Risk-Benefit Assessment for Foods

Workshop
Dissemination Material

Danubius Health Spa Resort Helia
Budapest, Hungary
9 – 10 September 2009

www.qalibra.eu
Summary

This deliverable, D22, contains the dissemination materials that were used at the first end-user workshop of the QALIBRA project, 9-10 September 2009. These materials are also intended for use in further training activities which may be organised after the end of the Qalibra project.

The overall objectives of QALIBRA are to develop a suite of quantitative methods for assessing and integrating beneficial and adverse effects of foods, and make them available to stakeholders as web-based software for assessing and communicating net health impacts.

Dissemination of, information about complex systems, such as the integrated assessment methodologies being developed in the Qalibra project, to end-users and stakeholders can be difficult. Similarly, knowledge transfer to potential end-users also represents a challenge. In QALIBRA, end-user uptake is promoted by a systematic program of dissemination activities adapted to the needs of all stakeholders, and by the development of targeted, tested materials and programs that allow use of the system by technical end-users during and after completion of the Qalibra project.

To promote end-user uptake of the web-based software developed in QALIBRA, a workshop format is used. A pilot workshop (effectively a “trial” workshop) was held in January 2009 to test the dissemination materials and the web-based software, which were subsequently extensively improved based on the feedback from participants. The design of the end-user workshop including the materials presented in this deliverable was based on a structured approach to training design (described in Appendix 2), feedback from the trial workshop, and the findings of a stakeholder analysis.

This report describes the first end-user workshop, which was carried out with project partners and 31 prospective end-users from food authorities, food companies and academia from 12 different Member States and 3 Associated States. Through these participants, the workshop will raise awareness and interest in the Qalibra assessment tool in their organisations, and thus initiate the development of a wider user network. A post-workshop feedback survey showed a very positive response by the participants, and was also useful in identifying areas for further improvement of the Qalibra tool in the final months of the project.

The report contains the dissemination material used at the workshop including presentations, scenarios and input data for practical examples.
Table of contents

Summary ................................................................. 2
Table of content .......................................................... 3
Presentation; General introduction to the workshop and the EU project QALIBRA ............ 4
Presentation; Introduction to risk-benefit assessment ................................................. 9
Presentation; QALIBRA findings on communication of risk-benefit information .......... 32
Presentation; Introduction to the QALIBRA risk-benefit assessment tool .................. 51
Presentation; Case study A: risk-benefit assessment for phytosterols in margarine ....... 59
Practical Session; QALIBRA tool and phytosterols example .................................... 74
Presentation; Case study B: risk-benefit assessment for oily fish ............................... 84
Appendix 1; Questionnaire .................................................................................... 108
Appendix 2; Methodology for developing QALIBRA training material ..................... 114
General introduction to the workshop and the QALIBRA project

Qalibra Workshop, Budapest, 9-10 September 2009

Presented by Helga Gunnlaugsdóttir

QALIBRA: Quality of life - integrated benefit and risk analysis

April 2006 – December 2009

Coordinator: Helga Gunnlaugsdottir, Matis, Iceland

Partners:

- RIVM, NL
- Food and Environment Research Agency, UK
- Wageningen University, NL
- University of Patras, GR
- Altagra Business Services, HU
- IPIMAR, PT

Clustered with:

Cooperation with:
Overall objectives

- Develop a suite of quantitative methods for assessing and integrating food risks & benefits
- Make them available to stakeholders as web-based software
- Develop effective strategies for risk/benefit communication
- Validate through comprehensive case studies on oily fish and functional foods

QALIBRA software

- Objective: develop web-based tools for risk-benefit assessment
- Primary target users: practitioners with expertise in risk and/or benefit assessment
- Usability of the QALIBRA-tool has been tested during the development

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Presentation
General introduction to the workshop and the QALIBRA project

QALIBRA timetable

● First training workshop, Wageningen, 20 Jan 2009
● Refinements of QALIBRA tool and training materials
● Practical session of the refined QALIBRA tool with SAP members in June 2009
● End-user workshop and training course Sept 2009
● Final improvements identified after the workshop with end-users
● Project ends December 2009

QALIBRA workshop

● Objectives:
  4 Communicate the key results of the QALIBRA project to food safety experts
  4 Introduction to the risk-benefit modelling approaches developed in the project
  4 Practical hands-on training on the QALIBRA tool
  4 Feedback on QALIBRA tool
Presentation
General introduction to the workshop and the QALIBRA project

QALIBRA workshop - Agenda

- Agenda Wednesday 9th of September:
  - General introduction to the workshop and the QALIBRA project
  - Introduction to risk-benefit assessment
  - Presentation of QALIBRA findings on communication of risk-benefit information
  - Introduction to the QALIBRA risk-benefit assessment tool
  - Case study A: risk-benefit assessment for phytosterols in margarine
  - Guided practical session with QALIBRA tool and phytosterols example

QALIBRA workshop - Agenda

- Agenda Thursday 10th of September:
  - Case study B: risk-benefit assessment for oily fish
  - Practical session with QALIBRA tool and oily fish example
  - Discussion
  - Feedback on workshop

- BRAFO members will stay for a follow up working meeting on Thurs and Friday, to test using the QALIBRA tool on their case studies
Thank you...
Introduction to risk-benefit assessment and the Qalibra framework

Qalibra Workshop, Budapest, 9-10 September 2009

Presented by Andy Hart
Main contributors: RIVM & Fera

Outline of presentation

- Why risk-benefit assessment?
- Basic concept
- Tiered approach & role of Qalibra
- Defining the risk-benefit question
- Measures of net health impact
- Calculation method
- Data inputs
- Variability, uncertainty and dependency
- Outputs & interpretation
Why risk–benefit?

- Changes in diet may pose both risks and benefits to health
- Balance of risk and benefit is of interest to:
  - Food authorities
  - Food industry
  - Health professionals
  - Consumers

Examples

<table>
<thead>
<tr>
<th>‘Benefits’</th>
<th>‘Risks’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traditional nutrition</td>
<td></td>
</tr>
<tr>
<td>Fish</td>
<td></td>
</tr>
<tr>
<td><strong>Coronary heart diseases ↓</strong></td>
<td><strong>Neurological damage in the fetus / microbiological contamination</strong></td>
</tr>
</tbody>
</table>
### Examples

<table>
<thead>
<tr>
<th>‘Benefits’</th>
<th>‘Risks’</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Functional foods</strong></td>
<td></td>
</tr>
<tr>
<td>Foods fortified with folic acid</td>
<td>Neural tube defects ↓</td>
</tr>
<tr>
<td>Neutro tube defects ↓</td>
<td>Colorectal cancer?</td>
</tr>
</tbody>
</table>

### Examples

<table>
<thead>
<tr>
<th>‘Benefits’</th>
<th>‘Risks’</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Functional foods</strong></td>
<td></td>
</tr>
<tr>
<td>Margarines with phytosteros / - stanols</td>
<td>Cholesterol level ↓</td>
</tr>
<tr>
<td>Plasma phytosterol levels ↑</td>
<td></td>
</tr>
</tbody>
</table>
Basic concepts

- Beneficial health effects
- Adverse health effects

- dose-response

- cases prevented (death, disease)
- extra cases (death, disease)

- integrated measure

- Health gain
- Health loss

- Intake scenario

- Baseline or reference scenario to assess against
- Common currency to compare gains and losses
- Tiered approach

Tiered approach (Brafo project)

- Refine assessment only as far as is needed to reach a decision:
  - Tier 1: Screening assessment of Rs & Bs
  - Tier 2: Qualitative integration of R-B
  - Tier 3: Deterministic integration of R-B
  - Tier 4: Probabilistic integration of R-B
Presentation
Introduction to risk-benefit assessment

Problem formulation

Defining the risk-benefit question:

- Dietary change to be assessed
  - e.g. food policy, dietary advice, new products…
- Baseline or Reference scenario
  - usually current diet
- Population to be considered
- Consequences of interest
  - Qalibra considers only health impacts
Measures of health impact

- Mortality (death)
  - mortality risk/rate, life expectancy, life years lost
- Morbidity (disease)
  - incidence, prevalence, morbidity risk
- Quality of life, functioning
  - physical functioning, mental health, health quality

Need an integrated measure of health impact

Net health impact

- Various measures exist, e.g.
  - Disability-adjusted life years (DALYs)
  - Quality-adjusted life years (QALYs)
  - Willingness to pay (WTP)
  - Etc.
- Qalibra focussing on DALYs
  - Used by WHO and Dutch government
- Qalibra tool can also calculate QALYs
Disability-adjusted life years

DALYs – take account of:

• Number of people affected
• Severity of disease
• Duration of disease
• Years of life lost due to early mortality

Calculation of DALYs

• Years lived with disease: YLD
• Severity of disease: w (DALY weight, 0-1)
• Years of life lost: YLL

\[ \text{DALY} = YLD \times w + YLL \]

• Sum up for all individuals in population

More DALYs bad, less DALYs good…
DALY weights

- Express reduction on health quality as a proportion (full health = 0, death = 1)

- Tables of values published in literature
  - E.g. WHO
    - Coronary heart disease: \( \approx 0.2 \)
    - Prostate cancer: 0.13
    - Dementia: 0.65
DALY issues

‘Efficiency’ vs. Equity

- Assumes adverse effects can be compensated by beneficial effects in different people
  → Maximising health may increase inequity

- Potential unwanted effects, e.g.
  - higher life expectancy of women → prioritise treatment to baby girls over baby boys
  - disable years of life are worth less → prioritise treatment to able people over disabled, etc.

