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Literature Review

An updated review of published human health risk-benefit assessment studies in the scientific literature

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Abstract

Background: Public health policies in the area of food and diets tend to separate recommendations on food safety and nutrition. However, food products can simultaneously have risks and benefits. Risk-benefit assessment (RBA) seeks to integrate the assessment of both risks and benefits to aid complex decision-making using a multidisciplinary approach. In this study, a systematic literature review of recent RBA studies was performed, focusing on food consumption and human health following earlier reviews by Boué, et al. (2015) and Thomsen, et al. (2021).

Results: A total of 50 new RBA studies were reviewed since 20 May 2014. Our current literature review shows that the majority of RBA studies conducted in recent years remain focused on seafood, with studies on fish alone comprising 34% of all studies; the focus being on the benefits of fish consumption versus contaminant exposure. Most of the studies have been conducted in Europe (n = 31) and Asia (n = 11).

Conclusion: RBA has the potential to be applied more widely to other food choices such as alternative proteins, yet application remains limited to specific applications and contaminant/nutrient case studies. In recent years, a few RBA studies have been reported on less mainstream food sources and one specifically on novel foods. Novel foods offer a unique application space for RBA as their development is focused heavily on the benefits to the consumer, society, and environment, yet there remains uncertainty as to their safety.

More Information

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Introduction

Public health policies in the area of food and diets typically separate recommendations on food safety and nutrition. Food safety risks, such as the presence of chemical and microbiological hazards, are looked at with an emphasis to eliminate and/or control them to levels of no toxicological concern or harm. Whereas for nutrients, attention is given to understanding the required levels for optimal health. For consumers, however, the risks and benefits of eating foods are not distinct and more often than not there is a choice to be made whether to consume or not. Such decisions can be challenging, especially when the broader impact of food outside of just human health and sustenance is considered. With increasing pressures on global food security and sustainability, it is clear that the choices around food have wider impacts on a person's lifestyle and the environment.

In most cases, risk assessment approaches use conservative, worst-case scenarios in order to limit any chance of risk. This is understandable. However, driving towards zero risk is a challenge, considering that the exposure to individual food products, added ingredients, and unintentionally added contaminants is a factor of our total diet and where it is sourced, not any one product or ingredient. Furthermore, when the population diet is considered, it is also necessary to consider how specific risks are accepted by the population as a whole and how the management of them can influence other risks as well as benefits across the entire food supply. Products can simultaneously have risks and benefits, and

mitigation strategies for single hazards can lead to confusing dietary recommendations [1-3].

Risk-Benefit Assessment (RBA) seeks to integrate the assessment of both risks and benefits and aid complex decision-making using a multidisciplinary approach [4]. RBA has been performed worldwide on health risks and benefits of consumption of various foods [1], with the World Health Organization (WHO) and Food and Agriculture (FAO) applying multi-criteria decision analysis to address food safety issues in pilot studies conducted in Thailand and Uganda [5,6]. There have also been several research endeavors focusing on RBA [7-10].

Despite the growing interest in RBA approaches, the uptake and application of RBA methodologies by regulatory authorities, however, has been limited. To date, the European Food Safety Authority (EFSA) is the only regulatory authority to publish a guide on how to perform human health risk-benefit assessment of foods [11,12], along with a recently published case study expanding on the application of RBA for assessing novel foods [13].

In this study, a systematic literature review of recent RBA studies was performed, focusing on food consumption and human health. The objective of this paper is to review the state of the literature around human health risk-benefit assessments related to foods and promote further discussion on the application of RBA approaches to the assessment of new and novel foods entering the market. It takes the form of earlier reviews by Boué, et al. [1] and Thomsen, et al. [14] and provides consolidated results on new studies published since 2014, as well as the directions and challenges that remain in the field. Specifically, attention is drawn to the application of RBA approaches in supporting the acceptance of novel foods. Further, the geographical focus of recent RBA studies is examined, as most studies have historically been conducted in Europe where the discussion around RBA approaches is the strongest.

