FSA Study on the Use of Quality Adjusted Life Years for Food Safety Risks (Phase 1)

Food Standards Agency

Final Report

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Final Report

A report submitted by Cohort Consulting

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Acronyms

CEA	Cost-effectiveness analysis
DALY	Disability adjusted life year
EQ-5D	Euro-Qol 5 Dimension (health classification system)
FBD	Foodborne disease
FSA	Food Standards Agency
HUI-3	Health Utilities Index version 3 (health classification system)
HYE	Healthy Year Equivalent
IgE	Immunoglobulin E
IID	Intestinal infectious disease
NICE	National Institute for Health and Care Excellence
QALY	Quality adjusted life year
SF-6D	Short-form 6 dimensions (health classification system)
SG	Standard gamble
TTO	Time trade-off
VAS	Visual analogue scale
VSL	Value of Statistical Life
WTP	Willingness-to-pay

Key Findings

The purpose of this research is to assess the feasibility of using Quality Adjusted Life Years (QALYs).

In the course of this research we have found the following:

- A review of the use of QALYs in UK government departments shows that they are widely used to measure health impacts and this is a growing trend
- A review of the use of QALYs to measure health impacts by international food safety regulators shows that there are only a handful of countries using this approach, but those that use the QALY are often at the cutting edge of research in the appraisal and evaluation of health interventions in this area (e.g. the US, New Zealand, Sweden).
- A review of QALYs and other approaches was undertaken to determine the advantages and disadvantages of QALYs: we recommend the development of QALYs for reasons of research quality and institutional reasons of widespread use by other bodies.
- The research undertaken overwhelmingly suggests that developing QALYs is both highly feasible and desirable:
  - Methodologically – although a number of obstacles to collecting data are identified, in particular the difficulty of valuing the "maintenance state" such as dietary management and avoidance of allergens for allergen sufferers, feasible solutions to any obstacles exist
  - Results – the QALYs estimated from the research in phase 1 are based on expert judgment of the relative severity of different conditions
  - For allergy/intolerance, IgE-mediated reactions had the most significant QALY loss, so may be considered to have the highest burden. This is closely followed by coeliac disease.
  - Due to the relatively short duration of morbidity reactions we found QALY losses for IIDs are generally low and are driven by the proportion of deaths. *Listeria monocytogenes* had a much higher QALY loss than other IIDs due to the high (25%) chance of death among people contracting the disease (listeriosis).

Executive Summary

Background

The FSA currently uses monetary impact valuation to monitor and evaluate food safety measures; assess the cost benefit of interventions; and quantify the foodborne disease (FBD) burden on the UK economy.

Adopting health outcome measures, such as Quality Adjusted Life Years (QALYs) or Disability Adjusted Life Years (DALYs) are therefore needed to complement measures of monetary impact valuation. One of the most useful aspects of QALYs is that they allow comparisons of the relative effectiveness of interventions from different food policy areas. This information can help to inform both policy decision making within food safety and resource allocation decisions across foodborne disease prevention and control.

Purpose

The FSA has decided to commission this study in two phases. The research reported here (Phase 1) explores and reviews the evidence to elicit valuations of health outcome impact measures relating to foodborne risks associated with Intestinal Infectious Diseases (IIDs) and food hypersensitivity, which includes IgE mediated food allergy; non-IgE mediated food allergy; Coeliac disease; and food intolerance. Phase two will look to build on this study by validating findings and addressing gaps identified in the initial phase of the research.

An initial aim of Phase 1 of the research was to compare and contrast the costs and benefits of using the Disability Adjusted Life Year (DALY) with the Quality Adjusted Life Year (QALY). Consideration of the DALY was initially deemed important given that the DALY has been especially important in the international context, in particular in the use of the World Health Organization's Global Burden of Disease studies in order to provide summary measures of population health which enabled comparison across countries. However, after early consultation with the FSA it was determined that pursuing the comparison of DALYs with QALYs was not necessary as the QALY was considered a better alternative between the two. This was so as the use of the DALY is largely a response to limited data on health states (such as can be obtained by hospital records) available in developing countries where data are sparse. As the DALY provides far less fine-grained classification of health states, if such data constraints were not present, and they were not present in this context, then the finer-grained health state data provided by the QALY were clearly preferred for the current research. Further considerations in favour of using the QALY are discussed in section 3, below.

This report describes research and presents results of Phase 1 of the FSA study into the use of Quality Adjusted Life Years (QALYs) as a health outcome measure for use in the regulation of food safety. To this end a number of steps were taken.

Research

We now provide a brief summary of the research results reported here:

- A review of the use of QALYs in UK government departments' shows that they are widely used to measure health impacts and this is a growing trend.
- The use of QALYs to measure health impacts by international food safety regulators shows that there are only a handful of countries using this approach, but those that use the QALY are often at the cutting edge of research in the appraisal and evaluation of health interventions (e.g., the US, New Zealand, Sweden).
- QALYs and other approaches was undertaken to determine the advantages and disadvantages of QALYs: it was found that the many benefits of using the QALY included reasons of research quality and institutional determinants based on widespread use by other bodies, hence an attempt to develop QALYs is recommended.
- The empirical research undertaken into developing QALYs for food-related illnesses overwhelmingly suggests that developing QALYs is both highly feasible and desirable.

Methodologically speaking, although a number of obstacles to collecting data are identified, in particular the difficulty of valuing the "maintenance state" for allergen sufferers, feasible solutions to most obstacles exists.

As important, the results of the present research into QALYs estimated for food related illnesses are based on expert judgment of the relative severity of different conditions.

Limitations

However, as noted a number of limitations to the current research were identified. First, it will be highly desirable to attempt to measure each individual intestinal infectious disease (IID) and food hypersensitivity type; particularly in the case of the latter, where "aggregated" categories developed were considered too crude for respondents. Second, health state classifications should be undertaken by sufferers - those who have experienced IID and/ or food hypersensitivity, not experts. Third, finding respondents from various types of food hypersensitivity is paramount. Most importantly, it was found that the most substantive methodological challenge will be to conduct extensive qualitative and quantitative research into the valuation of the "maintenance" state such as dietary management and avoidance of allergens for those suffering from food hypersensitivity. This is where the greatest loss of health-related quality of life took place and is far and away the most important concern of those suffering from food hypersensitivity.

Next Steps

The next steps of the research must, and can, address each of the challenges and limitations noted above. There are also a number of other areas that should be included in Phase 2 of the research.

First, working closely with Public Health England on their IID outbreak investigations to obtain data from those currently suffering from illness due to foodborne disease. Second, to conduct general tests from primary data on the sensitivity of the current “social tariff” data used to value QALYs as this might be applied to the case of food related illness. The social tariff refers to the data-set used by the generic measure, such as the EQ-5D, to determine the weights associated with various health states; for the EQ-5D this was derived from a population-level study of valuations of health states. As it is sometimes the case that the social tariff valuations for health states associated with particular conditions tend to over- or under-estimate health quality[1] it is important that the social tariff data for food-related illnesses be shown to be adequately representative.

Third, distributional issues should be addressed, both with respect to various disadvantaged groups, but in particular to geographic inequalities facing food hypersensitivity sufferers in terms of provision of information relating to the maintenance of their condition.

Fourth, the research should establish how the age-of-onset of a food hypersensitivity and IID, particularly where there is the possibility of fatality, impacts on QALY losses.

Lastly, primary research on the willingness-to-pay (WTP) for a food safety related QALY should be undertaken. This approach can then provide context-specific and distributional weights where required. This approach has a number of advantages, discussed below, and importantly is consistent with the Treasury Green Book. Thus, a WTP value for a food safety QAL enables comparability and hence grounds for priority between different FSA policies, as well as comparability with other government departments' monetised policies.

[1] See Zamora et al (2007) for a study showing that the social tariff data for health states associated with lower back pain is generally inaccurate.

1. Introduction

The primary role of the Food Standards Agency (FSA) is to protect UK consumers in relation to food safety risks including microbiological foodborne disease (FBD), food allergy and chemical and radiological safety ensuring food is safe and what it says it is for consumers

The FSA, through risk assessment, regulation and other interventions, attempts to reduce the incidence of food safety risks in the UK and minimise impacts on society. To assess the most efficient and effective ways to do this, the FSA needs to ensure it has a good understanding of the incidence of food safety risks in the population and associated impacts.

The FSA currently uses monetary impact evaluations for purposes of assessing the costs and benefits of interventions and to quantify the overall burden of disease caused by infectious intestinal diseases (IIDs) and food hypersensitivities.[2]

Objectives

The FSA decided that a two-phase research project would be commissioned to develop QALYs. Phase 1 (the current phase) of the research had the following objectives:

- To review current approaches to valuing health outcomes by different UK departments as well as food safety regulators in various countries
- Explore the advantages/disadvantages of various types of health outcome measures (e.g., QALYs, DALYs, Value for Preventing Statistical Injuries/Fatalities)
- Recommend and provide a rationale for the use of a specific health outcome measure by the FSA
- Develop and construct a provisional set of QALY values for the various types of food-related illness that are addressed by the FSA, and which could act as an interim measure to inform the Board's strategic priorities for 2015-2020.

This report describes research and results of Phase 1 of the FSA study into the use of Quality Adjusted Life Years (QALYs) as a health outcome measure for use in the regulation of food safety. The aim of developing a QALY is to measure and compare the burden of illness caused by different intestinal infectious diseases (IIDs) and food hypersensitivity.

