NORDIC WORKING PAPERS

Risk-benefit assessment of food

Report from a Nordic workshop September 2016

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<http://dx.doi.org/10.6027/NA2017-902>
NA2017:902
ISSN 2311-0562

This working paper has been published with financial support from the Nordic Council of Ministers. However, the contents of this working paper do not necessarily reflect the views, policies or recommendations of the Nordic Council of Ministers.

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Content

1. Introduction	3
2. Presentations	4
2.1 Introductory presentations	4
2.2 Organisation of RBA in the Nordic countries	8
2.3 RBA activities in the Nordic countries	9
3. Group discussions on future Nordic collaboration	13
4. Summary and conclusions	17
5. References	18
 Appendix I, Programme	 20
Appendix II, List of participants	21
Appendix III, List of literature	22
Appendix IV, Abstract Hans Verhagen	25
Appendix V, Abstract Géraldine Boué	28
Appendix VI, Abstract Maarten Nauta	30
Appendix VII, Group discussions	32

1. Introduction

This workshop on risk-benefit assessment (RBA) was organized by the National Food Agency (NFA) in Sweden and took place in Uppsala, Sweden 22-23 September, 2016. The main purpose of the two-day workshop was to increase collaboration between the Nordic countries in this area. Presentations of organizations and RBA activities in the respective countries served as a basis for discussions regarding future collaboration. All Nordic countries were represented by at least one participant.

The workshop was funded by the Nordic Council of Ministers (NKMT). Hanna Eneroth and Nils-Gunnar Ilbäck at NFA arranged the workshop with the assistance of Inger Therese Laugsand Lillegaard, the Norwegian Scientific Committee for Food Safety (VKM), Norway, Katrín Guðjónsdóttir, Iceland Food and Veterinary Authority (MAST), Iceland and Helga Gunnlaugsdóttir, MATÍS, Iceland, Morten Poulsen, Denmark Technical University (DTU), Denmark and Maria Rönnqvist, the Finnish Food Safety Authority (Evira), Finland.

2. Presentations

The workshop was divided in four sessions to give all participants an updated and general view of RBA activities in Europe, as well as individual presentations of the Nordic organizations and their present activities in the RBA area. The four sessions were;

1. Introductory presentations on state of the art of RBA in a European context by invited speakers
2. Short presentations on the organizations where RBA is performed in Nordic countries
3. Presentations on risk and benefit activities in Nordic countries
4. Discussions about future Nordic collaboration

Appendix I includes the programme, appendix II, a list of participants and appendix III a list of literature.

2.1 Introductory presentations

Per Bergman, head of the risk-benefit assessment department at the NFA, Sweden, opened the workshop by welcoming the participants and speakers to Uppsala.

Leif Busk moderated the first session and introduced the three invited speakers; Hans Verhagen (Head of Risk Assessment and Scientific Assistance Department, EFSA), Géraldine Boué (ONIRIS-INRA, Nantes, France), and Maarten Nauta (the Risk Benefit Research Group, DTU, Denmark).

Hans Verhagen: Risk-benefit assessment of foods in a European perspective (abstract in appendix III)

Food and nutrition are essential for life and the benefit of foods is, first and foremost to provide nutrition. Even though food contains necessary and beneficial ingredients, all ingredients are potentially adverse at certain intake levels. In his presentation, Hans Verhagen exemplified how food and food ingredients may be both beneficial and adverse, and that there is a delicate balance between these effects. In addition, food may also contain non-nutrients such as contaminants, natural toxins, or other substances that may have potential adverse effects. For such adverse effects, risk-ranking or risk-risk comparison methods are important to develop and Hans Verhagen reviewed the methodological developments for this.

Referring to the extensive RIVM project “Our food our health”, Hans Verhagen stated that the public health burden of unhealthy dietary behaviour (eating too much and unhealthy food choices) by far outweighs the public health burden from food safety topics (National Institute for Public Health and the Environment (RIVM) 2006). He also mentioned that there is a need for a general improvement of different tools to be used in risk assessments as well as risk-benefit assessments. EFSA is presently focusing on several of these areas and Verhagen presented ongoing activities, such as uncertainty in risk assessment, weight of evidence approach, biological relevance, update on the guidance on Benchmark Dose response, and PROMETHEUS (PROMoting METHods for Evidence Use in Scientific assessments).

Questions and comments to Hans Verhagen

Can we really compare risks of different types such as microbiological and chemical risks?

Verhagen: Yes, whereas it is likely that the risk assessment in the different disciplines will require different reflections, there are currencies that can be used for both risks such as disability-adjusted-life-years (DALYs), quality-adjusted life-years (QALYs) and other parameters.

Is there a need for more epidemiological studies to develop chemical risk assessment, in order to calculate DALYs?

Verhagen: It is not essential because it is possible to calculate DALYs based on animal studies. Of course, there will be uncertainties related to the use of data from animal studies that need to be incorporated into the calculated health impact assessments.

The RIVM report illustrated that the public health burden related to unhealthy food is much higher than the public health burden related to unsafe food. A reflection from the audience is that the relation between the two in media is the opposite, focusing a lot more on the risks of food than on unhealthy dietary behaviour.

Another reflection regarding the RIVM results is that the risk of unsafe food has been drastically reduced, leaving the consumer to focus only on what choices are healthy, not on what choices are unsafe.

Géraldine Boué: Previous risk-benefit assessments of foods in Europe (abstract in appendix IV)

Géraldine Boué gave an overview of the principles of risk-benefit analysis and how the likelihood of adverse and beneficial health effects can be estimated from exposure to specified agents in food. She further presented a literature review of the entire RBA area made as part of her ongoing PhD-studies (Boué, Guillou et al. 2015). There are less than 100 published RBA and the main topic of study has been RBA of fish consumption, integrating nutritional compounds (e.g. fatty acids DHA and EPA), chemicals (e.g. methylmercury, dioxins, PCB), and microbiological hazards (*Listeria monocytogenes*). However, a majority of the articles had a focus on nutrients and chemicals. Trends over time (1992-2016) for RBA comparisons showed that comparisons using safety reference levels dominated, with less comparisons using common metric, and only few comparisons used composite metric (DALY or QALY).

Géraldine Boué highlighted the consideration of variability and uncertainty in future development of RBA procedures. There are also limitations in scientific knowledge regarding RBA, such as size of data set needed, epidemiological data, agent identification (nutrition), and chemistry (dose-response, cocktail effects). Géraldine Boué presented a list of potential applications, e.g. RBA case studies of interest, covering food and food components as well as agricultural and manufacturing practices. Finally, Géraldine Boué emphasized the important extension of results from RBA to risk-benefit communication, consumer risk-benefit perception and consumer trust.

Questions and comments to Géraldine Boué

The number of published risk-benefit assessments has continuously increased up to a point a few years ago. May this be due to lack of data, knowledge or may this be due to the extensive work load when making a risk-benefit assessment, resulting in a limited interest from the academia to perform research in this area?

Boué: Several of the projects in this area have been funded by European Union projects that ended recently. Another explanation may be that many studies have not been published in peer reviewed papers or have been published in another language than English. RBA is a multidisciplinary and complex area and to achieve funding in the future, effort has to be made to convince funders as well as experts of the necessity and feasibility of RBA.

How is selection of end-points for the risks and benefit assessments done when there are several possible endpoints?

Boué: The selection of endpoints and more precisely of “pair of hazard/endpoint” for the risks and benefits assessment is a crucial starting point. Firstly the particular food/diet and a population of interest must be defined. Then, all possible hazards/endpoints involved in the case study must be identified. At this stage, it is often not necessary or possible to conduct an RBA for all of them. Subsequently, a list of hazards/endpoints is selected for the RBA. “Risk ranking” methods can be used to prioritize hazards/endpoints according to their relevance, severity and to their weight of evidence in terms of causality. Certainly, the list of selected hazards/endpoints can evolve and the RBA can be refined or updated.

Maarten Nauta: The Consumer as risk and benefit manager: the need for quantification (abstract in appendix V).