Methods

A systematic review of the literature was undertaken following PRISMA guidelines proposed by Moher, et al. [15] with search criteria adapted from Boué, et al. [1]. The search strings were designed to cover articles on risk-benefit assessment related to food consumption, particularly within the fields of public health, nutrition, chemistry, and microbiology. Only studies written in English that characterized human health risks and benefits related to food consumption were included in this review (Figure 1).

Databases searched included MEDLINE (National Library of Medicine of the United States), ScienceDirect™ (Elsevier Science), SciFinder® (Chemical Abstracts Service), Scopus™ (Elsevier Co.), and Web of Science® (Thomson Reuters) as well as Google Scholar. Articles already covered under reviews by Boué, et al. [2] and Thomsen, et al. [14] were excluded from the review. The search period was from 20 May 2014 to 31 August 2022 with the last search undertaken on 31 August 2022.

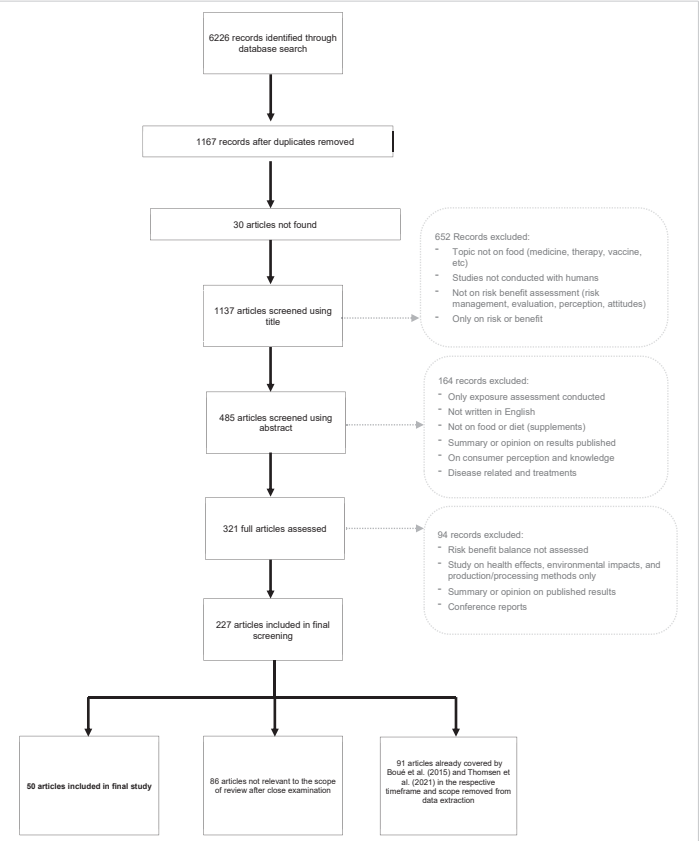

Figure 1: PRISMA Table.

The following information was extracted from the collected studies: (1) the region where the study was conducted, (2) the focus of the study - whether the risk-benefit study was performed on a food component, a substitution of food, or cooking method, (3) the food component studied, (4) the type of risk-benefit comparison (following the approach of Thomsen, et al. 2021 [14]).

Applying the same method of classification as the Thomsen, et al. [14] review on RBA in fish and seafood consumption, RBA studies were classified into (1) RBA studies estimating risk-benefit by integration into a common or composite metric such as the disability-adjusted life years – DALY (health-metrics studies), (2) risks and benefits characterized through comparison of exposures to nutrients and contaminants, via comparison to Dietary Reference Values (DRV) and Health-Based Guidance Values (HBGV), i.e. regulatory threshold based studies. Threshold approach studies were further categorized into whether or not they used (1) deterministic approaches – combining fixed values of consumption and concentration, or (2) probabilistic approaches, whereby probability distributions were assigned to different variables or on consumption data.

Results

Search strings and the total number of papers found are shown in Table 1.

Table 1: Search strings and the total number of papers found.