- Need to facilitate consideration of fairness
  - Show how DALY changes are distributed in population

Calculation methods

- Cumulative health impact*
  - Model multiple health effects and their interactions
  - With or without background diseases
  - Realistic but complex – simulate individual histories

- Directly attributable health loss*^:
  - Sum the DALY impacts of diseases incurred or avoided by the population in a single year
  - Interpret as measure of potential impact per year
  - Ignores delay, substitution and comorbidity
  - Much simpler and less data-demanding

*RIVM (2006) Our food, our health; *Hoekstra et al. (2008) folate paper
Calculation methods

• “Cumulative” method requires a level of data not practical – and probably not necessary – for most risk-benefit assessments:
  – Interactions between incidences, durations and severities of modelled effects
  – PLUS: incidences, durations and severities of major background diseases and their interactions with the modelled diseases
  – PLUS: need to model demographic development of population over period of dietary change (births, unrelated deaths, immigration, emigration)

• Qalibra tool uses “directly attributable health loss” method
  – Interpret total as potential health impact per year
  – Averages alternative outcomes for individual – but can still examine variation between individuals
  – Take account of limitations when interpreting results, e.g. ignoring comorbidity, delay and substitution will over-estimate DALY changes (see RIVM 2006)
  – Consider Cumulative method as additional tier to be used case-by-case when needed (e.g. RIVM Chronic Disease Model)
For quantal effects:

\[ \text{DALY} = I_{id} \cdot p_{\text{effect}} \left( p_{\text{rec}} \cdot YLD_{\text{rec}} \cdot w + p_{\text{die}} \cdot (YLD_{\text{die}} \cdot w + LE - CA - YLD_{\text{die}}) + (1 - p_{\text{die}} - p_{\text{rec}}) \cdot (LE - CA) \cdot w \right) \]

- DALYs if you recover
- DALYs if you die (including lost years)
- DALYs if effect continues to normal life expectancy

\[ I_{id} = \text{individual scaling factor (individuals to population)} \]
\[ p_{\text{effect}} = \text{probability of effect onset in current year (dose-response)} \]
\[ p_{\text{rec}} = \text{probability of recovery from effect} \]
\[ YLD_{\text{rec}} = \text{duration of disease for those who recover} \]
\[ w = \text{DALY weight (can differ for recover/die/chronic groups)} \]
\[ LE = \text{normal life expectancy (should be a function of age)} \]
\[ CA = \text{current age of individual in year of onset} \]
\[ p_{\text{die}} = \text{probability this effect causes death} \]
\[ YLD_{\text{die}} = \text{duration of disease for those who die of it} \]

- Sum result over individuals and over effects → net health impact for population
- Model relates to steady-state situation:
  - stable population structure
  - ongoing exposure to dietary scenario
  - no allowance for transition effects
For **continuous** effects:

- Requires modified calculation including age of onset and relationship between effect size and DALY or QALY weight

- Alternatively, **define a ‘Critical Effect Size’ and then treat as a quantal effect**
  - E.g. convert continuous dose-response for IQ to quantal dose-response for IQ falling below a threshold value (e.g. 80)

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Data needed

- Population info (age, sex, etc.)
- Intakes (reference & alternative)*
- Dose-response functions*
- Age of onset*
- Recovery probabilities*
- Mortality probabilities*
- Disease weights*
- Disease durations*
- Life expectancies

* Needed for each health effect considered
Main steps of assessment

- Define population & dietary change
  - Reference & Alternative scenarios
- Identify potentially relevant health effects
  - e.g. WHO, WCRF criteria
- Obtain required input data
- Calculate DALYs for each effect in each scenario
- Sum DALYs for each scenario & calculate net health impact
Input data: “individuals”

- **Representative sample of population** affected by diet change
- **Or a single “representative” individual**
- Need to specify **age**, plus any attributes that influence health effects (e.g. gender, weight)
- Specify **scaling factors** if needed
  - scale up to national population
  - account for bias in dietary surveys
- Need to specify **life expectancies**
  - usually a function of age
  - may be a function of other attributes

Main steps of assessment

Key to symbols:
- **Data input**
- **Decision point**
- **Display (output)**
- **Common Currency**
Input data: exposure

- **Intake of chemical or food type** associated with each health effect
  - for Reference & Alternative scenarios
- **Can be a single value** (e.g. typical or worst case) or **multiple values** for different individuals
- **Same units as dose-response**, e.g.
  - mg/kg bw/day of nutrient or contaminant
  - weight or portions per day of relevant food type (e.g. fish)
- **Can use output from existing dietary models** (e.g. MCRA)

Input data: dose-response

- **Dose-response can be**:
  - quantal or continuous (e.g. cancer, IQ)
  - chronic or acute (but difficult if recurrent)
  - an effect on next generation
  - a single value (threshold dose)
  - multiple values representing any form of dose response (Qalibra interpolates)
  - a function of age, sex, etc.

* requires data or assumptions on age of onset
Input data: dose-response

• Complications:
  – need probability of onset in current year
    • requires data or assumptions on age of onset of effect – usually highly uncertain for effects based on animal studies
  – need absolute not relative response
    • requires data on baseline effect levels
  – must relate to effects in humans
    • need to model extrapolation of animal studies to humans
  • Requires expertise in toxicology, epidemiology & modelling

Individuals
Exposure
Dose-response
Recovery/death
Severity
Duration

Input data: dose-response

• Combine outside Qalibra:
  – Sterol intake → %LDL cholesterol reduction
  – Baseline LDL cholesterol level
  – Absolute LDL cholesterol reduction → reduction in IHD incidence
  – Baseline IHD incidence

Example: Phytosterols

<table>
<thead>
<tr>
<th>Phytosterol intake (gr/day)</th>
<th>IHD probability</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean p5 p95</td>
</tr>
<tr>
<td>0</td>
<td>0.005 0.01 0.015</td>
</tr>
<tr>
<td>1</td>
<td>0.02 0.02 0.02</td>
</tr>
<tr>
<td>2</td>
<td>0.005 0.01 0.015</td>
</tr>
</tbody>
</table>

Example: Phytosterols

male, 68
Data inputs: recovery/death

- Need data on **recovery** and **mortality** rates* for each effect
  - e.g. from national health statistics
- **Often a single number**, but:
  - may be a function of age, sex, etc.
  - may be a function of intake
- **Complications**:
  - may depend on cause
  - uncertain for animal endpoints
  - recovery to less than full health

* total (not annual) proportions of affected individuals that recover or die

Data inputs: severity

- Need to select **DALY** or **QALY**
- **Weights** available in literature (e.g. WHO)
- Usually a single number, but:
  - may differ for those who recover or die
  - may depend on age, sex, etc.
  - may depend on intake
  - may be a function of a continuous effect (e.g. IQ)
- **Complications**:
  - national differences
  - disease with >1 stage or level of severity
  - uncertain for animal endpoints
Presentation
Introduction to risk-benefit assessment

Data inputs: effect duration

- **Average duration of health effect** (yrs)
  - e.g. from national statistics
- **Often a single number**, but:
  - may differ for those who recover/die
  - may depend on age, sex, etc.
  - may depend on intake
- **Complications**:
  - may depend on cause
  - uncertain for animal endpoints

Main steps of assessment

Key to symbols:
- **Data input**
- **Display (output)**
- **Decision point**

**Setup**
**Run**
**Dietary Scenarios**
**Individuals**
**Health effects**
**More Health Effects**
**Common Currency**
**Output: Net Health Impact**

**Exposure** (effect 1)
**Dose-Response** (effect 1)
**Recovery & mortality** (effect 1)
**Severity & duration** (effect 1)

**Exposure** (effect 2)
**Dose-Response** (effect 2)
**Recovery & mortality** (effect 2)
**Severity & duration** (effect 2)
### Quantifying variability

- **Exposure:**
  - variability can be represented by inputting intakes for sample of individuals

- **Other inputs:**
  - can enter different values for different subgroups of population, e.g. age, sex, any other attribute
  - could also use this function to represent distributions (with care)

### Quantifying uncertainties

- **May often not be necessary** (tiered assessment approach)
- **Options for quantifying uncertainty**
  - redo assessment with alternative assumptions
  - represent uncertainty with probability distributions for inputs
    - enter as a set of alternative values
    - Qalibra then generates distributions and confidence intervals for outputs
Quantifying dependencies

- **Dose-response:**
  - response dependent on dose

- **Other inputs:**
  - recovery, death, severity & duration can be dependent on dose

- Dependencies are also uncertain
  - can represent in same ways as other uncertainties (alternative runs, or input a set of alternative values)

Unquantified uncertainties

- Need to consider potential impact of uncertainties, variabilities & dependencies that are not quantified
- Also need to consider uncertainty due to assumptions and limitations in all parts of the model
Assumptions & limitations

• **Many additional assumptions & limitations**, including:
  - limitations of “Directly attributable effects” method:
    • ignores background diseases, comorbidity, delay, substitution
    • difficulty integrating effects of >1 stressor on same endpoint*
  - recovery, death, severity, duration, age of onset may depend on cause of effect → may differ from national statistics

• **Options for dealing with them:**
  - assess resulting uncertainties qualitatively (e.g. EFSA method)
  - alternative models (e.g. RIVM Chronic Disease Model)
    • addresses some limitations but needs more data & assumptions
  - simpler approaches (e.g. incidence only, or purely qualitative)
    • may be sufficient in many cases (Brafo Tiers 1 and 2)
    • very uncertain when both adverse & beneficial effects are expected

* e.g. fish: PUFAs & methylmercury may both affect IQ

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Tabular outputs

• Total DALY change for population
• Contribution of each health effect to total
• Intermediate results, e.g. incidence, years lost, etc.
• Probability intervals for quantified uncertainties
• Should be accompanied by evaluation of unquantified uncertainties & dependencies
  – partly intrinsic to Qalibra approach
  – partly related to user inputs
Graphical outputs

- Variation of individual contributions to total population impact*

- Relation of net health impact to age and other attributes

* Graphical outputs only available for runs with >1 individual

Interpretation of results

- Interpretation requires relevant expertise
- Do not present results as “real” impacts
- Results are an indication of the potential average annual health impact of a long-term* dietary change
  - Reflect knowledge & assumptions used
  - Limited by what is unknown or excluded
- Must characterise the associated uncertainty (how different the real impact could be) and communicate it to risk managers

*steady-state
Closing remarks

• Risk-benefit assessment is not easy
  – need high level of expertise in several fields
  – requires substantial data or assumptions
  – affected by many uncertainties