The general objective in RBA is to compare food intake scenarios and select the one that will provide largest positive health effect for the population. In his presentation, Maarten Nauta proposed to consider a complementary consumer-oriented approach to RBA. He stated that it is important not only to communicate that one food intake scenario is to be preferred over another but also to show how large the difference in health effect between these scenarios is expected to be. Maarten Nauta used three examples to illustrate that consumers will gain from the application of quantitative health metrics when they receive advice on dietary choices. The examples were the choice between raw milk and pasteurized milk, red meat cooking practices and cancers, and processed meat and colorectal cancer. In the examples, Nauta showed how the risks could be illustrated as days lost in an individual’s life rather than years lost at population level. However, challenges of quantification may be that this approach is more time and resource demanding and data may not be sufficient for a full quantification. Nevertheless, since consumers can be regarded as risk-benefit managers they need an estimate of the size of the health effect to individually weigh the overall risks and benefits in decision making. Sometimes, it may be useful to quantify health effects even if the risk-benefit balance is clear from the scientific evidence, Maarten Nauta explained. In that way, the impact of dietary choices can be better communicated and explained to the consumers.

Questions and comments to Maarten Nauta

Although there may be a risk related to for example eating grilled meat, there may also psychologically be beneficial effects related to it.

Nauta: In the way risk assessments are currently done, it is only possible to lose quality of life, not gain. Still, this might be something we should consider in the future.

Should the risk assessment be adapted when presented to the risk-benefit managers?

Nauta: Assessments can be complicated, and it is the assessor's task to make the report comprehensive and possible for the managers to interpret.

How far are we from using risk benefit assessment methods in our everyday work?

Nauta: The methods are still under development, but we should not wait for a perfect method until we start applying it.

Conclusions from Introductory presentations

The following take home messages from the speakers to the workshop participants initiated the discussion:

Communication. The biggest challenge is conveying the message of the usefulness of RBA to other experts and to consumers. Consumers are not as prone to listen to experts as they used to be, there are many sources of nutrition information of which only a minor part is evidence based. We should prioritize to make experts, media and consumers aware that risk benefit assessments are enabling consumers to make appropriate food choices.

Collaboration. Most experts have a narrow field of expertise and complete their restricted part of an RBA, not sufficiently discussing the results together with others. Although cooperation between experts from different disciplines may be challenging, it is necessary to develop methods ant to achieve high quality RBA.

Result-oriented. We have to present results where RBA make a difference, in order to give the area more attention. One way forward could be to include cost into a risk benefit assessments for food.

The introductory presentations put our work with RBA in Nordic countries into a European context. Not many RBAs have been performed in Europe, despite Europe being one of the more active players in this field. Several EU projects have been undertaken, and the number of publications in the RBA area reached a peak when these projects were finalized. There is a need to inform managers and consumers about the complexity of risks and benefits associated with food, as well as how this complexity can be handled in RBA. In order to make informed choices, both managers and consumers need facts, and often explanatory figures. However, to quantify risks and benefits increases complexity and outcomes must be appropriately communicated. The uncertainties associated with quantitative RBA were highlighted, and the need for reducing uncertainties as well as to better describe them was noted.

2.2 Organisation of RBA in the Nordic countries

During this session of Nordic presentations Nils-Gunnar Ilbäck acted as moderator.

Norway (Inger Therese Laugsand Lillegaard, VKM)

Risk assessment, which is the responsibility of VKM, is performed in different scientific panels, similar to those of EFSA. The VKM, Vitenskapskomiteen for mattrygghet does risk assessment as well as risk and benefit assessment usually through mandates from the Norwegian Food Safety Authority (NFSA), Mattilsynet, even though self-tasking is also possible. The NFSA manages chemical and microbiological risks of food, but also the control of food safety and cosmetics. The two agencies receive mandates from several governmental ministries. The responsibility of dietary habits lies on the Norwegian Directorate of Health.

Iceland (Katrín Guðjónsdóttir, MAST)

The Icelandic Food and Veterinary Authority (MAST), Matvælastofnun, is the central competent authority responsible for official controls and control programs for food safety in Iceland, and can also commission risk assessments. MATÍS is an independent governmentally owned research company with experience and expertise to carry out conventional risk assessment of food as well as RBA.

Finland (Maria Rönnqvist, Evira)

Several ministries and governmental agencies are involved in risk benefit assessments. In most cases the risk management and the risk assessment is divided between Evira and the National Institute for Health and Welfare (THL), Terveystieteiden tutkimuskeskus. Evira covers the food safety area while the THL work in the area of human disease and nutrition. That the risk assessment and the risk management are located at separate departments, make the risk assessments independent.

Denmark (Morten Poulsen, DTU)

RBA:s of food in Denmark is performed at the Technical University of Denmark, DTU. The main commission of DTU is research and education, but also advisory activities. DTU is partly funded by the ministries; thereby DTU can support other governmental agencies in the area of food safety and nutrition. This organization of DTU makes the risk and benefit assessments independent from the risk management performed at the authorities. Research disciplines related to RBA of food may also be performed at other universities in Denmark.

Sweden (Hanna Eneroth, NFA)

Risk and benefit- assessment, management and communication take place at the National Food Agency, NFA, Livsmedelsverket, a government agency under the ministry of enterprise and innovation. Assessments are usually initiated by managers at the department of Advice and emergency preparedness or other departments at the NFA. Experts at the Risk-and Benefit Assessment Department perform the risk-benefit assessment and act independently of the risk managers. Epidemiologists at IMM at Karolinska Institute (KI) also work with risks and benefits associated with food consumption.

Conclusions from the presentations of the Nordic organizations

The organization of assessors and managers of risk and benefit differs widely among the Nordic countries. Knowing about the differences in organization among the Nordic countries is a pre-requisite for future collaboration in projects. Thus, the short presentations of the organizations were appreciated by the workshop participants.

2.3 RBA activities in the Nordic countries

During this session of presentations of RBA activities in the Nordic countries Stina Wallin, NFA moderated the first two presentations (Norway and Iceland) and Anders Glynn, NFA the remaining three presentations (Finland, Denmark and Sweden).

Norway (Inger Therese Laugsand Lillegaard, VKM)

Disagreement between dietary guidelines on fish and VKM recommendations led to a request from NFSA to review the risks and benefits of fish and fish products (VKM 2014). The advice on fish consumption is specified as an interval from 1-2 dinner servings per week up to 3-4 dinner servings per week. Replacement of fish oil and fish protein with plant proteins and vegetable oils in farmed salmon feed has led to lower levels of dioxins, dioxin-like PCBs and mercury in farmed salmon than in wild fatty fish. VKM concludes that the benefits clearly outweigh the risk in terms of the current levels of the contaminants and other known undesirable substances in fish on the Norwegian market. The conclusions of the updated assessment led to removing the advice on specific amount of fatty fish consumption during childhood and pregnancy.

In 2013, the VKM published a RBA of breast milk for infant health (VKM 2013). Benefits were based on meta-analyses and reviews, while a systematic literature review was undertaken to identify potential risks, for example halogenated organic pollutants, heavy metals and pesticide residues. Methodological challenges included to disentangle the exclusive effect of breast milk on child health outcome, the use of different endpoints in the studies, confounders and exclusion criteria. The conclusion of the RBA was that the benefits associated with breast milk clearly outweigh the risk presented by current levels of contaminants in breast milk.

The most recent RBA at the VKM concerns benefits and risks associated with increasing potassium by replacement of sodium chloride (VKM 2014). While the general population may benefit from reduced sodium intakes, leading to estimated reduction in number of cases of stroke, kidney failure may be an adverse effect of increased potassium in the diet. VKM concludes that it is reasonable to anticipate that the percentage of population likely to face an increased risk is far greater than the percentage of population likely to benefit from the increased use of potassium chloride in foods as a substitute for sodium chloride.

Methods, evidence, uncertainties and expert judgement differ a lot between different disciplines and Inger Therese concluded her presentation by wishing that rather than being on

different planets, we should strive to be like apples and pears, at least they are in the same food group.

Iceland (Helga Gunnlaugsdóttir, MATÍS)

Risk benefit assessments have not been performed by Icelandic authorities but the staff of MATÍS has been involved in several EU projects on the topic. Helga Gunnlaugsdóttir, research group leader at MATÍS described the FP6 EU project QALIBRA (Hart, Hoekstra et al. 2013).

