Published in final edited form as:

J Food Prot. 2015 December ; 78(12): 2264–2278. doi:10.4315/0362-028X.JFP-15-146.

Application of a Rapid Knowledge Synthesis and Transfer Approach to Assess the Microbial Safety of Low-Moisture Foods

Ian Young^{1,2,*}, Lisa Waddell¹, Sarah Cahill², Mina Kojima³, Renata Clarke², and Andrijana Rajic²

¹Public Health Risk Sciences Division, Laboratory for Foodborne Zoonoses, Public Health Agency of Canada, 160 Research Lane, Suite 206, Guelph, Ontario, Canada, N1G 5B2 ²Food Safety and Quality Unit, Food and Agriculture Organization, Viale delle Terme di Caracalla, Roma 00153, Italy ³Department of Food Safety and Zoonoses, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland

Abstract

Low-moisture foods (LMF) are increasingly implicated in outbreaks of foodborne illness resulting in a significant public health burden. To inform the development of a new Codex Alimentarius code of hygienic practice for LMF, we applied a rapid knowledge synthesis and transfer approach to review global research on the burden of illness, prevalence, and interventions to control nine selected microbial hazards in eight categories of LMF. Knowledge synthesis methods included an integrated scoping review (search strategy, relevance screening and confirmation, and evidence mapping), systematic review (detailed data extraction), and meta-analysis of prevalence data. Knowledge transfer of the results was achieved through multiple reporting formats, including evidence summary cards. We identified 214 unique outbreaks and 204 prevalence and 126 intervention studies. 'Cereals and grains' (n=142) and *Salmonella* spp. (n=278) were the most commonly investigated LMF and microbial hazard categories, respectively. *Salmonella* spp. was implicated in the most outbreaks (n=96, 45%), several of which were large and widespread, resulting in the most hospitalizations (n=895, 89%) and deaths (n=14, 74%). *Salmonella* spp. had a consistently low prevalence across all LMF categories (0-3%), while other hazards (e.g. *B. cereus*) were found at highly variable levels. A variety of interventions were investigated in small challenge trials. Key knowledge gaps included under-reporting of LMF outbreaks, limited reporting of microbial concentration data from prevalence studies, and a lack of intervention-efficacy research under commercial conditions. Summary cards were a useful knowledge transfer format to inform complementary risk ranking activities. This review builds upon previous work in this area by synthesizing a broad range of evidence using a structured, transparent, and integrated approach to provide timely evidence-informed inputs into international guidelines.

Keywords

dry foods; low water activity; food safety; scoping review; systematic review; meta-analysis

* Author for correspondence: Telephone: +39 06 570 56623, Fax: +39 06 570 53057, ian.young@fao.org.

Introduction

Low-moisture foods (LMF) are naturally low in moisture or are produced from higher moisture foods through drying or dehydration processes. The low water activity (a_w) of these foods contributes to a long shelf life (7, 20, 47, 57). Examples of LMF products include cereals, grains, confections (e.g. chocolate), powdered-protein products (e.g. dairy and egg powders), dried fruits and vegetables, honey, spices, seeds, and nuts and nut-based products (e.g. peanut butter), among others. LMF are generally perceived as safe by consumers, and many LMF are consumed as ready-to-eat products with no consumer-level pathogen reduction step such as cooking (5, 7).

Although most microbial hazards cannot grow in LMF due to the low a_w , many pathogens can survive and remain viable for months to years in these foods, posing potential risks to consumers (7, 20, 47). For example, several national and international outbreaks of foodborne illness as well as product recalls have occurred in recent years due to *Salmonella* spp. contamination of LMF products such as spices, nuts (including peanut butter), cereal products (e.g. breakfast cereals), tahini paste, and chocolate, among many others (7, 15, 20, 34, 51, 57, 59, 63, 67, 68, 70). One of the most important steps in the control of microbial contamination of many LMF products is the application of pathogen-reduction treatments such as thermal and chemical pasteurization, high-pressure processing, or irradiation to reduce initial levels of microbial contamination of raw ingredients and materials (7, 20, 46, 65). The specific treatments used and their effectiveness differ by commodity and product composition, and should be accompanied by implementation of good manufacturing practices and hazard analysis critical control point (HACCP) systems throughout the production process to prevent and mitigate risks of post-treatment cross-contamination.

Recent high-profile outbreaks of foodborne illness and product recalls due to microbial contamination of LMF, particularly from *Salmonella* spp., have increased global attention and response to the microbial safety of LMF (5, 18, 29, 57, 65). Therefore, the Codex Committee on Food Hygiene acted to develop a Code of Hygienic Practice for LMF to set standardized and comprehensive international guidance in this area (13). The Food and Agriculture Organization of the United Nations (FAO) and World Health Organization (WHO) Joint Expert Meeting on Microbiological Risk Assessment (JEMRA) was requested to provide scientific advice into the development of this guideline.

Several expert reviews and industry and government guidance documents have been published in recent years which have comprehensively summarized many aspects of the microbial safety of LMF, including the mechanisms of microbial survival and resistance in LMF, key sources and risk factors of product contamination, and detailed recommendations for hygienic practices, control measures, and monitoring and verification processes (5, 7, 10, 11, 18, 20, 29, 47, 57, 65). However, none used a transparent and systematic methodology in their assessment and selection of the evidence reviewed and recommendations made, which limits the utility and user confidence of this evidence to inform decision-making and risk management (49, 54, 69). Therefore, JEMRA commissioned a structured and transparent knowledge synthesis approach to review the current state of global research on selected microbial hazards in LMF (49, 73). This manuscript highlights the overall process, results,

recommendations, and implications of the review. A more detailed and complementary technical report is also available online (22). The specific objectives of the review were to summarize and evaluate the evidence and limitations in the global literature on the burden of illness due to microbial contamination of LMF, the prevalence and concentration of microbial hazards in LMF, and interventions to reduce microbial contamination of LMF. A secondary objective of this manuscript is to share lessons learned from the application of knowledge synthesis and transfer methodologies to this area, including their utility to address an urgent and high-priority food safety policy issue and to inform risk and decision analysis (49). The end-users of this work may include decision-makers, researchers, and the broader food safety community interested in the current state of research on the microbial safety of LMF and the application of knowledge synthesis and transfer methods to food safety issues.

Materials and Methods

Knowledge synthesis approach and team

The review was conducted using a “rapid” (i.e. streamlined) approach to inform decision-making under a limited timeline and used an integrated combination of knowledge synthesis (scoping review, systematic review, and meta-analysis) and knowledge transfer methods (2, 24, 49). The review team consisted of all five co-authors, with diverse methodological and topic expertise: I.Y. and L.W. conducted the review activities with oversight and coordination from the other co-authors. The team convened via teleconference prior to initiating the review and exchanged correspondence regularly thereafter to discuss the protocol and review forms, to evaluate questions about review scope and eligibility criteria, and to review the study progress and results.

Scoping review questions, eligibility criteria, and definitions

The review questions were as follows: 1) what is the burden of illness in humans attributed to LMF contaminated with pathogenic bacteria?; 2) what is the frequency of contamination (prevalence and concentration) of selected microbial hazards in LMF?; and 3) what are the potentially effective interventions (from primary production to the end of processing) to mitigate risks associated with contaminated LMF? The review scope was limited to nine selected microbial hazards: *Bacillus cereus*, *Clostridium botulinum*, *Clostridium perfringens*, *Cronobacter* spp. (formerly *Enterobacter sakazakii*), *Escherichia coli* (including generic *E. coli* and pathogenic strains), *Salmonella* spp., *Staphylococcus aureus*, *Listeria monocytogenes*, and the indicator bacteria Enterobacteriaceae. Unless otherwise specified, the term *E. coli* is used in this article to refer to both generic and pathogenic strains.

LMF were defined as any food product with $a_w < 0.85$. Eight LMF product categories, each consisting of one or more sub-categories, were specified by the JEMRA secretariat in consultation with some subject matter experts and used to facilitate data organization, summarization, and reporting of this review (Table 1). Composite LMF products with multiple ingredients were assigned to only one category according to where the product best fit (e.g. mixed cereal/grain products were classified under “cereals and grains”) or based on the primary ingredient of concern for contamination. Powdered infant formula was

specifically excluded from the scope of this review because international guidelines for these products were recently updated based on a prior risk assessment (12, 21). Articles describing the validation of diagnostic tests for the detection of microbial hazards in LMF and those examining interventions at the consumer level (e.g. cooking) were also excluded.

For burden of illness information reported in this review, we defined an outbreak as two or more individuals with a similar illness resulting from consuming a common food product and with either an epidemiological or laboratory confirmation (27). We also included case studies where only one reported case of illness occurred due to a confirmed or suspected contaminated LMF product (e.g. infant botulism cases due to honey consumption). Only primary research on burden of illness information was included; foodborne illness attribution studies using outbreak data and/or expert elicitation to attribute foodborne illness to specific food groups or commodities (usually not specific LMF products) were excluded (4, 45). Information on LMF recalls were not summarized in this review. While we may have captured some of this information if it was indexed in the bibliographic databases included in the search, most would be contained only in food recall databases which were not searched in this review.