Search Terms	Scopus™	ScienceDirect™	MEDLINE	Google Scholar	SciFinder®	Web of Science®
TITLE(risk* AND (benefit* OR beneficial*)) and FULL-TEXT (food)	1867	714	829	93	741	824
TITLE((chemi* OR toxicolo* OR microbi* OR nutrition) AND (risk* AND (benefit* OR beneficial*))) and FULL-TEXT(food)	55	21	29	0	21	35
TITLE((risk* AND (benefit* OR beneficial*)) AND (health)) and FULL-TEXT(food)	223	81	110	11	114	132
TITLE((risk* AND (benefit* OR beneficial*)) AND (public health)) and FULLTEXT(food)	21	8	11	2	12	15
TITLE((risk* AND (Benefit* OR Beneficial*) AND (review)) and FULL-TEXT(food)	87	21	46	3	34	31
TITLE((risk* AND (benefit* OR beneficial*)) AND (state of the art)) and FULLTEXT(food)	7	7	7	2	5	7
Total number of articles (from all sources)	Grand Total: 6226 Duplicates: 5059 After removal of duplicates: 1167					

Note: Search strings were adapted according to the syntax unique to each database to maintain the same search logic.

After the removal of duplicates, there were a total of 50 new RBA studies reviewed since 20 May 2014. Tables 2,3 show that the majority of RBA studies have been conducted on food components (n = 43, 86%), namely fish, seafood, rice, red meat, tea, wild mushrooms, agricultural products, cereal, cocoa products, ethnic food, honey, nuts, seaweed, with the majority on seafood, namely fish alone (n = 17) and mixed seafood items (n = 13).

The focus of the remaining studies varied. Three studies were on rice, two on tea, and two on wild mushrooms. There was one study each on agricultural products, cereal, cocoa products, ethnic food, honey, nuts, and red meat. Four RBA studies were conducted on the substitution of one food for another, namely the substitution of red meat for fish, the substitution of food by seaweed, and the substitution of beef protein for insect protein. Additionally, one RBA study was conducted on the exposure to nitrate and nitrite in food, another on the RBA of iodine fortification of table salt, and one comparing cooking methods on the chemical risk and nutritional benefit of rice.

Most of the studies have been conducted in Europe (n = 31) and Asia (n = 11), as shown in Table 4. Three studies were conducted in North America, two in Africa, two in South America, and one in Siberia.

Thirty-five (35) out of 50 studies employed a threshold approach where risks and benefits were characterized by comparing exposures to contaminants and nutrients with Dietary Reference Values (DRV) and Health-Based Guidance Values (HBGV). Fifteen (15) out of 50 studies estimated risk-benefit by integration into a common health metric. Eleven of these studies applied the composite health metric disability-adjusted life years (DALY) where the burden of disease in a population was measured on the basis of the number of life years lost or saved. Four of these studies integrated risk and benefit into common health metrics, namely visual recall memory (VRM) points, coronary heart disease (CHD) risk, intelligence quotient (IQ) points, and liver cancer. For further details see Supplementary Data.

As Table 5, shows, out of the 35 threshold approach studies,

Table 2: Topic of RBA studies focusing on food consumption.

Topic	Number of Studies
Fish	17
Seafood	13
Rice	3
Substituting red meat by fish	2
Tea	2
Wild mushrooms	2
Agricultural products	1
Cereal	1
Cocoa products	1
Ethnic food	1
Honey	1
Iodine fortification of table salt	1
Nitrate and nitrite	1
Nuts	1
Red meat	1
Seaweed	1
Substituting beef by insects	1

Table 3: The focus of RBA studies.

Focus	Number of Studies
Food component	43
Chemicals in food	1
Substitution	4
Fortification	1
Cooking method	1

Table 4: The region where RBA studies have been conducted.

Region	Number of Studies
Europe	31
Asia	11
North America	3
Africa	2
South America	2
Siberia	1

Table 5: Types of RBA studies conducted.