[2] We will use the term "food-related illness" as an umbrella term to cover all cases of food allergy or intolerance or IIDs, and will also use the umbrella term "food hypersensitivities" to refer to "food allergy or intolerance", where the latter include IgE or non-IgE mediated conditions, intolerances and Coeliac disease.

By using a health outcome measure which is generic, enabling the comparison of different health states caused by different food-related causes, the FSA will have an enhanced evidence base upon which to establish its budgetary priorities in its work on food allergies and intolerance and IIDs.

Purpose

The purpose of this report is to provide the FSA with evidence on the relative burden of disease by different causes so as to inform their decision-making. The results presented here are preliminary but informative. Nevertheless the results are positive in terms of implications for a successful development of valid and reliable QALY estimates across the range of food-related illnesses in Phase 2.

Overview

This report will:

- Discuss the background to the present study
- Introduce and evaluate generic health-related outcome measures (e.g. DALYs, QALYs.)
- Explain the idea of a quality adjusted life year (QALY)
- Explain how the QALY is informed by a health state classification system and a measure of (health-related) quality of life or well-being associated with particular health states
- Survey the use of generic health outcome measures both by different UK Government Departments and internationally by different food safety regulatory bodies
- Describe the methods employed in collecting the data presented here
- Present analysis of the data and discuss the results
- Describe limitations and caveats to the current data
- Present conclusions of the current research, and how this research can potentially be used to establish budgetary priorities
- Describe next steps and recommendations in the development of QALYs for Phase 2 of the project

Technical details are set out in a number of technical annexes in the report.

2. Generic Health Outcome Measures: What They Are

The motivation behind the FSA QALY project is to deploy a measure that enables comparisons across the wide range of food-related illnesses under its remit, which the QALY is able to do when formulated as a generic health outcome measure.[3] Perhaps the simplest way to define and explain generic health outcome measures is to contrast them with condition-specific health outcome measures, which is illustrated using a hypothetical example below (see Box 1):

Box 1 – Generic Health Outcome Measures

Illustrated example

The FSA is tasked with allocating its limited budget so as to achieve the greatest health impact to improve health for only two conditions: food allergy (IgE mediated) and listeriosis. The FSA will therefore need to choose between one of two policy options, determined by how much benefit each policy will be provide. Policy option 1 is design specifically to reduce the likelihood of a food allergy IgE reaction, while policy option 2 will reduce the risk of contracting listeriosis. It is assumed that each policy costs exactly the same (approximately £1m). The FSA must now decide how to choose the policy that will produce the most health gains. To do this the FSA needs an outcome measure that will tell it the amount of improvement in health gained from the current level of health to the level of health provided by either policy.

The FSA must therefore determine what counts as health, and hence how to measure the health gain, for each condition. Suppose that for Listeria the FSA decides that the level of health is best measured by the length of illness"; i.e., the number of days of suffering experienced by a listeriosis-patient... And further suppose that for food allergy IgE, the FSA adopt a measure of health of self-reported worry free days (say on a scale from 1 to 5) as experienced and reported by allergy sufferers.[4]

Which policy produces the greatest health benefit? Should it be based on an improvement through the reduction of length of illness for listeriosis patients or a reduction of incidences of adverse reactions by those with allergy?

These measures enable the FSA to measure and compare impacts within a condition, but not health impacts between two (or more) conditions; therefore, to make a cost-effective decision the FSA needs a generic outcome measure of health. This is a measure that is capable of measuring health across all conditions addressed by different policies. Such a measure entails that it must be sensitive to changes in health across all conditions so that policy makers can gain the most health per pound spent when considering a wide variety of policies.

To illustrate this idea, suppose that there was a clinical unit measure of health called the "H", based on an "H-score" of between 0 and 1, with 0 being death and 1 being perfect health, and every value

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[3] Generic health outcome measures are more frequently referred to as "generic preference-based measures of health", as crucial to these methods is the fact that the health states are ultimately quantified by a preference measure saying how good or bad that health state is, which we discuss in the section on QALYs. We use the more general term "generic health outcome measure" here for simplicity.

[4] "Episode free days" and pain were both actually used as condition-specific measures for asthma and arthritis, respectively; see Drummond et al. (2005: 13, 125).

in between being a point-specific assessment of that individual's health on a continuous scale.

Using the H-score it is now possible for the FSA to compare the health gain between the health scores before and after the policy intervention for the two conditions (listeriosis and IgE cases), and whichever policy produces the greatest health gain from the two (equally costly) policies is the one the FSA should fund.

This example demonstrates how a generic health outcome measure is necessary for what health economists call "cross-programme (or –policy) comparability", and further how such cross-policy comparability enables decision makers to make the best use of their available financial resources in their decisions by being able to determine what policies can do the most good per-pound-spent.

The example in Box 1 (see above) introduced two different measures that were sufficiently different to make comparisons on relative efficacy basically impossible. Part of the reason for this is that this particular example used two very different metrics for health: one involved duration (the number of episode-free days), the other the quality of the health state (the severity of pain or the allergic reaction). Of course, almost any condition and treatment effect will vary by *both* duration and quality of health. Therefore a generic measure must somehow combine both the quality of a health state and its duration. It is to this issue in generic health outcome measures that we now turn.

QALYs

Thus, a Quality Adjusted Life Year is any measure that uses the year as a unit of duration or length, and is somehow adjusted for quality. However, a convention has emerged in the health economic literature that the term "QALY" refers to the measure used by NICE and employs the EQ-5D as a measure to classify health states. We will follow convention and adopt this usage. We discuss the QALY in the following section and more extensively in Technical Annex 1. For now, let us turn to other generic health outcome measures besides the QALY.

Alternatives to QALYs

There are various alternatives to the use of QALYs to capture the value of health impacts. Monetary measures are commonly used in economic evaluations and methods are described in the Treasury Green Book (HM Treasury, 2003). Although less common than QALYs for valuing health interventions in the UK, monetary measures have been used in health economic evaluations. In addition QALYs may be converted to monetary values for the purpose of calculating the net benefit of an intervention. Typically the value of £20,000 per additional QALY gained is used as the value reflecting the lower bound of the NICE cost-effectiveness threshold; however higher thresholds of £30,000 and £50,000 may be used depending on the nature of the condition and intervention.(17)

Healthy Year Equivalent

The healthy year equivalent (HYE) metric was originally proposed in the late 1980s.(30) One of the key differences between HYEs and QALYs is that the HYE values a profile of health over time, whereas in the QALY each health state is valued independently and then summed to form a profile. The advantage of the HYE is therefore that it is able to capture different values for ill health depending on when they occur in the overall profile of health; however, partly owing to complexities of valuation and calculation, HYEs are not routinely used for the evaluation of health interventions.

Disability Adjusted Life Years

Disability adjusted life years (DALYs) are also used to capture the health of populations and is the preferred measure of the World Health Organisation. DALYs are calculated as the sum of the Years of Life Lost (YLL) due to premature mortality in the population with the condition of interest and the sum of the Years Lost due to Disability (YLD) for people living with the condition. The quality weight, YLD, is calculated as the number of incident cases multiplied by a disability weight and the average duration. The weights used in DALY calculations have been heavily criticised; however amendments were made to the methodologies to improve them in 2010. The updated disability weights were based on data from household surveys conducted in five countries (Bangladesh, Indonesia, Peru, the United Republic of Tanzania and the United States of America) and a web-based survey. DALYs currently remain, however, more frequently used in evaluations of health in developing countries and for comparing population health internationally, than for economic evaluations of health interventions in the UK.

Healthy Life Years

More recently there have been new developments in the EU on the measurement of population health. The European Commission has developed an indicator referred to as Healthy Life Years (HLY). These reflect the number of years a person can expect to live without disability, adjusted for their age. There are two components to the HLY: mortality which is assessed through national life tables and data on activity limitation. The data on activity limitation are obtained from the General Activity Limitation Indicator (GALI)(31) included within an EU survey (Eurostat); however as this measure is not preference-based it does not reflect ‘value’ as usually required for economic evaluations.

3. The Construction of a QALY

In what follows we discuss the QALY and the methods by which it is constructed. We provide a non-technical introduction to QALYs here, and conclude with reasons for adopting the QALY for purposes of assessing food safety risks within FSA policy and practice.

The QALY: A Non-technical introduction

In theory, any health state classification system (or more specifically measure of Health-Related Quality of Life (HRQoL)) which can adjust for the quality of health gain and then be *combined with a description of longevity gains in terms of the number of years of life gained* produces a quality adjusted life year (QALY). That is, any measure able to simultaneously incorporate both adjustments in the quality of health and longevity adjustments measured in years provides a QALY measure. Thus one can construct QALYs by measuring health using any number of HRQoL health classification systems (see technical annex 1) when combined with years of life gained; all can inform the construction of a QALY.

However, the QALY as we describe it here follows current National Institute of Health and Care Excellence (NICE) practice and specifically assumes the use of the EQ-5D as the health state classification system. The EQ-5D was developed by the EuroQol group and is made up of five domains (hence "EQ-5D"); the five domains are mobility, (ability to undertake) self-care, pain/discomfort, anxiety/depression and (ability to undertake) usual activities, where each of these dimensions has three levels. Any specific health state is designated by the levels it achieves on each dimension, such as 11111 being perfect health, 11211 being some pain and discomfort. The value (quality adjustment weight for the life year lived in that state) for any specific health state is determined by an algorithm that also include a fixed parameter for any state less than 1. The EQ-5D is the preferred HRQoL measure of NICE and is the measure that is used most widely in the UK for calculating QALYs.

