample was tested	All cases confirmed
Mikhail et al., 2017	Case-case	Standardized STEC Enhanced Surveillance Questionnaire (SESQ).	36; 78	Unknown	Unknown	All samples were negative	All cases confirmed
Gobin et al., 2017	Case-control	Web-based questionnaire	21; 91	10 days before symptoms onset	10 days before recruitment	No food sample was tested	All cases confirmed
Gardiner et al., 2018	Retrospective case-control	Online questionnaire or Phone interviews	24; 156	8 days before the earliest case's symptom onset	Unknown	No food sample was tested	All cases confirmed
Kinnula et al., 2018	Retrospective cohort	Web-based questionnaire	30; 10	The time of attending event(s)	The time of attending event(s)	Food samples were positive and matched with the cases	Most of the cases were confirmed
Lagerqvist et al., 2020	Cohort	Web-based questionnaire	152; 149	Conference venue during the period 8 to 10 November 2017	Conference venue during the period 8 to 10 November 2017	No food sample was tested	3 samples were tested and positive

Table 11 The case and control definition, response rates and association between true cases and food vehicles of the 12 *E. coli* outbreaks (ordered by time frame).

Author	Case definition	Control definition	Response rates	Association between true case and food vehicle
Buchholz et al., 2011	Clinically diagnosed HUS in an adult who was hospitalized in one of three hospitals in northern Germany, located in the cities of Bremen, Bremerhaven, and Lübeck.	Control subjects were individually matched with case subjects on the basis of age group and neighbourhood.	Unknown	25% (6/24)
King et al., 2012	At the buffet who developed diarrhea (loose stools in 24 hours or 1 day's duration) or bloody diarrhea (blood visible to the eye in stools) or HUS (acute renal disease and microangiopathic haemolysis and thrombocytopenia) with a date of symptom onset between 8 and 23 June, 2011.	Individuals who ate at the buffet did not develop disease.	97% (93/96)	60.7% (17/ 28)
Launders et al., 2013	Individuals infected with the outbreak strain confirmed by the Gastrointestinal Bacteria Reference Unit, over the age of one year and resident in the UK, with onset of symptoms on or after 17 August, 2013.	Reference-cases were primary indigenous symptomatic cases of *Salmonella* infection confirmed by the Gastrointestinal Bacteria Reference Unit, over the age of one year and resident in the UK, with onset of symptoms on or after 17 August, 2013 (matched by age).	68.4% (13/19)	90.9% (10/11)
Peron et al., 2014	Individuals with onset of diarrhoea after 15 January, 2016 in Romania and laboratory confirmation for STEC O26.	Not Defined	53.3% (8/15)	100% (8/8)
Escher et al., 2014	FB employee who had consumed at least one meal prepared in the FB canteen between 9 and 14 April, 2012 and developed diarrhoea within the following 6 days.	Using the same criteria, except for clinical symptoms, as it was necessary that no signs of gastroenteritis were reported within 6 days after consuming the last meal.	17.8% (28/157)	22.3% (23/103)

Newitt et al., 2016	Person who consumed food from the restaurant during June 12–26, 2014, and within 7 days of exposure had diarrhoea or >2 of the following symptoms: vomiting, nausea, abdominal pain, fever, muscle ache or influenza–like symptoms, or headache; and who had no history of travel abroad or contact with anyone who had diarrhoea or vomiting during the 10 days before onset.	Person who had consumed food from the restaurant during the same time period (June 12–26, 2014) but who did not have diarrhoea, vomiting, nausea, abdominal pain, or fever and muscle ache or influenza-like symptoms since then.	76%（107/142）	Not report
Sinclair et al., 2016	A case of STEC O157 PT8 Stx1 + 2 as confirmed by GBRU or SERL with an onset of diarrhoea on or after 25 September, 2014.	Controls were recruited through a private company from a panel of registered participants. To register, participants must have been aged>18 years.	40.4% (36/89)	94.4% (28/346)
Mikhail et al., 2017	Primary symptomatic cases of STEC O157:H7 PT8stx2a, belonging to the same five SNP single linkage cluster confirmed by GBRU with onset of diarrhoea between 19 July and 30 September, 2015 and resident in England or Wales.	For each outbreak case, two control cases were selected from indigenous cases of STEC O157:H7 with PTs other than PT8 associated with illness in July and August reported to the national surveillance system during the preceding years (2010–2014).	76.5% (36/47)	49% (22/36)
Gobin et al., 2017	Individuals with onset or specimen date from 31 May, 2016 onwards and a cultured STEC O157 isolate confirmed at the PHE Gastrointestinal Bacterial Reference Unit (GBRU).	Aged 18 years and over (all cases at time of study were 18 years or older) and frequency matched by sex and region of residence. Four controls per case were recruited from a commercial online market research panel.	12.7% (21/165)	Not report
Gardiner et al., 2018	Individuals with a reference laboratory-confirmed isolate of *E. coli* O157 PT 34 eae+stx2+stx1 and compatible whole genome sequence (within 5 SNP single linkage cluster with address: 5.156.1329.2502.2965.3081.%), with onset of illness within 8 days of consuming food at Venue A or Venue B during the appropriate exposure reference period.	All employees in the office building who had access to Venue A.	57.8% (203/351)	95.8% (23/24)

Kinnula et al., 2018	Individuals with a stool sample positive for STEC or EPEC between 19.08.2016 and 22.09.2016, or with symptoms of diarrhoea more than three times a day between 20.08.2016 and 03.09.2016, who had participated in one of the events that the catering company had served between 19 and 21 of August, 2016.	Individuals who had participated in one of the events that the catering company had served between 19 and 21 of August, 2016, did not develop disease.	64% (427/670)	76.7% (23/30)
Lagerqvist et al.,2020	Individual who consumed food and/or beverage at the conference venue during the period 8 to 10 November, 2017 and reported symptoms of gastrointestinal illness including abdominal pain, nausea, diarrhea (more than three loose stools in 24 hours), bloody diarrhea and/or vomiting within 7 days after attending the venue, i.e. symptom onset before 15, 16 or 17 November, 2017.	Individual who consumed food and/or beverage at the conference venue during the period 8 to 10 November, 2017, did not develop disease.	72% (398/554)	33% (50/152)

*Response rate was calculated as: the number of identified case which involved in the food exposure study/the total number of identified case (case-control study); the number of people who response to the food exposure study/the number of people involved in the outbreak (cohort study)

* Association between true case and food vehicle was calculated as: the number of case who consumed identified food item/ the total number of case

Table 12 Food vehicles of the 12 *E. coli* outbreaks.

Authors	Food vehicles
Buchholz et al., 2011	Sprouts (OR 4.35 95% CI 1.05-18.0 P=0.04) Cucumbers (OR 3.53 95% CI 0.96-12.9 P=0.06) Apples (OR 3.91 95% CI 0.86-17.7 P=0.08) Strawberries (OR 2.33 95% CI 0.90-6.0 P=0.08)
King et al., 2012	Sprouts (RR 6.4 95% CI 2.6-15.7 P<0.000) Fenugreek sprouts (RR 4.4 95% CI 2.1-9.1 P<0.000) Lettuce (RR 4.3 95% CI 2.8-6.4 P=0.004) Carrots (RR 3.1 95% CI 1.3-7.1 P=0.009)
Launders et al., 2013	Watercress (OR 22.7, 95% CI 1.38–1414.94, p=0.025)
Peron et al., 2014	Fresh fruits (apples (8/8), pears (6/8), oranges (7/8), Bananas (7/8)), Vegetables (roots (8/8), Pepper (8/8), Zucchini (7/8)
Escher et al., 2014	Beet greens (OR 10.64 95% CI 1.63-∞ P=0.017) Green beans (OR 10.33 95% CI 1.42-460.11 P=0.008)
Newitt et al., 2016	Lettuce (OR 4.99 95%CI 2.01–12.42 P<0.001)
Sinclair et al., 2016	Mixed-leaf salad (OR 14.2 95% CI 5.3-38.1 P<0.2) Bananas (OR 4.9 95% CI 2.0-12.0 P<0.2) Tomatoes (OR 4.3 95% CI 1.8-10.6 P<0.2)

Mikhail et al., 2017	Prepacked salad from retailer X (OR 54, P<0.001, 95%CI 11-247)
Gobin et al., 2017	Mixed salad leaves (OR=4.56; 95% CI: 1.17–17.79) Salad eaten at one catering premises (OR=8.30; 95% CI: 1.96–35.15)
Gardiner et al., 2018	Baby mixed leaf (OR 19.7 95%CI 3.01-822.99 P<0.01)
Kinnula et al., 2018	Chicken fillet in oil with fresh herbs including rocket (risk ratio 7.67 95%CI 1.18-49.7 P<0.001)
Lagerqvist et al., 2020	Root vegetables (salad buffet) (RR 1.96 95%CI 1.28-2.99 P<0.001)

Table 13 The origins, periods, associated serotypes of pathogens, number of cases and patient groups of the 7 *Salmonella* outbreaks (ordered by time frame).

Articles	Countries	Outbreak time frame	Pathogens	No. of cases	No. of hospitalized	Outbreak population
Müller et al., 2011	Denmark	9.2011	*Salmonella* Strathcona	43	20	General (61% female)
Byrne et al., 2014	Multi-country	10.2011-02.2012	*Salmonella* Newport	63	13	General
Bayer et al., 2014	Germany	10.2011-11.2011	*Salmonella* Newport	106	28% of case	General (52% female)
Vestrheim et al., 2015	Norway	10.20.2013-01.04.2014	*Salmonella* Coeln	19	0	General
Knoblauch et al., 2015	Germany Switzerland	7.2014	*Salmonella* Bovismorbificans	74	0	General
Waldram et al., 2018	England	02.2013-03.2013	*Salmonella* Agona phage type 40	592	2	People who attended Street Spice, a food festival (53% female)
Colombe et al., 2019	Sweden	28.08.2019-19.10.2019	*Salmonella* Typhimurium	82	0	General (62% female)

Table 14 Relative information of study types, methods, exposure window and lab tests for the food exposure investigations extracted from study of the 7 *Salmonell*a outbreaks.

Articles	Food exposure study						
	Study types	Study methods	No of cases (exposed); No of control (unexposed)	Exposure window case	Exposure window control	Results of the food lab test	Results of the case lab test
Müller et al., 2011	Case-control	Standard hypothesis-generating questionnaire by telephone interview (shopping receipts).	17; 10	One week before illness onset	Unknown	Food samples (later batch) were negative	7 cases were confirmed
Byrne et al., 2014	Case-control	Questionnaire, different questionnaires were distributed to case and control group.	13; 91	7 days before illness	12.2012	Positive and matched	Cases identified from 31 October 2011 onwards
Bayer et al., 2014	Case-case	Questionnaire by telephone interview.	50; 45	3 days before disease onset	3 days before disease onset	Positive and matched	32 cases were confirmed
Vestrheim et al., 2015	Case-control	Standard trawling questionnaire by face-to face interview (case) or telephone interview (control).	7; 24	1 week before symptom onset	2 weeks preceding the interview.	All sample were negative	All cases confirmed
Knoblauch et al., 2015	Case-case	Questionnaire by telephone interview	20; 14	72 hours prior to symptom onset	72 hours prior to symptom onset	2 sample were positive	All cases confirmed
Waldram et al., 2018	Cohort	Web-based questionnaire	188; 619	During the Street Spice festival	During the Street Spice festival	Food samples were positive	29 samples were confirmed
Colombe et al., 2019	Case-control	Web-based questionnaire	45; 328	One week before illness onset	One week before answering the questionnaire	No food sample was tested	All cases confirmed

Table 15 The case and control definition, response rates and association between true case and food vehicles of the 7 *Salmonella* outbreaks (ordered by time frame).

Articles	Case definition	Control definition	Response rates	Association between true case and food vehicle
Müller et al., 2011	A patient with laboratory confirmed *S*. Strathcona infection in Denmark diagnosed during September–December 2011	Controls were selected from the Danish Civil Registration System and matched by age (birthday), sex, and municipality of residence	58% (25/43)	82.3% (14/17)
Byrne et al., 2014	(i) laboratory confirmed infection with fully antimicrobial-sensitive S. Newport exhibiting the outbreak PFGE profile designated as SNEWXB.0110 (defined by the watermelon isolate); (ii) symptoms including diarrhea or any two or more of: vomiting, fever or abdominal pain; (iii) onset of illness between 31 October 2011 and 31 January 2012; and (iv) who was reported in any of the six countries.	Staff from RKI department in Germany	73% (46/63)	59%
Bayer et al., 2014	At least one symptom of acute gastroenteritis (diarrhea or stomach pain or vomiting or fever) and onset of symptoms between 20 October and 8 November 2011.	Controls were defined as laboratory-confirmed *S*. Enteritidis infections in adults (18 years or older) notified to the public health authorities with at least one symptom of acute gastroenteritis and onset of symptoms between 14 November and 11 December 2011 (match with age and region).	47.1% (50/106)	42% (21/50)
Vestrheim et al., 2015	Person living in Norway with a laboratory-confirmed infection with *S*. Coeln, with onset of symptoms on 20 October 2013 or later (before 26th 11 2013), and with no history of travel outside Norway in the 2 weeks preceding onset of symptoms	Each case match with 3 controls. controls were matched by age, sex and municipality, using the Norwegian population registry and the phone registry.	36.8% (7/19)	71.4% (5/7)
Knoblauch et al., 2015	Salmonella cases that were confirmed to be caused by *S*. Bovismorbificans	*Salmonella* cases that were confirmed to be caused by other serovar	90% (20/22)	95% (19/20)

Waldram et al., 2018	A person who developed a diarrhea illness between 12 h and 5 days after attending the Street Spice festival	A person who did not develop a diarrhea illness between 12 h and 5 days after attending the Street Spice festival	71% (374/527)	24.7% (130/527)
Colombe et al., 2019	Case with a laboratory result matching the unusual phenotype of the *Salmonella* strain, infected in Sweden according to the clinician, and notified after 15 August 2019	Randomly selected from a national pool of controls (n = 5,900) available at PHAS	54.9% (45/82)	98% (44/45)

*Response rate was calculated as: the number of identified case which involved in the food exposure study/the total number of identified case (case-control study); the number of people who response to the food exposure study/the number of people involved in the outbreak (cohort study)

* Association between true case and food vehicle was calculated as: the number of case who consumed identified food item/ the total number of case

Table 16 Food vehicles of the 7 *Salmonella* outbreaks.

Articles	Food vehicles
Müller et al., 2011	Small, elongated tomatoes (OR 33.95 95% CI 2.4-463)
Byrne et al., 2014	Pre-sliced watermelon (OR 9.8 95% CI 2.6-37.3 P<0.01)
Bayer et al., 2014	Sprout (OR 31.9 95% CI 4.5-1346 P<0.001)
Vestrheim et al., 2015	Ready-to-eat baby leaf mix (OR 20 95% CI 2.7-∞)
Knoblauch et al., 2015	Sprout and salad (OR 14.3 95% CI 1.47-138 P=0.01)
Waldram et al., 2018	Coconut chutney (with fresh curry leaves) (OR 33 95% CI 20-57)
Colombe et al., 2019	Small tomatoes (OR: 10.8 95% CI 4.15-112.68 p<0.001)

3.1.3. Norovirus

Six studies reported norovirus outbreaks in different countries in EU area were identified from the database (Table 17). One outbreak resulted in 10 950 patients, which was the largest outbreak among all identified cases, followed by the outbreak in United Kingdom in 2016 that caused over 1 000 illness. Of six outbreaks, cases were drawn from specific facilities (worked in the same place or attended same restaurants or conferences).

