



Project no: 022936

Project acronym: Beneris

Project title: Benefit-risk assessment for food: an iterative value-of-information approach

Instrument: STP-Specific Targeted Project

## **Deliverable 38:**

# Full benefit risk analysis of fish

Due date of deliverable: 1 Dec, 2008 Actual submission date: 15 Nov, 2009

Dissemination level: PU

Start date of project: April, 1<sup>st</sup> 2006

Duration: 3,5 years

Organisation name of the lead contractor for this deliverable: THL

# Full benefit risk analysis of fish (D38)

In the WP3 "case study", two different open assessments have been carried out, which differ from each other both in terms of the scope of the assessment and the key methodology applied:

The first and smaller one (in terms of both scope and research efforts) of the assessments has been referred to in the <u>BENERIS</u> project as the "benefit-risk assessment of methyl mercury (MeHg) and omega-3 fatty acids in fish". This assessment is based on the method of Monte Carlo simulation and examines the health impact of fish consumption in terms of two fish-derived substances contributing to a narrow set of health variables.

The larger one of the assessments is referred to as the "full benefit risk analysis of fish", which is the main health impact assessment carried out within BENERIS. This assessment is based on a **Bayesian Belief Network** (BBN) representation of the problem – rather than conventional Monte Carlo simulation – and analyses the health impact of fish consumption in terms of a larger set of fish-derived substances contributing to a wider spectrum of health variables.

A more detailed description of the whole work package (WP3 Case 1: Fish) can be found in the Beneris wikipages at <a href="http://www.opasnet.org/beneris/index.php/WP3">http://www.opasnet.org/beneris/index.php/WP3</a> Case 1: Fish

**Deliverable 38** consists of the BBN-based assessment. The documentation of D38 is composed of the following sections:

- I) Printout of the assessment wikipage
- II) Description of the BBN model for the benefit-risk analysis of fish
- III) Main components of further information.

## I) Printout of the assessment wikipage

Below is a printout of the "assessment page" of the **full benefit risk analysis of fish**. This assessment aims to quantify the occurrence of a set of deleterious health outcomes consisting of cardiovascular, cancer, teeth aberrations and central nervous system effects (decline of the intelligence quotient) due to the consumption of fish in Finland. However, for a detailled description of the assessment, including hyperlinked access to its variable description pages listed on the assessment page, one should visit

http://heande.opasnet.org/wiki/Benefit-risk\_analysis\_of\_fish

Please use the following credentials: **username**=bioher, **password**=qADaC4h

## **CONTENT**

- 1 Scope
  - 1.1 Purpose
  - 1.2 Boundaries
  - 1.3 Scenarios
  - 1.4 Intended users
  - 1.5 Participants
- 2 Definition
  - 2.1 Decision variables
  - 2.2 Indicators
  - 2.3 Other variables
  - 2.4 Analyses
- 3 Result
  - 3.1 Results
  - 3.2 Conclusions
- 4 See also
- 5 References
- 6 Related files

## 1 Scope

## 1.1 Purpose

What are the current health risks and benefits of fish consumption in the general population of Finland? Risks and benefits should be assessed separately as well as combined.

There are additional questions related to the making of the assessment.

- How can we evaluate policy options regarding fish consumption?
- How to utilize Open\_assessment method to this benefit-risk assessment?

#### 1.2 Boundaries

This assessment focuses on a selected list of compounds and health endpoints.

Risks due to <u>dioxin</u>, <u>PCBs</u>, and <u>methylmercury</u> intake via fish consumption for the following health endpoints:

- Cancer Dioxins and PCBs
- Cardiovascular disease Methylmercury

- Adverse central nervous system effects Methylmercury
- Developmental defects in teeth Dioxins and PCBs

Benefits due to omega-3 fatty acid intake from fish for the following health endpoints:

- Beneficial effects for central nervous system
- Preventive effects for coronary heart diseases
- Fish consumption in Finland (other countries will follow after the Finnihs data)
- Population of Finland, age group specific data (see scenarios below)
- Included pollutants: dioxins, PCBs, methylmercury
- Included nutrients: eicosapentaenoic acid (<u>EPA</u>), docosahexaenoic acid (<u>DHA</u>)
- Age groups: 0-2 years, 2-18 years, 18-55 years, 55+ years

#### 1.3 Scenarios

• A theoretical scenario where (age-group-specific) DALYs are above the estimated median, or below the estimated median.