Search strategy

A comprehensive search algorithm was developed by extracting key terms from 14 known relevant articles and combining them into three broad categories: LMF product terms, microbial hazards terms, and outcome terms. The search was pre-tested in PubMed to ensure it was sufficiently sensitive, and then was implemented in two bibliographic databases (Scopus and PubMed) on January 13, 2014. No publication date or other restrictions were placed on the searches. The search was verified through multiple steps. Firstly, we reviewed a reference list of 464 relevant articles identified by the authors during preliminary review work on this subject. The preliminary work included a web search in Google using the terms “low-moisture food”, “low-water activity food” and “dry food pathogens”, it included a search of the reference lists of eight review articles and reports relevant to the review questions, and it included a hand search of the reference lists of all relevant articles. We conducted additional verification by reviewing the reference lists of eight additional articles and by hand-searching the reference lists of newly identified relevant articles. The full search algorithm and list of articles used for verification are available in the full technical report (22).

To identify additional sources of burden of illness information, we searched a comprehensive database of international foodborne disease outbreak reports maintained at the Public Health Agency of Canada (27). The database comprises >7,900 outbreak reports from multiple sources: journal articles, newspapers, listservs, press releases, country line lists, and government and laboratory websites (27). To search the database, all outbreaks implicating LMF products and the selected microbial hazards were queried on January 14, 2014, and used to obtain all recorded information about the outbreak.

Relevance screening and confirmation

Screening of the titles and abstracts of all unique citations identified in the search was conducted using an *a priori* developed screening form. The form contained one question to determine the relevance of citations to one or more of the review questions. If the title and abstract did not provide sufficient detail to determine the article's relevance (e.g., "confectionary items", "sweets", "snacks" may not refer to LMF), the article was included at this stage for further evaluation. Full texts of all relevant citations were obtained and articles were confirmed for relevance using a pre-specified form. Key characteristics were also extracted to facilitate evidence mapping and to prioritize subsequent review steps: article language; LMF product categories; and microbial hazards investigated. Only articles published in English, French, and Spanish were included in further data extraction and analysis unless there was sufficient extractable data from an English abstract. In addition, we excluded research on dried and/or fermented sausages, salamis, and jerky's from further analysis because we were not able to confirm the a_w of many of these products due to reporting limitations in the literature, and the a_w of these products is typically close to or variable around the 0.85 cut-off limit used in this review (56). For other products where a_w values were not specified and product eligibility as a LMF was not certain, we referred to previously published a_w values for common foods and ingredients to make a decision (56). Finally, we excluded all articles that investigated the prevalence or concentration of microbial hazards in LMF published prior to 1990, as these were not considered relevant or reflective of the current state of the industry and because of changes in diagnostic test methodologies since that time.

Evidence charts

Overall and LMF category-specific evidence charts were created to highlight cross-tabulations between combinations of the following variables: review question; LMF categories investigated; and microbial hazards investigated. The evidence charts were created using bubble figure plots in Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA), where each cross-tabulation value is represented by bubbles that are proportional in size to the total number of articles. The charts were used by the review team to evaluate the breadth and depth of data available for each review question and the feasibility of conducting meta-analysis in specific data subgroups under the study timelines.

Systematic review methods

Detailed data were extracted from each article confirmed as relevant using one of three specific data extraction forms developed for each review question. The burden of illness form contained 17 questions about: the source of the outbreak/case report; year; region/country; confirmation method (epidemiological or laboratory); LMF products and microbial hazards implicated; the number of exposed persons, cases, hospitalizations, deaths, attack rate, and other details (e.g. microbial hazard concentration in the implicated LMF). The prevalence form contained 21 questions about: general article details (e.g. publication year); study design and location; LMF products and microbial hazards investigated; outcome types (prevalence and/or concentration data); extent of reporting of outcome data; and quantitative results. The intervention form contained 20 questions about: general article details; study

design and location; LMF products and microbial hazards investigated; intervention type, details, and effectiveness; and reporting of quantitative results.

Data analysis

For all review questions, extracted data were summarized descriptively and key results reported in frequency tables and figures. Based on an assessment of the quantity and distribution of available data in scoping review evidence charts, the review team decided to conduct meta-analysis only on study estimates of the prevalence of microbial hazards in LMF. Additional meta-analysis on other data subsets (e.g. intervention efficacy) was not considered feasible within the project timelines.

Meta-analysis models were calculated for the prevalence of each microbial hazard in overall LMF categories and in sub-categories if prevalence data were available from ≥ 2 sampling surveys and when at least one of the surveys reported non-zero prevalence. We excluded Enterobacteriaceae from this analysis as it was captured in this review as an indicator of contamination and not a hazard. The models were calculated using the DerSimonian and Laird method for random-effects (vs. a fixed-effect approach) based on our assumption that the prevalence estimates followed a distribution across studies and that studies were not all estimating the same prevalence value (14). Additionally, we used a double arcsine transformation to stabilize the variance of the input data (3, 23). This transformation was necessary because the data subsets often contained low prevalence levels and a high proportion of zero values, a situation that adds undue weight to prevalence values between 25 and 75% when using a standard log transformation (3, 19). The unit of analysis was individual sampling surveys (i.e. unique food product and microbial hazard prevalence combinations reported in an article). In some cases there was more than one survey reported within an article; however, we did not account for this extra level of variation as it was unlikely to have much consequence on the overall estimates.

Heterogeneity in the meta-analysis estimates was assessed using I^2 , which measures the proportion of variation among surveys that is due to heterogeneity rather than random error (33). We categorized I^2 values into three descriptive categories to enable more intuitive interpretation of heterogeneity levels by end-users: $\leq 30\%$ was considered low; 31-60% medium; and $>60\%$ high (32). However, caution should be used in interpreting these categories as the cut-off percentages are subjective. When heterogeneity was high (i.e. $>60\%$), we also reported the median and range of the prevalence values within the data subset, as reporting meta-analytic average estimates alone can be misleading with so much variation (31). We reported meta-analysis estimates even when heterogeneity was high to allow a more complete assessment of prevalence trends across the LMF categories; however, in these cases, the specific estimates should be interpreted with caution.

Knowledge transfer

To facilitate the reporting, interpretation, and uptake of the results of this review for end-users, we presented results in the format of eight “summary cards” each corresponding to one of the LMF categories (52). The aim of the summary cards was to present the review results in a more intuitive and practical format to aid end-users in risk and decision analysis.

Each summary card provided a brief description of the LMF category, a summary of the well-researched areas and knowledge gaps (scoping review evidence charts), and detailed summaries of the evidence and results for each review question (burden of illness, prevalence, and interventions) supported by descriptive tables and figures.

Review management

All citations identified in the search were entered into RefWorks (Thomson ResearchSoft, Philadelphia, PA) and duplicates were removed using the automatic function and manually. Unique citations were imported into the web-based, systematic review software program DistillerSR (Evidence Partners, Ottawa, ON) for relevance screening and article characterization. Data extraction and descriptive analysis were conducted using Microsoft Excel. Meta-analysis was conducted using the Excel add-in MetaXL (EpiGear International Pty Ltd., Wilston, Australia). The forms used for relevance screening and confirmation were pre-tested by I.Y. and L.W. on a selection of 30 abstracts and six articles, respectively. Reviewing proceeded only when consistent inclusion and exclusion agreement was achieved between reviewers (kappa >0.8). Relevance screening was conducted by two independent reviewers (I.Y. and L.W.), and discrepancies or conflicts between reviewers were resolved by consensus. Relevance confirmation (I.Y.) and extraction (I.Y. and L.W.) were conducted by one reviewer. Copies of all forms used in this review are available in the full technical report (22).

Results

Knowledge synthesis evidence mapping

A flow chart of the knowledge synthesis and transfer process is shown in Figure 1 and scoping review evidence charts of the number of unique articles and outbreak/case reports summarized by review questions, LMF product categories, and microbial hazards investigated are shown in Figures 2 and 3. Overall, the most commonly investigated LMF category was cereals and grains (n=142), while the most commonly investigated LMF categories for each research question (burden of illness, prevalence, and interventions) were cereals and grains (n=72), spices/dried herbs/tea (n=77), and nuts and nut products (n=51), respectively (Figure 2). The most commonly investigated microbial hazard, overall and across each review question, was *Salmonella* spp. (Figure 3). LMF category-specific evidence charts and a citation list of all relevant articles identified in this review are available in the full technical report (22).

Burden of illness

Evidence charts included 214 unique outbreaks and case reports. The median year of occurrence was 2009 (range 1953-2013), indicating a steady increase in reported outbreaks implicating LMF products. Most identified outbreaks occurred in Europe (58%) and North America (28%). A descriptive summary of the overall proportion of burden of illness information stratified by LMF category is shown in Table 2, and the number and relative size of outbreaks in each LMF category by implicated microbial hazard is shown in Figure 4. *Salmonella* spp. was the most frequently implicated microbial hazard and had the potential to cause large, widespread outbreaks resulting in the highest proportion of reported

hospitalizations and deaths (Table 2 and Figure 4). *B. cereus* was mostly implicated in smaller outbreaks from rice and other cereal products (Table 2 and Figure 4). *S. aureus* caused some very large outbreaks due to contaminated powdered milk, thus overall a disproportionate number of cases is attributed to *S. aureus* (Table 2 and Figure 4). A more detailed summary of all outbreaks and case reports is presented in the full technical report (22).

