Best Practices for Risk-Benefit Analysis:
experience from out of food into food

Guest Editors
Brian G. Lake, Mariken J. Tijhuis and Hans Verhagen

L. B. Larsen, M. S. Sidhu, M. P. Schreiber and J. Castenmiller

1 Preface

2-4 State of the art in benefit-risk analysis: Introduction

5-25 State of the art in benefit-risk analysis: Food and nutrition

26-32 State of the art in benefit-risk analysis: Medicines

33-39 State of the art in benefit-risk analysis: Food microbiology

Available online at www.sciencedirect.com
SciVerse ScienceDirect

Food and Chemical Toxicology
VOLUME 50 (2012) ISSUE 1

Contents continued on inside back cover
State of the art in benefit–risk analysis: Introduction

H. Verhagen a,b,c,⇑, M.J. Tijhuis a,d, H. Gunnlaugsdóttir e, N. Kalogeras d, O. Leino i, J.M. Luteijn g, S.H. Magnússon e, G. Odekerken d, M.V. Pohjola f, J.T. Tuomisto f, Ø. Ueland h, B.C. White i, F. Holm j

a National Institute for Public Health and the Environment (RIVM), PO Box 1, 3720 BA Bilthoven, The Netherlands
b Maastricht University, NUTRIM School for Nutrition, Toxicology and Metabolism, PO Box 616, 6200 MD Maastricht, The Netherlands
c University of Ulster, Northern Ireland Centre for Food and Health (NICHE), Cromore Road, Coleraine, BT52 1SA Northern Ireland, United Kingdom
d Maastricht University, School of Business and Economics, PO Box 616, 6200 MD Maastricht, The Netherlands
e Matís, Icelandic Food and Biotech R&D, Vínlandsleið 12, 113 Reykjavík, Iceland
f National Institute for Health and Welfare (THL), PO Box 95, FI-00381 Helsinki, Finland
g University of Ulster, School of Nursing, Shore Road, Newtownabbey (Jordantown), BT37 0QQ Northern Ireland, United Kingdom
h Nofima, Osloveien 1, N-1430 Ås, Norway
i University of Ulster, Dept. of Pharmacy and Pharmaceutical Sciences, School of Biomedical Sciences, Cromore Road, Coleraine, BT52 1SA Northern Ireland, United Kingdom
j FoodGroup Denmark and Nordic NutriScience, Rugaardsvej 14, A2 Rugaard, DK-8400 Ebeltoft, Denmark

Article info
Article history:
Available online 12 June 2011
Keywords:
Benefit-risk
Best practice
BEPRARIBEAN

Abstract
Risk-taking is normal in everyday life if there are associated (perceived) benefits. Benefit–Risk Analysis (BRA) compares the risk of a situation to its related benefits and addresses the acceptability of the risk. Over the past years BRA in relation to food and food ingredients has gained attention. Food, and even the same food ingredient, may confer both beneficial and adverse effects. Measures directed at food safety may lead to suboptimal or insufficient levels of ingredients from a benefit perspective. In BRA, benefits and risks of food (ingredients) are assessed in one go and may conditionally be expressed into one currency. This allows the comparison of adverse and beneficial effects to be qualitative and quantitative. A BRA should help policy-makers to make more informed and balanced benefit-risk management decisions. Not allowing food benefits to occur in order to guarantee food safety is a risk management decision much the same as accepting some risk in order to achieve more benefits. BRA in food and nutrition is making progress, but difficulties remain. The field may benefit from looking across its borders to learn from other research areas. The BEPRARIBEAN project (Best Practices for Risk-Benefit Analysis: experience from out of food into food; http://en.opasnet.org/w/Bepraribean) aims to do so, by working together with Medicines, Food Microbiology, Environmental Health, Economics & Marketing-Finance and Consumer Perception. All perspectives are reviewed and subsequently integrated to identify opportunities for further development of BRA for food and food ingredients. Interesting issues that emerge are the varying degrees of risk that are deemed acceptable within the areas and the trend towards more open and participatory BRA processes. A set of 6 ‘state of the art’ papers covering the above areas and a paper integrating the separate (re)viewes are published in this volume.
State of the art in benefit–risk analysis: Food and nutrition


A R T I C L E   I N F O

Article history:
Available online 12 June 2011

A B S T R A C T

Benefit–risk assessment in food and nutrition is relatively new. It weighs the beneficial and adverse effects that a food (component) may have, in order to facilitate more informed management decisions regarding public health issues. It is rooted in the recognition that good food and nutrition can improve health and that some risk may be acceptable if benefit is expected to outweigh it. This paper presents an overview of current concepts and practices in benefit–risk analysis for food and nutrition. It aims to facilitate scientists and policy makers in performing, interpreting and evaluating benefit–risk assessments.