The QALY is constructed from essentially three sources:

1. *description of common possible symptom profiles* that arise from any given condition[5]; this task is generally undertaken by *clinical experts*.
2. *classification of a health state* derived from scoring the symptom description using a health state classification system, in this case the EQ-5D; this task is usually undertaken by *patients*.

[5] For example, the common categories of symptoms for Norovirus were described as "mild diarrhoea and vomiting", "diarrhoea and violent vomiting" and "diarrhoea, violent vomiting and fever". See Technical Annexe 5 for the descriptions of symptoms used in the present research.

3. *valuation of the health state* using a utility measure (to be described below); this task is generally undertaken by the *general public*. We will describe these last two steps here.

Classification of a Health State

The QALY, as noted above, enables the simultaneous comparison of gains/losses in the quality of health as well as gains/losses in the number of life years that a particular policy might produce. While the longevity gains of a treatment are estimated using clinical data, the descriptions of the quality of the health states are derived from patients experiencing the condition. That is, the patient scores their own health state according to how well they rate their own HRQoL on the five domains of the EQ-5D.

Until recently the EQ-5D has used 3 levels to describe how well or badly one may fare in each domain; e.g., with respect to mobility, these three levels are defined as: 1 - "No problems walking about"; 2 - "Some problems walking about"; or 3 - "Confined to bed". However, the EuroQol group has recently been piloting the use of a 5-level descriptive classification for each of the five domains, and we have used that method here. The 5L classification generally has the form: 1 – no problems; 2 – slight problems; 3 – moderate problems; 4 – severe problems; 5 – extreme problems (the full wording and mode of elicitation can be seen in technical annexe 2). We used the newer "EQ-5D-5L", as it is called, as it is most likely set to become the industry standard, and it was thought that the FSA should be using the most current methods for scoring the EQ-5D, especially given the likely widespread adoption of this method

Thus, a classification of a health state is simply that set of numbers used to score that state. For example, suppose a patient scored their own health state as follows: Mobility – 2; Self-care – 1; Usual activities – 2; Pain/discomfort – 1; Anxiety/depression – 3. This health state would then be scored or classified with the simple numerical representation: 21213.

Constructing QALYs: Measuring and valuing health

Above we provided an introduction to QALYs using the current NICE practice of using the EQ-5D to classify health and the "time trade off" (TTO) as a means of valuing that health state[6]. However, there are a number of other health state classification systems used to construct QALYs. We here describe in a non-technical manner other classification systems as used in health economics. This is partly for purposes of further exposition of the notion of a health state classification system, as well as providing further context for why the EQ-5D was the system employed in the present research. We also discuss different measures used to value health, which are generally measures of utility in the economist's sense, which refers to the degree that a state of affairs generally brings pleasure or dis-pleasure to an individual. In the case of health this entails measuring the level of satisfaction an individual enjoys from a positive health gain or suffers from a health loss.

[6] The time-trade off procedure is explained in greater detail in Box 2 below.

Measuring health with health-related quality of life measures

Health economists have developed generic measures of health state classification systems which attempt to measure Health-Related Quality of Life (HRQoL). To define HRQoL for purposes of developing an operational measure, health economists ask: how does one's health impact on how one feels and how well is one able to do the things in life that make a life better or worse? HRQoL measures use a number of general domains that measure health across all conditions. Scores on these domains must then be aggregated to provide an overall health-state classification. How HRQoL health state classification scores are then converted to *health utilities* so as to provide a unique continuous (i.e., cardinal) score for overall health is discussed in the following section on QALYs.

Which set of domains is to be used in measuring HRQoL is a long-standing and ongoing concern in the field of outcome evaluation in health economics. The reasons for adopting one health state classification system over another can range from philosophical concerns about what ought to matter when we evaluate health, to psychometric issues concerning how responses to items on domains should or should not be correlated. As an example of the latter, suppose that, in responding to a health state classification system containing two domains (X and Y) to classify a particular health state, half of the respondents reported having no problems in domain X and severe problems in domain Y, while the other half reported severe problems in domain X and no problems in domain Y. We would conclude that this health state classification does not perform well in measuring the health states it aims to measure.

These issues here are complex (and hence further discussed in Technical Annex 1), but to provide some idea of what the different health state classification systems focus on in terms of what is important in HRQoL, we will simply list the domains of quality of life used by the 3 most prominent systems currently used in the health economics profession: the EQ-5D, the SF-6D, and the health utilities index 3 (HUI3):

- EQ-5D: anxiety/depression; pain/discomfort; usual activities; self-care; mobility.
- SF-6D: physical functioning; role limitations; social functioning; pain; mental health; vitality.
- HUI3: vision; hearing; speech; ambulation; dexterity; emotion; cognition; pain.

As can be seen, there is some overlap: each health state classification system includes "pain". But even in the area of psychological consequences the systems vary in focus: the EQ-5D on "anxiety and depression", the SF-6D on the more general "mental health", and the HUI3 on "emotion" (which concerns happiness) and cognition (which concerns memory and clear thinking). And beyond this the domains are quite different, and one can see how the different systems of classification will be differentially sensitive to outcomes of different conditions.

As an example, it is often noted that the SF-6D is more sensitive to conditions that impact upon social life, with its domains of “role limitations” and “social functioning”. The HUI3, by contrast, would be less sensitive to impact on social life, but is likely to be more sensitive to loss of various types of physical functioning, with its domains of “speech”, “ambulation”, “dexterity” and “pain”.

Our primary purpose in explaining the different domains used by different health state classification systems is to illustrate how a generic health outcome measure is constructed by measuring different domains of quality of life to construct an overall measure of HRQoL which requires no actual clinical measures.

Our secondary purpose is to highlight that the choice of domains is itself a substantive methodological choice. We have taken some time to explain this research construct as it is crucial to understanding what the FSA is undertaking in its attempt to use a generic health outcome measure, and to understanding the results we present later.

Having explained the idea of a generic health outcome measure and its importance in enabling comparisons across a variety of health-related outcomes, hence enabling better comparison and evaluation of policies, we now turn to the more specific measure being developed by the FSA in this project, the QALY as constructed using the EQ-5D health state classification system.

However, note that this classification on its own does not tell us *how bad that health state actually is*. And it is this information that is needed for generic health outcome measures of different health states to be comparable to one another. Therefore, for each health state we also need to value that state with a measure of utility, or how good or bad that state is for the person experiencing it.

Valuing health with utility measures

The utility measure is constructed by having the general public examine a particular health state classification and then provide a utility scoring of that state. This utility score allows us to give a unique (cardinal[7]) value between 0 and 1 to each and every health state possible in that health state classification system. The utility-elicitation device favoured by NICE is what is known as the “time trade-off” (TTO) method. In this technique, respondents are asked to consider how many years in a state of full health would be equivalent to a longer period in a particular state of less than full health (say 10 years) [8] which is illustrated using a hypothetical example below (see Box 2):

[7] Cardinal - measurement of utility on an absolute scale. For instance like measurement of distance on a ruler. Not this is NOT a ratio scale – 0.5 is NOT twice as healthy as 0.25, in same way that on temperature scale 30 degree is not twice as hot as 15 degree.
[8] In both cases it is assumed that the period of whatever duration is followed by immediate death.

Box 2 – "Time Trade-Off" (TTO) Method

Suppose you are presented with 10 years in a very poor health state i.e. an EQ-5D of 33333 (worse in all domains). Now imagine the minimum number of years of life in full health you would be willing to accept in order to not experience the poor health state for 10 years. Suppose that you think that the state is so dire that rather than having 10 years in that state (followed by death) you would prefer at minimum to have 4 years of perfect health (followed by death).

You have traded off time (6 further years of life in the very poor health state) in order to gain greater quality of health (4 years in perfect health), hence the term "time trade-off". By taking the ratio of these two figures, 4/10, we are able to derive a unique number between 0 (death) and 1 (perfect health), in this case .4, which we take as the utility value for the health state 33333.

To provide utilities for all of the possible health states possible in the EQ-5D the UK Department of Health undertook a survey of approximately 3,000 respondents taken from the general public. This data set is what is now called the "social tariff". Studies that derive unique QALY values for conditions (say for clinical trials) elicit unique health state classifications from patients, but then derive the unique QALY value for those states by simply deriving their utility score from the social tariff data set. A problem with this approach is that many studies now show that the social tariff data set of utility values often over-values how bad a health state is, and so many researchers now elicit their own unique utility data to value different conditions (discussed in the Appendix describing next steps for Phase 2).

In summary, the QALY enables us to describe any possible set of symptoms using a health state classification system (in this case, the EQ-5D), and to further convert that health state into a unique numerical value of health (as determined using health-related quality of life measures) on a constant scale of 0 to 1 using a utility measure (in this case, the TTO).

We will be discussing this method further below in our methods and results sections, where the overall case for proceeding with QALYs is made.

4. QALYs and policy context: Use by other food safety regulatory bodies and other UK Government Departments

In this section we examine how QALYs are used both by different UK Government departments as well as different food safety regulatory bodies. However, it is worth noting that the use of QALYs for economic evaluations is not restricted to the UK, and the metric has become established in international guidelines for the evaluation of health outcomes by other healthcare agencies. Their use as the primary measure of outcomes is recommend in Belgium (Kleemput et al, 2012), Ireland (Health Information and Quality Authority (Ireland), 2010), New Zealand (PHARMAC (New Zealand), 2012), Sweden (Edling and Stenber, 2003) and Slovenia (Health Insurance Institute of Slovenia, 2010) or as one of a possible range of outcome metrics in Canada (CADTH, 2006), Norway (Norwegian Medicines Agency, 2012), Switzerland (Swiss Federal Office of Social Security, 1998), Taiwan (Taiwan Society for Pharmacoeconomics and Outcomes Research, 2006), Slovakia (Ministry of Health (Slovakia), 2011) and Egypt (Egyptian Drug Authority, 2013). Thus the QALY is internationally prominent in countries where cost-effectiveness analysis (CEA) is undertaken.