Prevalence

Evidence charts included a total of 204 articles reporting on 2,064 unique prevalence surveys. The median publication year was 2009 (range 1990-2014). Most prevalence studies were conducted in Europe (32%) and Asia/the Middle East (32%). Most surveys (85%) sampled products at retail (e.g. grocery stores, markets) and at a single point in time (90%). Articles more frequently reported prevalence (presence/absence) than concentration (e.g. CFU/g) outcomes (97% vs. 39%). Only 5% (n=37/795) of surveys measuring concentration outcomes reported mean counts with an associated measure of variability and sample size, precluding possible meta-analysis of these outcomes. Meta-analysis results of the weighted average prevalence of selected microbial hazards across LMF categories is shown in Table 3. *Salmonella* spp. was consistently found at very low prevalence levels across each of the LMF categories, with average prevalence values ranging from 0 to 3% (Table 3). A forest plot of the meta-analysis prevalence estimates for *Salmonella* spp. is shown in Figure 5 to visually illustrate these results. *E. coli* O157, *L. monocytogenes*, and *S. aureus* were also found at fairly low average prevalence levels across most categories; however, these hazards were less frequently investigated than *Salmonella* spp. (Table 3). *B. cereus* and *Cronobacter* spp. were found at highly variable average and median prevalence levels and ranges across most categories (Table 3). *C. botulinum* and *C. perfringens* were infrequently investigated in most categories; with the former investigated most in honey and preserves (found at a low median prevalence of 2.9%) and the latter investigated most in spices/dried herbs/tea (found at heterogeneous and variable prevalence levels ranging from 0 to 50%). More detailed prevalence results conducted at the LMF sub-category level, including additional forest plots, are reported in the full technical report (22).

Interventions

Evidence charts included a total of 126 articles reporting on 609 unique intervention trials. The median publication year was 2008 (range 1968-2014). Most intervention studies were conducted in North America (57%) followed by Asia/the Middle East (24%). A summary of intervention types investigated to control microbial hazards in LMF is shown in Table 4. The majority of trials identified (78-100%) were challenge trials with artificially inoculated samples, compared to controlled trials (Table 4), 97% were conducted under laboratory conditions, and sample sizes were typically small (84% of trials contained <10 samples or didn't report a sample size). The most commonly investigated intervention type (n=143 trials) was chemical treatments (e.g. chemical sprays and dips), followed by heat treatments (116 trials) and modified storage conditions (114 trials). Interventions were most often investigated in the nuts and nut products category and against *Salmonella* spp. (Table 4). Most trials (92%) reported that the investigated interventions resulted in statistically significant reductions in microbial hazard contamination. More detailed tables of specific

interventions investigated in each LMF category and sub-category are reported in the full technical report (22).

Summary cards

A copy of all summary cards can be found in the full technical report (22). The summary cards were presented to members of the JEMRA FAO/WHO Working Group on Ranking of Microbiological Hazards Associated with LMF during a technical meeting in May, 2014, to inform expert discussions and deliberations about the relative differences in burden of illness, prevalence, and intervention data across LMF categories. In addition, quantitative data on the burden of illness from each microbial hazard and meta-analytic prevalence estimates were used as evidence-informed and transparent inputs in a complementary multi-criteria decision-analysis (MCDA) model.

Discussion

Review implications

The highest proportion of research identified in this review was conducted in the cereals and grains category. This is not surprising given that cereals and grains are the most widely traded and consumed LMF category globally, with an estimated US\$118.5 billion in export value in 2011 and an average of 185 g consumed per person per day (22). It also contained the highest proportion of outbreaks across LMF categories, which were mostly small and isolated *B. cereus* and *S. aureus* outbreaks due to consumer and food-handler mishandling (time-temperature abuse) of cooked rice and pasta dishes. Consumer mishandling was also frequently a cause of outbreaks in the dried protein products category due to *S. aureus* and *Salmonella* contamination of reconstituted milk. Across all LMF categories, many of the medium to large LMF outbreaks were due to contaminated ready-to-eat products where the contamination occurred after the final pathogen-reduction stage of processing. The risk of large national and international outbreaks is magnified in ready-to-eat LMF products due to their long shelf life and wide distribution. For example, breakfast cereals, rice cake snacks, paprika-flavoured potato chips, peanut-flavoured kosher snacks, chocolate, and peanut butter have all been implicated in large and widespread outbreaks for these reasons (9, 30, 35, 38, 44, 51, 59, 64, 70). Related to this, associated product recalls also had the potential to be large and affect many countries (63). The implementation, monitoring, and review of good production, manufacturing, and hygienic practices, including HACCP systems, are just as critical for LFM products as other foods. This may not preclude in some cases the need to implement additional verified interventions prior to retain distribution to ensure the safety of these products.

Many LMF outbreaks were caused by a contaminated product or other ingredient being added to a composite food after the final microbial reduction stage (e.g. after kill steps during processing or after cooking). This was particularly notable for outbreaks related to spices, including an outbreak of 1000 salmonellosis cases due to contamination of paprika seasoning on potato chips in Germany in 1993 (38), and two outbreaks related to contaminated pepper that was primarily used in the production of dried and fermented sausages (25). As many LMF products are typically ingredients in composite foods, it is

likely that the burden of illness attributable to LMF is under-represented in the literature even more so than higher-moisture foods (65). Increased awareness is needed among food chain stakeholders on the potential for LMF contamination of complex foods and appropriate control measures, and LMF ingredients should be considered as possible sources of contamination in future outbreak investigations and product recalls involving composite foods.

We identified several outbreaks of LMF products that are designed or targeted towards vulnerable population groups such as infants and toddlers (e.g. infant cereals, powdered milk, and many snacks) (39, 41, 50, 60). Outbreaks due to contaminated LMF intended for special supplementary diets for hospitalized patients have also occurred (37, 40). Food safety concerns relating to powdered formulae for infants and young children have already been developed at the international level (12). Given that LMF products often represent a large part of the diet of vulnerable and malnourished populations globally, who may be at higher risk of infection, there is a need for greater awareness of the risks associated with these products and the appropriate guidance and control measures required to mitigate these risks.

Prevalence data captured in this review provide a baseline for the likely frequency of contamination across various LMF categories. While the prevalence of *Salmonella* spp. and other major foodborne pathogens (e.g. *L. monocytogenes* and *E. coli* O157) was generally very low across categories, the presence of contamination and some variability in the results signals a possible risk to the consumer. In addition, exposure to even very low doses of some pathogens such as *Salmonella* can be sufficient to cause foodborne illness (61). The largest proportion of prevalence studies evaluated products in the spices/dried herbs/tea category, which is not surprising given that several high-profile outbreaks of contaminated spices and seasonings have occurred over the past 20 years resulting in increased government and industry attention to these products (65, 66, 67, 75). Many spices and seasonings undergo various treatments to reduce microbial contamination; however, it is not a requirement for exporting countries to indicate if a pathogen reduction intervention has been applied. Van Doren et al. (2013) analyzed spice shipments imported into the United States from 2007-2009 and found that spices labeled as “treated” had a lower *Salmonella* prevalence compared to spice shipments that were untreated or of unknown treatment status (3% compared to 6.8%), although the difference was not statistically significant (66). While additional treatments may help to reduce microbial contamination of spices and other LMF, multi-barrier prevention and control strategies are also needed to mitigate possible risks to consumers. For example, in a risk profile of pathogens and filth in spices, the United States Food and Drug Administration recommended a need for enhanced capacity development, communication, training, education, and regulatory and enforcement strategies involving all stakeholders in supply chain (65). These recommendations could apply similarly to other LMF categories summarized in this review.

Unfortunately, concentration data were sparsely reported in studies captured in this review. This is a concern particularly for toxin-producing microbial hazards such as *B. cereus*, *C. perfringens*, and *S. aureus*, which are usually only considered a threat to public health if bacterial concentrations are found at elevated levels in the final product (e.g. 10^5 - 10^8

CFU/g) (16, 55). Therefore, although the average prevalence of some of these hazards (e.g. *B. cereus*) was very high in several LMF categories, the proportion present at levels needed to cause human illness may have been much lower. In addition, the point of sampling, product characteristics, and intended use should also be taken into account when evaluating the presence and contamination of such hazards in LMF, as for example, even low contamination levels in products that are subsequently reconstituted or used as an ingredient in complex foods could still present a risk to consumers if proper storage and handling practices are not observed. More complete reporting of concentration data is encouraged for future studies in this area so that the results can better inform risk assessment and decision-making.

Intervention data captured in this review comprised mostly of laboratory-based challenge trial studies. These studies are important to establish conditions under which an intervention might be effective. However, they often contain design features that may not be reflective of commercial conditions, including artificial exposures of food products to microbial hazards (typically using high doses and laboratory-adapted strains) and small sample sizes (53, 71). For these reasons the quantifiable measures of intervention effect may be different, likely less effective, under commercial conditions compared to studies conducted under strict laboratory conditions. Given that many of the interventions identified in this review are already implemented on a commercial scale in certain LMF sectors (e.g. nuts and spices) (1, 65, 66), we encourage these industries to make any data on intervention effectiveness under commercial conditions more widely accessible and available to support future synthesis, risk assessment, and decision analysis efforts.

While most intervention studies identified in this review reported a significant intervention effect on microbial reductions, most did not report their outcome data in a sufficient format for possible meta-analysis (e.g. extractable mean counts with a measure of variability and sample size). These results correspond with those of Wisener et al. (2014), who found that challenge trials for pre-harvest food safety interventions tended to have reporting deficiencies for key methodological features and reported more favorable outcomes than controlled trials (71). Another limitation of the intervention research in this review is that, in many cases, the reported reductions in microbial hazard concentrations were only minimal (e.g. <1-5 log CFU/g) and did not decrease counts below an acceptable threshold. For some LMF products, intervention efficacies may be limited due to high protein, fat, and/or sugar content acting as a protective barrier (26, 36, 58). In addition, the doses and/or duration of treatments required to achieve suitable reductions in microbial hazard concentrations may negatively affect the sensory quality (e.g. taste and texture) and consumer acceptability of some LMF products (6, 43, 48, 62). While it is critical that research into the efficacy and commercial application of hazard reduction interventions continues, due to the current difficulties in reliably reducing levels of microbial hazards on LMF products without unduly affecting their quality, primary emphasis in the industry should be placed on minimizing contamination during pre-harvest and preventing contamination during harvest and processing operations.