• Potential benefits of Qalibra
  – provides a common conceptual framework
  – helps to identify important issues
  – allows progressive refinement from deterministic to probabilistic
  – helps organise input data, saves writing own programs
  – can use outputs of other tools (e.g. MCRA)

Thank you…
Overview WP3 activities

Development of strategies for communicating and disseminating risk-benefit information and dissemination

Lynn Frewer, Heleen van Dijk, Meike Wentholt
Wageningen University

Qalibra end-user workshop
9-10 September 2009, Budapest, Hungary

Changes in the practice of risk analysis

- Increased transparency in decision-making process associated with risk governance, including risk assessment
- Implies need to develop effective communication with society about assessment
- Individual differences in perceptions – important for policy practice
- ALSO targeted communication to individuals
  
  A case study using QALYs
WP3 activities

- Consumer studies
  - Focus groups
  - Surveys
  - Stakeholder study

Consumer focus groups

- Aim: To develop insights for effective ways to communicate both risks and benefits associated with the consumption of a specific food product.
Presentation
QALIBRA findings on communication of risk-benefit information

Consumer focus groups

- The following issues were explored:
  - Consumer perceptions of the adequacy of current information provision about health risks and benefits associated with food consumption
  - Consumer preferences and reactions to different metrics describing the net health impact from risk-benefit assessment outputs
    - Life expectancy
    - QALY
    - DALY

Consumer focus groups: Method

- 33 consumers participated in the focus group discussions
  - Iceland (n = 9)
  - the Netherlands (n = 7)
  - Portugal (n = 9)
  - UK (n = 8)
Consumer focus groups: Results

- Perceived adequacy of current information about risks and benefits.
  - Biased information
    - promote the vested interests of manufacturers
  - Conflicting information
    - many different opinions
    - confusing
    - distrust in information
    - need for scientific proof

Consumer focus groups: Results

- Key positive and negative points from the discussions on the three measures for describing the net health impact.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life expectancy</td>
<td>• Useful for comparing and reaching conclusions, • Concrete.</td>
<td>• Effect size too small.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Not relevant for younger people.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Too much emphasis on health</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• No information about quality of life.</td>
</tr>
<tr>
<td>Quality of life (QALY)</td>
<td>• Important and relevant information.</td>
<td>• Terminology is counterintuitive.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emphasis is on negative aspects (e.g. disability and disease).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Complicated, difficult to understand.</td>
</tr>
<tr>
<td>Disability adjusted life years (DALY)</td>
<td>• Combination of life expectancy and quality of life.</td>
<td>• Difficult and confusing.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Not useful.</td>
</tr>
</tbody>
</table>
Focus groups: Conclusions

- Consumers
  - require balanced and scientifically derived information about both risks and benefits associated with food consumption.
  - do not understand DALYs
  - appreciate receiving information about
    - life expectancy and
    - quality of life and
    - risks and benefits.
- 6 months difference in DALYs will not influence decision-making.

Surveys: Research question

- Consumer reactions to integrated risk-benefit information in terms of QALYs.
  - People tend to weigh losses as more relevant than gains
  - People differentially process information about risks compared to benefits
QALIBRA findings on communication of risk-benefit information

Surveys: Method

- Two internet surveys (N = 1012, 443).
- Nationally representative samples from the Netherlands.

Surveys: Method

- Dependent variables
  - Perceived *importance* and *WTP* of QALY changes (Survey 1).
  - *Usefulness* of QALYs for decision making (Survey 2).
  - Impact information QALY change on *risk and benefit perceptions* and *behavioral intentions* (Survey 2).
Surveys: Method

- Independent variables
  - Survey 1 focused on *avoided* losses, Survey 2 on *gains obtained*.
  - Information format
    - Integrated *versus* separate risk-benefit information presented in one message (Survey 2).
  - Personal characteristics of participants (Survey 1 and 2).

Results: Usefulness of QALYs for decision making

- QALYs perceived as *useful information* for decision making regarding consumption of fatty fish.

<table>
<thead>
<tr>
<th></th>
<th>For me personally</th>
<th>For policy makers</th>
<th>For people working in health care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perceived usefulness</td>
<td>4.31</td>
<td>4.69</td>
<td>4.67</td>
</tr>
<tr>
<td>QALYs</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Very useful

Less useful
Results: Perceived importance of changes in QALYs

- Increased health gains are perceived as important
- Initial improvements in health are perceived as being as important as subsequent improvements
- Health gains lower than 3.5 QALYs are, on average, not perceived as more important than a health gain of zero QALYs
- Variance for WTP scores was higher than scores for perceived importance
  - WTP may be less suitable for measuring consumer valuation of health (in context of food consumption).

Results: Impact of changes in Qalys on decision-making

- On risk and benefit perceptions.
  - Information with a positive net effect
    - increased benefit perceptions *
    - no impact on risk perceptions **
  - Information with a negative net effect
    - increased risk perceptions ***
    - no impact on benefit perceptions ****
- On intentions to eat fatty fish.
  - Information had no impact on intentions to eat fatty fish.

* $\Delta M = -0.25, p = .09$
** $\Delta M = -0.13, p = .38$
*** $\Delta M = -0.29, p = .04$
**** $\Delta M = 0.15, p = .28$
Results: Prevention *versus* promotion

- Acting to avoid losing QALYs was perceived to be equally *important* as gaining the same amount of QALYs.
- People perceived that information about avoiding losses and gaining health were equally *understandable* and *credible*.
- This can be interpreted as people understanding both illness prevention and health promotion information when expressed in Qalys.

Results: Integrated *versus* separate risk-benefit information

- Both perceived to be equally *useful* for decision making.
- Similar impact on *perceptions* and *behavioral intentions*.
- *Understandability* depended on information format:
  - Positive net effect:
    - separate risk-benefit information more understandable
  - For a negative net effect:
    - integrated risk-benefit information more understandable.
**Personal characteristics: Age**

- Older people found QALYs more *useful* for decision making.
- Older people evaluated changes in QALYs as more *important*.
- Older people did NOT differentially utilize QALY information in developing *risk and benefit perceptions* and *behavioral intentions*.

**Personal characteristics: Gender**

- Men and women found QALYs equally *useful* for decision making.
- Women evaluated changes in QALYs as more *important* than men.
- *Risk perceptions* following negative net effect increased *more for women* than for men.
- Information on QALY changes had no differential impact on *benefit perceptions* and *behavioral intentions* related to gender.
Personal characteristics: Perceived personal health

- Perceived personal health did not influence perceived *usefulness* of QALYs for decision making
- People with better perceived personal health evaluated changes in QALYs as more *important*
- Information on QALY changes had no differential impact on *risk and benefit perceptions* and *behavioral intentions* related to current health status

Conclusions (1)

- QALYs are generally perceived by consumers as a useful measure for decision making regarding fish consumption
- Changes of 3.5 QALYs is the “threshold” for decision-making than no change in health
- Information concerning a gain or loss of 4 QALYs influenced benefit and risk perceptions but had no affect on behavioural intentions
- Impact on health may need to be larger than 4 QALYs to influence behaviour
- Useful to test these thresholds across other areas of human health
Conclusions (2)

- Focus on gains versus loss had no differential impact on valuations of importance of QALY changes.
- Integrated risk-benefit information and risks and benefits presented separately in one message can be equally useful for communicating risks and benefits associated with food consumption.
- Reactions to information about health changes in terms of QALYs depend on personal characteristics.

Stakeholder study

- QALIBRA aims to develop an integrated risk-benefit assessment web-enabled software tool and website
- Effective information towards, and the correct use of the system by prospective end-users, will be essential to disseminate the project outputs and ensure uptake of the QALIBRA tool/website by the end-users
- Stakeholder requirements need to be understood
Why conduct a stakeholder study?

- Different end-users will have different preferences in information delivery and formats according to their needs and understandings.

- Research applied to the identification of:
  - end-user needs
    - stakeholder analysis
  - requirements for the QALIBRA tool/website (e.g. output format)
    - expert elicitation exercise

---

Stakeholder analysis

- Aim: Identification of prospective end-users for the QALIBRA tool/website.
- Three levels of potential end-users:
  - at the top level: “general public”
  - at the second level: “policy community”
  - at the third level: those actively conducting RBA, researchers
Presentation
QALIBRA findings on communication of risk-benefit information

Stakeholder analysis (2)

<table>
<thead>
<tr>
<th>General public</th>
<th>Policy makers &amp; other interested end-users</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Consumer organisations</td>
<td></td>
</tr>
<tr>
<td>□ Other NGOs</td>
<td>□ Media, generally</td>
</tr>
<tr>
<td>□ Consumers</td>
<td>□ Communicators</td>
</tr>
<tr>
<td>□ Educational bodies in each country</td>
<td>□ Specialist press</td>
</tr>
<tr>
<td>□ Nutritionists</td>
<td>□ Consumer health media</td>
</tr>
<tr>
<td>□ Educators</td>
<td>□ Industry</td>
</tr>
<tr>
<td>□ Clinical-health professionals</td>
<td>□ Policy makers</td>
</tr>
<tr>
<td>□ Industry</td>
<td>□ Risk managers</td>
</tr>
<tr>
<td>□ Policy makers</td>
<td>□ Food authority</td>
</tr>
<tr>
<td>□ Risk managers</td>
<td>□ Academics, scientists (incl. some industry)</td>
</tr>
</tbody>
</table>

Expert elicitation exercise

- **Aim:**
  Identification of demands and preferences of selected stakeholders for the QALIBRA tool/website

- Expert opinion was sought through applying an online Delphi-like research method
  - *Round 1 - relevant issues and methods*
  - *Round 2 – in depth analysis*
Survey characteristics

<table>
<thead>
<tr>
<th></th>
<th>Round 1</th>
<th>Round 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Respondents #</strong></td>
<td>39</td>
<td>20</td>
</tr>
<tr>
<td><strong>Organisation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Government</td>
<td>25</td>
<td>14</td>
</tr>
<tr>
<td>Industry</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Academia</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>NGO</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>18</td>
<td>11</td>
</tr>
<tr>
<td>Male</td>
<td>21</td>
<td>9</td>
</tr>
<tr>
<td><strong>Work experience</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-5 years</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>6-10 years</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>11-20 years</td>
<td>17</td>
<td>7</td>
</tr>
<tr>
<td>21+ years</td>
<td>15</td>
<td>9</td>
</tr>
</tbody>
</table>