Food exposure studies were conducted in the way of case-control study (2 studies) or cohort study (4 studies). Online questionnaires were distributed to the participants to record their food consumption information (Table 18 & 19). All the studies accessed the control exposure window as the same period as the cases. In 4 out of 6 studies, food samples were collected and tested in microbiological laboratory. Among which, 2 studies reported that the results were positive. Of 3 studies, cases were also confirmed by lab test. In 4 studies, more than 75% of the cases population participated in the food exposure investigation. Higher association between cases population and the identified food vehicles can be found in four studies, with correlation over 50%. Table 20 shows the food vehicles of 6 studies. Salads were considered as the potential food vehicles for three of the outbreaks and strawberry was identified as the source of infection in the largest outbreak among these 6 studies (OR 3.85 95% CI 1.12-13.21 P=0.03).

Table 17 The origins, periods, associated serotypes of pathogens, number of cases and patient groups of the 6 Norovirus outbreaks (ordered by time frame).

Articles	Countries	Outbreak time frame	No. of cases	No. of hospitalized	Population
Mayet et al., 2011	French	12.04.2011-13.04.2011	147	Unknown	Staffs from French military parachuting unit
Bernard et al., 2012	Germany	20.09.2012-05.10.2012	10,950	38	People from 390 institutions (mainly from schools and childcare facilities) in five federal states in East Germany
Kaminska et al., 2014	Poland	19.12.2012-22.12.2012	97	0	Employees from National Institute of Public Health-National Institute of Hygiene (NIPH-NIH) (80% female)
Vo et al., 2016	Finland	29.01.2015-15.02.2015	27	0	Employees of electric companies A and B
Einöder-Moreno et al., 2016	Norway	11.2013	74	0	People attended two meetings held at a conference centre (84% female)
Morgan et al., 2016	United Kingdom	10.2016-11.2016	Over 1000	Unknown	Staffs and customers in branches of restaurant

Table 18 Relative information of the food exposure investigations extracted from study of the 6 Norovirus outbreaks.

Articles	food exposure study						
	Study types	Study methods	No. of cases (exposed); no. of controls (unexposed)	Exposure window: case	Exposure window: control	Results of the food sample lab test	Results of the case lab test
Mayet et al., 2011	Case-control	Standardized questionnaire	147; 148	11 and 12 April	11 and 12 April	Food sample were tested and positive	No case was tested
Bernard et al., 2012	Case-control	web base or Email questionnaire	36; 40	Three days before the start of outbreak	Three days before the start of outbreak	Food samples were tested and positive	40% of cases samples were tested positive
Kaminska et al., 2014	Retrospective cohort study	Email questionnaire	90; 98	One week before outbreak	One week before outbreak	No food sample was tested	Samples were test positive
Vo et al., 2016	Cohort study	Standardized questionnaire	9; 9	Lunch at Restaurant X on January 26, 2015	Lunch at Restaurant X on January 26, 2015	Food samples were tested and negative	No case was tested
Einöder-Moreno et al., 2016	Retrospective cohort study	Online questionnaire	88; 46	During the meeting	During the meeting	No food sample was tested	All samples were positive
Morgan et al., 2016	Cohort study	Online questionnaire	44; 14	Between 26 to 28 October for customers who went to the Cardiff, Edinburgh or London (branch 22) or between 27 to 29 October for customers who went to London (branch 23)	Between 26 to 28 October for customers who went to the Cardiff, Edinburgh or London (branch 22) or between 27 to 29 October for customers who went to London (branch 23)	Food samples were tested and negative	No case was tested

Table 19 The case and control definition, response rates and association between the true case and food vehicle of the 6 Norovirus outbreaks (ordered by time frame).

Articles	Case definition	Control definition	Response rates	Association between true case and food vehicle
Mayet et al., 2011	Member of the military unit staff who presented at least one measurable symptom of the following: diarrhoea defined by three or more liquid stools in 24 hours, vomiting, and oral temperature of ≥38°C between 11 and 15 April, 2011.	Staff who had eaten in the canteen on 11 and 12 April did not have symptom.	100%	Not report
Bernard et al., 2012	Pupil with onset of vomiting or diarrhoea from 24 to 30 September	Pupils from three school classes who did not report vomiting or diarrhoea during the outbreak period.	<1%	89% (32/36)
Kaminska et al., 2014	An employee of NIPH-NIH who ate food items served at the Christmas reception 19 December, 2012 and subsequently developed diarrhoea (C3 stools in 24 h) or vomiting within 1 week	An employee of NIPH-NIH who did not eat food items served at the Christmas reception 19 December, 2012 and did not develop diarrhoea (C3 stools in 24 h) or vomiting within 1 week.	78% (239/306)	68% (61/90)
Vo et al., 2016	An employee of companies A or B with diarrhoea and/or vomiting who ate lunch at Restaurant X on January 26, 2015	An employee of companies A or B without diarrhoea and/or vomiting who ate lunch at Restaurant X on January 26, 2015	77.8% (21/27)	78% (7/9)
Einöder-Moreno et al., 2016	Individuals who had diarrhoea and/or vomiting in a participant of either of the two meetings who became ill from noon on 4 November until midnight on 7 November, 2013, without household contacts with similar symptoms during the week before onset of symptoms.	People who attended the meetings but did not have diarrhoea and/or vomiting	88% (147/168)	65% (57/88)
Morgan et al., 2016	Persons who ate at one of the four branches who developed sever+I14e diarrhea (three or more episodes in 24 hours) or vomiting or two other symptoms (mild diarrhoea (less than	Persons who ate at one of the four branches did not develop disease	19.2% (159/825)	Not report

	three episodes in 24 hours), bloody stools, nausea, fever, stomach cramps and headache) within 72 hours of eating at a branch.

*Response rate was calculated as: the number of identified case which involved in the food exposure study/the total number of identified case (case-control study); the number of people who response to the food exposure study/the number of people involved in the outbreak (cohort study).

* Association between true case and food vehicle was calculated as: the number of case who consumed identified food item/ the total number of case.

Table 20 Food vehicles of the 6 Norovirus outbreaks.

Articles	Food sources
Mayet et al., 2011	Salads (OR: 2.1; 95% CI: 1.0–4.4; p=0.03) and raw vegetables (OR: 2.1; 95% CI: 1.1–3.8; p=0.01)
Bernard et al., 2012	Strawberries (OR 3.85 95%CI 1.12-13.21 P=0.03)
Kaminska et al., 2014	Vegetable salads (RR 1.7; 95 % CI 1.2–2.2) Frozen carrots (5.00;95%CI2.0–13.0)
Vo et al., 2016	Grated salads (RR 2.33 90%CI 1.02-5.34)
Einöder-Moreno et al., 2016	Raspberry mousse (RR 2·4, 95% CI 0·97–6·0, P=0·060)
Morgan et al., 2016	Chipotle mayo (RR 2.17 95%CI 1.06-4.88 P=0.035)

3.2. Evaluation of evidence

The GRADE methodology was applied towards the data collected in Table 10, 11, 14, 15, 18 and 19, based on which the evidence evaluation was conducted and reported in Table 21, 22 and 23. Table 24 shows the overall results of evidence evaluation of risk of bias, imprecision and indirectness for studies grouped by different pathogens. For risk of bias, by comparing the definition of case (exposed) and control (unexposed) group (Table 11, 15 and 19), only 6 out of 25 studies applied suitable criteria to match the control (unexposed) group with the case (exposed) group, while more than half of the control group could not match the case with one or more criteria as: age, sex, exposure window or geography. Besides, 19 out of 25 (76%) studies used the same methods to measure the food exposure of control (unexposed) group and the case (exposed) group. Two studies did not apply the same method. For one study of *Salmonella* outbreak (Vestrheim et al., 2015), both the case and control group were invited to answer the same questionnaire, however, the researchers reached the case population by face-to-face interview and reached the control group by telephone. In another study (Byrne et al., 2014), different questionnaires were distributed to the case and control. For recall bias, 56% of studies collected the information about food exposure through online questionnaire, which was ranked as a low-quality assessment method. It is worth noting that in one study, researchers collected the supermarket receipts of both the case and control group as a source of food consumption information. 8 studies conducted cohort study and were ranked as green level, while 17 studies conducted case-control (case) study to investigate food vehicles. 8 out of 25 studies reported having a high repose rate (≥75%) and 8 studies had a low repose rate or did not report the data.

For imprecision, all the studies reported wider OR or RR of food vehicles and illness, that lowing the quality of evidence. In majority studies (64%), the ratio of the control (unexposed) group and case (exposed) group was less than 1:1 or fixed. For all the cohort study, the number of unexposed depended on the range of people associated with the outbreak (the number of populations that eating at the same restaurant or attending the same conference as the case group), unlike the number of control group, which was recruited by researcher in case-control study. For indirectness, 17 out 25 studies properly met the criteria of PECO and were ranked in green level. In the studies, which ranked as yellow or orange level, the common missing points were: case did not confirmed by microbial lab test and lacking of food sample microbial lab test. E Peron (2014) was the only one study, which did not involve a comparator. No study failed to meet any criteria in indirectness and was ranked in red level.

Twenty out of the 25 identified studies evaluated the consistency and publication bias by forest plot and funnel plot, among which 13 of them were case-control (case) studies (6 studies of *E. coli*, 6 studies of *Salmonella*, 1 study of Norovirus) with the indicator of Odds Ratio (OR), while 7 of them were cohort studies (3 studies of *E. coli*, 1 studies of *Salmonella*, 3 study of Norovirus) with the indicator of Risk Ratio (RR). 5 studies were excluded because lacking valid data for calculation. Figure 8 and 9 show the association between consumption of fresh fruits and vegetables contaminated by three pathogens and the outbreaks. It can be observed from Figure 8 that, fresh fruits and vegetables contaminated by *Salmonella* were the most important risk factor for foodborne outbreak (OR 25.12 95% CI 12.07-52.30), followed by the food items contaminated by *E. coli* and

Norovirus, with the OR 16.27 and OR 3.85, respectively. Moderate heterogeneity can be observed from the I^2 (53%) of the studies of *E. coli* outbreak and no heterogeneity can be observed from the case of *Salmonella* outbreak (I^2 =0%). For the meta-analysis of cohort studies (Figure 9), results show that fresh fruits and vegetables can be the vehicle of foodborne outbreak, with the RR 2.76, RR 1.12 and RR 1.90 for *E. coli*, *Salmonella* and Norovirus, respectively. Similarly, moderate heterogeneity was detected from the studies of studies of *E. coli* outbreak (I^2 =72%) and no heterogeneity was detected from studies of Norovirus outbreak (I^2 =0%). Figure 10 and 11 show the funnel plot of analysis for publication bias. The results indicated a lack of complete symmetry around the estimated pooled OR and RR that most of the studies placed in the right side of the funnel plot. All the studies reported the OR or RR more than 1, which suggesting the favour of publishing positive results than negative results. Two points in each funnel plot fall outside the confidence region indicate that the asymmetry of funnel plot may cause by heterogeneity between the included studies. Besides, data search conducted from limited databases resulted in potentially missing studies.

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Table 21 The evaluation results of risk of bias, imprecision and indirectness for the 12 studies of *E. coli* outbreaks by GRADE system.

Dimension	Criteria in Dimension			Buchholz et al., 2011	King et al., 2012	Launders et al., 2013	Peron et al., 2014	Escher et al., 2014	Newitt et al., 2016	Sinclair et al., 2016	Mikhail et al., 2017	Gobin et al., 2017	Gardiner et al., 2018	Kinnula et al., 2018	Lagerqvist et al.,2020
Risk of bias	Failure to develop and apply appropriate eligibility criteria (age, sex, region, time lag≤2 weeks) Selection from same population in cohort study	number of inclusion criteria	4		√							√			
			3	√		√									
			2					√	√	√			√		√
			≤1				√				√			√	
	Differences in measurement of exposure	study methods	same method	√	√			√		√	√	√	√		√
			different method												
			not report			√	√		√					√	
	Recall bias	study methods	interview	√			√	√							
			telephone questionaire		√	√			√						
			online questionaire							√	√	√	√	√	√
		study type	cohort		√									√	√
			case-case			√					√				
			case-control or other	√			√	√	√	√		√	√		
	Incomplete follow-up (reponse rate)		reponse rate≥75%		√				√		√				
			reponse rate≥50%			√	√						√	√	√
			reponse rate<50% or not report	√				√		√		√			
Imprecision	Wide were the CI around the effect estimate		0.75-1.25OR(RR)												
			0.5-1.5OR(RR)							√					√
			wider or not report	√	√	√	√	√	√		√	√	√	√	
	Number of control: case		≈3:1	√								√	√		
			≈2:1							√	√				
			≈1:1 or fixed		√	√	√	√	√					√	√
Indirectness	Population (no lab confirmed/negative case)	number of points included	≤1		√				√	√			√	√	
	Exposure (no test or food sample(s) neagtive)		2			√	√				√	√			√
	Comparator missing		3	√				√							
	Outcome (low association (<50%) between true case and food)		4												

Table 22 The evaluation results of risk of bias, imprecision and indirectness for the 7 studies of *Salmonella* outbreaks by GRADE system.

Dimension	Criteria in Dimension			Müller et al., 2011	Byrne et al., 2014	Bayer et al., 2014	Vestrheim et al., 2015	Knoblauch et al., 2015	Waldram et al., 2018	Colombe et al., 2019
Risk of bias	Failure to develop and apply appropriate eligibility criteria (age, sex, region, time lag≤2 weeks) Selection from same population in cohort study	number of inclusion criteria	4							
			3	√		√	√			√
			2					√	√	
			≤1		√					
	Differences in measurement of exposure	study methods	same method	√		√		√	√	√
			different method		√		√			
			not report							
	Recall bias	study methods	interview							
			telephone questionaire	√		√	√	√		√
			online questionaire		√				√	
		study type	cohort						√	
			case-case			√		√		
			case-control or other	√	√		√			√
	Incomplete follow-up (reponse rate)		reponse rate≥75%					√		
			reponse rate≥50%	√	√				√	√
			reponse rate<50% or not report			√	√			
Imprecision	Wide were the CI around the effect estimate		0.75-1.25OR(RR)							
			0.5-1.5OR(RR)						√	
			wider or not report	√	√	√	√	√		√
	Number of control: case		≈3:1		√		√			√
			≈2:1	√						
			≈1:1 or fixed			√		√	√	
Indirectness	Population (no lab confirmed/negative case)	number of points included	≤1	√	√	√	√	√	√	√
	Exposure (no test or food sample(s) neagtive)		2							
	Comparator missing		3							
	Outcome (low association (<50%) between true case and food)		4							

Table 23 The evaluation results of risk of bias, imprecision and indirectness for the 6 studies of Norovirus outbreaks by GRADE system.

Dimension	Criteria in Dimension			Mayet et al., 2011	Bernard et al., 2012	Kaminska et al., 2014	Vo et al., 2016	Einöder-Moreno et al., 2016	Morgan et al., 2016
Risk of bias	Failure to develop and apply appropriate eligibility criteria (age, sex, region, time lag≤2 weeks) Selection from same population in cohort study	number of inclusion criteria	4			√	√	√	√
			3						
			2	√	√				
			≤1						
	Differences in measurement of exposure	study methods	same method	√	√	√	√	√	√
			different method						
			not report						
	Recall bias	study methods	interview						
			telephone questionaire						
			online questionaire	√	√	√	√	√	√
		study type	cohort			√	√	√	√
			case-case						
			case-control or other	√	√				
	Incomplete follow-up (reponse rate)		reponse rate≥75%	√		√	√	√	
			reponse rate≥50%						
			reponse rate<50% or not report		√				√
Imprecision	Wide were the CI around the effect estimate		0.75-1.25OR(RR)						
			0.5-1.5OR(RR)	√	√				
			wider or not report			√	√	√	√
	Number of control: case		≈3:1						
			≈2:1						
			≈1:1 or fixed	√	√	√	√	√	√
Indirectness	Population (no lab confirmed/negative case)	number of points included	≤1	√	√	√	√	√	
	Exposure (no test or food sample(s) neagtive)		2						
	Comparator missing		3						√
	Outcome (low association (<50%) between true case and food)		4						

Table 24 Overall results of quality evaluations of the evidence by GRADE.