Review strengths and limitations

A key strength of this review compared to previous reviews in this area is the use of a structured and transparent knowledge synthesis approach. These methods provide more credible and reliable data inputs and evidence to support risk ranking and decision-making on policy-relevant food safety issues (17, 49). In addition, the reproducible approach can be updated over time as new evidence and knowledge becomes available. Another strength of this review was the integrated knowledge transfer of the results through multiple evidence reporting formats, including innovative “summary cards”. Previous research has shown that science-to-policy professionals in the food safety sector desire more intuitive, practical, and tailored communication formats to enhance their interpretation and uptake of scientific evidence to inform policy- and decision-making (72, 74). The summary cards were useful to inform expert committee deliberations on the risk ranking process and to highlight and integrate key synthesis findings into the complementary MCDA model. The summary card format could be adapted and adopted in other food safety contexts to support risk and decision analysis, and warrants further application and evaluation.

We relied heavily on a database of international foodborne disease outbreaks maintained by the Public Health Agency of Canada to identify as many LMF outbreaks as possible (27). Access to this database provided added value to the review given that outbreak reports are often not indexed in bibliographic databases of peer-reviewed literature, including 56% of reports identified this project. However, many LMF products, especially those that are an ingredient in composite foods, are not traditionally considered as a possible vehicle for foodborne illness in outbreaks and sporadic case investigations. Thus, the burden of illness attributed to LMF products is likely significantly underestimated. Enhanced reporting and indexing of outbreak reports is warranted in the future to aid in determining a more accurate assessment of the burden of illness due to LMF.

While previous reviews of the microbial safety of LMF have also covered burden of illness, prevalence, and intervention topics (5, 7, 10, 11, 18, 20, 47, 57), none have provided the same breadth and depth of evidence compilation, synthesis, and presentation as covered and reported in this review. For example, the synthesis of burden of illness data from globally reported outbreaks and cases allows for an overall assessment of the relative burden of illness due to different microbial hazard-LMF category combinations. Similarly, the meta-analysis results provide an indication of the likely global distribution of microbial hazards in different LMF categories. These outcomes are of interest to risk assessors and managers, decision-makers, and future researchers in this area who need to understand the current state of knowledge about the microbial safety of LMF and where there are critical knowledge gaps that need to be addressed. We recommend more coordinated generation of future primary research in this sector and enhanced collaboration among science-to-policy stakeholders to ensure that key knowledge and reporting gaps are addressed, that research is targeted at priority areas from a policy perspective, and that findings will be relevant to key end-users.

A rapid review methodology was used to streamline the knowledge synthesis process to meet short timelines with limited human resources. Specifically, we streamlined the search (only two databases) and data extraction (one instead of two reviewers) phases of the review,

which may have resulted in missed articles and data extraction errors, respectively (8, 24, 28). In addition, the complexity and breadth of the topic may have resulted in missing key search terms that might have yielded additional relevant articles. We attempted to minimize these potential biases by employing a comprehensive search verification strategy and by pre-testing all extraction forms. Finally, we excluded a total of 60 potentially relevant articles prior to detailed data extraction that were published in languages other than English, French, and Spanish. The possible impact of excluding these articles on the results is not known.

Conclusion

Overall, this review provided a credible and robust assessment of global research about the microbial food safety of LMF to inform risk ranking, Codex guideline development, and future research opportunities. This compilation allows comparison of similarities and differences across broad LMF categories and readers may further evaluate categories in more detail in the full technical report (22). Burden of illness data highlight how contamination of LMF along the food chain can lead to occasional and sometimes large outbreaks of human illness. Prevalence data provide an understanding of the likely frequency of contamination detected in different LMF categories, and intervention data provide proof of concept for several broad categories of treatments that industry could use, or in some cases has already adopted, to control microbial contamination of LMF. The summary card format for presenting review results could be useful for future food safety policy issues to enhance evidence utility and uptake for risk and decision analysis. Future research should focus on addressing key knowledge gaps and improving outcome data reporting. Enhanced microbial food safety of LMF will require comprehensive and multi-faceted prevention, mitigation, and control efforts among all stakeholders across the farm-to-fork continuum.

Acknowledgements

We thank Laura Dysart for conducting a preliminary scoping review of the evidence and developing a technical protocol and preliminary report that formed the basis for this expanded review, and Judy Greig for providing a summary of international outbreaks from the Public Health Agency of Canada database. We also thank members of the FAO/WHO Working Group on Ranking of Microbiological Hazards Associated with LMF for their feedback on the preliminary results from this review, including Dr. Michael Batz, Dr. Gilberto Montibeller, Dr. Jeff Farber, Dr. Paul Cook, Mrs. Edyta Margas, Dr. Michelle Danyluk, Dr. Linda Harris, Dr. Jean-Louis Cordier, and Dr. Igimi Shizunobu. This review was supported in-kind by the Laboratory for Foodborne Zoonoses, Public Health Agency of Canada.

References

1. Almond Board of California. [Accessed 30 March 2015] Pasteurization. 2015. Available at: <http://www.almonds.com/processors/processing-safe-product#tc-pasteurization>
2. Arksey H, O'Malley L. Scoping studies: Towards a methodological framework. *Int J Soc Res Methodol*. 2005; 8:19–32.
3. Barendregt JJ, Doi SA, Lee YY, Norman RE, Vos T. Meta-analysis of prevalence. *J Epidemiol Community Health*. 2013; 67:974–978. [PubMed: 23963506]
4. Batz MB, Hoffmann S, Morris JG Jr. Ranking the disease burden of 14 pathogens in food sources in the United States using attribution data from outbreak investigations and expert elicitation. *J Food Prot*. 2012; 75:1278–1291. [PubMed: 22980012]
5. Beuchat L, Komitopoulou E, Betts R, Beckers H, Bourdichon F, Joosten H, Fanning S, Benno TK. Persistence and survival of pathogens in dry foods and dry food processing environments. *ILSI Eur*

- Rep Ser. 2011 [Accessed 30 March 2015] Doc. no. D/2011/10.996/29. Available at: <http://www.ilsa.org/Europe/Documents/Persistence%20and%20survival%20report.pdf>.
6. Beuchat LR, Mann DA. Inactivation of *Salmonella* on pecan nutmeats by hot air treatment and oil roasting. J Food Prot. 2011; 74:1441–1450. [PubMed: 21902912]
 7. Beuchat LR, Komitopoulou E, Beckers H, Betts RP, Bourdichon F, Fanning S, Joosten HM, Kuile BHT. Low-water activity foods: Increased concern as vehicles of foodborne pathogens. J Food Prot. 2013; 76:150–172. [PubMed: 23317872]
 8. Buscemi N, Hartling L, Vandermeer B, Tjosvold L, Klassen TP. Single data extraction generated more errors than double data extraction in systematic reviews. J Clin Epidemiol. 2006; 59:697–703. [PubMed: 16765272]
 9. Cavallaro E, Date K, Medus C, Meyer S, Miller B, Kim C, Nowicki S, Cosgrove S, Sweat D, Phan Q, Flint J, et al. *Salmonella* Typhimurium infections associated with peanut products. N Engl J Med. 2011; 365:601–610. [PubMed: 21848461]
 10. Chen YH, Scott VN, Freier TA, Kuehm J, Moorman M, Meyer J, Morille-Hinds T, Post L, Smoot L, Hood S, Shebuski J, et al. Control of *Salmonella* in low-moisture foods III: Process validation and environmental monitoring – part three of a three-part series. Food Prot Trends. 2009; 29:493–508.
 11. Chen YH, Scott VN, Freier TA, Kuehm J, Moorman M, Meyer J, Morille-Hinds T, Post L, Smoot L, Hood S, Shebuski J, et al. Control of *Salmonella* in low-moisture foods II: Hygiene practices to minimize *Salmonella* contamination and growth. Food Prot Trends. 2009; 29:435–445.
 12. Codex Alimentarius Commission. [Accessed 30 March 2015] Code of hygienic practice for powdered formulae for infants and young children. Doc. no. CAC/RCP 66. 2008. Available at: http://www.codexalimentarius.org/input/download/standards/11026/CXP_066e.pdf
 13. Codex Alimentarius Commission. Report of the 45th Session of the Codex Committee on Food Hygiene; Ha Noi, Viet Nam. 11–15 November 2013; 2014. Available at: http://www.codexalimentarius.org/download/report/805/REP14_FHe.pdf
 14. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986; 7:177–188. [PubMed: 3802833]
 15. Dey M, Mayo JA, Saville D, Wolyniak C, Klontz KC. Recalls of foods due to microbiological contamination classified by the U.S. Food and Drug Administration, fiscal years 2003 through 2011. J Food Prot. 2013; 76:932–938. [PubMed: 23726186]
 16. European Food Safety Authority. Opinion of the Scientific Panel on Biological Hazards on *Bacillus cereus* and other *Bacillus* spp in foodstuffs. EFSA J. 2005; 175:1–48.
 17. European Food Safety Authority. Application of systematic review methodology to food and feed safety assessments to support decision making. EFSA J. 2010; 8:1637.
 18. European Food Safety Authority. Scientific opinion on the risk posed by pathogens in food of non-animal origin. Part 1 (outbreak data analysis and risk ranking of food/pathogen combinations). EFSA J. 2013; 11:3025.
 19. Fazel S, Khosla V, Doll H, Geddes J. The prevalence of mental disorders among the homeless in Western countries: Systematic review and meta-regression analysis. PLoS Med. 2008; 5:1670–1681.
 20. Finn S, Condell O, McClure P, Amezcua A, Fanning S. Mechanisms of survival, responses and sources of *Salmonella* in low-moisture environments. Front Microbiol. 2013; 4:331. [PubMed: 24294212]
 21. Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO). [Accessed 30 March 2015] *Enterobacter sakazakii* and other microorganisms in powdered infant formula: Meeting report. Microbiological Risk Assessment Series No. 6. 2004. Available at: <ftp://ftp.fao.org/docrep/fao/007/y5502e/y5502e00.pdf>
 22. Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO). [Accessed 30 March 2015] Ranking of low moisture foods in support of microbiological risk management: Report of an FAO/WHO consultation process. 2014. Available at: <ftp://ftp.fao.org/codex/meetings/CCFH/CCFH46/LMF%20Part%201-3%2030Oct%202014.pdf>
 23. Freeman MF, Tukey JW. Transformations related to the angular and the square root. Ann Math Statist. 1950; 21:607–611.