Type of Study	Approach	Quotient
Threshold approach (n = 35)	Deterministic (n = 32)	Risk-benefit Quotient (n = 12)
		Target Hazard Quotient (n = 8)
		Others e.g. Health Benefit Value of Selenium (HBV-Se) (n = 12)
	Probabilistic (n = 3)	Others e.g. Health Benefit Value of Selenium (HBV-Se) (n = 3)
Health metrics (n = 15)	DALY (n = 11)	
	Others e.g. IQ (n = 4)	

32 were deterministic, with three studies making use of probabilistic approaches to model different intake scenarios. Among the studies that made use of the deterministic approach, twelve studies calculated a risk-benefit quotient where risk and benefit were considered in the same equation. Eight studies characterized risks using target hazard quotient, where risk and benefit were assessed using DRV and/or HBGV. Twelve studies either made a direct comparison with DRV or HBGV or made use of other ways of estimating specific risk-benefit such as the Health Benefit Value of Selenium (HBV-Se) where the health benefit value of selenium is estimated taking into account the simultaneous presence of methylmercury [16]. Full details of all studies are provided in the Supplementary Data.

Discussion

Despite more attention on RBA approaches, the majority of RBA studies conducted after Boué, et al. [1] Thomsen, et al. [14] were still on fish (n = 17, 34%) and mixed seafood (n = 13, 26%). While the Thomsen, et al. study [14] focused entirely on fish and seafood, the review by Boué, et al. [1] showed that 70% of RBA studies conducted between 1999 and 20 May 2014 were on fish and fish products. Fish and seafood are an important source of nutrients such as essential fatty acids (DHA and EPA), while at the same time they are likely to carry contaminants such as methylmercury and dioxins that are harmful to human health [14]. Nonetheless, fish and seafood are popular choices of food for consumers and commercially valuable [17], therefore it is still a topic of interest for RBA, especially for sensitive populations like children and women of childbearing age [18,19]. The trade-off of nutritional benefit and contaminant risk provides a solid application for RBA studies to be conducted. This is likely why there are so many case studies replicated on different fish and seafood species in different populations of interest.

One of the challenges of RBA that has been pointed out by Thomsen, et al. [14] is that most RBA studies have been conducted in high-income countries. Even though there is a significant level of fish and seafood consumption in lower-income countries, there are not many RBA studies being conducted in these countries. As of the timing of this study, this is still the case as most of the newly sourced RBA studies published have been conducted in Europe (n = 31, 62%).

Among the 35 threshold approach studies, 12 studies made use of a risk-benefit quotient (RBQ) where risk and benefit were considered in the same equation. RBA studies such as the ones by Barchiesi, et al. [20] and Fang, et al. [21] have made use of an RBQ proposed by Gladyshev, et al. [22]. This quotient represents the exposure to a contaminant (e.g. methylmercury) and whether it exceeds the HBGV when an adult aims to consume a sufficient portion of the food (e.g. fish) i.e. to obtain a recommended daily intake of essential nutrients (e.g. essential fatty acids). If the RBQ <1, consuming a portion of food to obtain a recommended daily intake of the nutrient considered does not result in exposure to a contaminant exceeding HBGV, hence there is no risk to human health. It is vice versa for an RBQ >1. In most of the studies, however, risk and benefit were compared individually using health-based guidance values and not integrated into the same equation or metric.

Only 11 out of 50 studies estimated risk-benefit using DALYs. This is likely due to the level and quality of data a DALY model requires. DALY is a composite metric that can aggregate mortality and morbidity measures associated with multiple health outcomes [2,23]. One of the challenges of applying DALYs in RBA is that a disability weight needs to be established for the health outcome considered [3,24]. Moreover, implementing a composite health metric such as DALY in an RBA study requires data such as life expectancy, disability weights, and duration associated with the health effects [1,9,25].

Smith and Hooper [3] have proposed that RBA has the potential to be more widely applied to other foods and especially to alternative proteins and novel/functional food. Existing food regulatory frameworks for novel food are primarily focused solely on food safety risks alone. RBA is a methodology that can integrate risk and benefit to assess the health impact of alternative proteins and novel food so that the health benefit of food is not negated by the presence of possible health risks in the regulatory context. This is one of the key drivers for consumer acceptance and interest in novel/functional foods thus having a measurable and quantifiable approach to weigh the risks and benefits will greatly aid discussion with consumers and help enhance novel food acceptance.