The QALIBRA project focused on the impact of dietary choices on health and the project group carried out comprehensive risk-benefit analyses for selected food groups including fatty fish and functional foods. The outcome of QALIBRA were methods for quantitative assessment that integrate the risks and benefits of dietary change into a single measure of net health impact, and allow quantification of associated uncertainties. These methods were implemented in the QALIBRA software, which is freely available at www.qalibra.eu. It was concluded in the BRAFO project that it is only necessary to refine the assessment as far as needed to reach a decision (Boobis, Chiodini et al. 2013). Thus, quantitative approaches such as QALIBRA are needed when there is some risk and some benefits but neither clearly dominate.

QALIBRA uses the “directly attributable health loss” developed at RIVM (National Institute for Public Health and the Environment (RIVM) 2006). The output is the sum of the DALY impact of diseases incurred or avoided by the population in a single year and should be interpreted as an indication of the potential average annual health impact of a long term dietary change. The associated uncertainty should be characterized and communicated to risk managers. Data on population, intakes, dose-response, probabilities of recovery and mortality, disease weights, durations and life expectancy is needed. However, assumptions can be made when all data is not available. The QALIBRA software has been available since 2009. There are no statistics on the number of users of the tool. It is currently administered and maintained by the UK Food and Environment Research Agency (FERA).

Finland (Maria Rönnqvist, Evira)

At Evira, a risk benefit assessment of Baltic herring was made in 2013-2014 (Evira 2015). Results were presented as DALYs. The conclusions were that benefits with n-3-fish fatty acids and vitamin D by far exceeded the risks of dioxins and PCBs in age groups above 50 years, and that consumption according to the recommendations were beneficial also for children and pregnant women. It was concluded that the Finnish recommendations were appropriate.

Some of the challenges with RBA identified in Finland are: 1) lack of analytical results from foods, 2) difficulties to single out effects of a certain component, 3) large uncertainties or lack of data on several parameters 4) the difference in consumption in different population groups and 5) difficulties to estimate cumulative effects of substances in foods.

Maria Rönnqvist also reported on an ongoing project about risk assessment and cost benefit analysis of salmonella in feed. Evira is planning for a risk-benefit assessment of edible seeds,

a burden of disease project and a project on common methods for ranking chemical and microbiological risks (together with NFA, Sweden).

Denmark (Morten Poulsen, DTU)

In Denmark, RBA of food is a relatively new discipline and is primarily carried out at DTU Food. In 2015 DTU Food, Fødevareinstituttet was reorganized and the Research Group for Risk-Benefit was established. A major external funding source for the research group is the Metrix project funded by the Danish National Food Authority. Morten Poulsen described the Metrix project which is focused on quantitative health assessment of foods and diets. The primary objectives are to develop new and improved ways of performing risk-benefit assessments, to estimate burden of food associated diseases and to rank risks and benefits of food. An additional aim is to estimate the economic impact of food-associated diseases, risk factors and interventions. The work within the Metrix project builds upon the methods and modelling frameworks developed in former EU-projects. Furthermore, Morten Poulsen presented the challenges within RBA that DTU believes should be further addressed: 1) the concept of risk-benefit, 2) tiered approaches, 3) uncertainty and data gaps, 4) RBA of whole diets, 5) to find the optimal scenario, 6) variability, and 7) top down approach versus bottom up approach (starting the assessment by the use of human epidemiological data down to the food, or starting with the food and go up to the human health risk using a risk assessment approach).

Heddie Mejborn gave an example of risk-benefit assessment of nuts performed in 2013 (DTU and Fødevareinstituttet 2015). The conclusions were that there is a net health gain of consuming 30 gram nuts per day, despite risks associated with aflatoxin produced by mould on nuts and that the cancer potency factor overestimates the risks of nuts. Health gain, expressed in DALYs depends on type of nuts, where the lowest health gain was estimated from consumption of Brazil nuts.

Helle Korsgaard presented a risk ranking study of vegetables and fruits where 115 product-pathogen combinations were scored (DTU and Fødevareinstituttet 2015). Some of the higher ranked combinations such as lettuce-salmonella and berries-norovirus were well known, while other combinations for example melon- salmonella were unexpectedly highly ranked. She concluded that we have to be observant to identify new risks of food-borne infections associated with trends in consumption and the globalization.

Sweden (Hanna Eneroth)

At NFA, previous work with RBA includes herring and salmonid fish from the Baltic Sea (NFA 2013), nitrate and sodium in processed meat at reduced storage temperature (NFA 2014) and increased nut consumption (NFA 2014). Hanna Eneroth described a project at the risk and benefit assessment department, initiated in 2012 with the aim to develop an in-house working procedure for RBA (National Food Agency 2014). This process of compiling a working procedure for RBA, using the EFSA Scientific opinion as a starting point (EFSA Scientific Committee 2010), increased the understanding among experts with a background in different disciplines. Although only a few full RBAs have been carried out at NFA, a way of working where both risks- and benefits are taken into account when evaluating and

communicating nutrition and food safety issues has evolved. Perceived challenges are: 1) time and resources for the holistic approach represented by a RBA versus the needs from risk managers to answer acute questions, 2) Knowledge base differs between disciplines (for example epidemiological evidence in nutrition versus extrapolations from animal studies in toxicology), 3) Methodology for common metrics, 4) Data gaps and estimation of uncertainties and 5) Risk-benefit communication, including the communication of uncertainties. In an ongoing collaboration, the NFA and Karolinska Institute are developing the assessments of benefits and risks of nut consumption.

Professor Agneta Åkesson, Institute of Environmental Health, Karolinska Institute reflected on how risks and benefits are identified in epidemiological data. For example, the intake of long chain-n3-fish fatty acids was not associated with myocardial infarction (MI) unless dietary PCB exposure was taken into account in two large cohorts of Swedish women and men. Thus, in mutually adjusted data, dietary PCB exposure was associated with 60-70% increased risk of MI, while the intake of long chain-n3-fish fatty acids was associated with lower risk of MI (Bergkvist, Berglund et al. 2015; Bergkvist, Berglund et al. 2016). Very similar results were obtained for stroke (Bergkvist, Kippler et al. 2014; Kippler, Larsson et al. 2016) with the strongest association observed for hemorrhagic stroke. These results demonstrate that the beneficial effects of long chain-n3-fish fatty acids were only apparent when the negative effect of PCB was accounted for. These results were complemented with a study where the association between fish consumption and all-cause and CVD mortality was assessed. A U-shaped association was observed where both low and high consumption of fish, especially fatty fish, was associated with higher mortality (Bellavia, Larsson et al. 2016).

Conclusions from RBA activities in Nordic countries

Several risk-and benefit assessments have been performed in the Nordic countries, most common examples are RBAs of fish. The RBAs were performed on the initiative of risk managers or were undertaken on risk benefit assessors own initiative to develop the methodology of RBA. In Denmark, DALYs have been used as a common metric to weigh risks and benefits to a larger extent than in the other countries. The challenges identified with RBA shared some common features: collaboration across different disciplines with different base of evidence, data gaps and quality of data and needs to develop methodology are perceived as challenging by all countries.

3. Group discussions on future Nordic collaboration

Before the workshop, participants received three key questions for group discussions.

1. Future RBA -What are the topics of risk-benefit assessments we see in the future?
2. Methodology needs -What are the methodological issues we need to work with in order to perform good quality risk-benefit assessments?
3. Nordic collaboration -How can we collaborate on risk benefit assessments in the Nordic countries?

During the coffee breaks of day 1 and 2, all workshop participants were asked to put their ideas on three boards, one board for each key question. Participants were divided into three groups, each group responsible for one key question (Appendix VII). On the second day, the three groups took one board each with its key question, discussed the questions and ranked the topics in terms of relevance for Nordic collaboration.

Group 1: Future RBA - What are the topics of risk-benefit assessments we see in the future

This group assigned the topics into high, medium and low priority according to the relevance for the Nordic population, urgency, and data and method availability. Anders Glynn was the rapporteur for the group.