24. Ganann R, Ciliska D, Thomas H. Expediting systematic reviews: Methods and implications of rapid reviews. *Implement Sci.* 2010; 5:56. [PubMed: 20642853]
25. Gieraltowski L, Julian E, Pringle J, Macdonald K, Quilliam D, Marsden-Haug N, Saathoff-Huber L, Von Stein D, Kissler B, Parish M, Elder D, et al. Nationwide outbreak of *Salmonella* Montevideo infections associated with contaminated imported black and red pepper: Warehouse membership cards provide critical clues to identify the source. *Epidemiol Infect.* 2013; 141:1244–1252. [PubMed: 23200262]
26. Grasso EM, Somerville JA, Balasubramaniam VM, Lee K. Minimal effects of high-pressure treatment on *Salmonella enterica* serovar Typhimurium inoculated into peanut butter and peanut products. *J Food Sci.* 2010; 75:E522–E526. [PubMed: 21535491]
27. Greig JD, Ravel A. Analysis of foodborne outbreak data reported internationally for source attribution. *Int J Food Microbiol.* 2009; 130:77–87. [PubMed: 19178974]
28. Grindlay DJC, Brennan ML, Dean RS. Searching the veterinary literature: A comparison of the coverage of veterinary journals by nine bibliographic databases. *J Vet Med Educ.* 2012; 39:404–412. [PubMed: 23187034]
29. Grocery Manufacturers Association. [Accessed 30 March 2015] Control of *Salmonella* in low-moisture foods. 2014. Available at: <http://www.gmaonline.org/downloads/technical-guidance-and-tools/SalmonellaControlGuidance.pdf>
30. Harker KS, Lane C, Gormley FJ, Adak GK. National outbreaks of *Salmonella* infection in the UK, 2000–2011. *Epidemiol Infect.* 2014; 142:601–607. [PubMed: 23721866]
31. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med.* 2002; 21:1539–1558. [PubMed: 12111919]
32. Higgins, JPT.; Green, S., editors. *Cochrane handbook for systematic reviews of interventions: Version 5.1.0.* The Cochrane Collaboration; 2011. Available at: <http://handbook.cochrane.org/> [Accessed 30 March 2015]
33. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ.* 2003; 327:557–560. [PubMed: 12958120]
34. Isaacs S, Aramini J, Ciebin B, Farrar JA, Ahmed R, Middleton D, Chandran AU, Harris LJ, Howes M, Chan E, Pichette AS, Enteritidis PT30 Outbreak Investigation Working Group. et al. An international outbreak of salmonellosis associated with raw almonds contaminated with a rare phage type of *Salmonella* Enteritidis. *J Food Prot.* 2005; 68:191–198. [PubMed: 15690826]
35. Killalea D, Ward LR, Roberts D, de Louvois J, Sufi F, Stuart JM, Wall PG, Susman M, Schwieger M, Sanderson PJ, Fisher IS, et al. International epidemiological and microbiological study of outbreak of *Salmonella* Agona infection from a ready to eat savoury snack—I: England and Wales and the United States. *BMJ.* 1996; 313:1105–1107. [PubMed: 8916693]
36. Krapf T, Gantenbein-Demarchi C. Thermal inactivation of *Salmonella* spp. during conching. *LWT - Food Sci Technol.* 2010; 43:720–723.
37. Kunz LJ, Ouchterlony OT. Salmonellosis originating in a hospital; a newly recognized source of infection. *N Engl J Med.* 1955; 253:761–763. [PubMed: 13266037]
38. Lehmacher A, Bockemuhl J, Aleksic S. Nationwide outbreak of human salmonellosis in Germany due to contaminated paprika and paprika-powdered potato chips. *Epidemiol Infect.* 1995; 115:501–511. [PubMed: 8557082]
39. Ling ML, Goh KT, Wang GC, Neo KS, Chua T. An outbreak of multidrug-resistant *Salmonella enterica* subsp. *enterica* serotype Typhimurium, DT104L linked to dried anchovy in Singapore. *Epidemiol Infect.* 2002; 128:1–5. [PubMed: 11895083]
40. McCall CE, Collins RN, Jones DB, Kaufmann AF, Brachman PS. An interstate outbreak of salmonellosis traced to a contaminated food supplement. *Am J Epidemiol.* 1966; 84:32–39. [PubMed: 5952710]
41. Miyakawa S, Takahashi K, Hattori M, Itoh K, Kurazono T, Amano F. Outbreak of *Salmonella* Oranienburg infection in Japan. *J Environ Biol.* 2006; 27:157–158. [PubMed: 16850895]
42. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, Atkins D, Barbour V, Barrowman N, Berlin JA, Clark J, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Med.* 2009; 6:e1000097. [PubMed: 19621072]

43. Mtenga AB, Kassim N, Shim W, Chung D. Efficiency of fractionated γ -irradiation doses to eliminate vegetative cells and spores of *Bacillus cereus* from raw rice. *Food Sci Biotechnol*. 2013; 22:577–584.
44. Nabae K, Takahashi M, Wakui T, Kamiya H, Nakashima K, Taniguchi K, Okabe N. A Shiga toxin-producing *Escherichia coli* O157 outbreak associated with consumption of rice cakes in 2011 in Japan. *Epidemiol Infect*. 2013; 141:1897–1904. [PubMed: 23127395]
45. Painter JA, Hoekstra RM, Ayers T, Tauxe RV, Braden CR, Angulo FJ, Griffin PM. Attribution of foodborne illnesses, hospitalizations, and deaths to food commodities by using outbreak data, United States, 1998–2008. *Emerg Infect Dis*. 2013; 19:407–415. [PubMed: 23622497]
46. Pan Z, Bingol G, Brandl MT, McHugh TH. Review of current technologies for reduction of *Salmonella* populations on almonds. *Food Bioprocess Technol*. 2012; 5:2046–2057.
47. Podolak R, Enache E, Stone W, Black DG, Elliott PH. Sources and risk factors for contamination, survival, persistence, and heat resistance of *Salmonella* in low-moisture foods. *J Food Prot*. 2010; 73:1919–1936. [PubMed: 21067682]
48. Prakash A, Lim FT, Duong C, Caporaso F, Foley D. The effects of ionizing irradiation on *Salmonella* inoculated on almonds and changes in sensory properties. *Radiat Phys Chem*. 2010; 79:502–506.
49. Raji A.; Young, I. [Accessed 30 March 2015] Knowledge synthesis, transfer and exchange in agri-food public health: A handbook for science-to-policy professionals. Available at: <https://atrium.lib.uoguelph.ca/xmlui/handle/10214/7293>
50. Rushdy AA, Stuart JM, Ward LR, Bruce J, Threlfall EJ, Punia P, Bailey JR. National outbreak of *Salmonella* Senftenberg associated with infant food. *Epidemiol Infect*. 1998; 120:125–128. [PubMed: 9593480]
51. Russo ET, Biggerstaff G, Hoekstra RM, Meyer S, Patel N, Miller B, Quick R, *Salmonella* Agona Outbreak Investigation Team. A recurrent, multistate outbreak of *Salmonella* serotype Agona infections associated with dry unsweetened cereal consumption, United States, 2008. *J Food Prot*. 2013; 76:227–230. [PubMed: 23433369]
52. Ruzante JM, Davidson VJ, Caswell J, Fazil A, Cranfield JAL, Henson SJ, Anders SM, Schmidt C, Farber JM. A multifactorial risk prioritization framework for foodborne pathogens. *Risk Anal*. 2010; 30:724–742. [PubMed: 19671103]
53. Sargeant JM, Kelton DF, O'Connor AM. Study designs and systematic reviews of interventions: Building evidence across study designs. *Zoonoses Public Health*. 2014; 61(Suppl 1):10–17. [PubMed: 24905992]
54. Sargeant JM, Torrence ME, Raji A, O'Connor AM, Williams J. Methodological quality assessment of review articles evaluating interventions to improve microbial food safety. *Foodborne Pathog Dis*. 2006; 3:447–456. [PubMed: 17199527]
55. Schelin J, Wallin-Carlquist N, Cohn MT, Lindqvist R, Barker GC, Radstrom P. The formation of *Staphylococcus aureus* enterotoxin in food environments and advances in risk assessment. *Virulence*. 2011; 2:580–592. [PubMed: 22030860]
56. Schmidt, SJ.; Fontana, AJ. Appendix E: Water activity values of select food ingredients and products. *Water Activity in Foods: Fundamentals and Applications*. Barbosa-Cánovas, GV., et al., editors. Blackwell Publishing Ltd; Oxford, UK: 2008. p. 407–420.
57. Scott VN, Chen YUH, Freier TA, Kuehm J, Moorman M, Meyer J, Morille-Hinds T, Post L, Smoot L, Hood S, Shebuski J, et al. Control of *Salmonella* in low-moisture foods I: Minimizing entry of *Salmonella* into a processing facility. *Food Prot Trends*. 2009; 29:342–353.
58. Shachar D, Yaron S. Heat tolerance of *Salmonella enterica* serovars Agona, Enteritidis, and Typhimurium in peanut butter. *J Food Prot*. 2006; 69:2687–2691. [PubMed: 17133812]
59. Sheth AN, Hoekstra M, Patel N, Ewald G, Lord C, Clarke C, Villamil E, Niksich K, Bopp C, Nguyen TA, Zink D, et al. A national outbreak of *Salmonella* serotype Tennessee infections from contaminated peanut butter: A new food vehicle for salmonellosis in the United States. *Clin Infect Dis*. 2011; 53:356–362. [PubMed: 21810748]
60. Sotir MJ, Ewald G, Kimura AC, Higa JJ, Sheth A, Troppy S, Meyer S, Hoekstra RM, Austin J, Archer J, Spayne M, et al. Outbreak of *Salmonella* Wandsworth and Typhimurium infections in