Dimension	Criteria in Dimension			*E. coli* (12)	*Salmonella* (7)	Norovirus (6)	Total (25)
Risk of bias	Failure to develop and apply appropriate eligibility criteria (age, sex, region, time lag≤2 weeks) Selection from same population in cohort study	number of inclusion criteria	4	2	0	4	6
			3	2	4	0	6
			2	5	2	2	9
			≤1	3	1	0	4
	Differences in measurement of exposure	study methods	same method	8	5	6	19
			different method	0	2	0	2
			not report	4	0	0	4
	Recall bias	study methods	interview	3	0	0	3
			telephone questionaire	3	5	0	8
			online questionaire	6	2	6	14
		study type	cohort	3	1	4	8
			case-case	2	2	0	4
			case-control or other	7	4	2	13
	Incomplete follow-up (reponse rate)		reponse rate≥75%	3	1	4	8
			reponse rate≥50%	5	4	0	9
			reponse rate<50% or not report	4	2	2	8
Imprecision	Wide were the CI around the effect estimate		0.75-1.25OR(RR)	0	0	0	0
			0.5-1.5OR(RR)	2	1	2	5
			wider or not report	10	6	4	20
	Number of control: case		≈3:1	3	3	0	6
			≈2:1	2	1	0	3
			≈1:1 or fixed	7	3	6	16
Indirectness	Population (no lab confirmed/negative case)	number of points included	≤1	5	7	5	17
	Exposure (no test or food sample(s) neagtive)		2	5	0	0	5
	Comparator missing		3	2	0	1	3
	Outcome (low association (<50%) between true case and food)		4	0	0	0	0

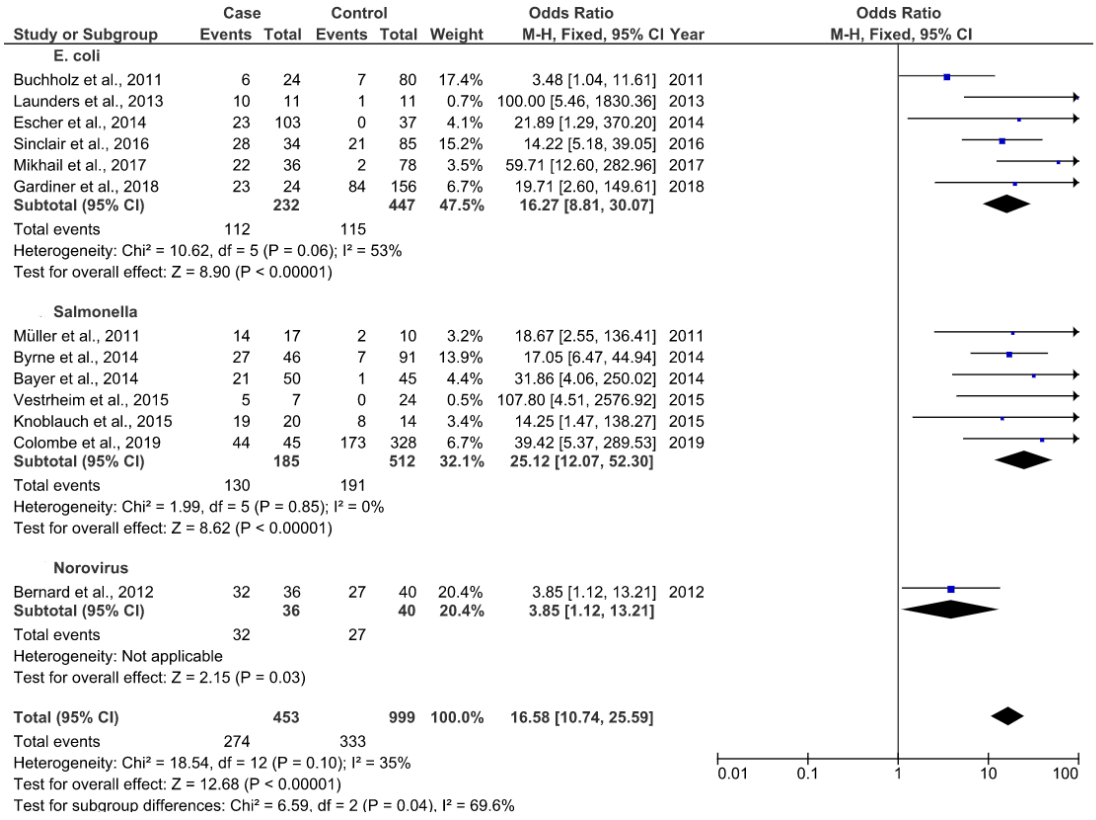

Figure 8 Forest plot of the risk of *E. coli*, *Salmonella* and Norovirus infections by consuming fresh fruits and vegetables, showing the OR with 95% CI.

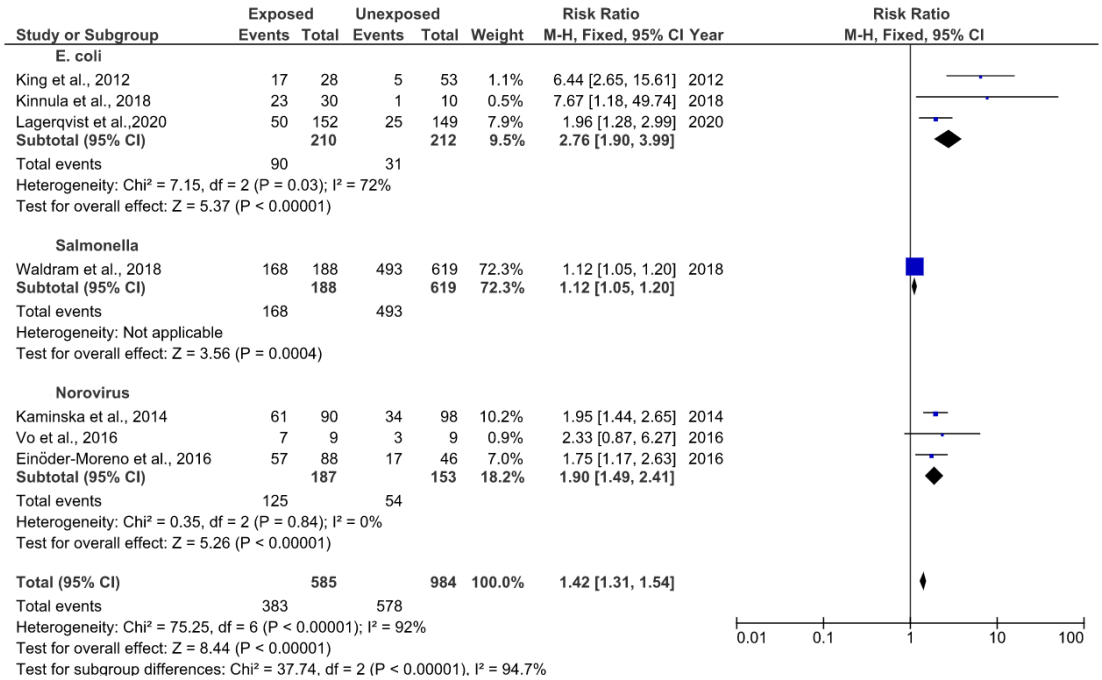

Figure 9 Forest plot of the risk of *E. coli*, *Salmonella* and Norovirus infection by consuming fresh fruit and vegetable, showing the RR with 95% CI.

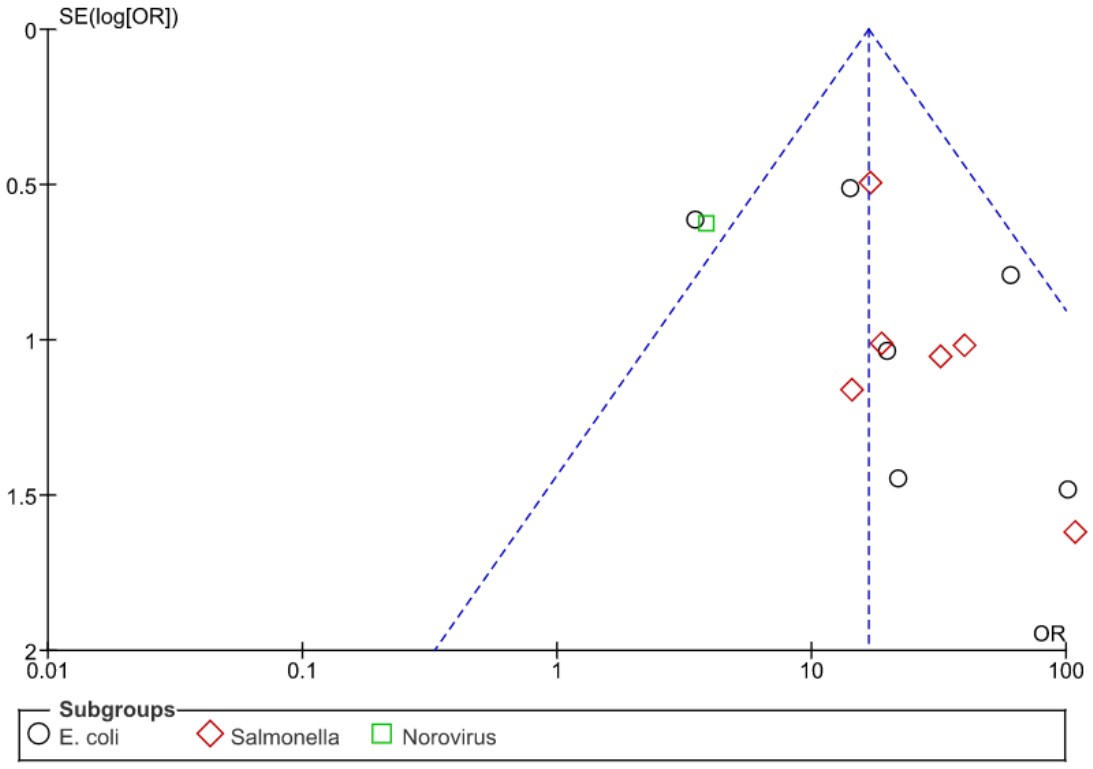

Figure 10 Funnel plot of the OR of 13 case-control (case) studies for evaluating the publication bias.

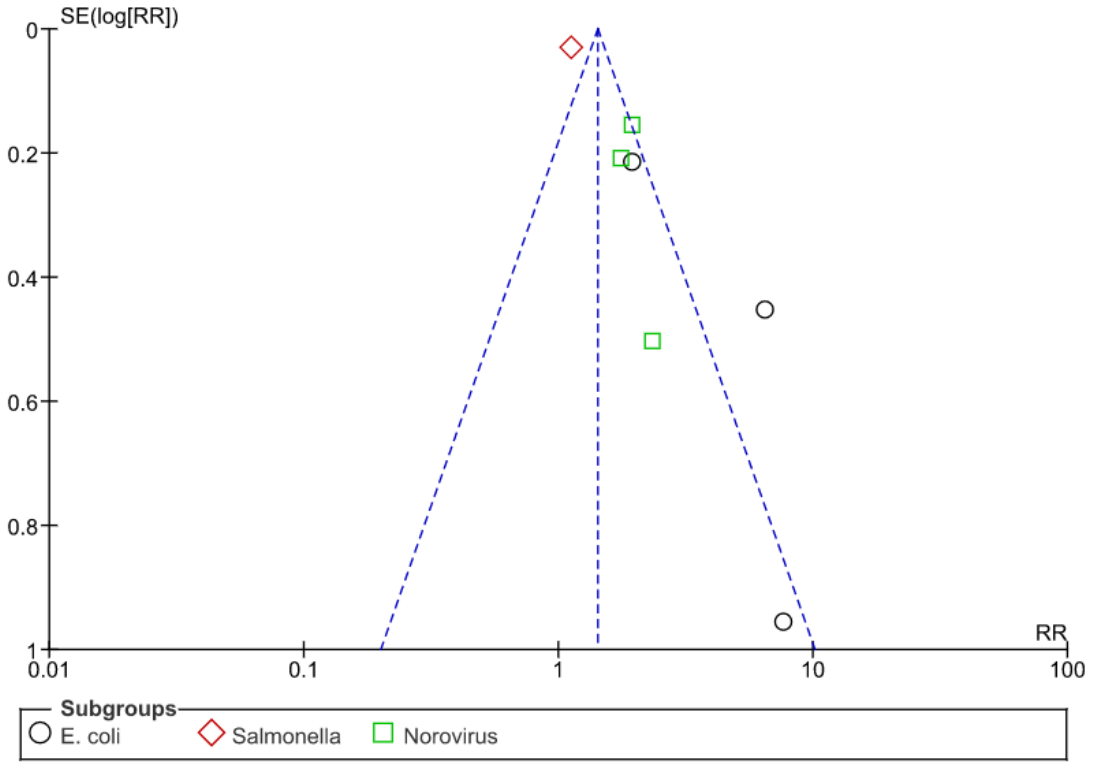

Figure 11 Funnel plot of the RR of 7 cohort studies for evaluating the publication bias.

4. Discussion

This study aims at searching for the epidemiological evidence of the foodborne outbreaks caused by the primary pathogens and the opportunistic pathogens. Food vehicle was focused on minimally processed fresh fruits and vegetables, as rising attention has been paid to a healthier diet with more plant-based foods. Collected studies were conducted within the European region during the recent ten years from 2011 to 2020. The quality of studies varies and the methodological criteria of GRADE system were applied to evaluate the identified studies. GRADE system was developed for quality assessment of clinical research and formulating related recommendation. It is hence quite challenging to apply it in the area of food safety.

4.1. Opportunistic pathogens

The investigation of opportunistic pathogens is an ongoing issue, which attracted the attention of researchers all over the world. Effort has been put into understanding the molecular detection and subtyping techniques, as well as the pathogenicity and virulence. Only limited number of articles have reported the foodborne outbreaks associated with fruits and vegetables consumption. In 2016, a *Citrobacter freundii* outbreak was reported in a German hospital. 76 cases were identified and most of them were not in the same ward. Vegetable salad was proved as the food vehicle of the outbreak, as *Citrobacter freundii* was isolated from the salad sample and the number of new cases was declined after banning serves the salad (Pletz et al., 2018). However, increasing incidence of infection related to animal-based food and wound infection has been apparent. *Cronobacter* spp. (*Enterobacter sakazakii*) has been considered as a concern in infant formulae or formulae for special medical purposes. Besides, the contaminated apparatus for formulae production and containers were also reservoirs for *Cronobacter* spp. A case of neonatal infection was reported in the U.S. and the potential vehicle were the expressed human breast milk and the associated breast pump (Bowen et al., 2016). *Vibrio vulnificus* infection is common cause of foodborne illness, which account for nearly 95% of seafood-related deaths in the U.S.. Interestingly, male was the majority of people who infected by *Vibrio vulnificus* (Jones & Oliver, 2009).