High priority

- *Whole grain foods* – Of large public health interest and recommended by Nordic food authorities, issue of higher levels cadmium and arsenic being found in whole grain foods than in refined foods, health effects on children not clear, data is probably available, of specific Nordic interest as intakes are high.
- *Iodine* – An increased awareness of potentially low intakes in the Nordic countries while high concentrations are found in for example algae products. There is ongoing biomonitoring and other activities in the Norjod project (Nystrom, Brantsaeter et al. 2016).
- *Pulses/legumes* – recommended by Nordic food authorities, risks associated with anti-nutrients such as lectines, although they are mainly associated with preparation of pulses. The group expressed an interest to assess health effects of pulses as an alternative to red meat.
- *Vegetable oils/margarine* – Recommended by Nordic food authorities and widely used. Consumers are concerned with risks of for example food additives in margarines. The presence of the process contaminant 3-MCPD is currently investigated in Sweden. There is an ongoing assessment of vegetable oils in Denmark.

- *Eggs organic versus conventional* – Ongoing Swedish assessment show higher dioxin levels in organic than in conventional eggs. Eggs are nutritious in many aspects but difficult to assess in dietary assessment and not easy to assess substitution by other foods. There is a possible microbiological risk if for example the eggs are in contact with soil or if the hens are kept outside. There was a discussion if this RBA could also contain aspects on sustainability and organic food in general.
- *Herbal teas* – claimed beneficial health effects versus natural plant toxins

Medium priority

- *Gluten-free diet* – lack of data
- *Folate* - already performed in Dutch project (Hoekstra, Verkaik-Kloosterman et al. 2008)
- *Fish oil* –too specialized
- *Coffee and tea* – too broad
- *Whole crab* – too specialized
- *Nitrate/nitrite in vegetables* – lack of data
- *Low carbohydrate diet*– too broad and DTU have ongoing activities

Low priority

- *Raw vs. pasteurized milk* – limited interest
- *Insects as food* – lack of data
- *Apples and pears, with or without peeling* – too specific
- *Ready-to-eat food vs. home-prepared food* -lack of data
- *Nuts* –ongoing activities

The following suggestions were not prioritized as the suggestions were thought to be too broad, and thus difficult to address in a constructive way:

- *Food supplements,*
- *Natural toxins in vegetables and fruit,*
- *Matrix effects* (for example differential effects between vitamins from fruit and vegetables and from food supplements).

The presentation was followed by a discussion on whether a joint project should be one that meets the need of managers in a topic of high public health relevance, or on a very specific topic mainly with the aim to develop methodology. In either case, the project must not be too extensive or complex and data has to be available. Whichever topic is chosen, the first step is to formulate a clearly defined risk-benefit question.

Group 2 Methodology needs- What are the methodological issues we need to work with in order to perform good quality risk-benefit assessments?

Anna Karin Lindroos was rapporteur for the group. The group found it difficult to prioritize based on the criteria given, but presented suggestions grouped into different themes:

- *Problem formulation*, including how to formulate good questions, the matrix problem with substance versus food (for example caffeine versus coffee) was discussed.
- *Different types of studies* for example epidemiological and animal studies-how can they be used and combined in the RBA? Are we overestimating the risk when using animal studies?
- *Identify and communicate data gaps*. The communication of ongoing and finished national projects between countries requires connections and routines for sharing data and reports.
- *Assumptions* must be clear and transparent in an RBA.
- *Other methodological challenges* includes how to work with risk-ranking, how to deal with uncertainties, and weight of evidence. How to deal with whole diets and substitution issues and how to deal with population mean versus personalized diets was also briefly mentioned

Group 3 Nordic collaboration – How can we collaborate on risk-benefit assessments in the Nordic countries?

Rapporteurs for this group were Per Bergman and Morten Poulsen. Ways to improve collaboration may be through improved awareness of the importance of RBA and by that increase possibilities for obtaining funding at different levels:

- At national level, risk assessors should approach risk managers to inform them about RBA and illustrate the possibilities. This could lead to an increase in mandates/questions relevant to public health.
- At Nordic level, we should continue to approach NKMT for funding of RBA projects. The possibilities to apply for funds from NordForsk should be investigated.
- At European level we should work to get RBA as a topic into Horizon 2020, and try to influence relevant work programs and joint EU projects on the topic.

The group suggested the following mechanisms to increase collaboration:

- A small group responsible for taking this initiative further should be appointed at this workshop. This group can plan for meetings and projects. One application for preparing a follow up meeting and one application for a specific project was discussed.
- One contact person per country to send and receive information to a network would increase communication to avoid similar projects in parallel without collaboration.

- Actively involve experts from other Nordic countries as partners when planning research.

The group discussed further how to decide on joint projects:

- A joint project on risk ranking was suggested because it is the first stage of RBA and it will set the needs for RBA in context and produce a time frame for upcoming projects.
- In joint projects on risk and benefit assessment with self-defined scope and resources, the aspect of communication must be included.
- In a joint effort, data from different countries can be combined and data gaps identified. The lack of data in certain areas could then be communicated to funding agencies and researchers.
- Prioritize the suggested RBAs based for instance on ongoing national activities and possibility of funding.

Conclusions of group discussions of the three key questions

The meeting appointed the following persons to be the Nordic Risk-Benefit group: Morten Poulsen, Denmark, Inger Therese L Lillegaard, Norway, Helga Gunnlaugsdóttir, Iceland, Maria Rönnqvist, Finland and Hanna Eneroth, Sweden. This group will finalize a report from this workshop and continue to work on activities to increase Nordic collaboration.

4. Summary and conclusions

The interest to participate in this NKMT financed workshop was large from the start. All Nordic countries were represented and there was a general view that this workshop has opened up for new possibilities for networking and continued collaboration between the Nordic countries.

The participants were enthusiastic about the future possibilities of RBA to serve as scientific basis on what healthy foods are. The workshop illustrated how important RBA is to assist professional managers as well as consumers in making the best choices on what to eat. Risk benefit assessors of different disciplines, managers and communicators need to work together to achieve this goal. This workshop gave participants an overview on what has been done in the field of RBA in the Nordic countries and in Europe. RBA-projects tend to be resource demanding, and there are many methodological challenges. Participants expressed their interest to develop the area of RBA further in collaboration with colleagues in the Nordic countries and to harmonize the approaches to RBA within the Nordic region.

The first result of the workshop was the establishment of a Nordic Risk Benefit group, with members from all Nordic countries. Besides reporting the outcome of this workshop, this group will explore the possibilities for a future collaborative project, including the possibilities for NKMT based funding.

To sum up the workshop, Hanna Eneroth and Nils-Gunnar Ilbäck concluded that it is the commitment of the participants, that make a workshop successful and during these two days everyone actively contributed. Per Bergman closed the workshop by thanking the participants and the organizers of the workshop.