- infants and toddlers traced to a commercial vegetable-coated snack food. *Pediatr Infect Dis J*. 2009; 28:1041–1046. [PubMed: 19779390]
61. Teunis PF, Kasuga F, Fazil A, Ogden ID, Rotariu O, Strachan NJ. Dose-response modeling of *Salmonella* using outbreak data. *Int J Food Microbiol*. 2010; 144:243–249. [PubMed: 21036411]
 62. Torlak E, Sert D, Serin P. Fate of *Salmonella* during sesame seeds roasting and storage of tahini. *Int J Food Microbiol*. 2013; 163:214–217. [PubMed: 23562834]
 63. Unicomb LE, Simmons G, Merritt T, Gregory J, Nicol C, Jelfs P, Kirk M, Tan A, Thomson R, Adamopoulos J, Little CL, et al. Sesame seed products contaminated with *Salmonella*: Three outbreaks associated with tahini. *Epidemiol Infect*. 2005; 133:1065–1072. [PubMed: 16274503]
 64. United States Centers for Disease Control and Prevention. Multistate outbreak of *Salmonella* serotype Agona infections linked to toasted oats cereal—United States, April–May, 1998. *Morb Mortal Wkly Rep*. 1998; 47:462–464.
 65. United States Food and Drug Administration. [Accessed 30 March 2015] Draft risk profile: Pathogens and filth in spices. 2014. Available at: <http://www.fda.gov/downloads/Food/FoodScienceResearch/RiskSafetyAssessment/UCM367337.pdf>
 66. Van Doren JM, Kleinmeier D, Hammack TS, Westerman A. Prevalence, serotype diversity, and antimicrobial resistance of *Salmonella* in imported shipments of spice offered for entry to the United States, FY2007–FY2009. *Food Microbiol*. 2013; 34:239–251. [PubMed: 23541190]
 67. Van Doren JM, Neil KP, Parish M, Gieraltowski L, Gould LH, Gombas KL. Foodborne illness outbreaks from microbial contaminants in spices, 1973–2010. *Food Microbiol*. 2013; 36:456–464. [PubMed: 24010629]
 68. Vij V, Ailes E, Wolyniak C, Angulo FJ, Klontz KC. Recalls of spices due to bacterial contamination monitored by the U.S. Food and Drug Administration: The predominance of salmonellae. *J Food Prot*. 2006; 69:233–237. [PubMed: 16416926]
 69. Waddell L, Raji A, Sargeant J, Parker S, Deckert A, McEwen S. The methodological soundness of literature reviews addressing three potential zoonotic public health issues. *Zoonoses Public Health*. 2009; 56:477–489. [PubMed: 19175572]
 70. Werber D, Dreesman J, Feil F, van Treeck U, Fell G, Ethelberg S, Hauri AM, Roggentin P, Prager R, Fisher IS, Behnke SC, et al. International outbreak of *Salmonella* Oranienburg due to German chocolate. *BMC Infect Dis*. 2005; 5:7. [PubMed: 15691371]
 71. Wisener LV, Sargeant JM, O'Connor AM, Faires MC, Glass-Kaasra SK. The evidentiary value of challenge trials for three pre-harvest food safety topics: A systematic assessment. *Zoonoses Public Health*. 2014; 61:449–476. [PubMed: 24219101]
 72. Young I, Kerr A, Waddell L, Pham MT, Greig J, Raji A, McEwen SA. A guide for developing plain-language and contextual summaries of systematic reviews in agri-food public health. *Foodborne Pathog Dis*. 2014; 11:930–937. [PubMed: 25383916]
 73. Young I, Waddell L, Sanchez J, Wilhelm B, McEwen SA, Raji A. The application of knowledge synthesis methods in agri-food public health: Recent advancements, challenges and opportunities. *Prev Vet Med*. 2014; 113:339–355. [PubMed: 24485274]
 74. Young I, Gropp K, Pintar K, Waddell L, Marshall B, Thomas K, McEwen SA, Raji A. Experiences and attitudes towards evidence-informed policy-making among research and policy stakeholders in the Canadian agri-food public health sector. *Zoonoses Public Health*. 2014; 61:581–589. [PubMed: 24528517]
 75. Zweifel C, Stephan R. Spices and herbs as source of *Salmonella*-related foodborne diseases. *Food Res Int*. 2012; 45:765–769.

Figure 1.

Flow chart of rapid knowledge synthesis and transfer process. Modified from PRISMA guidelines (42). NOTE: Some articles (n=8) contained data in more than one of the three evidence mapping categories (burden of illness, prevalence, and interventions). In addition, individual outbreak reports were sometimes reported in more than one article, so the total number of unique articles and outbreak reports was 536.

Figure 2.

Evidence chart of the number of research articles and unique outbreak and case reports investigating the burden of illness, interventions, and prevalence of microbial hazards in LMF, stratified by LMF category. Bubble size is proportional to the total number of articles and reports.

Figure 3.

Evidence chart of the number of research articles and unique outbreak and case reports investigating the burden of illness, interventions, and prevalence of microbial hazards in LMF, stratified by microbial hazards investigated. Bubble size is proportional to the total number of articles and reports.

Figure 4.

The number of outbreaks and case reports in each LMF category stratified by number of cases (<5, 5-49, 50-500, >500) and microbial hazard.

Figure 5.

Forest plot of the meta-analytic prevalence of *Salmonella* spp. across LMF categories.

CI = confidence interval; Med. = medium; No. obs. = number of total samples tested per category; Heter.=heterogeneity rating (see Table 3); Select. bias=selection bias rating (see Table 3). Prevalence estimates are from random-effects meta-analysis using a double arcsine transformation. Median and range prevalence values are only shown for categories where heterogeneity was high (i.e. $I^2 > 60\%$).

Table 1

LMF categories and examples of included food products.

LMF categories / sub-categories ^a	Examples of included food products
Cereals and grains	
<i>Whole grains</i>	Wheat, barley, maize/corn, oats, rye, millet, sorghum, buckwheat
<i>Rice/ rice products</i>	Rice, rice noodles
<i>Milled grains</i>	Milled grain products (e.g. flours, starches)
<i>Other dry cereals and cereal products</i>	Breakfast cereals, cereal and baking mixes, unspecified/mixed cereals
Confections and snacks	
<i>Cocoa/chocolate products</i>	Dried cocoa beans, cocoa powder, chocolate, cocoa and chocolate-based products (e.g. hot chocolate mix)
<i>Other/unspecified confections</i>	Fondants/creams, marshmallows, caramels/toffees, candies, chewing gum, other/unspecified confections and sweets
<i>Snacks</i>	Savoury snacks (e.g. chips, crackers, biscuits)
<i>Yeast</i>	Yeast extract (as additive or flavouring)
Dried fruits and vegetables	
<i>Dried fruits</i>	Raisins, prunes, dates, dried mangos, dried apricots, desiccated coconut, fruit powders
<i>Dried vegetables</i>	Dried vegetables (e.g. tomatoes), vegetable powders and mixes (e.g. dry soup mixes), dehydrated vegetables (e.g. potato flakes, carrot slices), vegetable flours (e.g. potato starch), dried legumes
<i>Dried mushrooms</i>	Dried/dehydrated mushrooms
<i>Dried seaweed</i>	Dried seaweed
Dried protein products	
<i>Dried dairy products</i>	Milk/whey powders, other dairy powders (e.g. cheese), milk-based powders and mixes
<i>Dried egg products</i>	Egg powders
<i>Dried fish/seafood products</i>	Dried fish and seafood, fish flour/meal
<i>Dried meats other than sausages/salamis/ jerky</i>	Meat powders, gelatin
Honey and preserves	
<i>Honey</i>	Honey
<i>Preserves</i>	Jams, syrups (e.g. corn syrup)
Nuts and nut products	
<i>Almonds</i>	Almonds
<i>Other tree nuts</i>	Brazil nuts, cashews, hazelnuts/filberts, macadamia nuts, pecans, pine nuts, pistachios, and walnuts
<i>Peanuts/peanut products</i>	Peanuts, peanut butter, peanut spreads
<i>Mixed/unspecified nuts</i>	Mixed/unspecified nuts
Seeds for consumption	
<i>Sesame seeds</i>	Sesame seeds
<i>Tahini</i>	Tahini (sesame seed paste)
<i>Halva/helva</i>	Halva/helva (confection made from sesame paste/tahini)
<i>Other and unspecified seeds</i>	Pumpkin seeds, sunflower seeds, poppy seeds, melon seeds, flax seeds, mixed/unspecified seeds for consumption (does not include sprouted seeds)
Spices, dried herbs, and tea	