Are you familiar with…

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>Somewhat</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Risk assessment</td>
<td>84%</td>
<td>14%</td>
<td>2%</td>
</tr>
<tr>
<td>2) Benefit assessment</td>
<td>51%</td>
<td>44%</td>
<td>5%</td>
</tr>
<tr>
<td>3) Risk-benefit assessment (RBA)</td>
<td>47%</td>
<td>47%</td>
<td>7%</td>
</tr>
</tbody>
</table>

- Experience with “other” risk-benefit assessment tools (or other assessment tools)
  - 64% reported **no experience** with these kind of tools
Integrated health outcome approach

- Both QALY and DALY are useful to assess risks-benefits
  - DALY: 70% useful, 10% useless, 20% don’t know
  - QALY: 68% useful, 12% useless, 20% don’t know
  - QALIBRA-tool based on DALY
- An overview of assumptions should be provided
  - all participants agree (round 2)

Other functionalities or features

- Some suggestions by respondents:
  - Tool functionalities
    - present a clear outcome: net risk or benefit
    - overview of what data is needed for the tool (‘checklist’)
  - Added features
    - inclusion of cost-benefit methods
    - information exchange with others performing RBAs
  - Information requirements
    - examples of how to communicate the results of RBAs
    - background and educational materials
    - harmonized method for intake estimations
Presentation
QALIBRA findings on communication of risk-benefit information

Output formats

- **Results at population level**
  - tabular output: relative / absolute results table
  - graphical output: bar chart (+ scenario result)

- **Results at individual level**
  - tabular output: relative / absolute results table
  - graphical output: histogram with confidence intervals; cumulative distribution
  - narrative option: textual format

Most understandable output formats

- Bar chart for population level results

Understandable way to present results
Yes 95%; No 5%; Don’t know 0%
Most understandable output formats

Predicted effect of proposed dietary policy

<table>
<thead>
<tr>
<th>Percent of population</th>
<th>Lose &gt;10 DALYs</th>
<th>Lose 5-10 DALYs</th>
<th>Lose up to 5 DALYs</th>
<th>No change in DALYs</th>
<th>Gain up to 5 DALYs</th>
<th>Gain 5-10 DALYs</th>
<th>Gain &gt;10 DALYs</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>10%</td>
<td>20%</td>
<td>30%</td>
<td>40%</td>
<td>50%</td>
<td>60%</td>
<td>70%</td>
</tr>
</tbody>
</table>

Understandable way to present results?
- Yes: 100%
- No: 0%
- Don’t know: 0%

population level results: histogram with confidence intervals

Conclusions

- **Stakeholder study to identify:**
  - *requirements ⇒ expert elicitation exercise*
  - Most participants were familiar with RBA (93%)
  - About half has used RBA as part of their work
  - DALYs are perceived to be useful to assess risks/benefits (70% agrees)
    - DALYs are used for the QALIBRA-tool

49
Recommendations regarding the web-tool

- Provide a checklist of data needed for the tool
- Provide a combination of data output options
  - graphical; tabular; overview of (model) assumptions
- Allow for multiple output formats
- Provide information regarding
  - background of model
  - educational materials
- Allow for information exchange with others performing RBAs
Introduction to the QALIBRA risk-benefit assessment tool

Qalibra Workshop, Budapest, 9-10 September 2009

Presented by Helen Owen
Main contributors: Fera, Patras

QALIBRA web tool

• Requirement of EU project specification:
  – ‘Make methods available to all stakeholders as web-based software’
QALIBRA web tool

- Flexible framework:
  - Follows stepwise assessment framework
  - User can specify as few/many health effects as required
  - Can accept outputs from other software as input (e.g. MCRA)
  - Each input can be deterministic or probabilistic
  - Proper use requires significant expertise in exposure, toxicology, etc.

QALIBRA web tool

- User-friendly design
  - Interface professionally designed and tested
  - “Assessment wizard” for new users
  - Extensive help (to be completed)
  - Hypertext glossary for specialised terms

FINAL REFINEMENTS IN PROGRESS - PLEASE BEAR WITH US!
QALIBRA web tool

Tour of website
QALIBRA web tool

- Assessments, Model Runs and Datasets

**Example**

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Model Runs</th>
<th>Datasets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risks and benefits of drinking wine</td>
<td>Run 1 - Red</td>
<td><em>All datasets used to produce the model runs</em></td>
</tr>
<tr>
<td></td>
<td>Run 2 - Rose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Run 3 - White</td>
<td></td>
</tr>
</tbody>
</table>
TOUR OF QALIBRA WEBSITE

Helen Owen, Fera

1. Introduction
   Aims of this session:
   • Overview of website content
   • Learn layout conventions & how to navigate
   • Introduce new and expert user options
   • Introduce concepts of assessments, model runs and datasets

2. Go to www.qalibra.eu

3. Home page
   Contains basic information about the project and the web tool
   • What is QALIBRA?
   • Why does it exist?
   • Who is it for?
   • How does it work?
     o Worked example RBAs using tool
     o Data requirements
     o Outputs
   • How to register
   Please note this content is under development – some links do not lead anywhere yet!

4. Logon links in top-right

5. Tabs along top:
   • Register
   • Support
   • Project
   • Contact Us
Presentation

Introduction to the QALIBRA risk-benefit assessment tool

The Home Page

6. Click on Support tab
   3 links on the side-bar:
   - Support Home: this is still under development, but Andy has delivered a lot of this material to go here in his presentation
   - Glossary: completed.
   - Model Parameters: These are the data inputs that the tool requires. I will explain these in more detail during the practical session

7. Click on Project tab
   Contains information about the project e.g.
   - Participant details
   - Project workplan – list of WPs

8. Click on Contact Us tab
   Email addresses for
   - Project enquiries
   - Scientific enquiries
   - Give feedback/ask for help

9. Return to homepage by clicking on QALIBRA logo or home icon in the ‘breadcrumbs’ (just below tabs along top)
10. Login using your user name and password (we will distribute these in the practical sessions)
   The Tool tab (only for registered users) has now appeared at the top!

11. Click on Tool
   From this page you can either be
   - Guided through the creation of your RBA – novice users
     - Click to show first step of wizard
     - Demonstrate hover links to glossary definitions
   - Or go straight to RBAs that you’ve already created (click to show table containing Assessments and their Model Runs)
     - Note the layout of the table:
       Assessment - a group of Model Runs investigating the same risk-benefit problem
       Model Run – a single RBA using a particular set of data inputs
       Datasets – every dataset you have used to construct all of your model runs
   See slide 7 in ‘Introduction to the QALIBRA risk-benefit assessment tool’
Table of Assessments and Model Runs

- Assessments can be shared with other QALIBRA users (click to demo)
- Assessments can be renamed
- Assessments can be discussed (with anyone you have shared with)
- Assessments can be deleted!
- You can also group Assessments that you have created using the 'Grouped Assessments' tab on the side-bar. This is intended to facilitate sharing of multiple assessments (e.g. all those for your organisation).
Presentation
Case study A: risk-benefit assessment for phytosterols in margarine

Risks and benefits of phytosterol enriched margarines

Case study of the Qalibra project on a functional food

Participants:
Rivm, Fera, Matis

Presenters: Nynke de Jong, Jeljer Hoekstra

Phytosterol enriched margarines

- Functional food:
  - Foods to which one or more ingredients (nutrients or non-nutrients) have been added, or in which ingredients by themselves or concentrations of already present ingredients have been modified to enhance their contribution to a healthful diet (claims)
  - different from novel foods
  - Contribution is communicated to the general public through claims
Phytosterol enriched margarine: SCF opinion (April 2000)

- April 2000: SCF opinion $\rightarrow$ safe for consumption
- Marketing: people who try to lower their blood cholesterol levels
- Patients on cholesterol-lowering medication: medical supervision
- $\beta$-carotene reduction relevant for people with suboptimal vitamin A status: dietary advice about adequate intake of fruits and vegetables

25 g / day $\rightarrow$ 10-15% LDL reduction
## Recommended intakes

<table>
<thead>
<tr>
<th>Product category</th>
<th>Common packing size</th>
<th>Recommended consumption</th>
<th>Phytosterol concentration</th>
<th>Daily intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Margarine</td>
<td>250 g</td>
<td>3* 8-10 g/day</td>
<td>7.5-8 g/100 g</td>
<td>2-2.3 g</td>
</tr>
</tbody>
</table>

## Phytosterol enriched margarines

- **Accepted motives for industry to market FF**
  - Increasing wealth and corresponding lifestyle
  - Increasing life expectancy
  - Increasing health problems and knowledge about health problems
  - → so people are interested and willing to buy

- **Societal questions**
  - Medicalisation of daily food intake?
  - Long term safety and effectiveness (e.g. exposure, overdosing, target-vs riskgroups, physiological or behavioural interactions?)
  - Marketing and advertising procedures (claims)?
Phytosterol enriched margarines

- Research should focus on safety and effectiveness
  - Quantitatively balancing positive vs negative effects:

![Risks and Benefits](image)

Problem definition

- From a policy making point of view:
  - What are the public health effects of a policy on margarine enrichment?
  - 20% / 50% / 100% of margarines are enriched

- Policy scenario: 7.5 g phytosterols / 100 g margarine (100%)
- Reference scenario: status quo: no enrichment
Case study A: risk-benefit assessment for phytosterols in margarine

Data needed

- Population info (age, sex, etc.)
- Intakes (reference & alternative)*
- Dose-response functions*
- Age of onset*
- Recovery probabilities*
- Mortality probabilities*
- Disease weights*
- Disease durations*
- Normal life expectancies

* Needed for each health effect considered
Case study A: risk-benefit assessment for phytosterols in margarine

Health effects of phytosterols

- Negative effect: carotenoid lowering *convincing evidence*, 21 papers
- Final health effect: vitamin A deficiency; nightblindness