Several factors heighten the susceptibility of nowadays population to opportunistic pathogens. First of all, the proportion of elderly people grows gradually due to the demographic transition. Besides, the unhealthy diets which contain large amount of fat and sugar result in the high incidence of chronic diseases, such as diabetes, and the loss of microbial diversity in human. Opportunistic pathogens grow and replace the residual microorganisms in intestine that leads to dysbiosis and eventually leads to disease (Josephs-Spaulding et al., 2016). Moreover, it was predicted that the number of opportunistic pathogen infections would further increase, as the development of multiplying antibiotic-resistant strains (Fusco et al., 2018). Although the detection technique and treatment approach improve during recent years, it is important to raise the awareness of Good Manufacturing Practice and proper way of food handling.

4.2. Identified evidence

4.2.1. Pathogens associated with outbreaks

The consumption of fresh fruits and vegetable is significantly associated with the outbreaks of *E. coli*, *Salmonella*, Norovirus in Europe. It is not surprising that fresh fruits and vegetables were proved as a potential food vehicle of the primary pathogen. In European Union, a growing tendency of the number of outbreaks can be observed from 2004 to 2012, highlighting 29 outbreaks in 2006, 34 outbreaks in 2009 and 44 outbreaks in 2010 (Callejón et al., 2015). Similarly in the U.S., fresh products accounted for a growing proportion of all-caused foodborne infections, increasing from 0.7% in the 1970s to 6% in the 1990s (Sivapalasingam et al., 2004). Yet from 2004 to 2012, there is no clear trend about the absolute number of outbreaks caused by consuming fresh products can be found (Callejón et al., 2015).

Among 25 identified articles, 12 of them were related to the infection of *E. coli*, indicating that *E. coli* is more likely to exist in fresh products and has a higher possibility to cause infection in Europe. Animal manure was considered the main source of *E. coli* contaminations. Animal manure would contact fruits and vegetables directly or indirectly through soil or irrigation water where *E. coli*, as an ecologically, fit microorganism, is able to survive and grow (Luna-Guevara et al., 2019; Delaquis et al., 2007; Durso et al., 2004). Pathogenic *E. coli* possesses adherence factors not only for human epithelial colonization but also used for adherence to raw vegetables (Luna-Guevara et al., 2019). Furthermore, *E. coli* may occur in fruits and vegetables due to cross-contamination by poor hygiene of food handlers and equipment (Lynch et al., 2009). In this case, *E. coli* transmitted from the environment would be able to attach to various plants, which would be consumed by people, then result in infection. Compared with other pathogens, low doses of *E. coli* O157:H7 infection (<100 or even <10 cfu) are sufficient to cause intestinal diseases (Ackers et al., 1998). Outside the EU region, *E. coli* was also identified as the most common pathogen caused multistate outbreaks in the U.S. and *E. coli* O157 was the most prevalent strain (Sivapalasingam et al., 2004; Callejón et al., 2015).

Salmonella and Norovirus are also identified as the significant foodborne pathogen responsible for outbreaks associated with fruits and vegetables consumption. Traditionally, plant-based food is not recognized as the vehicle of *Salmonella*. Indeed, avian, beef, pork, unpasteurized milk, poultry and eggs are the most common host of the pathogen (Munck et al., 2020; Ehuwa et al., 2021). However, a large investigation conducted in the UK, Ireland, Germany and the Netherlands proved that the prevalence of *Salmonella* in fruit and vegetable products ranged from 0.1% to 2.3% and an increasing number of outbreaks was observed in recent years (Dyda et al., 2020; Westrell et al., 2009). In the U.S., a similar trend was observed that foodborne outbreaks from raw eggs and seafood are on a decline while outbreaks due to fruits and vegetables keep rising (Gould et al., 2013). Norovirus is not a typical foodborne pathogen in the 1990s, while since 2005 the development of diagnostic technology led to growing number of Norovirus outbreaks associated with fresh fruits and vegetables. Unlike *E. coli* and *Salmonella*, most of the reported Norovirus outbreaks have been due to the contamination of foods from illness food handlers at or close to the service place (Berger et al., 2010).

In this study, no article about *L. monocytogenes* outbreak was identified from databases. The possibility of *L. monocytogenes* to contaminate fresh fruits and vegetables and cause infection in humans has been recognized for a long time. A number of surveys have been conducted to investigate the prevalence of *L. monocytogenes* in fresh products. The results show that *L. monocytogenes* can be isolated from cucumber, peppers, potato, leafy vegetables, beansprout, tomato and cabbage (Beuchat, 1998). Although *L. monocytogenes* is able to survive and grow on fresh products under refrigeration temperature during storage, the outbreak associated with fresh products is infrequent. One reason should be the high infective dose of *L. monocytogenes* (10^3-10^6 cfu) and the long incubation time before developing disease (McLauchlin et al., 2004). Fresh product has relatively shorter shelf-life, that the contamination amount of *L. monocytogenes* would not exceed the infection dose when the products were consumed. Moreover, as fresh products will be disposed if expiring shelf-life, food sample cannot be collected during the investigation of outbreak, that the link between microorganisms and food vehicles could not be established. Besides, the prevalence of *L. monocytogenes* in fresh fruits and vegetables decreased significantly in recent years and most of the *L. monocytogenes* outbreaks were linked with the consumption of cooked meat, sausage or gravid fish (McLauchlin et al., 2004; EFSA Panel on Biological Hazards, 2018).

4.2.2. Food vehicles of outbreaks

Various fresh fruits and vegetables have been recognized as the vehicle of the foodborne pathogens' transmission in this study. More than half of the identified articles reported that salad or pre-sliced bagged salad leaf was the potential risk factor for foodborne infection, with OR >1. Salad and pre-sliced bagged salad leaf provide a proper condition for microorganisms to survive and proliferate, as nutrients emanated from the cut surface can be utilized by the pathogens. Furthermore, pathogen like *L. monocytogenes* or *E. coli* is able to penetrate the plant tissue through the cut edge, avoiding contact with antibacterial agents (Takeuchi & Frank, 2000; Heaton & Jones, 2008). Compared with unprocessed fruits and vegetables, salad or pre-sliced bagged salad leaf would have higher a possibility of contaminating by pathogens during the processing stage. Unclean washing water, improper hygiene of the producing environment and the food handlers are considered as the main concern in terms of foodborne infections (Brackett, 1994).

Among the identified articles associated with *Salmonella* outbreaks, sprouts and tomatoes were the most frequent food vehicles. While in the U.S., tomatoes were the most involved in the *Salmonella* outbreaks, which in line with the results of this study. The food vehicles vary between different pathogens. In the report of EFSA about the risks ranking of the foodborne pathogen combinations (2013), the most frequently reported combinations are: *Salmonella* spp. and sprouted seeds (11 outbreaks), *Salmonella* spp. and green leafy eaten raw as salads (7 outbreaks), VTEC and sprouted seeds (3 outbreaks) and norovirus and bulb or stem vegetables (2 outbreaks) during 2007 to 2011. In reality, it is challenging to investigate the sources of contaminations and the food agents, as the fresh products have short shelf-life and would be consumed or disposal before the outbreaks were recognized and conducted the traceback studies.

4.3. Evaluation of evidence

Collected studies were conducted in a wide range of time periods and designed with different

settings, thus, the quality of identified evidence varies with each other. Overall, the evidence shows high quality in the aspect of directness, consistency according to the results of the GRADE traffic light system and forest plots. However, in the aspect of existing risk of bias, precision and publication bias, there are some deficiencies, which decrease the overall quality. First of all, most the studies fail to apply suitable inclusion criteria of the control group. The inclusion criteria are developed to properly match the control group to the case group in observational studies. It is an approach to eliminate the influence of confounding factors, which would obscure the effect of exposure when investigating the disease's ethology and causal relationships (Jager et al., 2008). In the foodborne outbreak study, the application of improper inclusion criteria will lead to underestimate or overestimate the OR of developing diseases by consuming specified food items. Secondly, recall bias is a potential problem in more than half of identified studies. In this study, study methods and study designs were considered as the source of recall bias. For study methods, compared with questionnaire, the information collected through face-to-face interview are more accurate and comprehensive, thus contribute to higher quality of evidence (Harris & Brown, 2010). However, online or telephone questionnaire are superior in a higher response rate, less time-consuming and cost-effectiveness (Siemiatycki, 1979). For study design, it is worth noting that all the cohort studies reported by identified articles were associated with the outbreaks occurred in restaurant or conference setting. The practicality and feasibility inherent in the study design typically decide whether a cohort study or case-control study is appropriate in a specified setting. Yet, a well-design cohort study can provide more powerful results (Song & Chung, 2010). In this case, to improve the overall quality of observational study, it is necessary to follow the standard reporting guidelines, such as STROBE or PRISMA.

In addition to the potential risk of bias, the imprecision of estimated results was another factor, which would rate down the quality of evidence. Confidence intervals (CIs) is considered as an indicator of precision, narrow CIs indicates more precision while wide CIs indicates less precision. In this study, although all the estimated OR or RR was large than one, the CIs appeared insufficient wide and the sample size of most studies was moderate, that rating downs the quality of evidence. Furthermore, the funnel plots have shown the potential publication bias. The missing part of bottom left in the funnel plot indicates that the results with smaller sample size and effect size might not be published. Publication bias has been confirmed present in the clinical cohort studies. Studies with the significant result and considerable sample size are more likely to be published, even in journals with high citation impact factor (Easterbrook et al., 1991). However, when it comes to foodborne outbreak investigation, the amount of infected people within an outbreak is impossible to predict and control, that it is inevitable to have a small sample size. The small outbreaks would sometimes be ignored by the researchers or authorities. Thus, in this study, significant identified publication bias may cause by study confounding or other biases rather than possible publication bias. Besides, in a few studies, data of food items that existed in the checklist did not include in the final report, as the OR was smaller than 1.5 or was considered as non-significant data (e.g., $P>0.05$). Therefore, to provide powerful evidence, the authors should report the questionnaires and raw data as complementary material.

Evaluating individual study should organize as: identifying key elements of research question under the study; assessing of internal validity; summarizing of study results (West, 2002). In the GRADE

system, all the criteria mentioned above have been covered and subdivided clearly. However, the GRADE system was developed based on the clinical trials, that some adjustments should be adapted when applying in appraisal of foodborne outbreak study. First of all, a formal strategy to clarify the key elements of research question is PICO (known as population, intervention, comparator and outcome). While in observational study, PICO need to be modified as PECO (population, exposure, comparator and outcome). Secondly, in GRADE system, evaluation of observational study starts as low-quality evidence. From an ethical point of view, it is impossible to conduct experimental study for foodborne outbreak investigation. Therefore, some guideline projects suggest that the quality of evidence assessments begin as high followed by downgrading rather than having these begin as low followed by upgrading, as recommended by the GRADE approach (Rehfuess & Akl, 2013). Some researchers indicated that the GRADE approach is unable to distinguish between those public health interventions that are reasonably well supported by evidence (e.g., by interrupted time series-studies) and those that are less supported by evidence (e.g., by cohort studies) (Rehfuess & Akl, 2013). Thirdly, differences of terminology can be observed. In the GRADE system, study limitation (risk of bias) of observational study was subdivided into 4 aspects: failure to develop and apply appropriate eligibility criteria; flawed measurement of both exposure and outcome; failure to adequately control confounding; incomplete follow-up (Guyatt et al., 2011). While in the guideline of scientific assessment published by EFSA, the systematic error (bias) was subdivided into: informatic bias (differential misclassification or non-differential misclassification); confounding and selection bias (EFSA, 2020). In this study, the quality evaluation table was design based on the criteria used in the GRADE system. The description of follow-up was replaced by the calculation of response rate.

Although the GRADE system has been adopted by several research groups as it is a transparent and systematic appraisal tool, the United States' Community Guide and the Public Health Guidance offered by the United Kingdom's NICE Centre for Public Health Excellence indicated that they would not employ GRADE in their study. The GRADE system was considered to lack an assessment of cost-effectiveness, ethics, equity and other issues in developing recommendations and lacking the ability to protect against threats to internal validity (Rehfuess & Akl, 2013). EFSA did not pilot GRADE system in its scientific assessments, while it has applied the NTP-OHAT since 2015. The NTP-OHAT tool provides a parallel approach to evaluate the risk of bias from human or animal study which shares common terminology, considering the internal validity among different study designs. However, using NTP-OHAT may overestimate the potential risk of bias (Eick et al., 2020). Thus, there is no single appraisal tool that can satisfy all the aspects of assessing quality of study.

4.4. Integration of nutrition and rural development

To achieve the Sustainable Development Goals at the global level, the planetary diets should not only be promoted in developed countries but also in developing countries. Thence, foodborne diseases brought by the shifting diet behaviour with consuming more fresh fruit and vegetable products may pose a threat to the health issue of developing countries. Study has reported, while making up 41% of the world population, individuals living in developing countries accounted for 53% of all the foodborne illnesses and 75% of all the foodborne deaths, as well as 72% of the global foodborne DALYs, especially in African and South-eastern Asian region (Devleesschauwer et al.,

2018). Although it was unclear that the linkage of fresh products consumption and incidence of foodborne diseases in underdeveloped area, people have shown a high level of concern based on following reasons: lacking sufficient clean water to washing food and utensils; human and animal manure are widely used in horticulture production; food system is complex that fragmented with large numbers of small-scale actors and informal organization, which increase the difficulty for supervision (WHO, 2014; Grace, 2015). Moreover, food safety problem has an ignorable impact on the income and trade, that foodborne diseases would result in a reduction in developing-country exports and increase the economic costs (Unnevehr & Ronchi, 2014). Commonly, food safety problems and foodborne diseases can be ameliorated by implementing Good Agricultural Practice and following the instruction of "The Five Keys to Safer Food Manual" developed by WHO. To integrate all the aspects of food chain in one strategy, "From farm to fork" provides a comprehensive solution for addressing the challenge of food safety in a sustainable way.

Food safety and nutrition are crucial components for sustainable development. Foodborne diseases and malnutrition have an adverse effect not only on individual health and producibility, but also on the prosper of country worldwide. Microbiologically and chemically contaminated food products were responsible for more than 200 different diseases, ranging from diarrhoea to serious health problems, including cancer. Children were considered as the most vulnerable group (WHO, 2015). It was reported by The World Bank that unsafe food costs low- and middle-income economies USD 95.2 billion in lost productivity and 15 billion in medical expenses per year. Other costs were estimated in the losses of farm and company sales, foregone trade income and environmental burden of food wastes (Jaffee et al., 2018). On the other hand, excessive intake of energy would result in coronary heart disease, hypertension and strokes. Insufficient intake of calories and micronutrients, such as vitamins and minerals, is associated with a high risk of stunting or mental retardation (WHO, 2011). Stunting is a predictor for future economic opportunities of individuals and the ability of a country to accumulate human capital, as the economic costs of undernutrition account for about 2% to 11% of the GDP (Micha et al., 2020).

Unsafe food creates a vicious cycle of diseases and malnutrition, especially for young children, pregnant, the elderly and the sick. Thus, food safety and nutrition problems are closely connected, that it is necessary to engage stakeholders from different sectors to establish standards, and to generate scientific evidence-based advice for risk assessment as well as food safety and nutrition recommendations. It is an innovation to conduct scientific research which covers both aspects of food safety and nutrition. Drawing comprehensive instruction and evaluation system of intervention development is a future study direction for achieving SDGs. The cross-cutting units from The Nutrition and Food Safety (NFS) Department of WHO are contributing themselves to develop evidence-informed guidance about: diets and health, to reduce related disease burden; and policy actions to enable sustainable food environment, and technical tools, such as nutrient profile models for different policy applications. This study shows the possibility of applying GRADE in the food safety area. However, large efforts are still required for redesigning the evaluation criteria of GRADE to adapt the content of food safety study.