LMF categories / sub-categories ^a	Examples of included food products
<i>Spices- fruit/seed-based</i>	<i>Capsicum</i> spp. (paprika, cayenne pepper, chili peppers, other hot and sweet dried capsicum peppers), <i>Piper</i> spp. (black, white, green, long pepper), Apiaceae (aniseed, caraway, celery, coriander, dill seed, fennel, chervil, cumin), allspice, nutmeg/mace, other (e.g. cardamom, fengreek, mustard, sumac)
<i>Spices- root-based</i>	Garlic, ginger, turmeric, other (e.g. galangal, onion, asafoetida)
<i>Spices- herb/leaf-based</i>	<i>Origanum</i> spp. (e.g. oregano, marjoram), basil, bay leaf, other (e.g. mint, rosemary, parsley, sage, thyme, dill weed/leaves)
<i>Spices- bark/flower-based</i>	Cinnamon, cloves, saffron, other (e.g. geranium, safflower)
<i>Spices- mixed/unspecified</i>	Curry powder, Indian spices (e.g. garam masala, tandoori), herb mixes (e.g. Herbs de province, other/unspecified), other mixed/unspecified spices
<i>Tea</i>	Herbal (e.g. chamomile, spearmint, peppermint, linden flower, hibiscus), other/unspecified (e.g. black, green, rooibos)

^aNote that data were extracted to the LMF sub-category level; however, for ease of interpretation and brevity purposes, only data at the overall category level is reported in this article. For results presented at the sub-category level, please refer to the full technical report (22).

Table 2

Summary of the burden of illness due to LMF products that were the source of reported outbreaks and case reports attributed to selected microbial hazards.

Microbial hazard ^a / LMF category ^b	% (count) ^c			
	Outbreaks / case reports	Cases	Hospitalizations	Deaths
<i>B. cereus</i>	25.7 (55)	3.7 (1,057)	1.4 (14)	0 (0)
Cereals and grains	20.6 (44)	2.2 (614)	1.4 (14)	0 (0)
Confections and snacks	0.5 (1)	0.0 (4)	0 (0)	0 (0)
Spices/dried herbs/tea	4.7 (10)	1.5 (439)	0 (0)	0 (0)
<i>C. botulinum</i>	15.0 (32)	0.3 (84)	6.0 (61)	21.1 (4)
Dried protein products	1.9 (4)	0.1 (16)	1.4 (14)	5.3 (1)
Honey/preserves	11.7 (25)	0.1 (39)	0.1 (39)	5.3 (1)
Nuts and nut products	0.9 (2)	0.1 (28)	0.8 (8)	10.5 (2)
Spices/dried herbs/tea	0.5 (1)	0.0 (1)	0 (0)	0 (0)
<i>C. perfringens</i>	4.7 (10)	1.5 (432)	0 (0)	0 (0)
Cereals and grains	2.3 (5)	1.3 (369)	0 (0)	0 (0)
Spices/dried herbs/tea	2.3 (5)	0.2 (63)	0 (0)	0 (0)
Pathogenic <i>E. coli</i>	2.3 (5)	1.2 (354)	3.3 (33)	5.3 (1)
Cereals and grains	0.9 (2)	1.1 (313)	0.7 (7)	0 (0)
Confections and snacks	0.5 (1)	0.0 (11)	0.4 (4)	0 (0)
Nuts and nut products	0.9 (2)	0.1 (30)	2.2 (22)	5.3 (1)
<i>S. aureus</i>	7.5 (16)	49.2 (14,006)	0.7 (7)	0 (0)
Cereals and grains	5.1 (11)	0.6 (172)	0.2 (2)	0 (0)
Confections and snacks	0.5 (1)	0.0 (5)	0 (0)	0 (0)
Dried protein products	1.4 (3)	47.8 (13,606)	0 (0)	0 (0)
Honey/preserves	0.5 (1)	0.8 (223)	0.5 (5)	0 (0)
<i>Salmonella</i> spp.	44.9 (96)	44.0 (12,515)	88.6 (895)	73.7 (14)
Cereals and grains	4.7 (10)	1.3 (367)	7.4 (75)	0 (0)
Confections and snacks	19.2 (41)	8.9 (2527)	14.6 (147)	0 (0)
Dried fruits/vegetables	1.4 (3)	2.5 (719)	24.5 (247)	5.3 (1)
Dried protein products	2.8 (6)	16.2 (4,618)	0 (0)	0 (0)
Nuts and nut products	7.5 (16)	7.7 (2,183)	28.5 (288)	52.6 (10)
Seeds for consumption	3.7 (8)	1.3 (376)	0.4 (4)	5.3 (1)
Spices/dried herbs/tea	5.6 (12)	6.1 (1,725)	13.3 (134)	10.5 (2)

^aNo outbreaks of LMF products were identified implicating *L. monocytogenes*, *Cronobacter* spp., and Enterobacteriaceae.

^bNot all LMF categories are shown for all microbial hazards; in these cases, no outbreaks or case reports were identified for that microbial hazard in that food category. The totals across categories within a microbial hazard sum to the total for that microbial hazard.

^cPercentages relate to the total number of outbreaks, cases, hospitalizations and deaths across all microbial hazards and LMF categories.

Table 3

Summary of the prevalence of selected microbial hazards in LMF categories. The overall robustness of the meta-analysis prevalence estimates can be inferred from the heterogeneity and selection bias ratings. Taking into consideration the number of studies in the meta-analysis, high confidence in the meta-analysis results can be inferred when heterogeneity is low and the risk of selection bias is low, and low confidence can be inferred when both are high.

Micobial hazard / LMF category ^a	Average prevalence (95% CI) ^b	Median (range) ^c	No. obs./ surveys/studies	Heterogeneity ^d	Selection bias ^e
<i>B. cereus</i>					
Cereals and grains	38.5 (27.3 – 50.5)	32.8 (0 – 100)	2818/68/29	High	High
Confections and snacks	19.0 (8.6 – 32.2)	9 (0 – 100)	748/10/7	High	Med.
Dried fruits/vegetables	76.3 (19.0 – 100)	98 (0.4 – 100)	786/8/6	High	High
Dried protein products	31.5 (14.2 – 51.7)	38.9 (0 – 60)	732/8/8	High	Med.
Honey/preserves	38.9 (24.1 – 54.7)	33.2 (22.9 – 77.8)	698/6/6	High	High
Nuts and nut products	7.3 (3.1 – 12.9)	-	108/12/4	Low	High
Seeds for consumption	6.7 (0.5 – 17.6)	-	34/7/3	Low	High
Spices/dried herbs/tea	24.5 (20.1 – 29.2)	10.1 (0 – 100)	5973/143/24	High	Low
<i>C. botulinum</i>					
Cereals and grains	0.0	-	25/1/1	-	High
Confections and snacks	7.6 (1.1 – 18.1)	-	103/5/1	Med.	High
Dried fruits/vegetables	0.0	-	48/1/1	-	High
Dried protein products	11.5	-	26/1/1	-	High
Honey/preserves	4.2 (2.0 – 7.1)	2.9 (0 – 23.9)	2938/24/21	High	Med.
Spices/dried herbs/tea	4.5 (0.1 – 12.9)	0.05 (0 – 26.1)	488/4/4	High	High
<i>C. perfringens</i>					
Cereals and grains	4.5 (1.2 – 9.6)	-	279/9/7	Med.	High
Confections and snacks	0.0	-	700/5/1	Low	Low
Dried fruits/vegetables	0.0	-	1/1/1	-	High
Dried protein products	0.0	-	100/1/1	-	Low
Honey/preserves	2.9 (0 – 10.6)	3.0 (0 – 6.0)	166/2/2	High	Med.
Nuts and nut products	0.0	-	4/2/1	-	High
Seeds for consumption	0.0	-	6/1/1	-	Low
Spices/dried herbs/tea	11.4 (8.3 – 14.9)	0 (0 – 50)	4630/90/11	High	Low
<i>Cronobacter spp.</i>					
Cereals and grains	8.0 (3.2 – 14.5)	0 (0 – 45)	959/20/12	High	High
Confections and snacks	8.5 (2.6 – 17.1)	0 (0 – 100)	203/11/7	High	High
Dried fruits/vegetables	11.1 (2.0 – 25.1)	0.1 (0 – 60)	124/7/4	High	Med.
Dried protein products	4.6 (3.1 – 6.4)	-	2722/30/18	Med.	High
Honey/preserves	0.0	-	30/1/1	-	High
Nuts and nut products	0.0	-	2/1/1	-	Low
Seeds for consumption	38.6 (7.5 – 75.1)	45.5 (9.1 – 66.7)	34/3/1	High	High
Spices/dried herbs/tea	25.6 (18.0 – 34.1)	23.1 (0 – 100)	570/67/15	High	High