- Positive effect: LDL chol. lowering *convincing evidence*, 49 papers
- Final health effect: IHD decrease

- Pubmed (until 2008)
- Criteria of WHO
  - evaluate quality of studies + consistency of evidence:
    - convincing – probable – possible – insufficient
- Consultation of experts in the field

*(little studies on toxicity show no mutagenic activity, no subchronic toxicity, no genotoxicity)*

Input for the tool

- Population and Intake
- $P_{effect} =$ probability of effect onset *in current year* (this will be a function of intake)
- $Prec =$ probability of recovery from effect
- $P_{die} =$ probability this effect causes death
- $YLD_{rec} =$ duration of disease for those who recover
- $YLD_{die} =$ duration of disease for those who die of it
- $LE =$ normal life expectancy (a function of age)
- $CA =$ current age of individual in year of onset
- $w =$ DALY weight
Intake scenario’s – Issues

- Intake natural sources: 150-400 mg / day
- For effective LDL reduction: 2-3 g / day

- Actual intake low compared to effective dose
  - Dutch Doetinchem cohort: 14 g margarine / day = 1.1 g/day phytosterols (Wolfs et al., 2006);
  - Dutch Hartslag study: 14±9 g/day (de Jong et al., 2007)

Intake scenarios assumptions & data sources

- Natural plant sterol intake (background) not taken into account
- Data of Dutch National Food Consumption Survey (DNFCS), 1997-1998, N=6250
- Margarines used as bread spread only
- In DNFCS: 70-88% of the population uses margarine
- Start with a 100% enrichment scenario
Presentation
Case study A: risk-benefit assessment for phytosterols in margarine

Intake scenarios
age, sex dependent distribution

Population phytosterols intake

• For 1000 representative (age and sex) individuals for the Dutch population a margarine intake is drawn from the intake distribution

• Margarine intake converted to sterol intake based on 7.5 g /100 g
Case study A: risk-benefit assessment for phytosterols in margarine

Qalibra data

<table>
<thead>
<tr>
<th>age</th>
<th>sex</th>
<th>sterol intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>62</td>
<td>0</td>
<td>3.34</td>
</tr>
<tr>
<td>48</td>
<td>0</td>
<td>1.09</td>
</tr>
<tr>
<td>14</td>
<td>0</td>
<td>0.72</td>
</tr>
<tr>
<td>19</td>
<td>0</td>
<td>1.23</td>
</tr>
<tr>
<td>53</td>
<td>0</td>
<td>1.10</td>
</tr>
<tr>
<td>34</td>
<td>1</td>
<td>0.48</td>
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<tr>
<td>50</td>
<td>0</td>
<td>2.20</td>
</tr>
<tr>
<td>51</td>
<td>0</td>
<td>2.36</td>
</tr>
<tr>
<td>71</td>
<td>1</td>
<td>1.76</td>
</tr>
<tr>
<td>53</td>
<td>1</td>
<td>0.16</td>
</tr>
</tbody>
</table>

Beneficial effect: lowering IHD risk

Peffect

- Sterol intake – %LDL chol. reduction (Katan, 2003)
  - Confirmed by Demonty (2009)

- absLDL chol. reduction- decrease in IHD incidence (Law, 1994 + 2003)
  - Cohort includes statin users; possible overestimation of effect
Beneficial effect
Peffect

• Other information that is needed:
  – Baseline LDL chol. level: by sex and age class (Verschuren, 2008)
  – IHD incidence in the Dutch population, by sex and age class (Nationaal Kompas Volksgezondheid, 2003)

Peffect; IHD vs. sterol intake depends on age and sex

**male, 68**

- IHD probability vs. phytosterol intake (gr/day)

- Line graph showing the relationship between IHD probability and phytosterol intake for male individuals aged 68 years.
Case study A: risk-benefit assessment for phytosterols in margarine

IHD

• \( w: \) Weight factor for IHD = 0.29
• \( \text{Prec: Chronic disease } P=0 \)

\( \text{Pdie} \)
  – Male mortality of IHD-patients 5.8%
  – Female mortality of IHD-patients 8.6%

• \( \text{YLDdie: 1 year} \)
  – (underestimate of benefit)

Adverse effect

• \( \text{absorption of fat-soluble vitamins (a.o. beta-carotene) decreases} \)
  – Advice to consumers: increase the consumption of fruit and vegetables while taking phytosterol enriched products BUT

62% of consumers are unaware of the importance of consuming fruit and vegetables (Hearty, 2007)
So worst case assumption: Phytosterol intake decreases beta-carotene levels

Adverse effect: low beta-carotene status

- Dose response
  - Not readily available
  - 2 g phytosterol/day results in 20% lowering of beta-carotene levels

- Effect of low beta-carotene status
  - Best case: no effect
  - Worst case: inadequate vitamin A status, first phase nightblindness
Adverse effect: nightblindness

- Simple model based on worst case
  - Individuals with an inadequate vitamin A status, who take phytosterols, become nightblind
  - They take extra vitamin A and are cured within a year

Information that is needed:

- Plant sterol intake; yes/no
- Distribution of vitamin A deficiency

- $P_{effect} = P_{vitAdef}$ if sterol intake $> 0$
- Else $P_{effect} = 0$
Vitamin A deficiency

- In the Netherlands
  - 7% of the children have an intake lower than their need
  - 30% of female adults too low intake
  - Effect potential deficiency symptoms in 4.8% of 19-50 year females (Waijers and Feskens, 2004)

Adverse effect: night blindness

- DALY calculation

- Weighing factor for nightblindness: not available, chosen for weighing factor for minor/moderate visual disturbance
  - minor = 0.02
  - moderate = 0.17
Presentation
Case study A: risk-benefit assessment for phytosterols in margarine

- Curable, Prec=1
- duration for calculation YLDrec= 1 year
- Pdie=0

Results
Coffee / Tea time
Guided practical session will reveal some results
Guided practical session with QALIBRA tool: phytosterols example

Getting started

1. Go to www.qalibra.eu
   Login to the website with your Login and Password (to be supplied by trainer).

2. It is advisable that you choose your own password for future use of the website. Click on Account Settings to do so.

3. Click on the Tool tab at the top of the page.

   Next click on the Assessments link on the side bar.

   Two assessments have been created for the practical sessions at this workshop. They were made visible to all workshop participants using the Share function. The data inputs required by the tool for these risk benefit assessments have already been uploaded to the tool.

4. In this session we will be working with the assessment named ‘Fortification of margarines with plant sterols’. There are currently no model runs within this assessment. To create one, click on the link Wizard model run creation.

5. Hopefully the diagram is familiar! It was described in Andy’s ‘Introduction to risk-benefit assessment and the Qalibra framework’ presentation.

   Step 1 of the assessment is to setup the run. This is where you select the Assessment you want to work on – ensure that ‘Fortification of margarines with plant sterols’ has been selected.
Deterministic calculations

Example 1: high phytosterol consumer

6. To begin with we will try some deterministic calculations with the tool. We will first consider an individual who is a high consumer of phytosterols, so you may wish to give your Model Run a name such as ‘[Your name] high consumer’ (fill in as appropriate).

Hints for naming conventions can be found by hovering your mouse over Hints until a floating box appears (tool tip).

Some technical terms used in the tool have tool tips. They are also written in green and the floating box contains the glossary definitions for these technical terms.

Click Next.

7. **Step 2** is where you name the two dietary scenarios you are going to consider. We shall compare the dietary scenario of high phytosterol consumption to a scenario of zero consumption in order to see what the additional risks and benefits are. Name the Reference Scenario ‘Zero sterol consumption’ and the Alternative Scenario ‘High sterol consumption’.

Click Next.

8. In Step 3 you need to provide the tool with some information about the individual. In the **Individuals** drop down box select **Specify single value**. In the expanded section you can see, firstly a description of what the individuals input is and secondly what a single value for this input represents.

You need to supply the age of your individual. For this example we will use age 42.

Repeat this procedure for the **Life Expectancy** input and enter the value 80.

Click Next.

9. Some of the known health effects associated with phytosterol consumption are a reduction in **Ischaemic Heart Disease** (IHD) and an increase in **Night Blindness**. At **Step 4** select both of these **Health Effects** for inclusion in your risk benefit assessment.

Click Next.
10. The exposure values that are entered at Step 5 need to relate to the dietary scenarios we defined in step 2. We defined scenarios: zero sterol consumption and high sterol consumption. Use **Specify single value** for each input, to enter a value of 0 for Exposure: Reference Scenario for each health effect to correspond to zero sterol consumption.

The units of exposure must be the same as the units in the dose-response function. We will use ‘g sterol enriched margarine per day’ (with an enrichment of 7.5g phytosterols/100g margarine) for the dose-response for IHD and a binary dose-response where the individual is either a consumer of enriched margarines or not for Night Blindness. Enter a value of 7 g sterol enriched margarine/day for Exposure: Alternative Scenario under health effect IHD and a value of 1 (to indicate consumer) for Exposure: Alternative Scenario under health effect Night Blindness.

Click Next.

11. A single value for the Dose-Response represents a threshold dose above which the individual will get the health effect. At Step 6 enter single values of 6 and 1 for the dose-responses for IHD and Night Blindness.

You will also be asked to specify whether your dose-response is quantal or continuous. Since the dose-responses are expressed in terms of the dose required to give a probability of the individual getting the effect equal to one, these dose-responses are quantal.

Click Next.

12. If the individual contracts the health effect, what are the probabilities of recovery and death? For this example, we will assume that IHD is not curable and is fatal in 5.8% of cases and Night Blindness is a mild, curable condition.

At Step 7, use **Specify single value** to set the Recovery Probability to 0 and the Death (from effect) Probability to 0.058 for IHD.

Use **Specify single value** to set the Recovery Probability to 1 and the Death (from effect) Probability to 0 for Night Blindness.

Click Next.

13. At Step 8, you can choose the Common Currency to express your health effects in. For this example, choose DALYs.

Click Next.
14. If the individual recovers or dies from or lives to the end of their life with the health effect, how many years do they have the health effect for and what is the severity of the health effect during that time? **Step 9** is where you supply this information.