4.5. Study limitation

Several limitations of this study can be found: Only 25 articles were qualified to be selected for the study that it was possible to have missing article as fewer databases were searched. Secondly, more than one food vehicles were reported by most of the identified study, with OR or RR >1. Some of the food samples did not be collected and sent to lab for microbiological tests. Thus, it was hard to assure which food vehicle/vehicles was responsible for the outbreak. Besides, the development of an appraisal tool needs the contribution of experts from various study area. Although the evaluation tool used in this study was adjusted based on the GRADE system, the experience of GRADE system applied in observational study is limited and there is still a lot of improvement of terminology and assessment criteria should be made. Moreover, publication bias was explored by funnel plots, which is typically only reliable when the included studies are 10 or more. Otherwise, the significant publication test results may bring by confounding. Finally, the evidence was only evaluated by GRADE, which was first used in the area of the food safety study. To evaluate the quality of the evidence more objectively, other evaluation tools can also be applied.

5. Conclusion

This master thesis focuses on identifying epidemiological evidence of foodborne outbreaks associated with fresh fruits and vegetables consumption within the European region during the time period of 2011 to 2020. Both the primary pathogens and the opportunistic pathogens were considered as the potential causes of infections. To evaluate the quality of evidence, the GRADE system was applied in this study, which has been adapted as a methodological integration of the research areas of clinical study, nutrition and food safety.

25 articles were identified from the database. Based on the epidemiological evidence extracted, fresh products were confirmed as the food vehicles of *Salmonella spp., Escherichia coli* and Norovirus outbreaks within the European region, with overall OR of 16.58 for 13 case-control studies and RR of 1.42 for 7 cohort studies. More than half of the outbreaks caused by *Escherichia coli* infection, with OR of 16.27 and RR of 2.76. Salads or pre-sliced bagged salad leafs were the most frequent food vehicles according to the evidence. Most of the infected population are people of all ages and with the majority of females. Only one outbreak reported the infected population was children. Five articles did not involve in meta-analysis due to missing data and no article about *L. monocytogenes* outbreak was identified. Opportunistic pathogens were not proved as potential causes of foodborne infections.

The criteria used in GRADE system were redesigned to fit into the situation of appraising epidemiological evidence of food safety area. The overall quality of evidence is relatively low. Significant defects can be found in the aspect of recall bias and imprecision of results. 14 out of 25 studies collected the personal and food exposure information by online questionnaire and 13 out of 25 studies were defined as case-control studies, that lowing the quality of evidence. Wide range of confidence interval was detected around the estimated OR or RR of 20 studies and most of the studies did not recruit sufficient control group. Large heterogeneity was found among 7 cohort studies, which included in the meta-analysis. The asymmetry funnel plot indicated potential publication bias that the negative results and small-size studies had not been published. On the other hand, most of the studies properly identified the PECO, which shows the directness between the food exposure and the population.

Fresh fruits and vegetables have been proved as reservoirs of foodborne pathogens and caused infections among human. Foodborne diseases were responsible for heavy the disease burden globally, which has a negative influence on human wellbeing and impedes the sustainable development. It is a priority to take actions to control food safety problems associated with fresh products. “From farm to fork” interventions are necessary to avoid contamination in fresh products and inactive existing microorganisms by proper methods. Further research should focus on improving regulation of quality management and the implementation of hazard analysis of critical control points HACCP program in the entire fresh fruit and vegetable foods production chain to ensure food safety. Moreover, the “Rapid Alert System” need to be implemented to inform the public that avoid the widespread of foodborne pathogens. The possibility of applying GRADE in the study of food safety area has been proved, but it is necessary to make adjustments to assessment criteria.

In order to provide high-quality evidence-based methodology, the coalition of researchers from different fields should contribute to developing a comprehensive evaluation tool, which not only can be used in food safety study but also in clinical or nutritional study.

References

Aadil, R. M., Zeng, X. A., Jabbar, S., Nazir, A., Mann, A. A., Khan, M. K. I., & Ramzan, A. (2017). Quality evaluation of grapefruit juice by thermal and high pressure processing treatment. *Pakistan Journal of Agricultural Research*, 30(3).

Abadias, M., Alegre, I., Oliveira, M., Altisent, R., & Viñas, I. (2012). Growth potential of Escherichia coli O157: H7 on fresh-cut fruits (melon and pineapple) and vegetables (carrot and escarole) stored under different conditions. *Food Control*, 27(1), 37-44.

Ackers, M. L., Mahon, B. E., Leahy, E., Goode, B., Damrow, T., Hayes, P. S.,& Slutsker, L. (1998). An outbreak of Escherichia coli O157: H7 infections associated with leaf lettuce consumption. *Journal of infectious diseases*, 177(6), 1588-1593.

Adams, M. R., & Moss, M. (2007). *Food microbiology*. Royal society of chemistry.

Akbas, M. Y., & Ölmez, H. (2007). Inactivation of Escherichia coli and Listeria monocytogenes on iceberg lettuce by dip wash treatments with organic acids. *Letters in applied microbiology*, 44(6), 619-624.

Al-Kharousi, Z. S., Guizani, N., Al-Sadi, A. M., Al-Bulushi, I. M., & Shaharoona, B. (2016). Hiding in fresh fruits and vegetables: opportunistic pathogens may cross geographical barriers. *International journal of microbiology*, 2016.

Alwi, N. A., & Ali, A. (2014). Reduction of Escherichia coli O157, Listeria monocytogenes and Salmonella enterica sv. Typhimurium populations on fresh-cut bell pepper using gaseous ozone. *Food Control*, 46, 304-311.

Anzil, A. P., Rao, C., Wrzolek, M. A., Visvesvara, G. S., Sher, J. H., & Kozlowski, P. B. (1991). Amebic meningoencephalitis in a patient with AIDS caused by a newly recognized opportunistic pathogen. Leptomyxid ameba. *Archives of pathology & laboratory medicine*, 115(1), 21-25.

Bae, Y. M., Choi, N. Y., Heu, S., Kang, D. H., & Lee, S. Y. (2011). Inhibitory effects of organic acids combined with modified atmosphere packaging on foodborne pathogens on cabbage. *Journal of the Korean Society for Applied Biological Chemistry*, 54(6), 993-997.

Bajželj, B., Richards, K. S., Allwood, J. M., Smith, P., Dennis, J. S., Curmi, E., & Gilligan, C. A. (2014). Importance of food-demand management for climate mitigation. *Nature Climate Change*, 4(10), 924-929.

Barata, A., Malfeito-Ferreira, M., & Loureiro, V. (2012). The microbial ecology of wine grape berries. *International journal of food microbiology*, 153(3), 243-259.

Bardsley, C. A., Truitt, L. N., Pfuntner, R. C., Danyluk, M. D., Rideout, S. L., & Strawn, L. K. (2019). Growth and survival of *Listeria monocytogenes* and *Salmonella* on whole and sliced cucumbers. *Journal of food protection*, 82(2), 301-309.

Bauernfeind, J. C., & Pinkert, D. M. (1970). Food processing with added ascorbic acid. *In Advances in food research* (Vol. 18, pp. 219-315). Academic Press.

Bayer, C., Bernard, H., Prager, R., Rabsch, W., Hiller, P., Malorny, B., ... & Rosner, B. M. (2014). An outbreak of Salmonella Newport associated with mung bean sprouts in Germany and the Netherlands, October to November 2011. *Eurosurveillance*, 19(1), 20665.

Beaulieu, J. C., & Gorny, J. R. (2002). Fresh-cut fruits. *The commercial storage of fruits, vegetables, and florist and nursery stocks*, *604*.

Benarde, M. A., Snow, W. B., Olivieri, V. P., & Davidson, B. (1967). Kinetics and mechanism of bacterial disinfection by chlorine dioxide. *Applied microbiology*, 15(2), 257-265.

Berg, G., Eberl, L., & Hartmann, A. (2005). The rhizosphere as a reservoir for opportunistic human pathogenic bacteria. *Environmental microbiology*, 7(11), 1673-1685.

Berg, G., Erlacher, A., Smalla, K., & Krause, R. (2014). Vegetable microbiomes: is there a connection among opportunistic infections, human health and our 'gut feeling'? *Microbial biotechnology*, 7(6), 487-495.

Berger, C. N., Sodha, S. V., Shaw, R. K., Griffin, P. M., Pink, D., Hand, P., & Frankel, G. (2010). Fresh fruit and vegetables as vehicles for the transmission of human pathogens. *Environmental microbiology*, 12(9), 2385-2397.

Berger, V. W., & Alperson, S. Y. (2009). A general framework for the evaluation of clinical trial quality. *Reviews on recent clinical trials*, 4(2), 79–88.

Bernard, H., Faber, M., Wilking, H., Haller, S., Höhle, M., Schielke, A., ... & Werber, D. (2014). Large multistate outbreak of norovirus gastroenteritis associated with frozen strawberries, Germany, 2012. *Eurosurveillance*, 19(8), 20719.

Beuchat, L. R. (1998). Surface decontamination of fruits and vegetables eaten raw.

Beuchat, L. R. (2000). Use of sanitizers in raw fruit and vegetable processing. *Minimally processed fruits and vegetables*, 63-78.

Bitler, E. J., Matthews, J. E., Dickey, B. W., Eisenberg, J. N. S., & Leon, J. S. (2013). Norovirus outbreaks: a systematic review of commonly implicated transmission routes and vehicles. *Epidemiology & Infection*, 141(8), 1563-1571.

Bowen, A., Wiesenfeld, H. C., Kloesz, J. L., Pasculle, A. W., Nowalk, A. J., Brink, L., ... & Tarr, C. L. (2017). Notes from the field: Cronobacter sakazakii infection associated with feeding extrinsically contaminated expressed human milk to a premature infant—Pennsylvania, 2016. MMWR. *Morbidity and mortality weekly report*, 66(28), 761.

Brackett, R. E. (1994). Microbiological spoilage and pathogens in minimally processed refrigerated fruits and vegetables. In: *Minimally processed refrigerated fruits & vegetables* (pp. 269-312). Springer, Boston, MA.

Brown, S. P., Cornforth, D. M., & Mideo, N. (2012). Evolution of virulence in opportunistic pathogens: generalism, plasticity, and control. *Trends in microbiology*, 20(7), 336-342.

Buchholz, U., Bernard, H., Werber, D., Böhmer, M. M., Remschmidt, C., Wilking, H., ... & Kühne, M. (2011). German outbreak of Escherichia coli O104: H4 associated with sprouts. *New England Journal of Medicine*, 365(19), 1763-1770.

Buschini, A., Carboni, P., Furlini, M., Poli, P., & Rossi, C. (2004). Sodium hypochlorite-, chlorine dioxide-and peracetic acid-induced genotoxicity detected by the Comet assay and Saccharomyces cerevisiae D7 tests. *Mutagenesis*, *19*(2), 157-162.

Buta, J. G., & Moline, H. E. (2001). Prevention of browning of potato slices using polyphenoloxidase inhibitors and organic acids. *Journal of food quality*, 24(4), 271-282.

Büyükcam, A., Tuncer, Ö., Gür, D., Sancak, B., Ceyhan, M., Cengiz, A. B., & Kara, A. (2018). Clinical and microbiological characteristics of Pantoea agglomerans infection in children. *Journal of infection and public health*, 11(3), 304-309.

Byrne, L., Fisher, I., Peters, T., Mather, A., Thomson, N., Rosner, B., ... & Lane, C. (2014). A multi-country outbreak of Salmonella Newport gastroenteritis in Europe associated with watermelon from Brazil, confirmed by whole genome sequencing: October 2011 to January 2012. *Eurosurveillance*, 19(31), 20866.

Calhan, O., Onursal, C. E., Güneyli, A., & Eren, I. (2013, June). Effect of harvest date on postharvest quality of'Kordia'sweet cherry during MAP storage. In *XI International Controlled and Modified Atmosphere Research Conference 1071* (pp. 667-674).

Callejón, R. M., Rodríguez-Naranjo, M. I., Ubeda, C., Hornedo-Ortega, R., Garcia-Parrilla, M. C., & Troncoso, A. M. (2015). Reported foodborne outbreaks due to fresh produce in the United States and European Union: trends and causes. *Foodborne pathogens and disease*, 12(1), 32-38.

Chuajedton, A., Uthaibutra, J., Pengphol, S., & Whangchai, K. (2017). Inactivation of Escherichia coli O157: H7 by treatment with different temperatures of micro-bubbles ozone containing water. *International Food Research Journal*, 24(3), 1006-1010.

Coggon, D., Barker, D., & Rose, G. (2009). *Epidemiology for the Uninitiated*. John Wiley & Sons.

Colombe, S., Jernberg, C., Löf, E., Angervall, A. L., Mellström-Dahlgren, H., Dotevall, L., Bengnér, M., Hall, I., Sundqvist, L., Kühlmann-Berenzon, S., Galanis, I., Lindblad, M., Hansen, A., & Rehn, M. (2019). Outbreak of unusual H2S-negative monophasic Salmonella Typhimurium strain likely associated with small tomatoes, Sweden, August to October 2019. *Eurosurveillance: bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, 24(47), 1900643.

Colugnati, F. A., Staras, S. A., Dollard, S. C., & Cannon, M. J. (2007). Incidence of cytomegalovirus infection among the general population and pregnant women in the United States. *BMC infectious diseases*, 7(1), 71.

Connor, A. M., Luby, J. J., Hancock, J. F., Berkheimer, S., & Hanson, E. J. (2002). Changes in fruit antioxidant activity among blueberry cultivars during cold-temperature storage. *Journal of agricultural and food chemistry*, 50(4), 893-898.

Critical Appraisal Skills Programme (CASP). (2018). CASP (randomised controlled trial) checklist.

Culyer, A. J. (2014). *Encyclopedia of health economics*. Newnes.

Daher, D., Le Gourrierec, S., & Pérez-Lamela, C. (2017). Effect of high pressure processing on the microbial inactivation in fruit preparations and other vegetable based beverages. *Agriculture*, 7(9), 72.

Daş, E., Gürakan, G. C., & Bayındırlı, A. (2006). Effect of controlled atmosphere storage, modified atmosphere packaging and gaseous ozone treatment on the survival of Salmonella Enteritidis on cherry tomatoes. *Food Microbiology*, 23(5), 430-438.

De Backer, G., & De Henauw, S. (2019). Dietary guidelines for the Belgian adult population.

De Bentzmann, S., & Plésiat, P. (2011). The Pseudomonas aeruginosa opportunistic pathogen and human infections. *Environmental microbiology*, 13(7), 1655-1665.

De Corato, U. (2020). Improving the shelf-life and quality of fresh and minimally processed fruits and vegetables for a modern food industry: A comprehensive critical review from the traditional technologies into the most promising advancements. *Critical Reviews in Food Science and Nutrition*, 60(6), 940-975.

De Noordhout, C. M., Devleesschauwer, B., Angulo, F. J., Verbeke, G., Haagsma, J., Kirk, M., ... & Speybroeck, N. (2014). The global burden of listeriosis: a systematic review and meta-analysis. *The Lancet Infectious Diseases*, 14(11), 1073-1082.

Delaquis, P., Bach, S., & Dinu, L. D. (2007). Behavior of Escherichia coli O157: H7 in leafy vegetables. *Journal of food protection*, 70(8), 1966-1974.

DeSA, U. N. (2013). World population prospects: the 2012 revision. Population division of the department of economic and social affairs of the United Nations Secretariat, New York, 18.