#### 1.4 Intended users

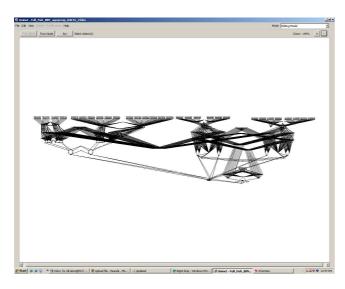
- Researchers
- Food safety authorities
- Risk assessment developers
- Policy makers

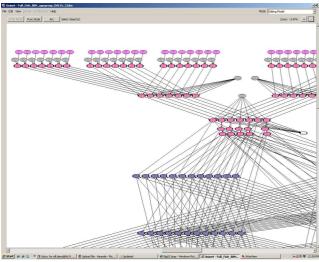
## 1.5 Participants

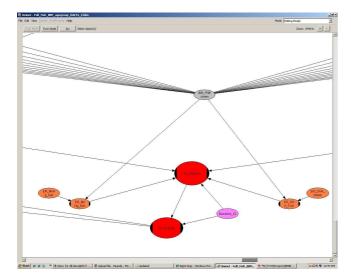
• Patrycja Gradowska, Olli Leino, Roger Cooke, Jouni Tuomisto

## 2 Definition

The case study is divided into more detailed questions, i.e. <u>variables</u>, which are described as entities utilizing the <u>Opasnet</u> platform. The model represents a set of variables and their dependences. Comparing policy options, and conditioning variables is executed by utilizing <u>Bayesian Belief Networks (BBN)</u>. The model file can be accessed from the website (see the chapter III of this deliverable). Graphical representations of the model are shown below, starting from a large scale picture containing the whole model with variables and connecting arrows between them. The close-up picture, located lowest, reveals more of the oval shaped variable nodes. Variables can contain either probabilistic input data or functional information about the variables.







## 2.1 Decision variables

We created a decision which is based on aggregated effects, i.e. combining the health end points using  $\underline{DALY}$  approach. The decisions are:

• A theoretical decision where DALYs are changed to above the estimated median, or below the estimated median.

• A theoretical decision where age-group-specific DALYs are changed to above the estimated median, or below the estimated median.

#### 2.2 Indicators

- DALYs for the total population
- Age-group-specific DALYs

#### 2.3 Other variables

The full model contains hundreds of nodes. Therefore, variables typically consist of a large number of nodes. Only variables have separate wiki pages. For more information about a particular variable of interest, open the case study page:

- <a href="http://heande.opasnet.org/wiki/Benefit-risk\_analysis\_of\_fish">http://heande.opasnet.org/wiki/Benefit-risk\_analysis\_of\_fish</a>
- username: bioher
- password: qADaC4h

There you can access all the links, including the variables. Model variables are described in Opasnet. The topics for the variables are:

- Domestic fish consumption of the general population in Finland
- Population of Finland
- Intake of PCDD/F from fish in Beneris
- Intake of PCB from fish in Beneris
- Body weight in Finland
- Height in Finland
- Risk for dental aberrations in children
- Exposure response function of dioxin on dental aberrations
- Concentrations of PCBs in fish
- Concentrations of PCDD/Fs in fish
- Methyl mercury intake from fish in Beneris
- Fish oil intake in Beneris
- Myocardial infarction risk in adults in Beneris
- Exposure response function of methyl mercury on CVD risk in adults
- Exposure response function of omega-3 fatty acids on CVD risk in adults
- Total cancer risk in adults in Beneris
- Concentrations of beneficial nutrients in fish
- Mercury and methyl mercury concentrations in fish

- Domestic fish consumption of the pregnant women in Finland
- Exposure response function of methyl mercury on intelligence quotient
- Exposure response function of omega-3 fatty acids on intelligence quotient
- Baseline intelligence quotient score in children
- <u>Intelligence quotient in children in Beneris</u>

## 2.4 Analyses

We carried out conditioning of the outcome variables of interests (DALYs and age-group-specific DALYs) and studied their effect on upstream variables of interests (age specific fish intakes, fish/sex specific intakes). We analyzed situations where DALYs are changed to above the estimated median, or below the estimated median. Our interest was to observe the changes in fish consumption. There are dozens of interesting comparisons and conditioning, the table captures variables with most substantial change in numerical value after conditioning.