Based on our review, we report a few new RBA studies being done on less mainstream food sources. For instance, a diet replacement study was done by Vellinga, et al. [26] on seaweed, which is considered a new source of food in parts of Europe. A study on Chinese dark tea was undertaken by He and Lyu [27] following a BRAFO approach. Benefit-Risk Analysis for Foods (BRAFO) is a tiered approach to risk-benefit assessment developed by a project funded by the European Commission. BRAFO is a framework that aims to compare human health risks and benefits of foods quantitatively based on a common scale of measurement [7,10].

However, despite the rapid interest and growth in alternative proteins and novel foods in the last 5 years, there has only been one study that has specifically applied RBA methodology to assessing novel foods. In this study by Naska et al. [13], published by EFSA, the complete replacement of a minced beef patty with edible insect dough was assessed based on health outcomes associated with nutrient intake, microbiological hazards, and compounds of toxicological concern and was quantified into a composite DALY metric. The expected change in DALYs when shifting from the reference scenario to the alternative one was estimated to be around

8,753 DALYs (per 100,000 population) saved in Greece, 6,572 DALYs in Denmark, and 21,972 DALYs in France. The change in DALY mostly came from the overall beneficial nutritional and microbiological impacts [14]. More such case studies need to be published to facilitate the harmonization and wider application of RBA.

A similar study on seaweed was published by Vellinga, et al. [26]. In this study, the authors attempted to investigate the impact of replacing 10% of foods commonly consumed in the Netherlands and Portugal, namely pasta, bacon, and lettuce, with novel seaweed-derived products made entirely with kelp (*Saccharina latissima*). The study compared a reference scenario of 0% seaweed consumption to the above alternative scenario in terms of nutrient intake of sodium and iodine, as well as exposure to contaminants arsenic, cadmium, lead, and mercury. Intake scenarios in the Netherlands and Portugal were compared with the current intake and exposure levels in Japan, where seaweed as a traditional food is a part of the normal diet. Nutrient intake and contaminant exposure were then compared to current health-based guidance values set by EFSA and Joint FAO/WHO Expert Committee on Food Additives (JECFA), and where there was no HBGV, a benchmark dose level. The results show that there are no consequences in the intake of sodium and exposure to cadmium, lead, and mercury in the alternative scenario. However, there is a significant increase in the mean iodine intake as well as exposure to arsenic.

RBA has the potential to be an added value in the novel food scene if it can be more widely applied. RBA studies can be applied to inform policymakers and consumers of the benefits of new food products that can outweigh any risks inherent to the product. With the growing interest in novel foods, especially alternative proteins, RBA also has the potential to be an important tool for policymakers to help answer pressing questions such as the trade-off between combatting climate change versus introducing a new allergenic protein onto the market. It will also aid consumers in making important, risk-based decisions about their diet.

Alternative proteins are often touted by investors and start-ups as a healthier and more environmentally friendly option held back by a lagging regulatory environment. In the absence of information about products like novel proteins, these claims are hard to support or refute and leave consumers to question the true reality around such products making them vulnerable to unscrupulous actors or missing out on potential benefits due to fear of the unknown.

Conclusion

A total of 50 new RBA studies since 20 May 2014 have been reviewed. Focus remains on seafood and the benefits of its consumption versus contaminant exposure. Most of the studies have been conducted in Europe (n = 31) and Asia (n = 11).

Based on our review, and the progress in the uptake of RBA methodologies since Boué, et al. [2], it is clear that more effort is needed to promote the use of RBA. We strongly believe that the application to novel foods is a key area of application that would benefit from the use of RBA approaches and hope to see a shift in the literature over the next 5-10 years as the novel food sector grows.

Supplementary materials

Supplementary Data (Excel Workbook): Risk-benefit assessment studies (n = 50) reviewed.

Author contributions

Conceptualization, BPCS; Literature review – TH and CK; writing—original draft preparation, TH; writing—review and editing, TH, BPCS, KH; funding acquisition, BPCS. All authors have read and agreed to the published version of the manuscript.

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