Devleesschauwer, B., Haagsma, J. A., Mangen, M. J. J., Lake, R. J., & Havelaar, A. H. (2018). The global burden of foodborne disease. *In Food safety economics* (pp. 107-122). Springer, Cham.

Diefenbach, M. A., Miller-Halegoua, S., & Bowen, D. J. (Eds.). (2016). *Handbook of health decision science*. New York: Springer.

Dietary Guidelines Advisory Committee. (2015). Dietary guidelines for Americans 2015-2020. Government Printing Office.

Do Nascimento Nunes, M. C. (2008). Impact of environmental conditions on fruit and vegetable quality. *Stewart Postharvest Review*, 4(4), 1-14.

Durso, L. M., Smith, D., & Hutkins, R. W. (2004). Measurements of fitness and competition in commensal Escherichia coli and E. coli O157: H7 strains. *Applied and environmental microbiology*, 70(11), 6466-6472.

Dyda, A., Nguyen, P. Y., Chughtai, A., & MacIntyre, C. R. (2020). Changing epidemiology of Salmonella outbreaks associated with cucumbers and other fruits and vegetables. *Global Biosecurity*, 1(3).

Easterbrook, P. J., Gopalan, R., Berlin, J. A., & Matthews, D. R. (1991). Publication bias in clinical research. *The Lancet*, 337(8746), 867-872.

EAT-Lancet Commission. (2019). Food Planet Health-Healthy Diets from Sustainable Food Systems. The Lancet website. https://www. thela ncet. com/journ als/lance t/artic le/PIIS0, 140-6736.

EFSA Panel on Biological Hazards (BIOHAZ), Ricci, A., Allende, A., Bolton, D., Chemaly, M., Davies, R., ... & Lindqvist, R. (2018). Listeria monocytogenes contamination of ready-to-eat foods and the risk for human health in the EU. *EFSA Journal*, 16(1), e05134.

EFSA Scientific Committee, More, S., Bambidis, V., Benford, D., Bragard, C., Hernandez-Jerez, A., ... & Halldorsson, T. I. (2020). Draft for internal testing Scientific Committee guidance on appraising and integrating evidence from epidemiological studies for use in EFSA's scientific assessments. *EFSA Journal*, 18(8), e06221.

Ehuwa, O., Jaiswal, A. K., & Jaiswal, S. (2021). *Salmonella*, Food Safety and Food Handling Practices. *Foods*, 10(5), 907.

Eick, S. M., Goin, D. E., Chartres, N., Lam, J., & Woodruff, T. J. (2020). Assessing risk of bias in human environmental epidemiology studies using three tools: different conclusions from different tools. *Systematic reviews*, 9(1), 1-13.

Einöder-Moreno, M., Lange, H., Grepp, M., Osborg, E., Vainio, K., & Vold, L. (2016). Non-heat-treated frozen raspberries the most likely vehicle of a norovirus outbreak in Oslo, Norway, November 2013. *Epidemiology & Infection*, 144(13), 2765-2772.

El-Senousy, W. M., Costafreda, M. I., Pintó, R. M., & Bosch, A. (2013). Method validation for norovirus detection in naturally contaminated irrigation water and fresh produce. *International journal of food microbiology*, 167(1), 74-79.

Escher, M., Scavia, G., Morabito, S., Tozzoli, R., Maugliani, A., Cantoni, S., ... & Caprioli, A. (2014). A severe foodborne outbreak of diarrhoea linked to a canteen in Italy caused by enteroinvasive Escherichia coli, an uncommon agent. *Epidemiology & Infection*, 142(12), 2559-2566.

Escobedo-Avellaneda, Z., Guerrero-Beltrán, J. Á., Tapia, M. S., Barbosa-Cánovas, G. V., & Welti-Chanes, J. (2018). Minimal Processing of Fruits. In: *Fruit Preservation* (pp.67-92). Springer, New York, NY.

European Centre for Disease Prevention and Control. Typhoid and paratyphoid fevers. In: *ECDC. Annual epidemiological report for 2017.* Stockholm: ECDC; 2020.

European Commission. (2005). Commission Regulation (EC) No 2073/2005 of 15 November 2005 on microbiological criteria for foodstuffs. Off. J. Eur. Union L, 338, 1-26.

European Food Safety Authority and European Centre for Disease Prevention and Control (EFSA and ECDC). (2018). The European Union summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks in 2017. *EFSA Journal*, 16(12), e05500.

European Food Safety Authority and European Centre for Disease Prevention and Control (EFSA and ECDC). (2019). The European Union one health 2018 zoonoses report. *EFSA Journal*, 17(12), e05926.

European Food Safety Authority, & European Centre for Disease Prevention and Control. (2018). Multi-country outbreak of Listeria monocytogenes serogroup IV b, multi-locus sequence type 6, infections linked to frozen corn and possibly to other frozen vegetables–first update. *EFSA Supporting Publications*, 15(7), 1448E.

Fardet, A. (2017). New concepts and paradigms for the protective effects of plant-based food components in relation to food complexity. *In Vegetarian and plant-based diets in health and disease prevention* (pp. 293-312). Academic Press.

Fatica, M. K., & Schneider, K. R. (2011). Salmonella and produce: survival in the plant environment and implications in food safety. *Virulence*, 2(6), 573-579.

Feliziani, E., Lichter, A., Smilanick, J. L., & Ippolito, A. (2016). Disinfecting agents for controlling fruit and vegetable diseases after harvest. *Postharvest biology and technology*, 122, 53-69.

Fierer, J., & Guiney, D. G. (2001). Diverse virulence traits underlying different clinical outcomes of Salmonella infection. *The Journal of clinical investigation*, 107(7), 775-780.

Foley, C., Harvey, E., Bidol, S. A., Henderson, T., Njord, R., DeSalvo, T., ... & Bosch, S. A. (2013). Outbreak of Escherichia coli O104: H4 infections associated with sprout consumption—Europe and North America, May–July 2011. MMWR. *Morbidity and mortality weekly report*, 62(50), 1029.

Forney, C. F., Song, J., Fan, L., Hildebrand, P. D., & Jordan, M. A. (2003). Ozone and 1-methylcyclopropene alter the postharvest quality of broccoli. *Journal of the American Society for Horticultural Science*, 128(3), 403-408.

Freitag, N. E., Port, G. C., & Miner, M. D. (2009). Listeria monocytogenes—from saprophyte to intracellular pathogen. *Nature Reviews Microbiology*, 7(9), 623-628.

Fusco, V., Abriouel, H., Benomar, N., Kabisch, J., Chieffi, D., Cho, G. S., & Franz, C. M. (2018). Opportunistic food-borne pathogens. In: *Food safety and preservation* (pp. 269-306). Academic Press.

Gardiner, D., Gobin, M., Verlander, N. Q., Oliver, I., & Hawker, J. (2018). Use of an ingredient-based analysis to investigate a national outbreak of Escherichia coli O157, United Kingdom, July 2016. *Eurosurveillance*, 23(26), 1700627.

Gil, M. I., Selma, M. V., López-Gálvez, F., & Allende, A. (2009). Fresh-cut product sanitation and wash water disinfection: problems and solutions. *International journal of food microbiology*, 134(1-2), 37-45.

Gobin, M., Hawker, J., Cleary, P., Inns, T., Gardiner, D., Mikhail, A., ... & Oliver, I. (2018). National outbreak of Shiga toxin-producing Escherichia coli O157: H7 linked to mixed salad leaves, United Kingdom, 2016. *Eurosurveillance*, 23(18), 17-00197.

Goh, E. L., Hocking, A. D., Stewart, C. M., Buckle, K. A., & Fleet, G. H. (2007). Baroprotective effect of increased solute concentrations on yeast and moulds during high pressure processing. *Innovative Food Science & Emerging Technologies*, 8(4), 535-542.

Gonzalez, R. J., Luo, Y., Ruiz-Cruz, S., & McEVOY, J. L. (2004). Efficacy of sanitizers to inactivate Escherichia coli O157: H7 on fresh-cut carrot shreds under simulated process water conditions. *Journal of food protection*, 67(11), 2375-2380.

Gordis, L., & Gold, E. B. (1984). Epidemiology of pancreatic cancer. *World journal of surgery*, 8(6), 808-821.

Gould, L. H., Demma, L., Jones, T. F., Hurd, S., Vugia, D. J., Smith, K., ... & Griffin, P. M. (2009). Hemolytic uremic syndrome and death in persons with Escherichia coli O157: H7 infection, foodborne diseases active surveillance network sites, 2000–2006. *Clinical Infectious Diseases*, 49(10), 1480-1485.

Gould, L. H., Walsh, K. A., Vieira, A. R., Herman, K., Williams, I. T., Hall, A. J., & Cole, D. (2013). Surveillance for foodborne disease outbreaks—United States, 1998–2008. *Morbidity and Mortality Weekly Report: Surveillance Summaries*, 62(2), 1-34.

Grace, D. (2015). Food safety in low- and middle-income countries. *International journal of environmental research and public health*, 12(9), 10490-10507.

Graves, L. M., Swaminathan, B., & Hunter, S. B. (2007). Subtyping Listeria monocytogenes. *Food science and technology-new york-marcel dekker-*, *161*, 283.

Griffin, P. M. (1995). Escherichia coli O157: H7 and other enterohemorrhagic Escherichia coli. *Infections of the gastrointestinal tract*, 739-761.

Guarino, A., Giannella, R., & Thompson, M. R. (1989). Citrobacter freundii produces an 18-amino-acid heat-stable enterotoxin identical to the 18-amino-acid Escherichia coli heat-stable enterotoxin (ST Ia). *Infection and immunity*, 57(2), 649-652.

Gupta, S., Chatterjee, S., Vaishnav, J., Kumar, V., Variyar, P. S., & Sharma, A. (2012). Hurdle technology for shelf stable minimally processed French beans (Phaseolus vulgaris): A response surface methodology approach. *LWT-Food Science and Technology*, 48(2), 182-189.

Guyatt, G., Oxman, A. D., Akl, E. A., Kunz, R., Vist, G., Brozek, J., ... & Schünemann, H. J. (2011). GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. *Journal of clinical epidemiology*, 64(4), 383-394.

Han, Y., Selby, T. L., Schultze, K. K., Nelson, P. E., & Linton, R. H. (2004). Decontamination of strawberries using batch and continuous chlorine dioxide gas treatments. *Journal of food protection*, 67(11), 2450-2455.

Han, Y., Sherman, D. M., Linton, R. H., Nielsen, S. S., & Nelson, P. E. (2000). The effects of washing and chlorine dioxide gas on survival and attachment of Escherichia coli O157: H7 to green pepper surfaces. *Food Microbiology*, 17(5), 521-533.

Hannan, E. L. (2008). Randomized clinical trials and observational studies: guidelines for assessing respective strengths and limitations. *JACC: Cardiovascular Interventions*, 1(3), 211-217.

Harris, L. R., & Brown, G. T. (2010). Mixing interview and questionnaire methods: Practical problems in aligning data. P*ractical Assessment, Research, and Evaluation*, 15(1), 1.

Health Canada, Public Health Agency of Canada, Canadian Food Inspection Agency. (2011). Weight of evidence: factors to consider for appropriate and timely action in a food-borne illness outbreak investigation.

Heaton, J. C., & Jones, K. (2008). Microbial contamination of fruit and vegetables and the behaviour of enteropathogens in the phyllosphere: a review. *Journal of applied microbiology*, 104(3), 613-626.

Hernández-Reyes, C., & Schikora, A. (2013). *Salmonella*, a cross-kingdom pathogen infecting humans and plants. *FEMS microbiology letters*, 343(1), 1-7.

Hever, J. (2016). Plant-based diets: A physician's guide. *The Permanente Journal*, 20(3).

Higgins, J. P., Altman, D. G., Gøtzsche, P. C., Jüni, P., Moher, D., Oxman, A. D., ... & Sterne, J. A. (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *Bmj*, *343*.

Hinsinger, P., Bengough, A. G., Vetterlein, D., & Young, I. M. (2009). Rhizosphere: biophysics, biogeochemistry and ecological relevance. *Plant and soil*, 321(1-2), 117-152.

Huang, H. W., Hsu, C. P., Yang, B. B., & Wang, C. Y. (2014). Potential utility of high-pressure processing to address the risk of food allergen concerns. *Comprehensive Reviews in Food Science and Food Safety*, 13(1), 78-90.

Huang, H. W., Wu, S. J., Lu, J. K., Shyu, Y. T., & Wang, C. Y. (2017). Current status and future trends of high-pressure processing in food industry. *Food control*, 72, 1-8.

Huang, T. S., Xu, C., Walker, K., West, P., Zhang, S., & Weese, J. (2006). Decontamination efficacy of combined chlorine dioxide with ultrasonication on apples and lettuce. *Journal of Food Science*, 71(4), M134-M139.

Huang, Y., & Chen, H. (2011). Effect of organic acids, hydrogen peroxide and mild heat on inactivation of Escherichia coli O157: H7 on baby spinach. *Food Control*, 22(8), 1178-1183.

In, Y. W., Kim, J. J., Kim, H. J., & Oh, S. W. (2013). Antimicrobial activities of acetic acid, citric acid and lactic acid against S higella species. *Journal of Food Safety*, 33(1), 79-85.

International, C. O. M. S. F. F. (2006). Use of epidemiologic data to measure the impact of food safety control programs. *Food Control*, 17(10), 825-837.

Jadad, A. R., Moore, R. A., Carroll, D., Jenkinson, C., Reynolds, D. J. M., Gavaghan, D. J., & McQuay, H. J. (1996). Assessing the quality of reports of randomized clinical trials: is blinding necessary?. *Controlled clinical trials*, 17(1), 1-12.

Jaffee, S., Henson, S., Unnevehr, L., Grace, D., & Cassou, E. (2018). *The safe food imperative: Accelerating progress in low-and middle-income countries*. World Bank Publications.

Jager, K. J., Zoccali, C., Macleod, A., & Dekker, F. W. (2008). Confounding: what it is and how to deal with it. *Kidney international*, 73(3), 256-260.

Johnson, J. R., & Russo, T. A. (2002). Extraintestinal pathogenic Escherichia coli: "the other bad E coli". *Journal of Laboratory and Clinical Medicine*, 139(3), 155-162.

Jones, M. K., & Oliver, J. D. (2009). Vibrio vulnificus: disease and pathogenesis. *Infection and immunity*, 77(5), 1723-1733.

Jones, R. N. (2010). Microbial etiologies of hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia. *Clinical infectious diseases*, 51(Supplement-1), S81-S87.

Josephs-Spaulding, J., Beeler, E., & Singh, O. V. (2016). Human microbiome versus food-borne pathogens: friend or foe. *Applied microbiology and biotechnology*, 100(11), 4845-4863.

Kamińska, S., Kruszewska, Ż., Lejbrandt, E., & Sadkowska-Todys, M. (2014). Lessons from norovirus outbreak in Warsaw, Poland, December 2012. *Food and environmental virology*, 6(4), 276-281.

Kanamori, H., Yano, H., Hirakata, Y., Endo, S., Arai, K., Ogawa, M., ... & Kaku, M. (2011). High prevalence of extended-spectrum β-lactamases and qnr determinants in Citrobacter species from Japan: dissemination of CTX-M-2. *Journal of antimicrobial chemotherapy*, 66(10), 2255-2262.

Karmali, M. A., Petric, M., Lim, C., Fleming, P. C., Arbus, G. S., & Lior, H. (1985). The association between idiopathic hemolytic uremic syndrome and infection by verotoxin-producing Escherichia coli. *Journal of Infectious Diseases*, 151(5), 775-782.