## 3 Result

#### 3.1 Results

Show results from the **Opasnet Base**:

<u>List of uploads</u> | The newest upload | Mean and SD | Sample (default 100 iterations)

Table 1. Analyses of conditioned variables.

Conditioned variable	Condition	Variable of interest	Unconditional mean	Conditional mean	Remarks						
net DALY	50% decrease	Fish intake 55+ years	19.064	17.375	Down by 8.9%						
		Total pike intake	0.977	0.890	Down by 8.9%						
DALY in age group 0-2	50% decrease	Total pike intake	0.056	0.046	Down by 18%						
DALY in age group 2-18	50% decrease	Fish intake in age group 2-18	2.409	1.533	Down by 36%						
DALY in age group 55+	50% decrease	Fish intake in age group 55+	19.064	16.536	Down by 13%						

Key results for the health end points are presented in table 2.

Table 2. Results for the health endpoints in the fish case study.

Health endpoint	Age group	Result	Standard deviation	Unit
Cancer risk	55+	0.34	1.3 x 10-4	Probability of remaining lifetime risk for cancer
Cancer risk	18-55	0.45	8.4 x 10-5	Probability of remaining lifetime risk for cancer
Coronary heart disease mortality	55+	74.75	39.74	# cases per 10000 person years
Coronary heart disease mortality	18-55	1.53	0.98	# cases per 10000 person years
Developmental defects in teeth	0-2	0.0087	0.075	Probability for fish users
Developmental defects in teeth	2-18	0.0094	0.101	Probability for fish users
Net central nervous system effects	All	0.0013	0.15	IQ points

## 3.2 Conclusions

Some results of the fish case study are quite well in harmony with the current knowledge, e.g. pike - because of its methylmercury - contributes the most to the DALYs in nearly all age groups and with both sexes. However, the current version of the model gives quite surprising results on fish consumption in age groups 18-55 and 55+, conditioned by decreasing DALY load below the median. The results suggest adults to radically decrease fish consumption. This is probably a result of high health loss estimates due to cancer vs. lower benefit estimates of cardiovascular health. The result is in sharp contrast with some previous assessments<sup>[2]</sup>. Before taking a strong position here, the preliminary DALY changes per one case that were used should be updated. Also, the dose-response relationships (compilation of dose-response literature) play significant roles. Further analysis of the model will focus on these issues.

## 3.3 Conclusions about making the assessment

The model offers freedom to scrutinize relationships between the variables and to find out relevant targets for making good policy. Opasnet environment connected to the model allows the information to be available for experts dealing with the issue but lay persons as well getting input from public participation. Opasnet base stores the numerical information in form of sample which is a practical format for others to make further analysis related to their own interests.

Additionally, we recognized needs for further developing the model, including:

- To more transparently categorize the variable information within the model.
- More flexible editing/sampling would improve the efficiency of the work done with the model.
- There is a need to run what-if scenario analysis, in addition to the current conditionalisation assessments.

The further development work will be done gradually as we improve in comprehending the model details.

#### 4 See also

- <u>Bayes' theorem</u> Theoretical background for Bayes analysis.
- Probability theory and decision theory Background information for theories.
- <u>Taylor expansion</u> Description of Taylor expansion, which has been utilized in the BBN model.
- Considered health end points. Discussion about the selection of endpoints.
- Description of this case study on an open website

As an individual part of this case study, we carried out a <u>benefit-risk assessment of MeHg and omega-3 fatty acids in fish</u>. This page contains description about the study and results with conclusions.