Using "**Specify single value**" set the Weight if Recover (from effect), Weight if Die (from effect) and Weight if Live (with effect) to 0.29 (from RIVM kompas) for IHD.

We have assumed that those who die from IHD only live 1 year with the disease before death. Set YLD if Recover to 0 (irrelevant since the recovery probability is 0) and YLD if Die (from effect) to 1.

Set the Weight if Recover (from effect), Weight if Die (from effect) and Weight if Live (with effect) to 0.02 (minor visual handicap, Stouthard) for Night Blindness.

We have assumed that those who contract Night Blindness only have the effect for 1 year before they are cured. Set YLD if Recover to 1 and YLD if Die (from effect) to 1 (irrelevant since the death probability is 0).

Click **Next**

15. **Step 10** is the final step – you are ready to calculate.

Click **Finish**

16. The next page lets you review your choices for each input.

Click **calculate**.

17. When the calculation is complete, take a look at the results.

You should see that using deterministic inputs gives rather limited results.

**Example 2: Average phytosterol consumer**

18. Try creating a new **Model Run** within the ‘Fortification of margarines with plant sterols’ **Assessment** (using the wizard), repeating the instructions above, but using input values of 2 g sterol enriched margarine/day and 1 (to indicate consumer) for **Exposure: Alternative Scenario**.

Could you have predicted these results yourself?
Practical Session
QALIBRA tool and phytosterols example

Probabilistic calculations

Example 3: introducing variability and uncertainty in the model inputs

19. Create a new Model Run within the ‘Fortification of margarines with plant sterols’ Assessment (using the wizard).

20. At Step 2, name the Reference Scenario ‘Zero sterol consumption’ and the Alternative Scenario ‘20% of margarines enriched’.

21. Individuals in a population vary significantly. Some will be male, some female and they all have different ages. We can incorporate this variability in the Qalibra model by providing a population of individuals contained in a .csv file.

Each row of the file represents one individual in the population. The first column of the file must contain the age of the individual. The last column must contain the ‘scaling factor’ - how many individuals in the true population this individual represents (this may come from dietary survey data). Columns in between are optional. They can be used to specify any personal attributes that may be needed for this assessment e.g. Sex.

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</table>

IMPORTANT:
- The first row of the file must contain column names.
- All the values in the file must be numeric e.g. sex may be represented by the enumeration 0 = Male, 1 = female.

A file representing the Dutch population, containing 1000 individuals has been created for you. You can select it at Step 3 by choosing Dutch Population from the drop down list.
22. **Life Expectancy** varies by age and sex. In each row of the file you can specify average life expectancy values for different ‘Subgroups’ of the population. The first column should contain upper bounds for age e.g. upper bounds 10, 20, 100 will specify life expectancy values for individuals aged 0-10, 11-20 and 21-100 respectively. The final column contains the life expectancy values. Columns in between provide upper bounds for any attributes you specify in the **Individuals** input.

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A file containing the Dutch life expectancy has been created for you. You can select it at **Step 3** by choosing **Dutch Life Expectancy** from the drop down list.

23. Select the health effects IHD and Night Blindness in **Step 4**.

24. **Exposure** will vary between individuals. By providing a file of exposures, where each row contains an average exposure value for the corresponding individual in the **Individuals** input, this variability can be quantified.

However, **Exposure** is also uncertain. For example, on any given day an individual may consume less than their average intake or they may consume more. To quantify this uncertainty, multiple columns of exposure values representing this uncertainty may be supplied.

In this example, if the individual is a margarine consumer, there is uncertainty around whether the margarine they have eaten contains phytosterols or not.

Exposure for the Reference Scenario are not shown here because they contain only zeros!
## Practical Session

### QALIBRA tool and phytosterols example

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### Exposure Night Blindness Alternative Scenario

**IMPORTANT:**
Correlations may exist between the different exposure inputs. For example, in the files above, when the individual has a non-zero intake of phytosterols there is a 1 in the corresponding position for the Night Blindness exposure because they have consumed enriched margarine. It is the user’s responsibility to ensure consistency in these correlations.

**Exposure** files containing the data for ‘zero enriched margarines consumed’ and ‘20% of margarines enriched’ have been created for you. You can select them at **Step 5** by choosing **Background exposure to sterols IHD**, **Background exposure to sterols NB**, **20% of margarines enriched with sterols IHD** and **20% of margarines enriched with sterols NB** from the drop down lists.
25. The response in the **Dose-Response** can be made more detailed by supplying multiple dose levels.

As with the life expectancy input, the dose-response may vary according the personal attributes that were supplied in the **Individuals** input.

The response may also be uncertain.

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Dose-response IHD
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13 | 1  | 1  | 0.02
18 | 1  | 0  | 0  
18 | 1  | 1  | 0.04
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50 | 1  | 1  | 0.05
65 | 1  | 0  | 0  
65 | 1  | 1  | 0.03
98 | 1  | 0  | 0  
98 | 1  | 1  | 0.02
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3  | 0  | 1  | 0  
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13 | 0  | 1  | 0.02
18 | 0  | 0  | 0  
18 | 0  | 1  | 0.03
50 | 0  | 0  | 0  
50 | 0  | 1  | 0.02
65 | 0  | 0  | 0  
65 | 0  | 1  | 0.01
98 | 0  | 0  | 0  
98 | 0  | 1  | 0.01

**Dose-response Night Blindness**

Files containing the **Dose-Response data** have been created for you. You can select them at **Step 6** by choosing **Sterols – IHD** and **Sterols – Night Blindness** from the drop down lists.

26. **At Step 7** you can use the single values you used in the previous 2 examples, but we can add more detail to the **Death (from effect) Probability** for IHD.

We have separate death probability values for males and females. But these probabilities are independent of age and exposure. By leaving the age and exposure columns blank, this independence can be indicated.
Practical Session
QALIBRA tool and phytosterols example

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<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td>0.058</td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td>0.086</td>
</tr>
</tbody>
</table>

Death (from effect) Probability IHD

The file containing the **Death (from effect) Probability** for IHD has been created for you. You can select it by choosing **Prob Death IHD** from the drop down list.

27. **Steps 8, 9 and 10** can be completed as in the previous 2 examples.

28. Explore the results and graphs you obtain.

We will discuss them as a group.

For more detail on the file formats for each parameter of the QALIBRA tool, see the **Model Parameters** link on the side-bar of the **Support** tab.
Risks and benefits of fish

Case study of the Qalibra project on a common food: fish

Participants:
Rivm, Fera, Matis, Iniap/Ipimar

Jeljer Hoekstra, Marco Zeilmaker, Bas Bokkers

Oily fish

- Oily fish (2-10% fat): A controversial food?
  - Beneficial ingredients:
    - N-3 fatty acids (EPA, DHA)
    - Macronutrients
    - Micronutrients (B-vitamins (B12); Vitamin D; Minerals (I,Se,Fe,P))
  - Harmful ingredients
    - Chemical contamination:
      - Heavy metals (MeHg)
      - Dioxins/Furans/PCBs
    - Microbiological contamination (Listeria)
Advice on oily fish consumption

- NL: fish twice per week, max 600 g / wk (i.e. max 4 meals/ wk)
  Pregnant women: max 300 g / wk
  (i.e. max 2 meals/wk), no predators

- UK: 4 meals/wk (boys and males)
  2 meals/wk (girls, women, including pregnancy and breastfeeding).
  No tuna, shark during pregnancy or before.

- US: fish low in methylmercury (women and young children)
  Up to 2 meals/wk

Problem definition

- What are the health effects if people were to consume 200 grams of fish per week instead of their current consumption

- almost according to the recommendation of the Dutch ‘voedingscentrum’ (nutrition education centre)
Case study B: risk-benefit assessment for oily fish

### Intake Scenario

- **Beneficial health effects**
  - Cases prevented (death, disease)
  - Health gain

- **Adverse health effects**
  - Extra cases (death, disease)
  - Health loss

- **Dose-response integrated measure**

### Choice of health effects

- **Strength of the evidence** at least probable according to WHO-criteria for those (beneficial) effects for which epidemiological data is available

- **Expert judgement** for toxicological effects based on animal experiments
  - TDI, ADI
**Health effects**

- Fatal Coronary Heart Disease (CHD)
- Stroke
- IQ gain, DHA
- IQ loss, MeHg
- Reduced sperm production, dioxins
- TT4 hormone decrease, dioxins
- Liver, diffuse fatty change, dioxins

**Data needed**

- Population info (age, sex, etc.)
- Intakes (reference & alternative)*
- Dose-response functions*
- Recovery probabilities*
- Mortality probabilities*
- Disease weights*
- Disease durations*
- Normal life expectancies

* Needed for each health effect considered
Input for the tool

- Population and Intake
  - $P_{\text{effect}} = \text{probability of effect onset in current year}$ (this will be a function of intake)
  - $P_{\text{rec}} = \text{probability of recovery from effect}$
  - $P_{\text{die}} = \text{probability this effect causes death}$
  - $Y_{\text{LDrec}} = \text{duration of disease for those who recover}$
  - $Y_{\text{LDdie}} = \text{duration of disease for those who die of it}$
  - $LE = \text{normal life expectancy (a function of age)}$
  - $CA = \text{current age of individual in year of onset}$
  - $w = \text{DALY weight}$

Population and intake

- Dutch population represented by 1000 individuals (age, sex, bodyweight) based on CBS database

- 2 scenarios
  - Reference: Current based on Dutch Food Consumption Survey, DNFCS
  - Alternative: 200 grams of fish/week
Current Fish intake distribution

Intake

- Fish intake drawn from DNFCS* distribution
- DHA conc. 0.61g/100g from Dutch food composition database (NEVO)
- MeHg 0.05 (0.02 to 20) mg/kg fish from RIKILT (2003)
- Dioxins 1.6 (0.3-11)ng TEQ/kg fish
  Anal Bioanal Chem (2007)

* Dutch National Food Consumption Survey
Fatal CHD

Method for Peff fatal CHD

- Assumption log-linear relation between fish intake (dose) and relative risk (response)
- Based on DR meta-analysis Greenland and Longnecker (1992) and Berlin et al. (1993)

\[ \ln(RR) = \beta_{fish} \]