Historically, the assessments of risks and benefits have been separate processes. Risk assessment is mainly addressed by toxicology, as demanded by regulation. It traditionally assumes that a maximum safe dose can be determined from experimental studies (usually in animals) and that applying appropriate uncertainty factors then defines the ‘safe’ intake for human populations. There is a minor role for other research traditions in risk assessment, such as epidemiology, which quantifies associations between determinants and health effects in humans. These effects can be both adverse and beneficial. Benefit assessment is newly developing in regulatory terms, but has been the subject of research for a long time within nutrition and epidemiology. The exact scope is yet to be defined. Reductions in risk can be termed benefits, but also states rising above ‘the average health’ are explored as benefits. In nutrition, current interest is in ‘optimal’ intake; from a population perspective, but also from a more individualised perspective.

In current approaches to combine benefit and risk assessment, benefit assessment mirrors the traditional risk assessment paradigm of hazard identification, hazard characterization, exposure assessment and risk characterization. Benefit–risk comparison can be qualitative and quantitative. In a quantitative perspective, benefits and risks are expressed in a common currency, for which the input may be determined or (increasingly more) probabilistic. A tiered approach is advocated, as this allows for transpar-
Benefit–risk assessment in medicine has been a valuable tool in the regulation of medicines since the 1960s. Benefit–risk assessment takes place in multiple stages during a medicine’s life cycle and can be conducted in a variety of ways, using methods ranging from qualitative to quantitative. Each benefit–risk assessment method is subject to its own specific strengths and limitations. Despite its widespread and long-time use, benefit–risk assessment in medicine is subject to debate and suffers from a number of limitations and is currently still under development.

This state of the art review paper will discuss the various aspects and approaches to benefit–risk assessment in medicine in a chronological pathway. The review will discuss all types of benefit–risk assessment a medicinal product will undergo during its lifecycle, from Phase I clinical trials to post-marketing surveillance and health technology assessment for inclusion in public formularies. The benefit–risk profile of a drug is dynamic and differs for different indications and patient groups. In the end of this review we conclude benefit–risk analysis in medicine is a developed practice that is subject to continuous improvement and modernisation. Improvement not only in methodology, but also in cooperation between organizations can improve benefit–risk assessment.
State of the art in benefit–risk analysis: Food microbiology

S.H. Magnússon a,e, H. Gunnlaugsdóttir a, H. van Loveren b, F. Holm c, N. Kalogerass d, O. Leino e, J.M. Luteijn f, G. Odekerken d, M.V. Pohjola e, M.J. Tijhuis b,d, J.T. Tuomisto e, Ø. Ueland g, B.C. White h, H. Verhagen b,i,j

a Matís, Icelandic Food and Biotech R & D, Vínlandsleið 12, 113 Reykjavík, Iceland
b National Institute for Public Health and the Environment (RIVM), P.O. Box 1, 3720 BA Bilthoven, The Netherlands
FoodGroup Denmark & Nordic NutriScience, Rugaardsvej 14, A2, Rudaard, DK-8400 Ebeltoft, Denmark
m Maastricht University, School of Business and Economics, P.O. Box 616, 6200 MD Maastricht, The Netherlands
National Institute for Health and Welfare (THL), P.O. Box 95, FI-70701 Kuopio, Finland
University of Ulster, School of Nursing, Shore Road, Newtownabbey (Jordanstown) BT37 0QB, United Kingdom
University of Ulster, Department of Pharmacy and Pharmaceutical Sciences, School of Biomedical Sciences, Cromore Road, Coleraine BT52 1SA, United Kingdom
Maastricht University, NUTRIM School for Nutrition, Toxicology and Metabolism, P.O. Box 616, 6200 MD Maastricht, The Netherlands
University of Ulster, Northern Ireland Centre for Food and Health (NICHE), Cromore Road, Coleraine BT52 1SA, United Kingdom

A R T I C L E   I N F O

Article history:
Available online 12 June 2011

Keywords:
Risk assessment
Microbiological risk assessment
Benefit–risk assessment
Food microbiology

A B S T R A C T

Over the past years benefit–risk analysis (BRA) in relation to foods and food ingredients has gained much attention; in Europe and worldwide. BRA relating to food microbiology is however a relatively new field of research. Microbiological risk assessment is well defined but assessment of microbial benefits and the weighing of benefits and risk has not been systematically addressed. In this paper the state of the art in benefit–risk analysis in food microbiology is presented, with a brief overview of microbiological food safety practices.