5. References

- Bellavia, A., S. C. Larsson, et al. (2016). "Fish consumption and all-cause mortality in a cohort of Swedish men and women." *J Intern Med*.
- Bergkvist, C., M. Berglund, et al. (2016). "Dietary exposure to polychlorinated biphenyls and risk of myocardial infarction in men - A population-based prospective cohort study." *Environ Int* 88: 9-14.
- Bergkvist, C., M. Berglund, et al. (2015). "Dietary exposure to polychlorinated biphenyls and risk of myocardial infarction - a population-based prospective cohort study." *Int J Cardiol* 183: 242-248.
- Bergkvist, C., M. Kippler, et al. (2014). "Dietary exposure to polychlorinated biphenyls is associated with increased risk of stroke in women." *J Intern Med* 276(3): 248-259.
- Boobis, A., A. Chiodini, et al. (2013). "Critical appraisal of the assessment of benefits and risks for foods, 'BRAFO Consensus Working Group'." *Food Chem Toxicol* 55: 659-675.
- Boué, G., S. Guillou, et al. (2015). "Public Health Risk-benefit Assessment Associated with Food Consumption—A Review." *European Journal of Nutrition & Food Safety* 5(1 (January-March)): 32-58.
- DTU and Fødevareinstituttet (2015). Helhetssyn på nødder -en risk-benefit vurdering (Risk benefit assessment of nuts).
- DTU and Fødevareinstituttet (2015). Risikorangering af sygdomsfremkaldende mikroorganismer i frisk frugt og grønt. Frugt og grønt indsatser 2013-2016.
- EFSA Scientific Committee (2010). "Guidance on human health Risk-benefit assessment of foods." *EFSA Journal* 8(7).
- Evira (2015). Itämeren silakka ravintona – Hyöty-haitta-analyysi (Benefit- risk assessment of Baltic herring).
- Hart, A., J. Hoekstra, et al. (2013). "Qalibra: a general model for food risk-benefit assessment that quantifies variability and uncertainty." *Food Chem Toxicol* 54: 4-17.
- Hoekstra, J., J. Verkaik-Kloosterman, et al. (2008). "Integrated risk-benefit analyses: method development with folic acid as example." *Food Chem Toxicol* 46(3): 893-909.
- Kippler, M., S. C. Larsson, et al. (2016). "Associations of dietary polychlorinated biphenyls and long-chain omega-3 fatty acids with stroke risk." *Environ Int* 94: 706-711.
- National Food Agency (2014). A review of risk and benefit assessment procedures -development of a procedure applicable for practical use at NFA. Report 24/2014. Uppsala, Sweden, National Food Agency (NFA).
- National Institute for Public Health and the Environment (RIVM) (2006). Our food, our health. Healthy diet and safe food in the Netherlands. Bilthoven, The Netherlands, National Institute for Public Health and the Environment (RIVM).
- NFA (2013). Risk and Benefit assessment of Herring and Salmonid Fish from the Baltic Sea Area. Rapport 21-2013. Uppsala, Sweden, Livsmedelsverket.

NFA (2014). Risk- och nyttovärdering av nötter –sammanställning av hälsoeffekter av nötkonsumtion (Risk- benefit assessment of nuts, summary of health effects of nut consumption). Rapport 16-2014. Uppsala, Sweden, Livsmedelsverket.

NFA (2014). Risk- och nyttovärdering av sänkt halt av nitrit och koksalt i charkuteriprodukter i samband med sänkt temperatur i kylkedjan (Risk- and benefit assessment of reduced nitrate and sodium in processed meat at reduced storage temperature). Rapport 13-2014. Uppsala, Sweden, Livsmedelsverket.

Nyström, H. F., A. L. Brantsaeter, et al. (2016). "Iodine status in the Nordic countries - past and present." Food Nutr Res 60: 31969.

VKM (2013). Benefit and risk assessment of breastmilk for infant health in Norway. Opinion of the Norwegian Scientific Committee for Food Safety.

VKM (2014). Benefit-risk assessment of fish and fish products in the Norwegian diet - an update. Opinion of the Norwegian Scientific Committee for Food Safety. VKM Report 2014: 15

VKM (2014). Benefit and risk assessment of increasing potassium by replacement of sodium chloride with potassium chloride in industrial food production. Opinion of the Scientific Steering Committee.

Appendix I, Programme

Thursday 22 September, Radisson Blu, Stationsgatan 4, Uppsala.

8.30	Registration	
9.00	Welcome	Per Bergman, NFA
9.15	Risk-benefit assessment (RBA) of foods in a European perspective	Hans Verhagen, EFSA
10.30	<i>Coffee/tea</i>	
10.50	Previous risk-benefit assessments of foods in Europe	Géraldine Boué, ONIRIS-INRA, France
11.30	The consumer as risk and benefit manager: the need for quantification	Maarten Nauta, DTU
12.15	Discussion of morning presentations	Leif Busk, NFA
12.30	<i>LUNCH</i>	
13.45	Introduction to workshop	Hanna Eneroth, Nils-Gunnar Ilbäck, NFA
14.00	Where are RBA performed in Nordic countries? Presentation of participants.	
15.30	<i>Coffee/tea</i> and post it exercise key question 1+2	
16.00	RBA in Norway	Inger Therese L Lillegaard and colleagues
16.45-17.15	RBA in Iceland	Helga Gunnlaugsdóttir
18.00	<i>Guided walk in Uppsala followed by dinner at restaurant Basilico</i>	

Friday 23 September

8.30	RBA in Finland	Maria Rönnqvist
9.00	RBA in Denmark	Morten Poulsen and colleagues
9.45	<i>Coffee/tea</i> and post it exercise key question 3	
10.15	RBA in Sweden	Hanna Eneroth and colleagues
11.00	Group discussions questions 1-3	
12.00	<i>LUNCH</i>	
13.15	Presentations from groups +discussion	All groups, moderated by Hanna and Nils-Gunnar
14.45-15.00	Summary and way forward	Hanna, Nils-Gunnar

Appendix II, Participants

<i>Surname</i>	<i>First Name</i>	<i>Representing</i>
Andersen	Rikke	Denmark Technical University
Aspenström Fagerlund*	Bitte	National Food Agency, Sweden
Bergman	Per	National Food Agency, Sweden
Bjerselius*	Rickard	National Food Agency, Sweden
Boué	Geraldine	ONIRIS-INRA, France
Busk*	Leif	National Food Agency, Sweden
Darnerud	Per Ola	National Food Agency, Sweden
Egevärn*	Mia	National Food Agency, Sweden
Eneroth	Hanna	National Food Agency, Sweden
Glynn	Anders	National Food Agency, Sweden
Guðjónsdóttir	Katrin	Iceland Food and Veterinary Authority
Gunnlaugsdóttir	Helga	MATiS, Iceland
Gyllenhammar*	Irina	National Food Agency, Sweden
Halldin Ankarberg	Emma	National Food Agency, Sweden
Hallström*	Helena	National Food Agency, Sweden
Ilbäck	Nils-Gunnar	National Food Agency, Sweden
Jemtland	Rune	Norwegian Food Safety Authority
Korsgaard	Helle	Denmark Technical University
Laugsand Lillegaard	Inger Therese	Norwegian Scientific Committee for Food Safety
Lindqvist	Roland	National Food Agency, Sweden
Lindroos	Anna Karin	National Food Agency, Sweden
Mangschou	Bente	Norwegian Scientific Committee for Food Safety
Mathisen	Gro	Norwegian Scientific Committee for Food Safety
Mattisson*	Irene	National Food Agency, Sweden
Mejborn	Heddie	Denmark Technical University
Nauta	Maarten	Denmark Technical University
Moraeus*	Lotta	National Food Agency, Sweden
Nälsén*	Cecilia	National Food Agency, Sweden
Poulsen	Morten	Denmark Technical University
Rosseland	Carola	Norwegian Scientific Committee for Food Safety
Rönnqvist	Maria	Evira, Finland
Sand	Salomon	National Food Agency, Sweden
Svanström*	Åsa	National Food Agency, Sweden
Säve-Söderbergh	Melle	National Food Agency, Sweden
Tesdal Håland	Julie	Norwegian Food Safety Authority
Wallin	Stina	National Food Agency, Sweden
Verhagen	Hans	EFSA
Widenfalk*	Anneli	National Food Agency, Sweden
Åkesson	Agnetta	Karolinska Institutet, Sweden