- Estimate \( \beta \) and \( \text{var}(\beta) \) for each study, adjust for within-study covariances due to common reference dose group
- Estimate overall \( \beta \), mixed effect model (weighted average)
Data

- 8 studies qualified.
  - report necessary data

- Input (possibly estimated from other reported numbers)
  - Dose (group)
  - and associated RR
  - Number of cases per dose group
  - or number of person years per dose group
  - Number of subjects per dose group
  - Total number of cases
  - Variance in RR (confidence intervals)
Case study B: risk-benefit assessment for oily fish

**Result β**

<table>
<thead>
<tr>
<th>Study</th>
<th>β</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kromhout (1985)</td>
<td>-0.030</td>
<td>-0.030 to -0.009</td>
</tr>
<tr>
<td>Albert (1998)</td>
<td>-0.009</td>
<td>-0.011 to -0.013</td>
</tr>
<tr>
<td>Ascherio (1995)</td>
<td>-0.013</td>
<td>-0.014 to -0.020</td>
</tr>
<tr>
<td>Daviglus (1997)</td>
<td>-0.002</td>
<td>-0.004 to -0.005</td>
</tr>
<tr>
<td>Oomen (2000)</td>
<td>0.004</td>
<td>0.005 to 0.013</td>
</tr>
<tr>
<td>Mozaffarian (2003)</td>
<td>-0.007</td>
<td>-0.008 to 0.001</td>
</tr>
<tr>
<td>Hu (2002)</td>
<td>-0.012</td>
<td>-0.013 to 0.011</td>
</tr>
<tr>
<td>Mann (1977)</td>
<td>0.027</td>
<td></td>
</tr>
</tbody>
</table>

**RR fatal CHD**

- Kromhout (1985)
- Ascherio (1995)
- Daviglus (1997)
- Albert (1998)
- Oomen (2000) Italy
- Hu (2002)
- Mann (1997)

Fish [gram/day] vs. RR fatal CHD
Unaccounted uncertainty

- distribution over dose group
  - e.g. 1-2 servings/week estimated at 150 grams/7 days
- assumption log-linear relation between RR and fish intake
- differences in age groups, male and female, smokers non-smokers
- different studies adjust for different confounders
- studies excluded
  - not reporting the right numbers e.g. ref. dose not no fish
  - cohorts of non-Europeans/Americans were excluded (Chinese and Japanese)

Absolute risk, RR to Peff

- \( \text{Peff} = \text{Po} \times \text{RR} \)
- Current intake must result in current incidence per age and sex

\[
\text{inc} = \sum_{1}^{100} \frac{\text{Peff}(\text{Intake(percentile)})}{100}
\]
Presentation
Case study B: risk-benefit assessment for oily fish

Incidence fatal CHD, CBS

- 5 year age groups
- 0 - 85+
- Men and women

Different \( P_0 \) for each sex and age group

<table>
<thead>
<tr>
<th>Mortality (ICD-10 code I21-22)</th>
<th>( 1/100000 ) men</th>
<th>( 1/100000 ) women</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>0.2</td>
</tr>
<tr>
<td>15</td>
<td>0</td>
<td>0.21</td>
</tr>
<tr>
<td>20</td>
<td>0.2</td>
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</tr>
<tr>
<td>25</td>
<td>0.6</td>
<td>0.2</td>
</tr>
<tr>
<td>30</td>
<td>1.79</td>
<td>0.82</td>
</tr>
<tr>
<td>35</td>
<td>4.78</td>
<td>2.17</td>
</tr>
<tr>
<td>40</td>
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<td>5.46</td>
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<tr>
<td>45</td>
<td>26.11</td>
<td>10.82</td>
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<tr>
<td>50</td>
<td>43.52</td>
<td>14.35</td>
</tr>
<tr>
<td>55</td>
<td>72.63</td>
<td>21.91</td>
</tr>
<tr>
<td>60</td>
<td>105.2</td>
<td>38.12</td>
</tr>
<tr>
<td>65</td>
<td>187.31</td>
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<td>70</td>
<td>305.19</td>
<td>134.39</td>
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<td>75</td>
<td>511.84</td>
<td>259.4</td>
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<tr>
<td>80</td>
<td>840.76</td>
<td>467.99</td>
</tr>
<tr>
<td>85</td>
<td>1331.27</td>
<td>960.05</td>
</tr>
</tbody>
</table>

Peff, fatal CHD

68, female

\( \text{Peff} \) vs. fish [grams/day]
Other parameters fatal CHD

- Pdie=1,
- Prec=0,
- YLDdie=0
- W=1

Stroke
Presentation
Case study B: risk-benefit assessment for oily fish

Peff stroke

- Like fatal CHD
- Based on DR meta-analysis Greenland and Longnecker (1992) and Berlin et al. (1993)

\[ \ln(RR) = \beta_{fish} \]

RR Stroke

Orencia (1996)
He (2002)
Iso (2001)
Gillum (1996)
Mozaffarian (2005)
estimate
max
min

\[ RR \text{ stroke} \]

\[ 0 \quad 0.5 \quad 1 \quad 1.5 \quad 2 \]

\[ 0 \quad 2 \quad 4 \quad 6 \quad 8 \]

fish [servings/week]
Presentation
Case study B: risk-benefit assessment for oily fish

Incidence stroke, RIVM

- 5 year age groups
- 0 - 85+
- Men and women

- Different P0 for each sex and age class

<table>
<thead>
<tr>
<th>1/1000</th>
<th>Incidence stroke</th>
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<tbody>
<tr>
<td>age</td>
<td>male</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>0.04</td>
</tr>
<tr>
<td>10</td>
<td>0.02</td>
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<tr>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>25</td>
<td>0</td>
</tr>
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<td>30</td>
<td>0.1</td>
</tr>
<tr>
<td>35</td>
<td>0.26</td>
</tr>
<tr>
<td>40</td>
<td>0.17</td>
</tr>
<tr>
<td>45</td>
<td>0.82</td>
</tr>
<tr>
<td>50</td>
<td>1.55</td>
</tr>
<tr>
<td>55</td>
<td>1.91</td>
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<td>60</td>
<td>3.68</td>
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<tr>
<td>65</td>
<td>5.64</td>
</tr>
<tr>
<td>70</td>
<td>9.8</td>
</tr>
<tr>
<td>75</td>
<td>15.92</td>
</tr>
<tr>
<td>80</td>
<td>19.86</td>
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<tr>
<td>85</td>
<td>24.08</td>
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</table>

Peff Stroke

<table>
<thead>
<tr>
<th>58, male</th>
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<tbody>
<tr>
<td>fish [grams/day]</td>
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<tr>
<td>0.0E+00</td>
</tr>
<tr>
<td>50</td>
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<tr>
<td>100</td>
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<td>150</td>
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<tr>
<td>200</td>
</tr>
<tr>
<td>250</td>
</tr>
<tr>
<td>300</td>
</tr>
</tbody>
</table>
Presentation
Case study B: risk-benefit assessment for oily fish

Other parameters stroke

- Pdie=0, (underestimate)
- Prec=0,

- \( W=0.61 \) (Stouthart, medium)
- \( W=0.27 \) WHO, long-term survivors

IQ effects
Presentation
Case study B: risk-benefit assessment for oily fish

- Effect on new-borns
  - DALYs assigned to mother (her intake)
- Dose-response IQloss vs MeHg intake
  - Intake – equilibrium hair conc. PBPK model Clewel et al.
  - Hair conc. – IQloss meta-analysis Cohen et al.
- Dose-response IQgain vs DHA intake
  - DHA – IQgain meta-analysis Cohen et al.
- Probability of having a child (depends on age) in the current year

![Dose-response MeHg IQloss](image-url)
### CBS newborn data

<table>
<thead>
<tr>
<th>age mother</th>
<th>probability of birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>0</td>
</tr>
<tr>
<td>20 - 25 year</td>
<td>0.035823</td>
</tr>
<tr>
<td>25 - 30 year</td>
<td>0.098602</td>
</tr>
<tr>
<td>30 - 35 year</td>
<td>0.129673</td>
</tr>
<tr>
<td>35 - 40 year</td>
<td>0.060005</td>
</tr>
<tr>
<td>40 - 45 year</td>
<td>0.009442</td>
</tr>
<tr>
<td>&gt;45</td>
<td>0</td>
</tr>
</tbody>
</table>

### IQ

- **Standard IQ distribution**
- **Mean 100, sd=15**

<table>
<thead>
<tr>
<th>IQ</th>
<th>w</th>
<th>max</th>
<th>min</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;85</td>
<td>0.82</td>
<td>0.98</td>
<td>0.534</td>
</tr>
<tr>
<td>70-84</td>
<td>0.43</td>
<td>0.518</td>
<td>0.353</td>
</tr>
<tr>
<td>50-69</td>
<td>0.29</td>
<td>0.496</td>
<td>0.091</td>
</tr>
<tr>
<td>35-49</td>
<td>0.09</td>
<td>0.137</td>
<td>0.04</td>
</tr>
<tr>
<td>20-34</td>
<td>0.09</td>
<td>0.137</td>
<td>0.04</td>
</tr>
<tr>
<td>&lt;20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Quality of life lost due to IQ-change

Other parameters IQ

- IQchange is for life
- Prec=0
- Pdie=0
Dioxines

Risk: Dioxins (issues)

Dioxins: same mechanism of action $\rightarrow$ TEQ
bioaccumulating properties
risk proportional to whole/tissue concentration
(liver/fat)

Background exposure: 0.9 pg TEQ/kg bw/day (NL)

Whole Body Concentration (W.B.C.) after intervention depends on individual's body composition:

W.B.C. after intervention
**Risk: Dioxins (effect assessment)**

Human epidemiological data: discarded (SCF/WHO/JECFA)

**Animal toxicity:**
- Carcinogenicity discarded (SCF/WHO/JECFA)
- Acute: single exposure during pregnancy → effects on sperm count
- Chronic: sustained exposure → survival/hepatic/thyroid toxicity