In the following section we discuss two different categories of use of generic health outcome measures. First, we examine the current use of such measures across a range of 12 different UK Government departments. This is in order to review the “state of the art” in valuing health in UK policy so as to better understand how the FSA QALY project would sit in the larger UK policy context.

The second is to similarly review how the QALY in particular has been used by a variety of international governmental bodies tasked with food safety regulation for their policy appraisal and evaluation. This is in order to better understand how the QALY has been applied to food safety, and to learn lessons for best practice for the use of the QALY given the FSA’s objectives.

Use of generic health outcome measures across UK Government departments

Many government departments routinely engage in decision making that will have effects on the life, health or safety of UK citizens. For this reason government departments often need to measure health, and put a financial value on life and health. UK government departments use a variety of methods and approaches to value life and health, and it is useful for the FSA to be aware of cross-departmental practice with respect to the measurement and valuation of health.

As part of a previous project conducted by one of the researchers[9] on the present project, a survey was undertaken with senior economists at a variety of UK government departments to determine whether they used measures of health for their policy appraisal and evaluation in order to provide a survey of cross-departmental practice, and if so, what method? We summarise the results of this research here.

The review showed great variation in departmental practice, but it appears that there are a small number of common themes in the valuation of life and health, which we discuss below. However, the overwhelming result is that the measurement and valuation of health by UK Government departments is essentially a "two-horse race", with *all* departments surveyed using either the QALY or the Department for Transport's figure of willingness-to-pay (WTP) to reduce the risk of death or injury, which is known generally as the Value of Statistical Life (VSL).

Given the prominence of the VSL figure in valuing health and life across government departments we must very briefly explain this idea. In WTP studies to value the prevention of injury or death, subjects are asked how much they would be willing to pay to reduce their (very small) risk of either minor injury, major injury, or death. This method is widely used, but is extremely limited in terms of valuing health: only three states are valued, minor or major injury or death. Given the wide range of possible health states which can occur, it is easy to see how the QALY has such appeal in being able to value perfect health, death, and every health state in between. Nevertheless, the DfT VSL figure has been much longer established in UK government policy than the QALY, hence, perhaps, an explanation for its relative prominence in the valuation of health.

Cross-Government Survey

Let us now turn to the results of this cross-government survey. For this research senior economists in 12 government departments were interviewed. Each departmental economist was asked about their use of measures and values[10] of life and health: whether quality and length of life adjustments were made, and if so how. As stated, all used either a WTP-for-VSL[11] measure or the QALY. Of those who used a WTP-for-VSL approach, most used the measures and values transferred from the DfT figure, with only DEFRA and the HSE conducting their own original research in addition to using the DfT figure. The results of this survey are presented in Table 1 below. For each department we list what method of

[9] Shepley Orr, who along with Professor J. Wolff, was commissioned to produce a report by the Interdepartmental Group for the Valuation of Life and Health, a group founded and led by DfT and HM Treasury. The aim of the report was to (1) examine current governmental practice in the measurement and valuation of life and health and, (2) to determine how best to develop greater inter-departmental consensus in the practice of health measurement and valuation. The results summarized here are discussed in: J. Wolff and S. Orr, *Cross-Sector Weighting and Valuing of QALYs and VPFs: A Report for the Inter-Departmental Group for the Valuation of Life and Health* (2009). http://www.ucl.ac.uk/cpjh/docs/IGVLH.pdf

[10] How the health state is *valued* refers to how a health state, once measured, is then given some monetary value.

[11] Again, the VSL figure includes measures and valuations of minor and major injury.

health measurement they used, and what health states were measured. Regarding the health states measured, there are basically two responses which follow as a matter of necessity.

Where the "VSL transferred from DfT" measure was used then "fatalities and two injury states (i.e., minor and major)" will be the health states measured; where the QALY is used, "all health states" are measured. When original research was used by the department to measure health in combination with either VSL or QALY we describe those states specifically.

Table 1: Methods used for measuring health across UK Government departments

Government Department/ Agency	Methodology	Health States Measured and Valued
Department for Transport	VSL	▪ Fatalities and two injury states
Scottish Government (Transport Department)	VSL transferred from DfT	▪ Fatalities and two injury states
Local Communities and Government	VSL transferred from DfT	▪ Fatalities and two injury states
Department of Health	QALY	▪ All health states
Environment Agency	Transferred from DfT and from DEFRA-WTP study	▪ Fatalities and two injury states
DEFRA	WTP to avoid health effects from air pollution (DEFRA-WTP study)	▪ Life year gained in normal health ▪ Life year gained in poor health ▪ Value of avoiding a hospital admission ▪ Value of avoiding a days breathing discomfort
Food Standards Agency	A range including: VSL transferred from DfT QALY[12]	Fatalities and two injury states All health states
Health Protection England	VSL transferred from DFT QALY	Fatalities and two injury states All health states
HSE	DfT VSL figure HSE WTP study on injuries QALY approach	Fatality, major injury, injury over 3 days, minor injury All health states
NICE	QALY	All health states
Home Office	VSL transferred from DfT (for homicide) QALY approach for other crimes.	Fatalities and two injury states All health states (associated with crimes of robbery, wounding, sexual offences and common assault).
Scottish Government (Health	VSL transferred from DfT	Fatalities and two injury states

[12] This research was undertaken when nutrition was part of the FSA remit, which is now covered by the Department of Health. The FSA has not since used QALYs in any other respect.

Government Department/ Agency	Methodology	Health States Measured and Valued
Department)	QALY	All health states

Summary of Survey Results

Our summary of this research is as follows:

- All the departments that were tasked specifically with health policy used the QALY.
- Many government departments borrowed the DfT VSL approach despite its limited scope to minor and major injury and death.
- The QALY is now used by many departments.
- Many departments used both the VSL and the QALY

Thus, this research shows that many government departments have adopted the QALY to measure health. Although this is far from universal practice, use of the QALY to measure health is certainly growing, especially as cost-effectiveness becomes increasingly important to Government departments given the current financial climate.

Adopting QALYs

Two reasons for the FSA to adopt the QALY as a measure of health:

- First, the increased use of QALYs by different UK Government departments entails that an evidence base and guidance for best practice is emerging in a variety of contexts beyond their narrow use by NICE and the DoH, and,
- Second, the more that different departments adopt the QALY as a measure of health, the greater will be the possibility of cross-departmental, i.e., “joined-up”, initiatives where common aims can be established and achieved. Given that FSA policy intersects with that of so many other departments, this should increase its scope and impact.

Use of the QALY by different food safety regulatory bodies

The use of the QALY by different food safety regulatory bodies has been limited in scope, but its increasing uptake by such bodies is informative for seeing the FSA QALY research project in its larger, international policy context.

Space considerations preclude a thorough description of each example of the use of QALYs (and preference based measures) by a food safety regulatory body. Therefore, we here note focus on recent *primary research* commissioned by regulatory bodies: one by the FDA to develop QALY values for food borne diseases, two Swedish studies, and the development of a disease-specific food allergy quality of life questionnaire. We then briefly list other examples we have found in our research.

United States

The US FDA recently undertook a large-scale study to determine the health loss associated with IIDs which was an important input to the current research. The EQ-5D was used in this study to estimate the QALY loss associated with 14 foodborne pathogens (Batz et al, 2012; Hoffman et al, 2012[DN. Check References]) This study did not use EQ-5D as intended; instead of administering the instrument for self-completion by people suffering from a FBD, an EQ-5D health state associated with each FBD was described based on the researchers' opinion. Values were then assigned to each EQ-5D health state based on the published general population value set for the USA.

Sweden

Of the two Swedish studies, one reported the use of the EQ-5D in a sample of 79 people with documented allergy to cow's milk, hen's egg and/or wheat (Jansson et al, 2013). It found that EQ-5D did not distinguish between people with and without reported asthma, with and without a prescription for an epinephrine auto injector, and with or without anaphylaxis; however it is not clear if the study was statistically powered to detect these differences and few details of the EQ-5D results are reported (for example, the results of the statistical tests are not reported).

The second Swedish study reached different conclusions and found that EQ-5D distinguished between groups with and without allergies (Covaciu et al, 2013). This study collected EQ-5D data from parents of 3236 children and reported on the children's symptoms of allergic disease such as asthma, rhinitis, eczema, and food hypersensitivity. It found that the median EQ-VAS[13] score was significantly lower in children with allergic diseases, and that children with asthma had the highest prevalence of problems of "pain or

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[13] This is a version of the EQ-5D which uses a visual analogue scale (VAS) in order to measure the utility associated with health states. For further clarification see Technical Annex 1, under "*direct measurement and valuation*".

discomfort" and lowest VAS scores of all.