The quality and safety of foods is commonly best preserved by delaying the growth of spoilage bacteria and contamination by bacterial pathogens. However, microorganisms in food can be both harmful and beneficial. Many microorganisms are integral to various food production processes e.g. the production of beer, wine and various dairy products. Moreover, the use of some microorganisms in the production of fermented foods are often claimed to have beneficial effects on food nutrition and consumer health. Furthermore, food safety interventions leading to reduced public exposure to foodborne pathogens can be regarded as benefits. The BRA approach integrates an independent assessment of both risks and benefits and weighs the two using a common currency.

Recently, a number of initiatives have been launched in the field of food and nutrition to address the formulation of the benefit–risk assessment approach. BRA has recently been advocated by EFSA for the public health management of food and food ingredients; as beneficial and adverse chemicals can often be found within the same foods and even the same ingredients. These recent developments in the scoping of BRA could be very relevant for food microbiological issues. BRA could become a valuable methodology to support evaluations and decision making regarding microbiological food safety and public health, supplementing other presently available policy making and administrative tools for microbiological food safety management.

© 2011 Elsevier Ltd. All rights reserved.


* Corresponding author. Tel.: +354 422 5000; fax: +354 422 5001.
E-mail address: sveinnh@matis.is (S.H. Magnússon).
State of the art in benefit–risk analysis: Environmental health


Abstract

Environmental health assessment covers a broad area: virtually all systematic analysis to support decision making on issues relevant to environment and health. Consequently, various different approaches have been developed and applied for different needs within the broad field. In this paper we explore the plurality of approaches and attempt to reveal the state-of-the-art in environmental health assessment by characterizing and explicating the similarities and differences between them. A diverse, yet concise, set of approaches to environmental health assessment is analyzed in terms of nine attributes: purpose, problem owner, question, answer, process, use, interaction, performance and establishment. The conclusions of the analysis underline the multitude and complexity of issues in environmental health assessment as well as the variety of perspectives taken to address them. In response to the challenges, a tendency towards developing and applying more inclusive, pragmatic and integrative approaches can be identified. The most interesting aspects of environmental health assessment are found among these emerging approaches: (a) increasing engagement between assessment and management as well as stakeholders, (b) strive for framing assessments according to specific practical policy needs, (c) integration of multiple benefits and risks, as well as (d) explicit incorporation of both scientific facts and value statements in assessments. However, such approaches are yet to become established, and many contemporary mainstream environmental health assessment practices can still be characterized as relatively traditional risk assessment.

© 2011 Elsevier Ltd. All rights reserved.

Abbreviations: BENEFIS, benefit–risk assessment for food: an iterative value-of-information approach; CSA, chemical safety assessment; DALY, disability adjusted life years; ECHA, european chemical agency; EIA, environmental impact assessment; EU, european union; HIA, health impact assessment; HEIMTSA, health and environment integrated methodology and toolbox for scenario assessment; IEHA, integrated environmental health impact assessment; INTARESE, integrated assessment of health risks of environmental stressors in Europe; IRGC, international risk governance council; LCA, life cycle assessment; NGO, non-governmental organization; NRC, national research council (USA); OECD, organization for economic co-operation and development; PBT, persisten, bioaccumulative, and toxic; PSSP, purpose, structure, state, performance; QALY, quality adjusted life years; REACH, registration, evaluation, authorization, and restriction of chemical substances (EU); SAIC, scientific applications international corporation; TEKES, national technology agency of finland; WHO, World Health Organization; YVA, Ympäristövaikutusten arviointi (Finnish for EIA).

* Corresponding author. Tel.: +358 17 201470; fax: +358 17 201480.
E-mail address: mikko.pohjola@thl.fi (M.V. Pohjola).

0278-6915/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.fct.2011.06.004
Review

State of the art in benefit–risk analysis: Economics and Marketing-Finance


⇑Corresponding author. Tel.: +31 43 388 4827; fax: +31 43 388 4875.
E-mail address: N.Kalogeras@maastrichtuniversity.nl (N. Kalogeras).