Khadre, M. A., Yousef, A. E., & Kim, J. G. (2001). Microbiological aspects of ozone applications in food: a review. *Journal of food science*, 66(9), 1242-1252.

Kim, B. F., Santo, R. E., Scatterday, A. P., Fry, J. P., Synk, C. M., Cebron, S. R., ... & Neff, R. A. (2020). Country-specific dietary shifts to mitigate climate and water crises. *Global environmental change*, 62, 101926.

Kim, Y., Keogh, J. B., & Clifton, P. M. (2016). Polyphenols and glycemic control. *Nutrients*, 8(1), 17.

King, L. A., Nogareda, F., Weill, F. X., Mariani-Kurkdjian, P., Loukiadis, E., Gault, G., ... & de Valk, H. (2012). Outbreak of Shiga toxin–producing Escherichia coli O104: H4 associated with organic fenugreek sprouts, France, June 2011. *Clinical Infectious Diseases*, 54(11), 1588-1594.

Kingsley, D. H., Pérez-Pérez, R. E., Niemira, B. A., & Fan, X. (2018). Evaluation of gaseous chlorine dioxide for the inactivation of Tulane virus on blueberries. *International journal of food microbiology*, 273, 28-32.

Kinnula, S., Hemminki, K., Kotilainen, H., Ruotsalainen, E., Tarkka, E., Salmenlinna, S., ... & Rimhanen-Finne, R. (2018). Outbreak of multiple strains of non-O157 Shiga toxin-producing and enteropathogenic Escherichia coli associated with rocket salad, Finland, autumn 2016. *Eurosurveillance*, 23(35), 1700666.

Kirch, W. (Ed.). (2008). *Encyclopedia of Public Health*: Volume 1: A-H Volume 2: I-Z. Springer Science & Business Media.

Klaiber, R. G., Baur, S., Wolf, G., Hammes, W. P., & Carle, R. (2005). Quality of minimally processed carrots as affected by warm water washing and chlorination. *Innovative Food Science & Emerging Technologies*, 6(3), 351-362.

Klerks, M. M., Franz, E., van Gent-Pelzer, M., Zijlstra, C., & Van Bruggen, A. H. (2007). Differential interaction of Salmonella enterica serovars with lettuce cultivars and plant-microbe factors influencing the colonization efficiency. *The ISME journal*, 1(7), 620-631.

Klevens, R. M., Edwards, J. R., Richards Jr, C. L., Horan, T. C., Gaynes, R. P., Pollock, D. A., & Cardo, D. M. (2007). Estimating health care-associated infections and deaths in US hospitals, 2002. *Public health reports*, 122(2), 160-166.

Knoblauch, A. M., Bratschi, M. W., Zuske, M. K., Althaus, D., Stephan, R., Hächler, H., ... & Kiefer, S. (2015). Cross-border outbreak of *Salmonella enterica* spp. enterica serovar Bovismorbificans: multiple approaches for an outbreak investigation in Germany and Switzerland. *Swiss Med Wkly*, 2015; 145: w14182.

Lagerqvist, N., Löf, E., Enkirch, T., Nilsson, P., Roth, A., & Jernberg, C. (2020). Outbreak of gastroenteritis highlighting the diagnostic and epidemiological challenges of enteroinvasive Escherichia coli, County of Halland, Sweden, November 2017. *Eurosurveillance*, 25(9), 1900466.

Lalkhen, A. G., & McCluskey, A. (2008). Statistics V: Introduction to clinical trials and systematic reviews. *Continuing Education in Anaesthesia, Critical Care & Pain*, 8(4), 143-146.

Lan, R., Reeves, P. R., & Octavia, S. (2009). Population structure, origins and evolution of major Salmonella enterica clones. *Infection, Genetics and Evolution*, 9(5), 996-1005.

Landl, A., Abadias, M., Sárraga, C., Viñas, I., & Picouet, P. A. (2010). Effect of high pressure processing on the quality of acidified Granny Smith apple purée product. *Innovative Food Science & Emerging Technologies*, 11(4), 557-564.

Lane, D. J., & Richardson, D. R. (2014). The active role of vitamin C in mammalian iron metabolism: much more than just enhanced iron absorption!. *Free radical biology and medicine*, 75, 69-83.

Lattanzio, V., Lattanzio, V. M., & Cardinali, A. (2006). Role of phenolics in the resistance mechanisms of plants against fungal pathogens and insects. *Phytochemistry: Advances in research*, 661(2), 23-67.

Launders, N., Byrne, L., Adams, N., Glen, K., Jenkins, C., Tubin-Delic, D., ... & Outbreak Control Team. (2013). Outbreak of Shiga toxin-producing E. coli O157 associated with consumption of watercress, United Kingdom, August to September 2013. *Eurosurveillance*, 18(44), 20624.

Le Guyader, F. S., Le Saux, J. C., Ambert-Balay, K., Krol, J., Serais, O., Parnaudeau, S., ... & Atmar, R. L. (2008). A French oyster-related gastroenteritis outbreak: Aichi virus, norovirus, astrovirus, enterovirus and rotavirus all involved in clinical cases. *Journal of Clinical Microbiology*.

Lee, E. Y., Jun, Y. S., Cho, K. S., & Ryu, H. W. (2002). Degradation characteristics of toluene, benzene, ethylbenzene, and xylene by Stenotrophomonas maltophilia T3-c. *Journal of the Air & Waste Management Association*, 52(4), 400-406.

Lee, S. Y., Costello, M., & Kang, D. H. (2004). Efficacy of chlorine dioxide gas as a sanitizer of lettuce leaves. *Journal of food protection*, 67(7), 1371-1376.

Li, Y., Hruby, A., Bernstein, A. M., Ley, S. H., Wang, D. D., Chiuve, S. E., ... & Hu, F. B. (2015). Saturated fats compared with unsaturated fats and sources of carbohydrates in relation to risk of coronary heart disease: a prospective cohort study. *Journal of the American College of Cardiology*, 66(14), 1538-1548.

Likotrafiti, E., Smirniotis, P., Nastou, A., & Rhoades, J. (2013). Effect of Relative Humidity and Storage Temperature on the Behavior of L isteria monocytogenes on Fresh Vegetables. *Journal of Food Safety*, 33(4), 545-551.

Looney, W. J., Narita, M., & Mühlemann, K. (2009). Stenotrophomonas maltophilia: an emerging opportunist human pathogen. *The Lancet infectious diseases*, 9(5), 312-323.

Lopez-Galvez, F., Gil, M. I., Truchado, P., Selma, M. V., & Allende, A. (2010). Cross-contamination of fresh-cut lettuce after a short-term exposure during pre-washing cannot be controlled after subsequent washing with chlorine dioxide or sodium hypochlorite. *Food Microbiology*, 27(2), 199-204.

Luna-Guevara, J. J., Arenas-Hernandez, M. M., Martínez de la Peña, C., Silva, J. L., & Luna-Guevara, M. L. (2019). The role of pathogenic E. coli in fresh vegetables: Behavior, contamination factors, and preventive measures. *International journal of microbiology*, 2019.

Lund, B. M., & O'Brien, S. J. (2011). The occurrence and prevention of foodborne disease in vulnerable people. *Foodborne pathogens and disease*, 8(9), 961-973.

Lynch, M. F., Tauxe, R. V., & Hedberg, C. W. (2009). The growing burden of foodborne outbreaks due to contaminated fresh produce: risks and opportunities. *Epidemiology & Infection*, 137(3), 307-315.

Mariani, A. W., & Pego-Fernandes, P. M. (2014). Observational studies: why are they so important?. *Sao Paulo Medical Journal*, 132(1), 01-02.

Martin, R. M., & Bachman, M. A. (2018). Colonization, infection, and the accessory genome of Klebsiella pneumoniae. *Frontiers in cellular and infection microbiology*, 8, 4.

Martínez-Ferrer, M., Harper, C., Pérez-Muntoz, F., & Chaparro, M. (2002). Modified atmosphere packaging of minimally processed mango and pineapple fruits. *Journal of Food Science*, 67(9), 3365-3371.

Matz, C., Deines, P., Boenigk, J., Arndt, H., Eberl, L., Kjelleberg, S., & Jürgens, K. (2004). Impact of violacein-producing bacteria on survival and feeding of bacterivorous nanoflagellates. *Applied and Environmental Microbiology*, 70(3), 1593-1599.

Mayet, A., Andreo, V., Bedubourg, G., Victorion, S., Plantec, J. Y., Soullie, B., ... & Migliani, R. (2011). Food-borne outbreak of norovirus infection in a French military parachuting unit, April 2011. *Eurosurveillance*, 16(30), 19930.

McLauchlin, J., Mitchell, R., Smerdon, W. J., & Jewell, K. (2004). Listeria monocytogenes and listeriosis: a review of hazard characterisation for use in microbiological risk assessment of foods. *International journal of food microbiology*, 92(1), 15-33.

McMacken, M., & Shah, S. (2017). A plant-based diet for the prevention and treatment of type 2 diabetes. *Journal of geriatric cardiology: JGC*, 14(5), 342.

Mendes, R., Garbeva, P., & Raaijmakers, J. M. (2013). The rhizosphere microbiome: significance of plant beneficial, plant pathogenic, and human pathogenic microorganisms. *FEMS microbiology reviews*, 37(5), 634-663.

Micha, R., Mannar, V., Afshin, A., Allemandi, L., Baker, P., & Battersby, J. (2020). Global nutrition report: action on equity to end malnutrition 2020.

Mikhail, A. F. W., Jenkins, C., Dallman, T. J., Inns, T., Douglas, A., Martín, A. I. C., ... & Hawker, J. (2018). An outbreak of Shiga toxin-producing Escherichia coli O157: H7 associated with contaminated salad leaves: epidemiological, genomic and food trace back investigations. *Epidemiology & Infection*, 146(2), 187-196.

Miller, F. A., Silva, C. L., & Brandão, T. R. (2013). A review on ozone-based treatments for fruit and vegetables preservation. *Food Engineering Reviews*, 5(2), 77-106.

Morgan, M., Watts, V., Allen, D., Curtis, D., Kirolos, A., Macdonald, N., ... & Decraene, V. (2019). Challenges of investigating a large food-borne norovirus outbreak across all branches of a restaurant group in the United Kingdom, October 2016. *Eurosurveillance*, *24*(18), 1800511.

Müller, L., Kjelsø, C., Frank, C., Jensen, T., Torpdahl, M., Søborg, B., ... & Ethelberg, S. (2016). Outbreak of Salmonella Strathcona caused by datterino tomatoes, Denmark, 2011. *Epidemiology & Infection*, 144(13), 2802-2811.

Munck, N., Smith, J., Bates, J., Glass, K., Hald, T., & Kirk, M. D. (2020). Source attribution of Salmonella in Macadamia nuts to animal and environmental reservoirs in Queensland, Australia. *Foodborne pathogens and disease*, 17(5), 357-364.

Neumann, G., & Romheld, V. (2000). The release of root exudates as affected by the plant's physiological status. In *The rhizosphere* (pp. 57-110). CRC press.

Newitt, S., MacGregor, V., Robbins, V., Bayliss, L., Chattaway, M. A., Dallman, T., ... & Hawker, J. (2016). Two linked enteroinvasive Escherichia coli outbreaks, Nottingham, UK, June 2014. *Emerging infectious diseases*, 22(7), 1178.

Nunes, M. C. N., Ėmond, J. P., & Brecht, J. K. (2002, August). Predicting shelf life and quality of raspberries under different storage temperatures. In *XXVI International Horticultural Congress: Issues and Advances in Postharvest Horticulture 628* (pp. 599-606).

Ochman, H., & Groisman, E. A. (1994). The origin and evolution of species differences in Escherichia coli and Salmonella typhimurium. *In Molecular Ecology and Evolution: Approaches and Applications* (pp. 479-493). Birkhäuser, Basel.

Odriozola-Serrano, I., Soliva-Fortuny, R., & Martín-Belloso, O. (2008). Effect of minimal processing on bioactive compounds and colour attributes of fresh-cut tomatoes. *LWT-Food Science and Technology*, 41(2), 217-226.

Ohe, M. (2013). A "Blind Spot" Regarding the Norovirus Infection Pathway. *The Tohoku Journal of Experimental Medicine*, 229(2), 125-128.

Ohlsson, T. (1996). Minimal processing and heat treatment. *European food and drink review*, (WINTER), 33-34.

Ohlsson, T., & Bengtsson, N. (Eds.). (2002). *Minimal processing technologies in the food industries*. Elsevier.

Pandey, K. B., & Rizvi, S. I. (2009). Plant polyphenols as dietary antioxidants in human health and disease. *Oxidative medicine and cellular longevity*, 2.

Pang, W., Shang, P., Li, Q., Xu, J., Bi, L., Zhong, J., & Pei, X. (2018). Prevalence of opportunistic infections and causes of death among hospitalized HIV-infected patients in Sichuan, China. *The Tohoku journal of experimental medicine*, 244(3), 231-242.

Park, S. H., Choi, M. R., Park, J. W., Park, K. H., Chung, M. S., Ryu, S., & Kang, D. H. (2011). Use of organic acids to inactivate Escherichia coli O157: H7, Salmonella Typhimurium, and Listeria monocytogenes on organic fresh apples and lettuce. *Journal of Food Science*, 76(6), M293-M298.

Parry, R. T. (Ed.). (2012). Principles and applications of modified atmosphere packaging of foods. *Springer Science & Business Media*.

Patras, A., Brunton, N., Da Pieve, S., Butler, F., & Downey, G. (2009). Effect of thermal and high pressure processing on antioxidant activity and instrumental colour of tomato and carrot purées. *Innovative food science & emerging technologies*, 10(1), 16-22.

Pennington, J. A., & Fisher, R. A. (2009). Classification of fruits and vegetables. *Journal of Food Composition and Analysis*, 22, S23-S31.

Pérez, A. G., Sanz, C., Rios, J. J., Olias, R., & Olías, J. M. (1999). Effects of ozone treatment on postharvest strawberry quality. *Journal of Agricultural and Food Chemistry*, 47(4), 1652-1656.

Peron, E., Zaharia, A., Zota, L. C., Severi, E., Mårdh, O., Usein, C., ... & Pistol, A. (2016). Early findings in outbreak of haemolytic uraemic syndrome among young children caused by Shiga toxin-producing Escherichia coli, Romania, January to February 2016. *Eurosurveillance*, 21(11), 30170.

Peterkofsky, B. (1991). Ascorbate requirement for hydroxylation and secretion of procollagen: relationship to inhibition of collagen synthesis in scurvy. *The American journal of clinical nutrition*, 54(6), 1135S-1140S.

Pletz, M. W., Wollny, A., Dobermann, U. H., Rödel, J., Neubauer, S., Stein, C., ... & Maschmann, J. (2018). A nosocomial foodborne outbreak of a VIM carbapenemase-expressing Citrobacter freundii. *Clinical Infectious Diseases*, 67(1), 58-64.

Poli, G., P. A. Biondi, F. Uberti, W. Ponti, A. Basari, and C. Cantoni. 1979. Virucidal activity of organic acid. *Food Chemistry* 4:250–8.

Porta, M. (Ed.). (2014). *A dictionary of epidemiology*. Oxford university press.

Potter, M. E., & Tauxe, R. V. (1997). Epidemiology of foodborne diseases: tools and applications. World health statistics quarterly. *Rapport trimestriel de statistiques sanitaires mondiales*, 50(1-2), 24-29.