*Participate only on September 22 th before lunch

Appendix III, Literature

Scientific papers

- Berjia F.L., Hoekstra J., Verhagen H., Poulsen M., Andersen R., Nauta M. (2014). Finding the Optimum Scenario in Risk-benefit Assessment: An Example on Vitamin D. *European Journal of Nutrition & Food Safety*: 4(4): 558-576.
- Boobis, A., A. Chiodini, J. Hoekstra, P. Lagiou, H. Przyrembel, J. Schlatter, K. Schutte, H. Verhagen and B. Watzl (2013). "Critical appraisal of the assessment of benefits and risks for foods, 'BRAFO Consensus Working Group'." *Food Chem Toxicol* 55: 659-675.
- Hart, A., Hoekstra, J., Owen, H., Kennedy, M., Zeilmaker, M.J., Jong, N. de, Gunnlaugsdottir, H. (2013), Qalibra: A general model for food risk–benefit assessment that quantifies variability and uncertainty. *Food and Chemical Toxicology*. 54(4): 4-17
- Hendriksen MA, Tijhuis MJ, Fransen HP, Verhagen H, Hoekstra J. (2010). Impact of substituting added sugar in carbonated soft drinks by intense sweeteners in young adults in the Netherlands: example of a benefit-risk approach. *Eur J Nutr*. 50 :41-51
- Hoekstra, J.; Fransen, H.P.; van Eijkeren, J.C.H.; et al. Benefit-risk assessment of plant sterols in margarine: A QALIBRA case study. *Food and Chemical Toxicology* 54(4): 35-42
- Hoekstra, J., Hart, A., Owen, H., Zeilmaker, M., Bokkers, B., Thorgilsson, B., Gunnlaugsdóttir, H. (2013) Fish, contaminants and human health: Quantifying and weighing benefits and risks. *Food and Chemical Toxicology* 54(4): 18-29
- Hoekstra J., Verkaik-Kloosterman J., Rompelberg C., van Kranen H., Zeilmaker M., Verhagen H, de Jong N. (2008). Integrated risk–benefit analyses: Method development with folic acid as example. *Food Chem. Tox.* 46: 893-909.
- Husøy, T., et al Reducing added sugar intake in Norway by replacing sugar sweetened beverages with beverages containing intense sweeteners – a risk benefit assessment. *Food Chem Toxicol*, 2008. 46 (9): p. 3099-105
- de Jong, N.; Verkaik-Kloosterman, J.; Verhagen, H.; et al. An appeal for the presentation of detailed human derived data for dose-response calculations in nutritional science *Food and Chemical Toxicology* 54(4): 43-49
- Renwick A.G., Flynn A., Fletcher R.J., Müller D.J.G., Tuijelaars S., Verhagen H. (2004). Risk-Benefit analysis of micronutrients. *Food and Chemical Toxicology* 42: 1903-1922.
- Tijhuis M.J., de Jong N., Pohjola M.V., Gunnlaugsdottir H., Hendriksen M., Hoekstra J., Holm F., Kalogeras N., Leino O., van Leeuwen R., Luteijn J.M., Magnusson S.H., Odekerken G., Rompelberg C., Tuomisto J.T., Ueland O., White B.C., Verhagen H. (2012). State of the Art in Benefit-Risk Analysis: Food and Nutrition *Food and Chemical Toxicology* 50: 5-25.
- Tijhuis MJ, Pohjola MV, Gunnlaugsdóttir H, Kalogeras N, Leino O, Luteijn JM, Magnússon SH, Odekerken-Schröder G, Poto M, Tuomisto JT, Ueland O, White BC, Holm F, Verhagen H. (2012). Looking beyond borders: Integrating best practices in benefit-risk analysis into the field of Food and Nutrition. *Food and Chemical Toxicology* 50: 77-93.

Ueland O., Gunnlaugsdottir H., Holm F., Kalogeras N., Leino O., Luteijn J.M., Magnusson S.H., Odekerken G., Pohjola M.V., Tjshuis M.J., Tuomisto J.T., White B.C., Verhagen H. (2012). State of the Art in Benefit-Risk Analysis: Consumer Perception . *Food and Chemical Toxicology* 50: 67-76.

Zeilmaker, M.J., Hoekstra, J., van Eijkeren, J. C.H., de Jong, N., Kennedy, M., Owen, H., Hart, A., Gunnlaugsdottir, H. (2013) Fish consumption during child bearing age: A quantitative risk-benefit analysis on neurodevelopment. *Food and Chemical Toxicology* 54(4): 30-34

Reports ("Grey literature")

DTU and Fødevareinstituttet, 2015 Helhetssyn på nødder -en risk-benefit vurdering.

http://orbit.dtu.dk/files/116492285/N_dderapporten.pdf

Evira, 2015 Benefit- risk assessment of Baltic herring

<https://www.evira.fi/globalassets/tietoa-evirasta/julkaisut/julkaisusarjat/elintarvikkeet/itameren-silakka-ravintona--hyoty-haitta-analyysi.pdf>

Livsmedelsverket 2014, Risk- och nyttovärdering av nötter sammanställning av hälsoeffekter av nötkonsumtion. Rapport 16-2014.

http://www.livsmedelsverket.se/globalassets/rapporter/2014/2014_livsmedelsverket_16_risk_nyttovar_dering_notter.pdf

A review of Risk and Benefit Assessment procedures- development of a procedure applicable for practical use at NFA. Rapport 24-2014.

http://www.livsmedelsverket.se/globalassets/rapporter/2014/2014_livsmedelsverket_24_risk_benefit_assessment_procedures.pdf

Livsmedelsverket 2014, Risk- och nyttovärdering av sänkt halt av nitrit och koksalt i charkuteriprodukter i samband med sänkt temperatur i kylkedjan. Rapport 13-2014.

http://www.livsmedelsverket.se/globalassets/rapporter/2014/2014_livsmedelsverket_13_risk_nytta_nitrit_koksalt_chark.pdf

VKM, 2014. Benefit and risk assessment of increasing potassium by replacement of sodium chloride with potassium chloride in industrial food production. Opinion of the Scientific Steering Committee.

<http://www.vkm.no/dav/b186a12b17.pdf>

VKM 2014. Benefit-risk assessment of fish and fish products in the Norwegian diet - an update.

Opinion of the Norwegian Scientific Committee for Food Safety. VKM Report 2014: 15

<http://www.vkm.no/dav/0a646edc5e.pdf>

VKM, 2013, Benefit and risk assessment of breastmilk for infant health in Norway. Opinion of the Norwegian Scientific Committee for Food Safety. <http://www.vkm.no/dav/820a1a0bf8.pdf>

Livsmedelsverket 2013, Risk and Benefit assessment of Herring and Salmonid Fish from the Baltic Sea Area. Rapport 21-2013

http://www.livsmedelsverket.se/globalassets/rapporter/2013/2013_livsmedelsverket_21_risk_benefit_herring_salmonid_fish_ver2.pdf?id=4013

Livsmedelsverket 2007, Risks and Benefits of Fish Consumption. A Risk-Benefit Analysis Based on the Occurrence of Dioxin/PCB, Methyl Mercury, n-3 Fatty Acids and Vitamin D in Fish. Rapport 12-2007.

http://www.livsmedelsverket.se/globalassets/rapporter/2007/2007_12_risks_and_benefits_of_fish_consumption.pdf

Fødevaredirektoratet 2003, Helhedssyn på fisk og fiskevarer.

<https://www.foedevarestyrelsen.dk/Publikationer/Alle%20publikationer/2003017.pdf>

Appendix IV

Nordic Risk-Benefit Assessment Workshop

Summary of presentation and literature recommendation
22-23 September 2016
Uppsala, Sweden

Hans Verhagen

European Food Safety Authority (EFSA)
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43126 Parma - Italy

Risk-benefit assessment of foods in a European perspective

Risk-taking is normal in everyday life if there are associated (perceived) benefits such as self-improvement, emotional engagement, and control. Food and nutrition are essential for life. The benefit of foods is, first and foremost, to provide nutrition. Additional potential health benefits are associated with nutrition and health claims. These are currently managed under EU Regulation 1924/2006, for which EFSA evaluates the scientific substantiation (Verhagen & van Loveren, 2016). Food contains many ingredients: macronutrients, micronutrients and non-nutrients. Non-nutrients are either contaminants, natural toxins or other substances, some of which are claimed to have beneficial effects. Food placed on the market is assumed to be safe if correctly handled, and many laws are in place to secure the safety of food in the EU. Risk-benefit analysis, also for food safety and nutrition, is the comparison of the risk to its related benefits.

Thus, on the one hand, food contains necessary and beneficial ingredients, whereas, on the other hand, all ingredients are potentially adverse (the dose makes the toxin...). Moreover, food and food ingredients may be both beneficial as well as adverse. For example, vitamins and minerals are necessary micronutrients for which Dietary Reference Values are set (<https://www.efsa.europa.eu/en/topics/topic/drv>). However, too high levels of intake could result in adverse effects; therefore maximum safe levels (tolerable upper intake levels) have been established (<http://www.efsa.europa.eu/en/scdocs/oldsc/ndaintakevitaminsminerals.htm>).