Maastricht University, School of Business and Economics, P.O. Box 616, 6200 MD Maastricht, The Netherlands
Matís, Icelandic Food and Biotech R&D, Vínlundaborg 12, 113 Reykjavik, Iceland
FoodGroup Denmark & Nordic NutriScience, Rudsørvej 14 A2, Ruda, DK-8400 Ebeltoft, Denmark
National Institute for Health and Welfare (THL), P.O. Box 95, FI-70701 Kuopio, Finland
University of Ulster, School of Nursing, Shore Road, Newtownabbey (Jordanstown) BT37 0QB, United Kingdom
National Institute for Public Health and the Environment (RIVM), P.O. Box 1, 3720 BA Bilthoven, The Netherlands
Nofima, Osloveien 1, N-1430 Ås, Norway
University of Ulster, Department of Pharmacy & Pharmaceutical Sciences, School of Biomedical Sciences, Cromore Road, Coleraine BT52 1SA, Northern Ireland, United Kingdom
Maastricht University, NUTRIM School for Nutrition, Toxicology and Metabolism, P.O. Box 616, 6200 MD Maastricht, The Netherlands
University of Ulster, Northern Ireland Centre for Food and Health (NICHE), Cromore Road, Coleraine BT52 1SA, Northern Ireland, United Kingdom

A R T I C L E   I N F O

Article history:
Available online 18 August 2011

Keywords:
Benefit-risk trade-offs
Decoupling
Utility
Economics
Marketing-Finance

A B S T R A C T

All market participants (e.g., investors, producers, consumers) accept a certain level of risk as necessary to achieve certain benefits. There are many types of risk including price, production, financial, institutional, and individual human risks. All these risks should be effectively managed in order to derive the utmost of benefits and avoid disruption and/or catastrophic economic consequences for the food industry. The identification, analysis, determination, and understanding of the benefit–risk trade-offs of market participants in the food markets may help policy makers, financial analysts and marketers to make well-informed and effective corporate investment strategies in order to deal with highly uncertain and risky situations.

In this paper, we discuss the role that benefits and risks play in the formation of the decision-making process of market-participants, who are engaged in the upstream and downstream stages of the food supply chain. In addition, we review the most common approaches (expected utility model and psychometrics) for measuring benefit–risk trade-offs in the economics and marketing-finance literature, and different factors that may affect the economic behaviour in the light of benefit–risk analyses.

Building on the findings of our review, we introduce a conceptual framework to study the benefit–risk behaviour of market participants. Specifically, we suggest the decoupling of benefits and risks into the separate components of utilitarian benefits, hedonic benefits, and risk attitude and risk perception, respectively. Predicting and explaining how market participants in the food industry form their overall attitude in light of benefit–risk trade-offs may be critical for policy-makers and managers who need to understand the drivers of the economic behaviour of market participants with respect to production, marketing and consumption of food products.

© 2011 Elsevier Ltd. All rights reserved.
Benefit and risk perception with respect to food consumption, have been a part of human daily life from beginning of time. In today’s society the food chain is long with many different types of actors and low degree of transparency. Making informed food choices where knowledge of benefits and risks is part of the decision making process are therefore complicated for consumers. Thus, to understand how consumers perceive benefits and risks of foods, their importance in relation to quality evaluations are aspects that need to be addressed. The objective of this paper is to discuss state of the art in understanding consumer perceptions of benefits and risks of foods in order to improve understanding of consumer behaviour in the food domain.

Risks may be associated with both acute and long term consequences, some of which may have serious effects. Perceived risks are connected to morbidity and mortality along two dimensions relating to unknown risk, and to which extent the risk is dreaded by the consumer. Unfamiliar, uncertain, unknown, uncontrollable, and severe consequences are some factors associated with risk perception. Novel food processing techniques, for instance, score high on several of these parameters and are consequently regarded with suspicion and perceived as risky by consumers.

On a daily basis, benefits of foods and food consumption are more important in most consumers’ minds than risks. Benefits are often associated with food’s ability to assuage hunger, and to provide pleasure through eating and socialising. In addition, two main categories of benefits that are important for acceptance of product innovations are health and environmental benefits.

Benefit and risk perception of foods seem to be inversely correlated, so when something is perceived as being highly beneficial, it is correspondingly perceived as having low risk. However, slightly different paths are used in the formation of these perceptions; benefit perception is based on heuristics and experience, while risk perception is to a larger extent the result of cognitive information processing.