## **5** References

- 1. ↑ Forming the list of pollutants
- 2. \(\gamma\) Wiener and Graham. Risk vs. risk. 1996#

#### 6 Related files

File name Date modified Size

Full Fish BBN.zip 15.10.2009 7:13:06 3694.02 kB

zipped rvinfo-file

zipped tps-file

## II) Description of the BBN model for the benefit-risk analysis of fish

The full documentation of the BBN model is given in the report "A Bayesian Belief Network model for the benefit-risk analysis of fish consumption in the BENERIS project" by P. Gradowska and R. M. Cooke (TU Delft, 2009). However, to save paper, only the cover and contents pages of this comprehensive report are displayed below. The complete report (63 pages) can be downloaded from:

http://heande.opasnet.org/wiki/File:TU\_Deflt\_-\_Model\_Documentation.pdf

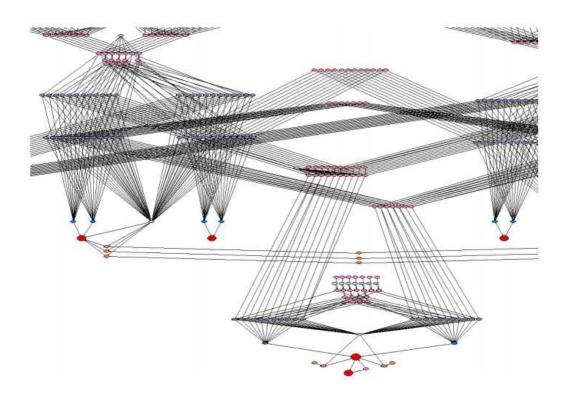
Please use the following credentials: **username**=bioher, **password**=qADaC4h

## A Bayesian Belief Network model for the benefit-risk analysis of fish consumption in the BENERIS project

P. Gradowska, R. M. Cooke

Delft Institute of Applied Mathematics

The Netherlands, November 2009



# Table of contents

1.	Introduction	3			
2.	2. Scope and boundaries of the fish case study				
3.	Bayesian Belief Networks	6			
	Discrete BBN	6			
	Normal (or discrete-normal) BBN	7			
	Non-parametric continuous/discrete BBN	7			
1.	Bayesian Belief Network for BENERIS fish case study	10			
5.	Model quantification	13			
	5.1. Consumption of fish in Finland	13			
	5.2. Content of nutrients and environmental pollutants in fish Methyl mercury Omega-3 fatty acids (DHA and EPA) PCDD/Fs and PCBs	17 17 18 18			
	5.3. Personal/demographic variables  Body weight and height Body mass index and percent body fat in children Age and gender	20 20 21 22			
	5.4. Intake of nutrients and environmental pollutants from fish	22			
	5.5. Quantitative exposure-response assessments 5.5.1. Effects of MeHg and omega-3 fatty acids on cognitive development of children 5.5.2. Effects of PCDD/Fs and PCBs on teeth development 5.5.3. Effect of MeHg and omega-3 fatty acids on cardiovascular disease 5.5.4. Effects on cancer	25 25 26 28 30			
5.	Modeling and assessment of benefits and risks	31			
	6.1. Generalized approach for modeling exposure-response relationships	31			
	6.2. Health effects of eating fish in Finland	34			
7.	Non-parametric BBNs and UniNet	41			
	7.1. Summary of UniNet features	45			
	7.2. BBNs for Uncertainty Analysis/ Stochastic Modeling	45			
	7.3. Analytic conditioning	46			
	7.4. Sample based conditioning	49			
	7.5. Ordinal data mining	52			
	7.5.1. Saturated BBN	53			
	7.5.2. Assessing model adequacy	55			
	7.5.3. Import/export model feature	59			
R	References				
4	bbreviations	63			

## III) Main components of further information

## The BBN model code of the fish case

The code specifying the BBN model utilized for the case study is accessible from the wikipage displayed above, via the links under the subtopic "Related files".

Please use the following credentials: **username**=bioher, **password**=qADaC4h

## Benefit-risk assessment of MeHg and omega-3 fatty acids in fish

As stated above, a separate benefit-risk assessment was carried out before applying the BBN model. This assessment is also accessible from the wikipage printed above, via the links under the subtopic "See also". Please use the credentials given above.