Risk-benefit analysis is a relatively new aspect in the area of food safety and nutrition. In this new field, it is important to realise the opposing starting points. Risk assessment for food safety is typically done by toxicologists, who start from dose levels with clear (adverse) effects down to doses that are without effect (from lowest observed adverse effect levels to no observed adverse effect levels), to which additional safety/uncertainty factors are applied to achieve safe levels for human exposure, i.e. intake levels that are essentially *without effect*. In contrast, benefit assessment for nutrition is typically done by nutritionists/epidemiologists, who work with dose levels with clear (beneficial) effects (e.g. minimal effective doses, scientific substantiation of health claims), i.e. intake levels that are essentially *with effect*. Risk-benefit assessment envisages expressing both risks and benefits of foods and food ingredients into one currency, thereby allowing for a qualitative and also quantitative comparison of health impact assessments of adverse and beneficial effects.

A risk-benefit assessment can help policy-makers to make informed risk management decisions. The risk-benefit manager may weigh the benefits versus the risks in a balanced way. In Europe, recently several major projects were concluded to explore the area of risk-benefit analysis for food and nutrition. All of these projects were developing methods and approaches to qualitatively and quantitatively compare risks and benefits, including by the European Food Safety Authority (EFSA 2010; overview in Verhagen et al. 2012). In general, for a risk-benefit comparison at least two scenarios need to be identified. For practical reasons it is advisable to perform a risk-benefit in a tiered approach and stop the assessment once sufficient information is available to weigh the one scenario versus the other. The approaches developed have been validated in a series of test cases reported as part of or alongside those projects.

In the debates around risk-benefit assessment of food safety and nutrition several considerations are important. From a theoretical point of view, risk-benefit assessments may actually better be considered as comparing one risk with another risk rather than with a benefit (risk-risk comparisons). This is widely illustrated by the 2006-RIVM report ‘Our Food Our Health’ (http://www.rivm.nl/en/Documents_and_publications/Scientific/Reports/2006/mei/Our_food_our_health_Healthy_diet_and_safe_food_in_the_Netherlands; translated into English with support from EFSA). This huge work was in essence a comparison of public health burden estimates of food safety issues versus (un)healthy nutrition, indicating that the public health burden of unhealthy dietary behaviour (eating too much and eating wrong) outweighs by far the public health burden coming from food safety topics. More recently, the WHO published another estimate of the ranking the global burden of foodborne diseases (http://www.who.int/foodsafety/areas_work/foodborne-diseases/ferg/en/). And also EFSA published on the development of a risk-ranking toolbox (<http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2012.2724/epdf>, <http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2015.3939/epdf>) and procured an overview of methodology and application of risk-ranking for prioritisation of food and feed related issues on the basis of the size of anticipated health impact (<http://onlinelibrary.wiley.com/doi/10.2903/sp.efsa.2015.EN-710/pdf>).

When taking risk-benefit further, there are ample scientific and other opportunities and challenges. Alongside, the development of approaches and entering new test cases, also the developments in science in the area of food safety risk assessment merit attention. To this end EFSA recently started exploring topics such as Uncertainty, Weight-of-Evidence, and Biological Relevance, all contributing to refinement of scientific risk assessment (Hardy et al. 2015) and most certainly also applicable in the area of risk-benefit assessment. In addition, the EFSA’s Prometheus framework (Promoting Methods for Evidence Use in Scientific assessments), aims at further defining the process and guiding principles for evidence use in scientific assessments and critically evaluating the available methods to fulfil these principles.

Literature recommendation

EFSA Scientific Committee; Guidance on human health risk-benefit assessment of food. EFSA Journal 2010;8(7)1673. [41 pp.]. doi:10.2903/j.efsa.2010.1673

Hardy A, Dorne JLCM, Aiassa E, Alexander J, Bottex B, Chaudhry Q, Germini A, Nørrung B, Schlatter J, Verloo D, Robinson T. (2015). Increasing robustness, transparency and openness of scientific assessments. EFSA Journal 2015;13(3):e13031. Doi: 10.2903/j.efsa.2015.e13031

Verhagen H. & van Loveren H. (2016). Status of nutrition and health claims in Europe by mid 2015. Trends in Food Science & Technology 56: 39-45. <http://dx.doi.org/10.1016/j.tifs.2016.07.005>

Verhagen H., Tjhuis M.J., Gunnlaugsdottir H., Kalogeras N., Leino O., Luteijn J.M., Magnusson S.H., Odekerken G., Pohjola M.V., Tuomisto J.T., Ueland O., White B.C., Holm F. (2012). State of the Art in Benefit-Risk Analysis: Introduction. Food and Chemical Toxicology 50: 2-4.

Appendix V

Nordic Risk-Benefit Assessment Workshop

Summary of presentation and literature recommendation
22-23 September 2016
Uppsala, Sweden

Géraldine Boué

ONIRIS-INRA, UMR1014 Secalim
F-44307 Nantes, France

Previous Risk-Benefit Assessments of Foods in Europe

Quantifying the overall impact of food on human health with a risk-benefit analysis is an emerging strategy to improve public health. Up to the last decade, risks and benefits associated with food consumption were assessed separately in microbiological, chemical and nutritional fields leading to rather incomplete or unsatisfying dietary recommendations. Risk-benefit analysis integrates three interconnected parts: assessment undertaking the scientific evaluation, management setting up actions to improve public health and communication between managers, assessors and all other bodies concerned by the assessment and the implementation of management options.

Risk-benefit assessment (RBA) methodology has been set up by European scientists with EFSA contributions and international projects (BRAFO, QUALIBRA, BEPRARIBEAN and BENERIS). It is now well established that RBA needs to start by a definition of the problem to define the case study (a diet, a food or a food compound), the (sub)population targeted, and different scenarios of consumer exposure to be assessed (reference and alternative scenarios). Then, to estimate all risks and benefits an assessment is conducted in microbiology, chemistry and nutrition for the different scenarios of consumer exposure. It follows traditional steps of risk assessment and in addition requires a comparison of all risks and benefits together in order to predict the overall health impact in terms of quality and duration of life gained or lost.

There are not yet many RBA carried out in food (less than 100). So far, main topic of interest has been RBA of fish consumption integrating nutritional compounds (e.g. fatty acids DHA and EPA), chemicals (e.g. Methylmercury, dioxins and PCB) as well as microbiological hazards (e.g. *Listeria monocytogenes*). With fish, and more generally in RBA, risks and benefits have been compared in several ways. The most common method has been based on a comparison of consumer levels of exposure with regard to safety reference levels such as TWI (Tolerable Weekly Intake) in chemistry and RDI (Recommended Daily Intake) in nutrition. This approach requires only an exposure assessment but gives the same importance to all potential health effects without considering the associated severity. Another option has been to compare the change in endpoint trends like the increase of number of deaths due to a risk with the decrease of number of deaths thanks to a benefit but it is limited to similar endpoints and often cannot enable to compare all endpoints considered in the case study. Alternatively, the use of a composite metric like the DALY (Disability-Adjusted-Life-Year) enables to convert all risks and benefits in a same metric and provides a comprehensive assessment of the consequences of a disease by integrating the quality of life lost and premature death. This requires a finalized assessment of each risk and benefit (up to the prediction of the number of cases) which is not always possible due to missing data. There is a growing interest in applying advanced probabilistic tools in RBA to capture the population diversity. The uncertainty is also more and more carefully qualified and even quantified to increase transparency.

To conclude, there are still methodological limits in RBA but it is now established enough to be recommended as a tool to assess inter-disciplinary public health issues associated with food consumption.

Literature recommendation

Boobis, A., A. Chiodini, J. Hoekstra, P. Lagiou, H. Przyrembel, J. Schlatter, K. Schutte, H. Verhagen and B. Watzl (2013). "Critical appraisal of the assessment of benefits and risks for foods, 'BRAFO Consensus Working Group'." *Food Chem Toxicol* 55: 659-675.

Boué, G., Guillou, S., Antignac, J. P., Le Bizec, B., & Membré, J. M. (2015). Public Health Risk-benefit Assessment Associated with Food Consumption-A Review. *European Journal of Food Research & Review*, 5(1), 32.