Consumers are particularly conservative when it comes to perception and acceptance of foods compared to other products. Benefit-risk evaluations tend to be skewed towards acceptance of all that is traditional and well-known (benefits), and rejection or suspicion towards anything that is novel or highly processed (risks) regardless of actual risk. Knowledge of how consumers perceive benefits and risks of foods, may contribute to understanding benefit-risk perception in other areas related to personal, societal or environmental perspectives.
Looking beyond borders: Integrating best practices in benefit–risk analysis into the field of Food and Nutrition

M.J. Tijhuis a,b,* M.V. Pohjola c H. Gunnlaugsdóttir d N. Kalogeras b O. Leino c J.M. Luteijn e S.H. Magnússon d G. Odekerken-Schröder b M. Poto f,g J.T. Tuomisto c Ø. Ueland h B.C. White i, F. Holm j, H. Verhagen a,k,l

a National Institute for Public Health and the Environment (RIVM), P.O. Box 1, 3720 BA Bilthoven, The Netherlands
b Maastricht University, School of Business and Economics, P.O. Box 616, 6200 MD Maastricht, The Netherlands
c National Institute for Health and Welfare (THL), P.O. Box 95, FI-70701 Kuopio, Finland
d Matís, Icelandic Food and Biotech R&D, Vínlandsleið 12, 113 Reykjavik, Iceland
e University of Ulster, School of Nursing, Shore Road, Newtownabbey (Jordanstown), BT37 0QB Northern Ireland, United Kingdom
f University of Turin, Facoltà di Giurisprudenza, Dipartimento di Scienze Giuridiche, vi San’Ottavio 54, 10124 Torino, Italy
g Precon Food Management BV, Regulierenring 16 Bunnik, The Netherlands
h Nofima, Oslovn 1, N-1430 Ås, Norway
i University of Ulster, Department of Pharmacy & Pharmaceutical Sciences, School of Biomedical Sciences, Cromore Road, Coleraine, BT52 1SA Northern Ireland, United Kingdom
j FoodGroup Denmark & Nordic NutriScience, Rugaardsvej 14, A2, Rugaard, DK-8400 Ebeltoft, Denmark
k Maastricht University, NUTRIM School for Nutrition, Toxicology and Metabolism, P.O. Box 616, 6200 MD Maastricht, The Netherlands
l University of Ulster, Northern Ireland Centre for Food and Health (NICHE), Cromore Road, Coleraine, BT52 1SA Northern Ireland, United Kingdom

Abstract

An integrated benefit–risk analysis aims to give guidance in decision situations where benefits do not clearly prevail over risks, and explicit weighing of benefits and risks is thus indicated. The BEPRAIBEAN project aims to advance benefit–risk analysis in the area of food and nutrition by learning from other fields. This paper constitutes the final stage of the project, in which commonalities and differences in benefit–risk analysis are identified between the Food and Nutrition field and other fields, namely Medicines, Food Microbiology, Environmental Health, Economics and Marketing–Finance, and Consumer Perception. From this, ways forward are characterized for benefit–risk analysis in Food and Nutrition. Integrated benefit–risk analysis in Food and Nutrition may advance in the following ways: Increased engagement and communication between assessors, managers, and stakeholders; more pragmatic problem-oriented framing of assessment; accepting some risk; pre- and post-market analysis; explicit communication of the assessment purpose, input and output; more human (dose–response) data and more efficient use of human data; segmenting populations based on physiology; explicit consideration of value judgments in assessment; integration of multiple benefits and risks from multiple domains; explicit recognition of the impact of consumer beliefs, opinions, views, perceptions, and attitudes on behaviour; and segmenting populations based on behaviour. The opportunities proposed here do not provide ultimate solutions; rather, they define a collection of issues to be taken account of in developing methods, tools, practices and policies, as well as refining the regulatory context, for benefit–risk analysis in Food and Nutrition and other fields. Thus, these opportunities will now need to be explored further and incorporated into benefit–risk practice and policy. If accepted, incorporation of these opportunities will also involve a paradigm shift in Food and Nutrition benefit–risk analysis towards conceiving the analysis as a process of creating shared knowledge among all stakeholders.

© 2011 Elsevier Ltd. All rights reserved.

Abbreviations: CVD, cardiovascular disease; DALY, disability adjusted life year; EFSA, European Food Safety Authority; HTA, health technology assessment; QALY, quality adjusted life year.

* Corresponding author at: National Institute for Public Health and the Environment (RIVM), P.O. Box 1, 3720 BA Bilthoven, The Netherlands. Tel.: +31 30 2742637; fax: +31 30 2744466.
E-mail address: mariken.tijhuis@rivm.nl (M.J. Tijhuis).