EU

A food allergy quality of life questionnaire (FAQLQ-AF) has recently been developed as part of the EuroPrevall project (Flokstra-de Blok et al, 2008; Flokstra-de Blok et al, 2009a; Flokstra-de Blok et al, 2009b; Flokstra-de Blok et al, 2010). The questionnaire has four dimensions: Allergen Avoidance and Dietary Restrictions (AADR), Emotional Impact (EI), Risk of Accidental Exposure (RAE) and Food Allergy related Health (FAH). Although this system has a scoring system, it is not preference-based, not a 0 (dead) to 1 (full health) scale and cannot be used to estimate QALYs. Interestingly, as this is the first study to attempt to develop a condition-specific HRQL measure for food related illnesses, in the most recent review of the literature from this team (Flokstra-de Blok and Dubois, 2012) the researchers conclude that their next step should be to further investigate the use of the QALY for food allergy.

Other Countries

There is a small but growing number of other cases of the use of QALYs or generic health outcome measures by food safety regulatory bodies. These include the following:

- The use of disability-adjusted life years (DALYs) by Food Standards Australia and New Zealand. The DALY is essentially a type of QALY, where the quality adjustment is made by a weight added to a particular life-year/longevity profile for different types of disability.
- The HSE used both the QALY and a WTP-for-a-VOLY (value of a life year) approach to valuing reductions in risks of a nuclear accident.
- A joint FSA/Ofcom regulatory impact assessment into the regulation of food advertising used the QALY to measure health impacts.
- A number of other food safety regulatory bodies have begun to take notice of the QALY and enquire as to the possibility of its use in the area of food safety, for example, EUFIC – The European Food Information Council (see: http://www.eufic.org/article/en/artid/Measuring-burden-disease-concept-QALY-DALY/)
- It is lastly worth noting that a small but emerging number of academic studies have recently begun to apply QALYs to measure the health loss associated with food-related illness, and the QALY features in many food safety textbooks and edited volumes.

Summary: QALYs as preferred alternative for the FSA

In summary, QALYs are the most commonly used metric for economic evaluations of health interventions, particularly in the UK. The EQ-5D is the most commonly used measure of health status for estimating the quality component (or ‘utility’) for QALY estimation. There is very limited published data on the use of QALYs and EQ-5D for capturing the health impacts of FBDs and food hypersensitivity to date; however given that FBDs and food hypersensitivity potentially affect morbidity and mortality QALYs may be an appropriate metric to use to capture their health impacts. In addition capturing the impacts in this way could facilitate comparisons with other health conditions and interventions. This is an area that would benefit from further research.

We now turn to our empirical research, beginning with a discussion of our research methods.

5. Research methods

This research was undertaken in four main steps.

Step 1 – Determining Scope of Food Related Illness

At the outset, what types of food-related illness to be considered in the present research had to be determined. The full set of possible causes of illness initially considered included 21 food related IIDs and 16 types of food hypersensitivity (see technical annexe 5 for the originally proposed list of food related illnesses). However, the number of food related IIDs was reduced from 21 to 18; and as the result of an expert workshop it was determined that food hypersensitivity could be collapsed into four different categories: IgE mediated food allergy; non-IgE mediated food allergy; Coeliac disease; and food intolerance.[14] This collapsing of categories was undertaken for two reasons:

- First and most importantly, the demands of data collection of 37 different types of food-related illness would simply not be possible given the limited scope of Phase 1, so some sort of alternative solution was required, therefore,
- It was then determined that the four categories of food hypersensitivity were *similar enough* in their common symptoms that they could be categorised together for present purposes.

Given this, it is obvious that there is a great deal of "missing variance" in the data by collapsing 16 causes of food hypersensitivity into 4 categories. Nevertheless, this was a necessary step needed to produce useful data on these categories as defined.

Step 2 – Elicitation of Symptom Descriptions

We elicited symptom descriptions for different severities of reaction from experts for the four categories of food-related illness. These included external experts from: Public Health England, Coeliac UK, and the Anaphylaxis Campaign. We followed the method employed in the US FDA research mentioned above (Batz et al, 2012; Hoffman et al, 2012), and the four categories of symptom descriptions elicited were used to construct a "disease outcome tree" which would contain (at least) 4 possible types of outcome for any given episode, namely: mild, moderate, severe, and life-threatening (with the latter including the possibility of death). However, respondents were encouraged to develop their own more fine- (or less-) grained outcomes and symptom descriptions.

Step 3 – Elicitation of Health State Classifications (EQ-5D)

[14] We also class IgE mediated, non-IgE mediated illnesses and Coeliac disease as types of *food hypersensitivity*.

We sought to elicit EQ-5D health state classifications for all of the symptoms. To this end, online surveys were developed to elicit the health state classifications:

- For IIDs, experts from Public Health England working in the area of food safety completed the EQ-5D questionnaire for health states.
- For food allergy/intolerance, sufferers of allergy/intolerance completed EQ-5D questionnaires for health states. Technical annexe 3 shows the characteristics of the survey respondents. The survey was posted as a news story on the FSA website and distributed by email to various groups that work to promote the interest of people with food hypersensitivity.

Step 4 – Derivation of Utility Values

Lastly, as is the practice of NICE and most other bodies using the EQ-5D, utility values for the health states were derived by the researchers using the “social tariff” of utilities established for all of the health states elicited (see above for discussion).

6. Results

EQ-5D health state classifications elicited from the allergy/intolerance and IID surveys were converted to utilities using the EQ-5D value set for the UK. The utilities represent UK general public preferences for health states anchored by 1 (perfect health) and 0 (dead). Table 2 reports the mean utilities by condition and severity of reaction.

Table 2.1 Utility values for allergy and intolerance health states

	IgE-mediated		Non-IgE-mediated		Coeliac		Food intolerance	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Mild	**0.717**	0.240	**0.668**	0.337	**0.711**	0.226	**0.726**	0.201
Moderate	**0.396**	0.353	**0.536**	0.349	**0.570**	0.264	**0.606**	0.237
Severe	**-0.210**	0.409	**0.260**	0.438	**0.280**	0.363	**0.311**	0.376
Life-threatening	**-0.470**	0.310	**-0.076**	0.560	**0.092**	0.384	**-0.016**	0.500

Table 2.2 Utility values for IID health states

	Campylobacter		Listeria		Salmonella (Non-typhoidal)		Salmonella (Typhoidal)		Enteropathogenic Escherichia coli		Enteroaggregative Escherichia coli	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Mild	**0.695**	0.078	**0.637**	0.083	**-0.311**	-0.311	**0.594**	0.056	**0.665**	0.061	**0.670**	0.069
Moderate	**0.451**	0.208	**0.057**	0.312	**0.449**	0.449	**0.179**	0.177	**0.290**	0.213	**0.525**	0.051
Severe	**0.120**	0.334	**-0.311**	0.293	**0.158**	0.222	**-0.560**	0.046	**-0.259**	0.407	**0.130**	0.110

	Norovirus		Hepatitis A		Hepatitis E		Clostridium perfringens		Clostridium botulinium		Bacillus cereus	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Mild	**0.704**	0.208	**0.702**	0.247	**0.563**	0.203	**0.590**	0.242	**0.371**	0.283	**0.742**	0.369
Moderate	**0.521**	0.176	**0.484**	0.162	**0.402**	0.296	**0.526**	0.172	**-0.021**	0.379	**0.601**	0.227
Severe	**0.165**	0.405	**0.398**	0.220	**0.454**	0.263	**0.289**	0.148	**-0.308**	0.461	**0.437**	0.211

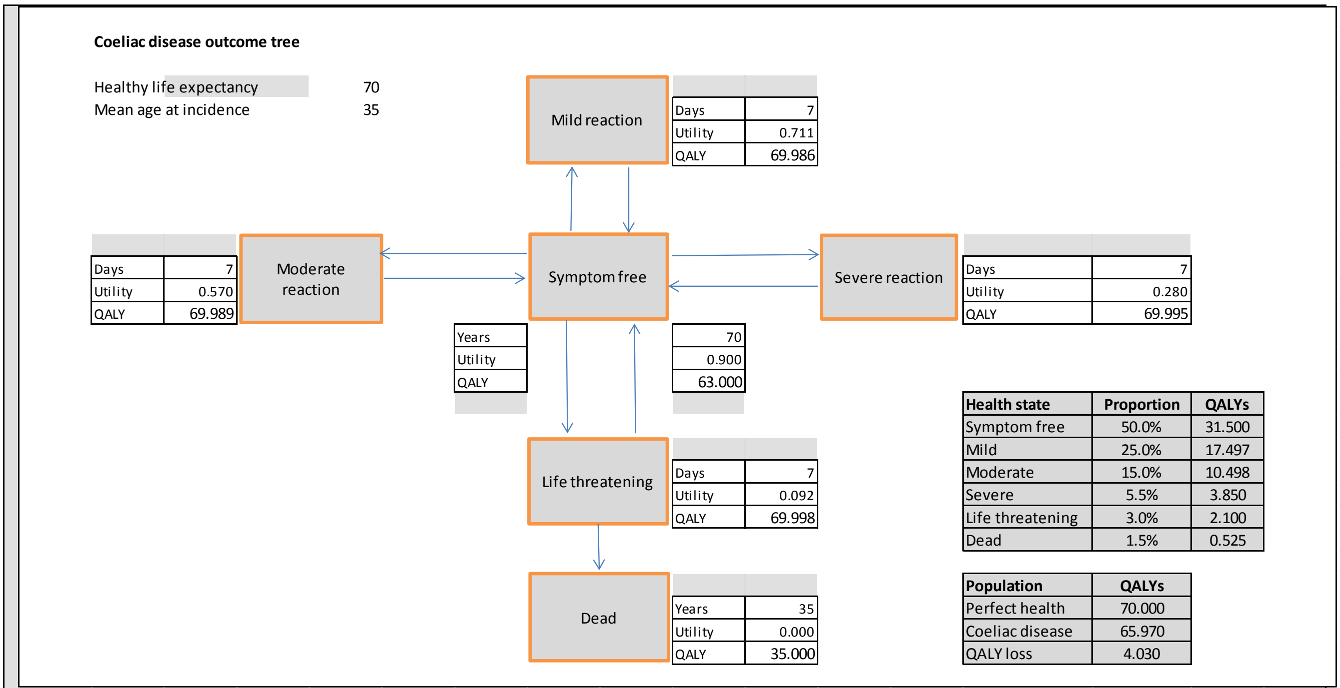
	Giardia lamblia		Staphylococcus aureus		Yersinia enterocolitica		Cryptosporidium parvum		Shigella		Rotavirus	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Mild	**0.877**	0.108	**0.900**	0.103	**0.863**	0.118	**0.932**	0.118	**0.891**	0.094	**0.900**	0.103
Moderate	**0.754**	0.016	**0.763**	0.132	**0.790**	0.208	**0.769**	0.064	**0.542**	0.266	**0.778**	0.068
Severe	**0.744**	0.149	**0.584**	0.294	**0.564**	0.029	**0.647**	0.086	**-0.071**	0.318	**0.597**	0.262