Micobial hazard / LMF category ^a	Average prevalence (95% CI) ^b	Median (range) ^c	No. obs./ surveys/studies	Heterogeneity ^d	Selection bias ^e
Generic <i>E. coli</i>					
Cereals and grains	15.5 (6.0 – 28.1)	8.9 (0 – 100)	4520/19/12	High	Med.
Confections and snacks	2.5 (0.1 – 7.2)	0 (0 – 42.3)	960/9/5	High	Low
Dried fruits/vegetables	0.2 (0 – 0.9)	-	838/9/5	Low	High
Dried protein products	1.5 (0 – 4.3)	-	108/2/2	Low	Med.
Honey/preserves	0.0	-	71/2/2	Low	High
Nuts and nut products	0.8 (0.3 – 1.4)	0 (0 – 4.8)	7823/36/7	High	Low
Seeds for consumption	9.1 (8.2 – 10.0)	-	3741/3/3	Low	Low
Spices/dried herbs/tea	11.1 (8.4 – 14.1)	0 (0 – 70.6)	4412/112/18	High	Med.
<i>E. coli</i> O157					
Cereals and grains	6.4 (0 – 18.3)	0 (0 – 26.7)	133/7/3	High	High
Confections and snacks	0.0	-	752/8/3	Low	Low
Dried protein products	0.0	-	100/1/1	-	Low
Honey/preserves	0.0	-	30/1/1	-	High
Nuts and nut products	0.0 (0 – 0.1)	-	10266/12/3	Low	High
Seeds for consumption	0.0	-	66/4/1	Low	High
Spices/dried herbs/tea	0.0	-	285/20/4	Low	High
<i>L. monocytogenes</i>					
Cereals and grains	2.2 (0 – 6.8)	0.5 (0 – 18.5)	410/5/5	High	High
Confections and snacks	0.8 (0.3 – 1.7)	-	1951/16/7	Med.	Low
Dried fruits/vegetables	0.0	-	555/1/1	-	Low
Dried protein products	0.7 (0 – 2.1)	-	200/2/2	Low	Low
Honey/preserves	0.0	-	30/1/1	-	High
Nuts and nut products	0.9 (0 – 2.9)	-	585/13/2	Med.	Med.
Seeds for consumption	0.0	-	15/3/1	Low	High
Spices/dried herbs/tea	0.0	-	432/62/6	Low	High
<i>S. aureus</i>					
Cereals and grains	4.0 (0.9 – 9.0)	3.1 (0 – 11.5)	500/8/7	High	High
Confections and snacks	0.5 (0 – 1.9)	0 (0 – 75)	714/7/3	High	Low
Dried fruits/vegetables	1.7 (0 – 6.1)	0 (0 – 25)	782/4/4	High	High
Dried protein products	0.0	-	100/1/1	-	Low
Honey/preserves	0.0	-	30/1/1	-	High
Nuts and nut products	0.0	-	63/8/4	Low	High
Seeds for consumption	0.0	-	75/3/3	Low	Med.
Spices/dried herbs/tea	4.6 (3.7 – 5.6)	-	1729/160/15	Low	Low
<i>Salmonella</i> spp.					
Cereals and grains	0.7 (0.3 – 1.4)	0 (0 – 46.2)	11443/29/14	High	Med.
Confections and snacks	0.6 (0.1 – 1.4)	-	870/12/7	Low	Med.
Dried fruits/vegetables	2.0 (0.2 – 5.2)	0 (0 – 33.3)	1150/14/10	High	Med.
Dried protein products	0.0 (0 – 0.1)	-	5175/15/9	Low	Low
Honey/preserves	0.0	-	604/9/9	Low	High

Micobial hazard / LMF category^a	Average prevalence (95% CI)^b	Median (range)^c	No. obs./ surveys/studies	Heterogeneity^d	Selection bias^e
Nuts and nut products	0.6 (0.4 – 0.9)	0 (0 – 66.7)	29226/60/15	High	Low
Seeds for consumption	1.9 (0.8 – 3.3)	0.1 (0 – 16.7)	4571/22/11	High	Low
Spices/dried herbs/tea	3.0 (2.6 – 3.4)	-	22461/319/34	Low	Med.

CI = confidence interval; Med. = medium; No. obs. = number of total samples tested per category.

^aNot all LMF categories are shown for all microbial hazards; in these cases, no studies were identified that investigated the prevalence of the microbial hazard in that food category.

^bEstimates from random-effects meta-analysis using a double arcsine transformation.

^cValues in this column only calculated if heterogeneity was high (i.e. $I^2 > 60\%$).

^dHeterogeneity rating definitions: low = I^2 0-30%; medium = 31-60%; high = $>60\%$.

^eSelection bias definitions: high = 0-30% of surveys used a representative sample; medium = 31-60% of surveys used a representative sample; low = $>60\%$ of surveys used a representative sample. Studies that conducted random or systematic sampling were considered representative.

Table 4
Summary of interventions investigated to control selected microbial hazards in LMF products.

Intervention type	LMF categories investigated (no. trials/ studies) ^a	Microbial hazards investigated (no. trials/ studies) ^a	Total no. trials/ studies	% challenge trials ^b	% of trials with extractable data	% of trials finding statistically significant reduction
Chemical treatments	Nuts and nut products (70/10)	<i>Salmonella</i> spp. (99/18)	143/26	90	22	91
	Cereals and grains (23/2)	<i>B. cereus</i> (27/4)				
	Dried protein products (18/3)	Generic <i>E. coli</i> (6/4)				
	Spices/dried herbs/tea (17/4)	Pathogenic <i>E. coli</i> (6/3)				
Drying	Dried fruits/vegetables (15/7)	<i>C. perfringens</i> (4/2)	36/10	100	22	97
		Enterobacteriaceae (1/1)				
	Nuts and nut products (17/4)	<i>Salmonella</i> spp. (22/9)				
	Dried protein products (12/2)	Pathogenic <i>E. coli</i> (6/4)				
Heat treatments	Dried fruits/vegetables (3/1)	<i>L. monocytogenes</i> (5/3)	116/45	96	46	88
	Confections and snacks (2/2)	<i>Cronobacter</i> spp. (2/1)				
	Spices/dried herbs/tea (2/1)					
	Nuts and nut products (53/18)	<i>Salmonella</i> spp. (98/38)				
Irradiation	Confections and snacks (21/8)	<i>Cronobacter</i> spp. (8/3)	73/25	78	60	92
	Cereals and grains (13/4)	Pathogenic <i>E. coli</i> (5/2)				
	Dried protein products (11/5)	<i>B. cereus</i> (3/2)				
	Dried fruits/vegetables (9/5)	Generic <i>E. coli</i> (2/1)				
Modified storage conditions	Spices/dried herbs/tea (8/4)		114/32	98	16	95
	Seeds for consumption (1/1)					
	Spices/dried herbs/tea (28/9)	<i>Salmonella</i> spp. (33/14)				
	Nuts and nut products (23/8)	Generic <i>E. coli</i> (10/5)				
Multiple/ combined interventions	Cereals and grains (9/3)	Pathogenic <i>E. coli</i> (9/4)	58/14	95	33	100
	Dried fruits/vegetables (9/1)	<i>B. cereus</i> (9/1)				
	Confections and snacks (3/3)	Enterobacteriaceae (5/5)				
	Honey/preserves (1/1)	<i>C. perfringens</i> (3/2)				
Ozone treatments		<i>S. aureus</i> (3/1)	15/7	93	7	93
		<i>C. botulinum</i> (1/1)				
	Nuts and nut products (35/13)	<i>Salmonella</i> spp. (56/20)				
	Confections and snacks (21/3)	Pathogenic <i>E. coli</i> (26/9)				
	Dried protein products (18/8)	<i>S. aureus</i> (16/2)	58/14	95	33	100
	Cereals and grains (16/4)	<i>B. cereus</i> (6/1)				
	Dried fruits/vegetables (13/3)	<i>Cronobacter</i> spp. (6/1)				
	Seeds for consumption (7/4)	Generic <i>E. coli</i> (2/2)				
	Spices/dried herbs/tea (4/2)	Enterobacteriaceae (2/1)	58/14	95	33	100
		<i>L. monocytogenes</i> (2/1)				
	Nuts and nut products (30/10)	<i>Salmonella</i> spp. (30/10)				
	Cereals and grains (21/2)	<i>B. cereus</i> (22/3)				
	Spices/dried herbs/tea (4/2)	<i>Cronobacter</i> spp. (3/1)	15/7	93	7	93
	Dried fruits/vegetables (2/1)	Generic <i>E. coli</i> (3/1)				
	Dried protein products (1/1)					
	Nuts and nut products (7/2)	<i>B. cereus</i> (6/3)				
	Dried fruits/vegetables (3/1)	Generic <i>E. coli</i> (5/3)	15/7	93	7	93

Intervention type	LMF categories investigated (no. trials/ studies) ^a	Microbial hazards investigated (no. trials/ studies) ^a	Total no. trials/ studies	% challenge trials ^b	% of trials with extractable data	% of trials finding statistically significant reduction
Other ^c	Spices/dried herbs/tea (2/2) Dried protein products (2/1) Cereals and grains (1/1) Nuts and nut products (30/8) Cereals and grains (21/2) Confections and snacks (2/2) Spices/dried herbs/tea (1/1)	<i>Salmonella</i> spp. (2/2) <i>Cronobacter</i> spp. (2/1) <i>Salmonella</i> spp. (26/9) <i>B. cereus</i> (20/1) Generic <i>E. coli</i> (4/2) Pathogenic <i>E. coli</i> (3/1)	54/13	96 ^d	4	85

^aSome studies investigated more than one LMF category/microbial hazard.

^bRefers to the percentage of trials that were challenge trial studies vs. controlled trials.

^cOther includes electrolyzed water (n=20 trials), high-hydrostatic pressure (n=12), non-thermal/cold plasma (n=9), nut extracts (n=8), fermentation (n=2), mincing (n=1), and vacuum atmospheric pressure (n=1).

^dOne of the non-challenge trials was a quasi-experiment (before-after study); others were all controlled trials.