EFSA (2010). "Guidance on human health risk-benefit assessment of foods. Scientific opinion." *EFSA Journal* 8(1673): 1-40.

Eneroth, H., & Zetterberg, L. A. (2016). Risk-benefit Assessment of Foods in Sweden-Developing a Working Procedure. *European Journal of Food Research & Review*, 6(2).

Hart, A., J. Hoekstra, H. Owen, M. Kennedy, M. J. Zeilmaker, N. de Jong and H. Gunnlaugsdottir (2013). "Qalibra: a general model for food risk-benefit assessment that quantifies variability and uncertainty." *Food Chem Toxicol* 54: 4-17.

Hoekstra, J., A. Hart, A. Boobis, E. Claupein, A. Cockburn, A. Hunt, I. Knudsen, D. Richardson, B. Schilter, K. Schutte, P. R. Torgerson, H. Verhagen, B. Watzl and A. Chiodini (2012). "BRAFO tiered approach for benefit-risk assessment of foods." *Food Chem Toxicol* 50: S684-S698.

Verhagen, H., M. J. Tjhuis, H. Gunnlaugsdóttir, N. Kalogeras, O. Leino, J. M. Luteijn, S. H. Magnússon, G. Odekerken, M. V. Pohjola, J. T. Tuomisto, Ø. Ueland, B. C. White and F. Holm (2012). "State of the art in benefit–risk analysis: Introduction." *Food and Chemical Toxicology* 50(1): 2-4.

Appendix VI

Nordic Risk-Benefit Assessment Workshop

Summary of presentation and literature recommendation
22-23 September 2016
Uppsala, Sweden

Maarten Nauta

Risk Benefit Research Group
National Food Institute
Technical University of Denmark

The Consumer as Risk and Benefit Manager: the Need for Quantification

In the past decade, different approaches to risk-benefit assessment have been developed in Europe. A well-known example is the tiered approach, developed in the BRAFO project (Hoekstra *et al.*, 2012). It defines different tiers that allow risk-benefit assessors to select the most appropriate method in terms of complexity of the assessment, depending on the risk-benefit question at stake. The general objective in these risk-benefit questions is to compare food intake scenarios and select the one that will provide the largest positive health effect for the population. This can be used by food and health authorities when they advise the public.

In this presentation it is proposed to consider a complementary consumer-oriented approach to risk-benefit assessment. After all, the final decision maker and risk manager with regards to food consumption in daily life is not the food authority, but the consumer. For the consumer, the authorities have the role of assessor, i.e. they are the party that provides the scientific information that is to be evaluated by the consumer. To facilitate this evaluation of health risks and benefits by the consumer, it is important that it is not only communicated that one food intake scenario is to be preferred over another, but also how large the difference in health effect between these scenarios is expected to be. This fits with the current ambition to move from hazard-based to risk-based approaches (Barlow *et al.*, 2015).

Three examples are given to illustrate that consumers will gain from the application of quantitative health metrics when they receive advice on dietary choices:

The first example considers the choice between raw milk and pasteurized milk, where the scientific evidence clearly suggests that the health risks of raw milk prevail the benefits (Claeys *et al.*, 2013). Yet, if arguments outside the health area are taken onboard, consumers would need an estimate of the size of the health effect to individually weigh the overall risks and benefits in a more holistic decision making process.

The second example compares different red meat cooking practices (Berjia *et al.*, 2014). Here the evidence suggests that roasting is to be preferred over frying or barbequing when considering the risk of different types of cancer. A quantitative analysis of the available data allows estimation of the burden disease consequential to the different cooking practices and gives a better insight in the actual size of the cancer risks. This may help consumers when evaluating the health risks associated to their preferred cooking practices.

The last example considers the intake of processed meat, which has been found to be carcinogenic by the IARC (Bouvard *et al.*, 2015). In a simplified approach, it will be shown what the communicated relative risk of 1.18 for an increased intake of 50 g processed meat per day could imply for different population groups in Denmark, if it is expressed in alternative risk metrics. This illustrates again that adequate communication of anticipated health effects can be important for consumers and can contribute to ongoing discussions on the impacts of dietary choices.

Regarding consumers as risk and benefit managers can be one of the reasons to put more emphasis on the quantification of health effects, as we aim to do in Denmark. In the discussion the challenges of quantification, for example with regards to uncertainties and in risk communication, will be addressed.

Literature recommendation

Barlow, S.M., Boobis, A.R., Bridges, J., Cockburn, A., Dekant, W., Hepburn, P., Houben, G.F., König, J., Nauta, M.J., Schuermans, J., Bánáti, D., 2015. The role of hazard- and risk-based approaches in ensuring food safety. *Trends Food Sci. Technol.* 46, 176–188. doi:10.1016/j.tifs.2015.10.007

Berjia, F.L., Poulsen, M., Nauta, M., 2014. Burden of diseases estimates associated to different red meat cooking practices. *Food Chem. Toxicol.* 66, 237–244. doi:10.1016/j.fct.2014.01.045

Bouvard, V., Loomis, D., Guyton, K.Z., Grosse, Y., Ghissassi, F. El, Benbrahim-Tallaa, L., Guha, N., Mattock, H., Straif, K., 2015. Carcinogenicity of consumption of red and processed meat. *Lancet Oncol.* 16, 1599–1600. doi:10.1016/S1470-2045(15)00444-1

Claeys, W.L., Cardoen, S., Daube, G., De Block, J., Dewettinck, K., Dierick, K., De Zutter, L., Huyghebaert, A., Imberechts, H., Thiange, P., Vandenplas, Y., Herman, L., 2013. Raw or heated cow milk consumption: Review of risks and benefits. *Food Control* 31, 251–262. doi:10.1016/j.foodcont.2012.09.035

Hoekstra, J., Hart, A., Boobis, A., Claupein, E., Cockburn, A., Hunt, A., Knudsen, I., Richardson, D., Schilter, B., Schütte, K., Torgerson, P.R., Verhagen, H., Watzl, B., Chiodini, A., 2012. BRAFO tiered approach for benefit–risk assessment of foods. *Food Chem. Toxicol.* 50, S684–S698. doi:10.1016/j.fct.2010.05.049

Appendix VII, Group discussions

1. **Future RBA** -What are the topics of risk-benefit assessments we see in the future?

Helle Korsgaard, DTU
Rikke Andersen, DTU
Inger Therese L. Lillegaard, VKM
Julie Tesdal Håland, NFSA
Anders Glynn, NFA
Emma Halldin Ankarberg, NFA
Stina Wallin, NFA
Per Ola Darnerud, NFA

- a) Add topics if you find it necessary
- b) Prioritize topics based for example on relevance for Nordic population, urgency, data availability, available methods (you may want to discuss this with group 2)
- c) Prepare to present your suggestion on what RBA to prioritize in Nordic collaboration with motivation

2. **Methodology needs** -What are the methodological issues we need to work with in order to perform good quality risk-benefit assessments?

Helga Gunnlaugsdóttir, MATÍS
Heddie Mejborn, DTU
Maarten Nauta, DTU
Carola Rosseland, VKM
Bente Mangschou VKM
Salomon Sand, NFA
Anna Karin Lindroos, NFA
Melle Sæve-Söderbergh, NFA

- a) Add methodological issues if necessary
- b) Prioritize the methodological issues based for example on relevance for upcoming RBA (You may want to discuss this with group 1), availability of expertise
- c) Prepare to present your suggestion on what methodological aspects to prioritize in Nordic collaboration, with motivations

3. Nordic collaboration -How can we collaborate on risk benefit assessments in the Nordic countries?

Maria Rönnqvist, Evira
Katrín Guðjónsdóttir, MAST
Morten Poulsen, DTU
Gro Mathisen, VKM
Rune Jemtland, NFSA
Per Bergman, NFA
Agneta Åkesson, Karolinska Institutet
Roland Lindqvist, NFA

- a) Do you find additional ways to increase collaboration?
- b) Prioritize the suggestions based for example on availability of experts, possibility of funding,
- c) Prepare to present your suggestion on how to increase collaboration with motivations

Full workshop discussion

After lunch, the three groups present their highest prioritized topics/methods/actions. All participants then discuss the ranking and how to collaborate on what topics and on what methodology.