In general, more severe reactions are associated with lower utility values, as might be expected given the more serious symptoms experienced. Some reactions, such as a severe IgE mediated reaction, received negative utility values, indicating they are considered 'worse than death'.

Box 3: Calculating and interpreting QALYs – Coeliac Example

In order to calculate the QALY burden of a given condition, the utility of a health state was combined with information on the duration of that health state and the frequency of that health state. This information is presented as a 'disease outcome tree' in Figure [1]

Figure [1] Example of coeliac disease outcome tree used to calculate a QALY loss



In the example of coeliac disease, six possible health states were described by experts:

- Symptom free
- Mild reaction (*mild abdominal pain, bloating, excess wind, lethargy, itchy skin, mouth ulcers)*
- Moderate reaction (*diarrhoea, vomiting, weight loss, dermatitis herpetiformis flare, fatigue*)
- Severe reaction *(chronic diarrhoea, failure to thrive or faltering growth, persistent gastrointestinal symptoms including nausea and vomiting, prolonged fatigue, recurrent abdominal pain, cramping or distension sudden or unexpected weight loss, unexplained iron-deficiency anaemia, ataxia, neuropathy, epilepsy, diabetes, severe dermatitis herpetiformis)*
- Life-threatening reaction *(bowel cancer, non-responsive CD)*
- Death

Each state was associated with a duration by the expert. In the case of coeliac disease, a reaction would last for 7 days. The duration of reaction was combined with the utility value for the health state description elicited from patients answering the EQ-5D to calculate a QALY of living with that state. For a mild state, the utility expressed by patients was 0.711 and the duration of a mild reaction stated by experts was 7 days. This gives a QALY loss of 0.711x(7/365)=0.014 for a mild reaction in coeliac disease.

The QALYs for each state were weighted by the relative proportions of people living in each state to give a QALY for people living with coeliac disease of 65.970. This is equivalent to a QALY loss of 4.030 compared with a person living in perfect health for 70 years (i.e. 65.970 = 70 - 4.030).

Results: food allergy/intolerance

Two important simplifying assumptions have been made for the QALY calculations for this pilot phase of work that should be borne in mind when interpreting the absolute results:

- The utility associated with living with the disease (i.e., "maintenance") while not experiencing a reaction (symptom free) was not assessed as part of this phase of research due to the heterogeneity of the state. For the purposes of estimating QALYs for this phase of work, a small decrement was assumed to give a value of 0.90 for this state across all allergy/intolerance.[15] It will be important for the utility of the maintenance state to be estimated accurately in future work since it has a large bearing on the QALY calculation due to the length of time people spend in this state.
- It is assumed for this phase of work that all allergy/intolerance has an equal chance of affecting young and old and therefore the average age of death was 35 (half of a 70 year healthy life). If a disease predominantly affects the young, the QALY loss associated with death would be higher and vice versa.

The QALY losses may be compared to indicate their relative severity in terms of mortality and morbidity on a common scale. For allergy, IgE-mediated reactions had the most significant QALY loss, so may be considered to have the highest burden. This is closely followed by coeliac disease. QALY loss estimates and distribution according to severity of illness by food allergy/intolerance type are presented in table 3.1 below:

Table 3.1 - Food allergy/intolerance QALY loss estimates

Food Hypersensitivity	QALY Loss per Case
IgE-mediated food allergy	4.202
Coeliac	4.030
Non-IgE-mediated food allergy	2.805
Food intolerance	1.969

[15] In particular the researchers proposed that generally speaking maintenance would have some effect on the EQ-5D domains of Anxiety/Depression and Usual Activities, possible effect on Self-care, and probably no effect on Pain/discomfort or Mobility. Using the EQ-5D-5L system and assuming maintenance implied a departure from perfect health (11111), we then defined "some effect" as counting as a reduction of 2 units out of 5, "possible effect" as a reduction of 1, and discounted "probably no effect". In the order presented above this would give a QALY profile of 33211, and we use the utility of that state as an additive constant or "maintenance discount" that we apply to construct the utility values for food hypersensitivity.

Results: Food related IIDs

Due to the relatively short duration of morbidity reactions, QALY losses for IIDs are generally low and are driven by the proportion of deaths. Listeriosis caused by *Listeria monocytogenes* had a much higher QALY loss than other FBDs due to the high (25% chance of death among people contracting the disease. QALY loss estimates and distribution according to severity of illness by IID type are presented in table 3.2 below:

Table 3.2 IID QALY loss

IID Type	QALY Loss per Case
Listeria monocytogenes	8.872
Clostridium botulinium	3.532
Enteropathogenic *Escherichia coli*	0.715
Hepatitis A	0.412
Salmonella (Typhoidal)	0.377
Hepatitis E	0.376
Salmonella (Non-typhoidal)	0.362
Cryptosporidium parvum	0.025
Giardia lamblia	0.019
Shigella	0.015
Rotavirus	0.010
Yersinia enterocolitica	0.010
Campylobacter	0.005
Staphylococcus aureus	0.004
Enteroaggregative *Escherichia coli*	0.004
Norovirus	0.002
Clostridium perfringens	0.002
Bacillus cereus	0.002

Summarising the results for foodborne disease is difficult as there is great variability between conditions with no common pattern for the distribution of symptoms and their severity. Nevertheless there are certain larger-scale trends across conditions. First, we can note that all conditions, with the exception of listeria, have a small proportion of infections resulting in death. Furthermore, there is a great deal of variability between conditions in terms of the proportion of cases being mild versus moderate. Finally, it is worth noting that these proportions do not represent overall population burden of illness, but instead distribution of symptoms within a condition

7. Limitations and caveats

Caution should be taken in making absolute comparisons between diseases due to some of the methodological simplifications discussed above, which we briefly list here:

- This research used only experts to classify health states, unlike NICE's practice of using patients. This was due to the limitations of data collection in the short period of time, but because these experts work closely with many patients as well, this practice was largely justifiable and produced results based on expert judgement.
- The health state classifications for food hypersensitivity were from a non-random, convenience-sampling method, potentially biasing the results.
- The valuation of the "maintenance" state for all types of food hypersensitivity was a measure based on the researchers' judgment. This is an area identified as potentially the most important challenge for phase 2 of the research
- Phase 1, QALY estimates according to IID and allergens type have not distributed by cases pertaining to non-hospitalisations, hospitalisations, fatalities, age of onset and long term chronic complications such as permanent disability hospitalisations

Importantly, however, the research meets the most important stated objectives for Phase 1 of the research:

First, the results demonstrate the feasibility, and indeed desirability, of estimating the burden of food-related illness by taking into account quality of life, length of life and frequency of occurrence into a generic and comparable measure: the QALY.

Second, the results presented here are derived from a sufficiently rigorous research methodology to be used for purposes of policy appraisal by the FSA, despite the limitations we have noted.

8. Conclusions

The research reported here is extremely promising in terms of its recommendations for Phase 2. For the “research highlights” we refer the reader to the earlier sections “Key findings” and “Executive summary”.

Here we wish to note an overwhelmingly positive conclusion for pursuing the research into QALYs in Phase 2.

Our research suggests that, first, conducting such research is entirely feasible. We have identified a number of research challenges that presented themselves in Phase 1 (and which provide limitations on the current data), though through exploring the issues both sensitively and with an eye to the quantitative demands of the research, we have identified necessary steps to overcoming these obstacles with relative ease. Perhaps more importantly, the research reported here suggests that by pursuing original research into the use of QALYs to measure food-related illness, the FSA has the opportunity to surpass all other current research work by other food safety regulatory bodies, becoming a world-leading agency in evaluating food safety risks in the process. Indeed, the research suggested here for Phase 2 would be a significant research achievement in its own right, creating a unique primary data set on the valuation of food safety risks that is currently unparalleled in policy, industry, or academic research.

9. Next steps and recommendations

Phase 1 of the FSA QALY study was conducted to an extremely brief time scale (project start and delivery of this Summary Note taking less than 3 months). The purpose of Phase 1 was two-fold. First, to develop a set of preliminary, interim QALY values for the various types of food-related illness addressed by the FSA Board so as to inform decision-making for setting the strategic priorities for 2015-2020. Second, Phase 1 was also a feasibility study to explore the possibility of developing QALYs and to identify issues and challenges to be addressed in Phase 2.