Praeger, U., Herppich, W. B., & Hassenberg, K. (2018). Aqueous chlorine dioxide treatment of horticultural produce: Effects on microbial safety and produce quality–A review. *Critical reviews in food science and nutrition*, 58(2), 318-333.

Raaijmakers, J. M., Paulitz, T. C., Steinberg, C., Alabouvette, C., & Moënne-Loccoz, Y. (2009). The rhizosphere: a playground and battlefield for soilborne pathogens and beneficial microorganisms. *Plant and soil*, 321(1-2), 341-361.

Ramos, B., Miller, F. A., Brandão, T. R. S., Teixeira, P., & Silva, C. L. M. (2013). *Innovative Food Sci. Emerging Technol*, 20, 1.

Ransley, J. K., Taylor, E. F., Radwan, Y., Kitchen, M. S., Greenwood, D. C., & Cade, J. E. (2010). Does nutrition education in primary schools make a difference to children's fruit and vegetable consumption? *Public health nutrition*, 13(11), 1898-1904.

Rathnayaka, R. M. U. S. K. (2013). Antibacterial Effect of Malic Acid Against Listeria monocytogenes, Salmonella en teritidis and Escherichia coli in Mango, Pineapple and Papaya Juices. *American Journal of Food Technology*, 8(1), 74-82.

Rehfuess, E. A., & Akl, E. A. (2013). Current experience with applying the GRADE approach to public health interventions: an empirical study. *BMC public health*, 13(1), 1-13.

Reid, K. C., Cockerill III, F. R., & Patel, R. (2001). Clinical and epidemiological features of Enterococcus casseliflavus/flavescens and *Enterococcus gallinarum* bacteremia: a report of 20 cases. *Clinical infectious diseases*, 32(11), 1540-1546.

Reiss, G., Kunz, P., Koin, D., & Keeffe, E. B. (2006). Escherichia coli O157: H7 infection in nursing homes: review of literature and report of recent outbreak. *Journal of the American Geriatrics Society*, 54(4), 680-684.

Rico, D., Martin-Diana, A. B., Barat, J. M., & Barry-Ryan, C. (2007). Extending and measuring the quality of fresh-cut fruit and vegetables: a review. *Trends in Food Science & Technology*, 18(7), 373-386.

Rivera, E. V. 2005. A review of chemical disinfection methods for minimally processed leafy vegetables. Ph.D. Thesis, Kansas State University, Manhattan, Kansas, USA

Robilotti, E., Deresinski, S., & Pinsky, B. A. (2015). Norovirus. *Clinical microbiology reviews*, 28(1), 134-164.

Sabaté, J., Sranacharoenpong, K., Harwatt, H., Wien, M., & Soret, S. (2015). The environmental cost of protein food choices. *Public health nutrition*, 18(11), 2067-2073.

Sanderson, S., Tatt, I. D., & Higgins, J. (2007). Tools for assessing quality and susceptibility to bias in observational studies in epidemiology: a systematic review and annotated bibliography. *International journal of epidemiology*, 36(3), 666-676.

Sant'Ana, A. S., Barbosa, M. S., Destro, M. T., Landgraf, M., & Franco, B. D. (2012). Growth potential of Salmonella spp. and Listeria monocytogenes in nine types of ready-to-eat vegetables stored at variable temperature conditions during shelf-life. *International journal of food microbiology*, 157(1), 52-58.

Santosa, A., Wall, S., Fottrell, E., Högberg, U., & Byass, P. (2014). The development and experience of epidemiological transition theory over four decades: a systematic review. *Global health action*, 7(1), 23574.

Satija, A., & Hu, F. B. (2018). Plant-based diets and cardiovascular health. *Trends in cardiovascular medicine*, 28(7), 437-441.

Satija, A., Bhupathiraju, S. N., Spiegelman, D., Chiuve, S. E., Manson, J. E., Willett, W., ... & Hu, F. B. (2017). Healthful and unhealthful plant-based diets and the risk of coronary heart disease in US adults. *Journal of the American College of Cardiology*, 70(4), 411-422.

Sharma, S., Hagbom, M., Carlsson, B., Nederby Öhd, J., Insulander, M., Eriksson, R., Simonsson, M., Widerström, M., & Nordgren, J. (2020). Secretor Status is Associated with Susceptibility to Disease in a Large GII.6 Norovirus Foodborne Outbreak. *Food and environmental virology*, 12(1), 28–34.

Shigehisa, T., Ohmori, T., Saito, A., Taji, S., & Hayashi, R. (1991). Effects of high hydrostatic pressure on characteristics of pork slurries and inactivation of microorganisms associated with meat and meat products. *International journal of food microbiology*, 12(2-3), 207-215.

Shin, Y., Ryu, J. A., Liu, R. H., Nock, J. F., & Watkins, C. B. (2008). Harvest maturity, storage temperature and relative humidity affect fruit quality, antioxidant contents and activity, and inhibition of cell proliferation of strawberry fruit. *Postharvest Biology and Technology*, 49(2), 201-209.

Silva, B. N., Cadavez, V., Teixeira, J. A., & Gonzales-Barron, U. (2017). Meta-analysis of the incidence of foodborne pathogens in vegetables and fruits from retail establishments in Europe. *Current Opinion in Food Science*, 18, 21-28.

Sinclair, C., Jenkins, C., Warburton, F., Adak, G. K., & Harris, J. P. (2017). Investigation of a national outbreak of STEC Escherichia coli O157 using online consumer panel control methods: Great Britain, October 2014. *Epidemiology & Infection*, 145(5), 864-871.

Sivapalasingam, S., Friedman, C. R., Cohen, L., & Tauxe, R. V. (2004). Fresh produce: a growing cause of outbreaks of foodborne illness in the United States, 1973 through 1997. *Journal of food protection*, 67(10), 2342-2353.

Smith, J. L., & Fratamico, P. M. (2017). Escherichia coli as a Pathogen. In: *Foodborne diseases* (pp. 189-208). Academic Press.

Söderström, A., Österberg, P., Lindqvist, A., Jönsson, B., Lindberg, A., Blide Ulander, S., ... & Andersson, Y. (2008). A large Escherichia coli O157 outbreak in Sweden associated with locally produced lettuce. *Foodborne pathogens and disease*, 5(3), 339-349.

Song, J. W., & Chung, K. C. (2010). Observational studies: cohort and case-control studies. *Plastic and reconstructive surgery*, 126(6), 2234.

Springmann, M., Godfray, H. C. J., Rayner, M., & Scarborough, P. (2016). Analysis and valuation of the health and climate change cobenefits of dietary change. *Proceedings of the National Academy of Sciences*, 113(15), 4146-4151.

Sram, R. J., Binkova, B., & Rossner Jr, P. (2012). Vitamin C for DNA damage prevention. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*, 733(1-2), 39-49.

Sydnor, E. R., & Perl, T. M. (2011). Hospital epidemiology and infection control in acute-care settings. *Clinical microbiology reviews*, 24(1), 141-173.

Tadesse, T. N., Ibrahim, A. M., & Abtew, W. G. (2015). Degradation and formation of fruit colour in tomato (Solanum lycopersicum L.) in response to storage temperature. *American Journal of Food Technology*, 10(4), 147-157.

Takeuchi, K., & Frank, J. F. (2000). Penetration of Escherichia coli O157: H7 into lettuce tissues as affected by inoculum size and temperature and the effect of chlorine treatment on cell viability. *Journal of food protection*, 63(4), 434-440.

The Netherlands, October to November 2011. *Euro Surveillance*, 19(1), 20665

Tilman, D., & Clark, M. (2015). Food, agriculture & the environment: can we feed the world & save the earth? *Daedalus*, 144(4), 8-23.

Timmermans, R. A. H., Mastwijk, H. C., Knol, J. J., Quataert, M. C. J., Vervoort, L., Van der Plancken, I., ... & Matser, A. M. (2011). Comparing equivalent thermal, high pressure and pulsed electric field processes for mild pasteurization of orange juice. Part I: Impact on overall quality attributes. *Innovative Food Science & Emerging Technologies*, 12(3), 235-243.

Top, J., Willems, R., & Bonten, M. (2008). Emergence of CC17 *Enterococcus faecium*: from commensal to hospital-adapted pathogen. *FEMS Immunology & Medical Microbiology*, 52(3), 297-308.

Torres, J.A., V elazquez, G. Hydrostatic pressure processing of foods. In Food Processing Operations Modeling: Design and Analysis, 2nd ed. *CRC Press: Boca Raton, FL, USA*, 2008 pp. 173–212.

Tsouvaltzis, P., & Brecht, J. K. (2017). Inhibition of enzymatic browning of fresh-cut potato by immersion in citric acid is not solely due to pH reduction of the solution. *Journal of food processing and preservation*, 41(2), e12829.

Tzortzakis, N., Borland, A., Singleton, I., & Barnes, J. (2007). Impact of atmospheric ozone-enrichment on quality-related attributes of tomato fruit. *Postharvest Biology and Technology*, 45(3), 317-325.

Unnevehr, L., & Ronchi, L. (2014). Food safety and developing markets: research findings and research gaps.

Uyttendaele, M., NEYTS, K., VANDERSWALMEN, H., NOTEBAERT, E., & Debevere, J. (2002). Control of Aeromonas on minimal processed vegetables by decontamination with lactic acid, chlorinated water or essential oil solution. In *18th International ICFMH Symposium Food Micro 2002, Lillehammer (Norway), 18-23 augustus 2002* (pp. 47-50).

Uzeh, R. E., Alade, F. A., & Bankole, M. (2009). The microbial quality of pre-packed mixed vegetable salad in some retail outlets in Lagos, Nigeria. *African Journal of Food Science (ACFS)*, 3(9), 270-272.

Van Haute, S., Sampers, I., Holvoet, K., & Uyttendaele, M. (2013). Physicochemical quality and chemical safety of chlorine as a reconditioning agent and wash water disinfectant for fresh-cut lettuce washing. *Applied and environmental microbiology*, 79(9), 2850-2861.

Vandekinderen, I., Devlieghere, F., Van Camp, J., Kerkaert, B., Cucu, T., Ragaert, P., ... & De Meulenaer, B. (2009). Effects of food composition on the inactivation of foodborne microorganisms by chlorine dioxide. *International journal of food microbiology*, 131(2-3), 138-144.

Velez Rivera, E. (2005). A review of chemical disinfection methods for minimally processed leafy vegetables (Doctoral dissertation, Kansas State University).

Vestrheim, D. F., Lange, H., Nygård, K., Borgen, K., Wester, A. L., Kvarme, M. L., & Vold, L. (2016). Are ready-to-eat salads ready to eat? An outbreak of Salmonella Coeln linked to imported, mixed, pre-washed and bagged salad, Norway, November 2013. *Epidemiology & Infection*, 144(8), 1756-1760.

Vila, J., Sáez-López, E., Johnson, J. R., Römling, U., Dobrindt, U., Cantón, R., ... & Bosch, J. (2016). Escherichia coli: an old friend with new tidings. *FEMS microbiology reviews*, 40(4), 437-463.

Vincent, J. L., Marshall, J. C., Ñamendys-Silva, S. A., François, B., Martin-Loeches, I., Lipman, J., ... & Jimenez, E. (2014). Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit. *The lancet Respiratory medicine*, 2(5), 380-386.

Vivek, K., Singh, S. S., & RC, P. (2019). A review on postharvest management and advances in the minimal processing of fresh-cut fruits and vegetables. *Journal of Microbiology, Biotechnology and Food Sciences*, 2019, 1178-1187.

Vo, T. H., Okasha, O., Al-Hello, H., Polkowska, A., Räsänen, S., Bojang, M., ... & Jalava, K. (2016). An outbreak of norovirus infections among lunch customers at a restaurant, Tampere, Finland, 2015. *Food and environmental virology*, 8(3), 174-179.

Waldram, A., Lawler, J., Jenkins, C., Collins, J., Payne, M., Aird, H., ... & Foster, K. (2018). Large outbreak of multiple gastrointestinal pathogens associated with fresh curry leaves in North East England, 2013. *Epidemiology & Infection*, 146(15), 1940-1947.

Wang, F., Zheng, J., Yang, B., Jiang, J., Fu, Y., & Li, D. (2015). Effects of vegetarian diets on blood lipids: a systematic review and meta-analysis of randomized controlled trials. *Journal of the American Heart Association*, 4(10), e002408.

Warriner, K. (2005). Pathogens in vegetables. *In Improving the safety of fresh fruit and vegetables* (pp. 3-43). Woodhead Publishing.

Waterlander, W. E., de Boer, M. R., Schuit, A. J., Seidell, J. C., & Steenhuis, I. H. (2013). Price discounts significantly enhance fruit and vegetable purchases when combined with nutrition education: a randomized controlled supermarket trial. *The American journal of clinical nutrition*, 97(4), 886-895.

Wells, G. A., Shea, B., O'Connell, D. A., Peterson, J., Welch, V., Losos, M., & Tugwell, P. (2000). The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses.

West, S. (2002). Systems to rate the strength of scientific evidence. *Evidence report/technology assessment*, No. 47.

Westrell, T., Ciampa, N., Boelaert, F., Helwigh, B., Korsgaard, H., Chríel, M., ... & Mäkelä, P. (2009). Zoonotic infections in Europe in 2007: a summary of the EFSA-ECDC annual report. *Eurosurveillance*, 14(3), 19100.

White, G. C. (1999). Chemistry of chlorination. *Handbook of chlorination and alternative disinfectants*, 212-287.

WHO Working Group. (2000). Evaluation and use of epidemiological evidence for environmental health risk assessment: WHO guideline document. *Environmental health perspectives*, 997-1002.

WHO, G. (2013). WHO methods and data sources for global burden of disease estimates 2000-2011. *Geneva: Department of Health Statistics and Information Systems*.

WHO/UNICEF Joint Water Supply, & Sanitation Monitoring Programme. (2014). *Progress on drinking water and sanitation: 2014 update*. World Health Organization.

Willett, W., Rockström, J., Loken, B., Springmann, M., Lang, T., Vermeulen, S., ... & Jonell, M. (2019). Food in the Anthropocene: the EAT–Lancet Commission on healthy diets from sustainable food systems. *The Lancet*, 393(10170), 447-492.

World Health Organization. (2014). WHO initiative to estimate the global burden of foodborne diseases: fourth formal meeting of the Foodborne Disease Burden Epidemiology Reference Group (FERG): sharing new results, making future plans, and preparing ground for the countries.

World Health Organization. (2015). *WHO estimates of the global burden of foodborne diseases: foodborne disease burden epidemiology reference group 2007-2015*. World Health Organization.

Wu, C. T. (2010). An overview of postharvest biology and technology of fruits and vegetables. In *Technology on Reducing Post-Harvest Losses and Maintaining Quality of Fruits and Vegetables: Proceedings of 2010 AARDO Workshop*.

Yeni, F., Yavaş, S., Alpas, H. A. M. I., & Soyer, Y. (2016). Most common foodborne pathogens and mycotoxins on fresh produce: a review of recent outbreaks. *Critical Reviews in Food Science and Nutrition*, 56(9), 1532-1544.

Zagory, D. (1999). Effects of post-processing handling and packaging on microbial populations. *Postharvest Biology and Technology*, 15(3), 313-321.

Zheng, D. P., Ando, T., Fankhauser, R. L., Beard, R. S., Glass, R. I., & Monroe, S. S. (2006). Norovirus classification and proposed strain nomenclature. *Virology*, 346(2), 312-323.

Zhu, Q., Gooneratne, R., & Hussain, M. A. (2017). Listeria monocytogenes in fresh produce: outbreaks, prevalence and contamination levels. *Foods*, 6(3), 21.