**Extrapolation/risk assessment strategy:**
- Define suitable “Effect Size” (animal)
- Calculate corresponding “Effect Dose” (animal)
- Extrapolate to effect dose in humans population

---

**Risk: Dioxins (extrapolation)**

- Distribution of effect dose in animal → human population
  - Interspecies extrapolation
  - Intraspecies extrapolation (mean=1/upper tail=10)

![Graph showing distribution of effect dose]

-5% sperm count
- Diffuse fatty change
-5% TT4
Dioxines, Spermcel production

- Effect in sons of exposed mothers
  - DALYs assigned to the mother (her intake)
- 15% reduction = infertile
- Probability of having a child (depends on age) next year
- Probability it is a son 51%, CBS

Peff spermcel production

30 year old mother
Other parameters sperm cell production

- Pdie=0,
- Prec=0,
- W=0.18 WHO, infertility

Peff TT4

50 year

Pefect

0.06
0.05
0.04
0.03
0.02
0.01
0
0
2
4
6
TEQ pg/kg BW
Other parameters TT4

- Pdie=0,
- Prec=0,
- W=0.09?? WHO, Iron-deficiency anemia (severe) WHO GBD update 2004

Risk: Dioxins (hepatic toxicity)

- Hepatic toxicity, rat (NTP, 2006)
- Effect Size: --
- Diffuse Fatty Change (dose metric: ng/kg liver)
- Aggregate measure for lower dose toxicity
- AoO unknown

<table>
<thead>
<tr>
<th>Effect</th>
<th>Internal conc liver</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pigmentation</td>
<td>2082.993</td>
</tr>
<tr>
<td>Toxic hepatopathy</td>
<td>4200.063</td>
</tr>
<tr>
<td>Multinucleated hepatocyte</td>
<td>4712.246</td>
</tr>
<tr>
<td>Hepatocyte hypertrophy</td>
<td>3127.275</td>
</tr>
<tr>
<td>Oval cell hyperplasia</td>
<td>4979.339</td>
</tr>
<tr>
<td>Diffuse fatty change</td>
<td>5588.079</td>
</tr>
<tr>
<td>Nodular hyperplasia</td>
<td>8422.326</td>
</tr>
<tr>
<td>Cholangiofibrosis</td>
<td>9031.534</td>
</tr>
</tbody>
</table>
Peff DFC

- Peff=0
- Smaller than numerical resolution of the toxicological model

Results

Coffee / Tea time

Guided practical session will reveal some results
Appendix 1

Post - Questionnaire for Qalibra Tool

Answering to questions 1 - 4 is optional.

1. Name:

2. Gender
   - Male
   - Female

3. Age .... years

4. What is your profession and main job responsibilities?

5. Were you familiar with the Qalibra framework before the workshop?
   - No
   - Yes, I have seen a presentation.
   - Yes, I have read some documents describing it.
   - Yes, a colleague has explained it to me
   - Yes, other. Please specify: ..........................

6. Have you used the Qalibra tool before the workshop?
   - No
   - Yes, I have used it once
   - Yes I have used it twice
   - Yes I have used it more than 2 times

7. I cannot decide if the Qalibra tool will deliver the analysis I want.
   - Strongly Disagree
   - Disagree
   - Neutral
   - Agree
   - Strongly Agree
8. I would trust to use the services offered by the Qalibra tool in my work/research.

- [ ] Strongly Disagree
- [ ] Disagree
- [ ] Neutral
- [ ] Agree
- [ ] Strongly Agree

Because:

9. I need more detailed information on what research findings and methodologies the Qalibra tool is based on.

- [ ] Strongly Disagree
- [ ] Disagree
- [ ] Neutral
- [ ] Agree
- [ ] Strongly Agree

Such as:
10. Learning to use the Qalibra tool is difficult.

- Strongly Disagree
- Disagree
- Neutral
- Agree
- Strongly Agree

Comment:

11. Everything in the Qalibra tool is easy to comprehend.

- Strongly Disagree
- Disagree
- Neutral
- Agree
- Strongly Agree

Comment:

12. The current workflow (sequence of dialogues/screens) was logical and easy for me to follow.

- Strongly Disagree
- Disagree
- Neutral
- Agree
- Strongly Agree
13. Could the workflow be organized in any other way or improved in certain cases to accommodate better your needs?

14. The terminology used is hard to understand.
   - Strongly Disagree
   - Disagree
   - Neutral
   - Agree
   - Strongly Agree

For example:

15. The Qalibra tool prevents me from making errors.
   - Strongly Disagree
   - Disagree
   - Neutral
   - Agree
   - Strongly Agree
16. Can you think of any specific services or functionalities of the Qalibra tool that would be useful for you?

17. How did you perceived the presentations of the Qalibra tool during the workshop? How can we improve?
18. What did we forget to ask you? Any other comments?

Thank you for your time.
APPENDIX 2

1. Methodology for developing training material and training courses for QALIBRA

The following two major steps are proposed to be included for developing training material considering the QALIBRA project:

a) **Design** of training material that is necessary to prepare relevant and useful training units

b) **Development** of training material which is a process for organizing, developing, revising and finalizing training units.

**Design of the training material** (detailed proposals are given in sections 1.1 to 1.4):

- Define the **target population** for training (see as well section 1.1).
- List the **tasks** to be performed by the target population (see as well section 1.2).
- List the **skills and knowledge needed to do the tasks** (see as well section 1.3).
- Select the **skills and knowledge to be taught** (These make up the “training objectives.”) (see as well section 1.4).

Following approach could be adopted for designing teaching units for the QALIBRA tool. For each teaching unit there should be defined: a) introductory background knowledge and criteria for applicability by explicitly outlining the training objectives and tasks for the participants (target population) b) more specific knowledge and skills needed to perform the tasks c) specific knowledge and skills to be taught.

![Diagram](image-url)
1.1 Defining the participants

The participants are the group of learners for whom the training is intended. It is critical to define this group(s) in order to design the training appropriately. We need this information as well for the forthcoming usability evaluations (see as well action point 24 from the partners meeting). For example, it is assumed that training for risk assessors could be different from training for modellers, even though they may do some of the same tasks. To define the target population, ask questions such as:

- What are the job titles of the intended participants in the training?
- How they were originally trained for their jobs?
- What are their educational and professional backgrounds?
- How are they accustomed to learning?
- What languages do they speak and read?
- What types of risk-benefit analysis do they work in, and what software tools are they using already?
- Is it possible for them to attend a training course away from their jobs?

1.2 Listing the tasks to be performed by the participants

The tasks to be performed by the participants should be defined according to the teaching unit and the training objectives. To define and analyze the tasks the training material developers should have deep domain knowledge and should have access to:

- Domain and technical experts who can accurately describe the task to be performed,
- good performers who can be observed doing the task by using the QALIBRA tool, and/or
- documents and manuals that accurately describe the task.

1.3 Listing the skills and knowledge needed to do the tasks

For each task involved, the training developers next list the skills and knowledge required to perform the task. Skills are generally actions related to the functionality of the QALIBRA tool such as creating assessments, editing and maintaining assessments, create datasets and explore results etc.. Required knowledge is the information needed to do a task correctly and is connected mainly with theoretical background knowledge. The final list of skills and knowledge can be very lengthy, and it becomes obvious that choices must be made about which skills and knowledge are most important to teach.

1.4 Selecting the skills and knowledge to be taught (training objectives)

Experts use a list of criteria to decide which skills and knowledge to include in the training. These will make up the training objectives for the course. The selection criteria may include such factors as the following. The first list below shows factors that would lead to inclusion in the course; the second list shows factors that would suggest that the skill or knowledge could be excluded (not taught) in the course. Some of the factors may be more or less relevant in different situations.

Possible criteria for inclusion

115
Many members of the target population lack the skill or knowledge.
Training (including practice and feedback) is required to learn the skill or knowledge because it is new or difficult.
The task for which the skill or knowledge is needed is important to the outcome.
The skill or knowledge is needed frequently.
It is practical to teach the skill or knowledge in the given training setting.

Possible criteria for exclusion

- The task, skill or knowledge cannot be described specifically and thoroughly enough to be a meaningful part of training.
- Teaching the skill or knowledge is not practical in the time or with the resources available.
- Most members of the target population already have the skill or knowledge.
- The task, skill or knowledge is straightforward and could be done correctly after reading guidelines such as a checklist or manual. Practice and feedback are not required.
- The task is done or the skill/knowledge is used infrequently (e.g. it deals with a condition that is extremely rare).
- There are substantial obstacles to doing the task (such as lack of equipment, or time) that would prevent participants from doing the task even if they knew how. These obstacles would have to be overcome before the training could be useful.
- Another training course is available to teach the task/skill/knowledge.

Similar criteria can be used to decide which of the included tasks, skills and knowledge will receive more emphasis and practice in the training course.

1.5 Designing and developing the training course

**Development of the training material (which is a step to be performed by domain experts):**

- Organize the selected skills and knowledge into suitable teaching units (modules) and develop the training design (including brief outlines of module content and planned training methods).
- Draft expanded outlines of modules, including instructional objectives, main theoretical background, and descriptions of training methods, examples and exercises.
- Experts provide realistic examples and information for use in exercises.
- Draft the complete teaching units.
- Field-test the training materials.
- Revise and finalize training materials based on the field test.

As part of the design process, the training developers organize the selected skills and knowledge to be taught into logical teaching units called modules. The design for each module includes its training objectives and a brief outline of the information, examples and exercises that will provide opportunities for practise using the skills and knowledge.

Development of each module progresses from the brief design outline, to an expanded outline, to the complete module. Expanded outlines of the modules specify more completely the information and the types of examples and exercises to be provided. For example, examples might be given
through pictures, live demonstrations or video. Exercises might include written exercises, group discussions or role plays. To develop realistic examples and exercises, the training developers rely on interviews with technical experts who are familiar with the target population, job setting, tasks and conditions.

Development of complete modules includes preparation of guidelines for the facilitators who will conduct the course. Finally, the modules and associated guidelines are reviewed by technical experts and field-tested with the target population. The training materials are then revised and finalized based on reviews and results of the field test.