Next Steps

While we believe we have shown that developing QALYs is certainly feasible, indeed desirable, we have also emphasized the limitations of the data presented here. Nevertheless, we have concluded that any limitations of the current research are the result of the short time-scale of Phase 1, and not due to any intrinsic barriers to the overall FSA QALY project or identifiable obstacles in Phase 2.

To illustrate this last point, we have identified a number of issues for Phase 2 of the FSA QALY study to address and resolve the problems of any limitations of the current study. We also propose a number of other possibly desirable objectives for Phase 2 that we believe will contribute to the successful development of QALYs.

Recommendations

Phase 1 of our research has led us to conclude that Phase 2 of the FSA QALY project should have the following objectives:

- Provide a systematic evidence review on the use of health outcome measures, both by
    - different UK government departments, and by
    - food safety regulators internationally.

- Conduct small-scale primary-data collection on EQ-5D classification of health states associated with food-related illness, in particular,
    - EQ-5D scores for *each* of the types of food-related illness, not in the collapsed categories as used in Phase 1.
    - Ensure that health state classifications provided by sufferers themselves support those obtained by experts, and determine whether a larger-scale data collection exercise from sufferers is required.
    - For food hypersensitivity use a more systematic sampling approach so the sample of respondents is representative and unbiased, and, further,
    - Conducting extensive qualitative and quantitative research into valuing the disutility associated with “maintenance” of the condition, which has been identified by many respondents as producing a far greater loss in HRQoL than the intermittent experience of an episode.

    - Working with Public Health England and the FSA on their IID outbreak investigations to collect data from respondents who are currently experiencing illness due to particular pathogens.

- Establish how the age-of-onset of food hypersensitivity and FBD, where there are possible fatalities, impacts on QALY loss (given some assumed life-span).

- Develop a monetary value for food-related QALYs. This could occur through one of three methods. Future research is likely to take the first path of collecting primary WTP values, though the other two options are included for purposes of consideration for inclusion as possible means of validating primary WTP data:
    - Conducting primary research on the willingness-to-pay (WTP) for a food-related QALY (following similar research commissioned by the NIHR into the "Social Value of a QALY").
    - Mapping the QALY values obtained in Phase 2 to the existing WTP-based monetisations used by the FSA to value the health-loss associated with food-related illness.
    - Mapping the QALY values obtained to some inferred threshold based on the FSA's own spending (sometimes known as a "league table" or "threshold searcher" approach) which is how NICE defines its own value of between £20,000-30,000/QALY

- Deliver a report that describes the research process and method and its results.

- Deliver a dataset and model with final values for QALYs for various food-related illnesses and any possible weightings according as revealed by different WTP values.

- Deliver a manual for FSA staff outlining how to use these QALY weights and their WTP values to inform decision making across all FSA regulatory decisions.

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10. Technical Annexes

Technical Annexe 1: The QALY: A Technical introduction

Quality adjusted life years (QALYs) are the most commonly used outcome metric in economic evaluations of health interventions in the UK. QALYs combine data on mortality with data on morbidity, where morbidity is captured using values representing the quality of life of individuals (sometimes referred to as ‘utilities’ or ‘preference weights’).

QALYs are the recommended outcome measure by the National Institute for Health and Care Excellence (NICE) in the UK. The strength of the NICE recommendation to use QALYs varies between its different guidance producing programmes ranging from being essential in the Technology Appraisal programme to optional in the Public Health programme. QALYs are commonly used to evaluate the health impacts of interventions in other UK institutions and The Treasury Green book notes the use of QALYs for the valuation of health benefits.

There are several reasons why QALYs have become a standard measure of health outcomes in economic evaluations. As they incorporate data on survival and quality of life they can reflect a range of different health impacts arising from health interventions. In addition the utility values are derived from the preferences of a population, usually a sample of the general public, and therefor incorporate a notion of value, which is important for economic evaluation. The generic nature of QALYs enable them to be used to compare a wide range of interventions, including those designed to improve life expectancy, quality of life or a combination of the two.

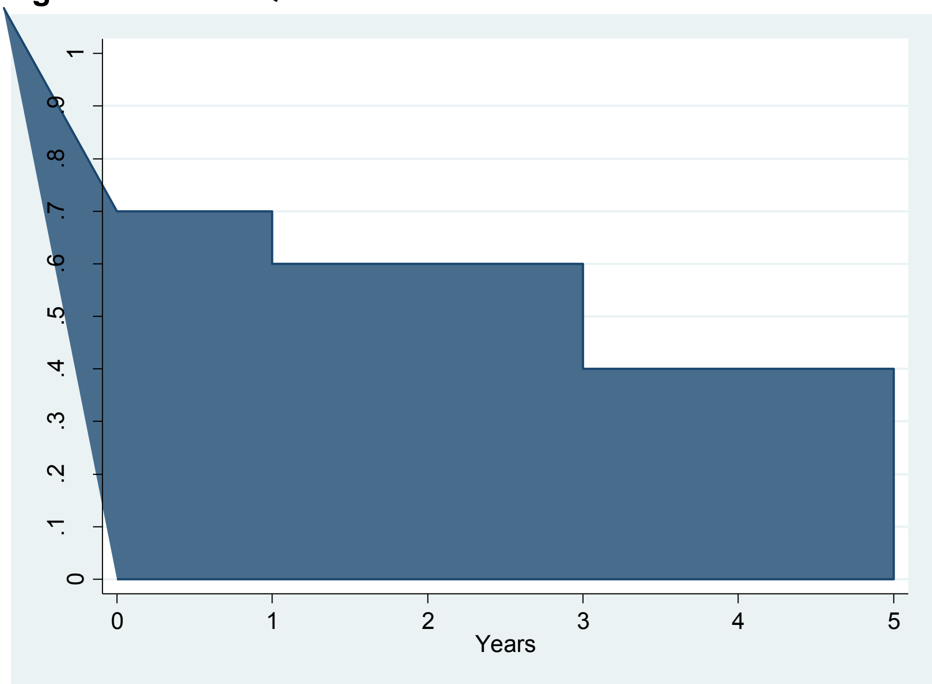
Calculation of QALYs

QALYs are measured on a scale where 0 represents ‘dead’ and 1 represents ‘full health’. Negative values are possible and reflect that the quality of life associated with the health state is perceived as being ‘worse that being dead’. QALYs are calculated by applying a quality of life weight to the duration of that state of health (QALY= duration*quality of life weight). For example, simply, one year spent in full health would accrue 1 QALY (1*1=1); Two years spent in health state considered to be 50% of full health would also accrue 1 QALY (2*0.5=1).

The length of time over which QALYs are measured depend on the intervention or condition of interest and the duration of the expected impact on health. In the evaluation of health interventions, QALYs are commonly estimated for the full life expectancy of the individual or population. They are able to reflect changing patterns of health over time. Figure 1 below illustrates this using a simple example. In the example, remaining length of survival is 5 years, at a decreasing level of quality of life. In the first year quality of life is valued at 0.7, 0.6 in years 2 and 3, and then 0.4 in the final two years of life. The total amount of QALYs in this case would be 2.7 QALYs [(0.7*1) + (0.6*2) + (0.4*2)= 2.7

QALYs.] There are various methods available for deriving the quality of life 'weights' used in the calculation of QLYs; these are described in Section 2.

Figure 1. Plot of QALY



Measuring and valuing health status

In order to calculate QALYs it is necessary to estimate the 'Q' component; that is, the quality of life values associated with different levels of health and used to weight survival in the QALY. There are various methods for deriving these quality of life values. Often, these methods are categorised into two groups: direct measurement and indirect measurement.

Direct measurement and valuation

Direct measurement involves asking people to consider their own health status, usually at the time of asking, and for them to *value* their health status using of one of range of valuation techniques. Currently the most common methods used to value health status are visual analogue scales (VAS), the time trade-off method and the standard gamble method.

The visual analogue scale method is arguably the simplest of the measurement techniques. Respondents are presented with a vertical or horizontal scale, and requested to indicate how they value their health state on that scale. VAS can differ in terms of the presentation of the scale, the numerical values attached to the scale, the definitions of the 'anchors' or limits at the top and bottom of the scale, and the wording of the question posed to respondents, including the recall period over which the respondent should consider their health. In order to be used in QALY calculations, respondents must also value a state of 'dead' on the VAS in order to be converted to the QALY scale on which 0 represents 'dead'.

One commonly used example of a VAS is the EQ-VAS which was developed by the EuroQol Group as part of the EQ-5D questionnaire. This is a 20cm vertical 0 to 100 scale, presented in the form of a thermometer. The anchor at the top of the scale represents the ‘best imaginable’ health states (value = 100) and the anchor at the bottom of the scale represents ‘worst imaginable’ health (value = 0). Respondents are asked to mark on the scale the value that best indicates their ‘current health today’ on the scale. The standard version of the EQ-VAS does not include a question requesting the valuation of the state ‘dead’ and therefore, it is argued, cannot be used to value QALYS; however valuation survey may include additional questions to anchor on the QALY scale.

The standard gamble method of valuation incorporates elements of valuation under uncertainty and trade-offs between uncertain states of health. Respondents are asked to consider spending a specified amount of time, t, in their current health state. They are then asked to make a hypothetical choice of remaining in that health state or accepting a risky treatment, which could lead to either perfect health or immediate death. The utility or value attached to their health state is then obtained by varying the chance or probability of the perfect health and death until the respondent considers the risky option to be equivalent to the certain option of their current health state. Essentially this approach is asking people their maximum risk of death that they would be prepared to accept in return for the chance of a cure for their condition.

The time trade-off (TTO) method has been frequently used in health state valuation as it embodies the notion of sacrifice between quality of life and length of life, and therefore intuitively reflects the trade-off encapsulated in the QALY metric. Respondents are asked to choose between two certain options: (i) a specified time period (e.g. remaining life expectancy) in their current health state and (ii) a shorter period of time in ‘full’ health. The time spent in full health is then varied until the respondent thinks both options are similarly desirable.

There are advantages and disadvantages associated with all three methods. The VAS method is arguably the simplest to conduct and can be completed using on-line or postal surveys; however it is prone to some form of bias and weakness upon examination of psychometric properties. In addition, it has been criticised by some economists for a lack of theoretical foundation. The standard gamble and TTO methods are more commonly used by economists; however these are more difficult for respondents to complete, in particular evidence has shown that the trade-offs and use of sometimes small change in probabilities are difficult for people to process. Both SG and TTO are usually conducted in interview settings making them more time-consuming and costly to conduct.

Indirect measurement and valuation

Indirect methods of valuation of health status are more commonly used than direct valuation methods in the economic evaluation of health interventions. This is for a variety of reasons including the time and expense of repeating valuation surveys for each intervention, a lack of consistency between studies arising from differences in designs of the surveys and, that some decision-makers prefer valuations from the perspective of tax-payers or the general population rather than only a specific group of people currently affected.

Indirect measures usually consist of a quality of life instrument (questionnaire) which is completed by the respondent to provide a self-assessment of their health status. The responses to the questionnaire are then used to describe the respondents' health states. Values may then be assigned to each possible health state from a predefined set of values.

The derivation of the utility weights for the QALY is obtained in two stages using the indirect measures. In the first stage the instrument (questionnaire) is completed by the population of interest. The responses are then used to categorise each respondent into one of the health states described by the instrument. Then, each individual's health state is assigned a value from the pre-defined set to give an individual preference or utility value. The pre-defined value sets are usually obtained from general population samples.

The EQ-5D is the most commonly used of these instruments for the economic evaluation of health interventions. Other widely used measures include the SF-6D, the Health Utilities Index (HUI) and the more recently developed Assessment of Quality of Life-8D (AQoL).

EQ-5D

The EQ-5D is a generic instrument for the measurement and valuation of health status(12). It was developed by the EuroQoL Group; a multi-national and multi-disciplinary group of researchers. Although originally developed and tested for use in Europe, its use has expanded internationally and there are currently 141 official language versions of the three-level version of the instrument.

The EQ-5D consists of a descriptive system and a VAS. Respondents are requested to complete both parts of the questionnaire with regard to their own health 'today'. The descriptive system includes five dimensions of health: mobility; self-care; ability to carry out usual activities; pain and discomfort; and anxiety and depression. In the well-established EQ-5D-3L, each dimension is described in terms of three levels of severity, although a five level version has been recently developed and is now increasingly used. The three level version describes 243 unique health states, and the five level describes 3125 possible health states. An example of the EQ-5D-5L descriptive system is provided in technical annexe 2.

Value sets have been developed by the EuroQol group to enable each health state described by the EQ-5D to be assigned a utility value. The original EQ value set was developed for the general population of England, funded by the Department of Health (Dolan 1997). These were obtained from a representative sample of 3395 members of the English general population through face-to-face interviews (Dolan et al, 1996). These people were asked to consider a selection of health states described by the EQ-5D and then to value them using the time-trade off method. A value set for the EQ-5D-5L version for England is expected to be published soon and an interim method for deriving utilities has been published in the interim (EuroQol Group, 2014). Value sets are currently available for 13 other countries for the EQ-5D-3L.

The EQ-5D has been validated in many different conditions and settings, and is the commonly used measure of health outcomes in economic evaluations of health technologies (Rasanen et al, 2006). In the UK, it is recommended by NICE as the preferred instrument for measuring health status for QALY calculations (NICE, 2013). It has also been used in large general population surveys including health Survey for England and Understanding Society. More recently it has been adopted by the Department of Health as part of its Patient-Reported Outcome Measures (PROMS) programme to routinely measure changes in the health of all patients undergoing selected health interventions (Health and Social Care information service, 2014).

Health Utilities Index

The Health Utilities Index (HUI) was developed by researchers from Canada (Feeny et al, 2002; Furlong et al, 2001). There are three versions (‘Mark 1, 2 and 3’), although Versions 2 and 3 are most frequently used. Respondents are asked to consider their own health over one of four possible recall periods ('Usual health', 'during the past 4-weeks', '...2-weeks', '...1-week'). HUI-2 was originally adapted to measure the health status of survivors of childhood cancer. It has seven attributes, each with between 3 and 5 levels: sensation; mobility; emotion; cognition; self-care; pain; and fertility. The HUI-3 was adapted for use in population health studies. It has eight attributes (each with 5 or 6 levels): vision; hearing; speech; ambulation; dexterity; emotion; cognition; and pain. The HUI-2 can describe 24,000 unique health states and the HUI-3 972,000 health states. Both have population value sets to enable utility scores to be assigned to each health state; however only the HUI-2 has a value set derived from the UK population. These values are estimated from a sample of 199 members of the UK general population who together valued a selection of 51 health states using the standard gamble method.

SF-6D

The Short-Form (SF)-12 and the SF-36 are commonly used measures of self-reported health status, developed originally in the USA. The SF-measures were not designed to facilitate the estimation of utility values and QALYs; however algorithms have since been developed that enable this (Brazier et al, 1998; Brazier et al, 2002). The SF-6D algorithm uses information from a subset of questions in the original SF-questionnaires to describe six dimensions: physical functioning, role limitations, social functioning, pain, mental health and vitality (each with between four and six levels). It can describe 18,000 unique health states. A value set is available for the SF-6D based on a survey of 836 members of the UK general population who, in total, valued 249 selected health states using the standard gamble method.

Assessment of Quality of Life – 8D (AQoL)

The more recently developed AQoL measures were created by researchers in Australia (Hawthorne et al, 1999; Richardson et al, 2014). There are two versions available and both have much more extensive descriptive systems than the other measures described above. The dimensions of the AQoL include Independent living (self-care, household tasks, mobility) social relationships (intimacy, friendships, family role), physical senses (seeing, hearing, communication), psychological well-being (sleep, anxiety and depression, pain), each with 4 levels. The AQoL-2 dimensions include Independent living (self-care, household tasks, mobility) social relationships (intimacy, friendships, family role), physical senses (seeing, hearing, communication), psychological well-being (sleep, anxiety and depression, pain), each with between 4 and 6 levels. The AQoL-1 describes 16.8 million unique health states and the AQoL-2 describes 64 billion health states. Value sets for the UK are not currently available for the AQoL measures.

Technical Annexe 2: The EQ-5D-5L

Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY

I have no problems in walking about	❑
I have slight problems in walking about	❑
I have moderate problems in walking about	❑
I have severe problems in walking about	❑
I am unable to walk about	❑

SELF-CARE

I have no problems washing or dressing myself	❑
I have slight problems washing or dressing myself	❑
I have moderate problems washing or dressing myself	❑
I have severe problems washing or dressing myself	❑
I am unable to wash or dress myself	❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities	❑
I have slight problems doing my usual activities	❑
I have moderate problems doing my usual activities	❑
I have severe problems doing my usual activities	❑
I am unable to do my usual activities	❑

PAIN / DISCOMFORT

I have no pain or discomfort	❑
I have slight pain or discomfort	❑
I have moderate pain or discomfort	❑
I have severe pain or discomfort	❑
I have extreme pain or discomfort	❑

ANXIETY / DEPRESSION

I am not anxious or depressed	❑
I am slightly anxious or depressed	❑
I am moderately anxious or depressed	❑
I am severely anxious or depressed	❑
I am extremely anxious or depressed	❑

Technical Annexe 3: Survey respondents by disease, age and time of last reaction

Figure 1a. Adults (n=640)

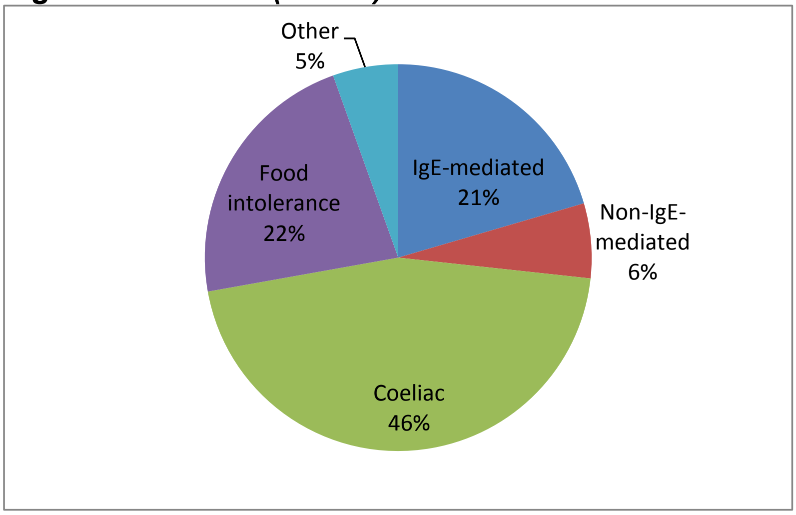


Figure 1b. Children – proxy responses by parent/ guardian (n=293)

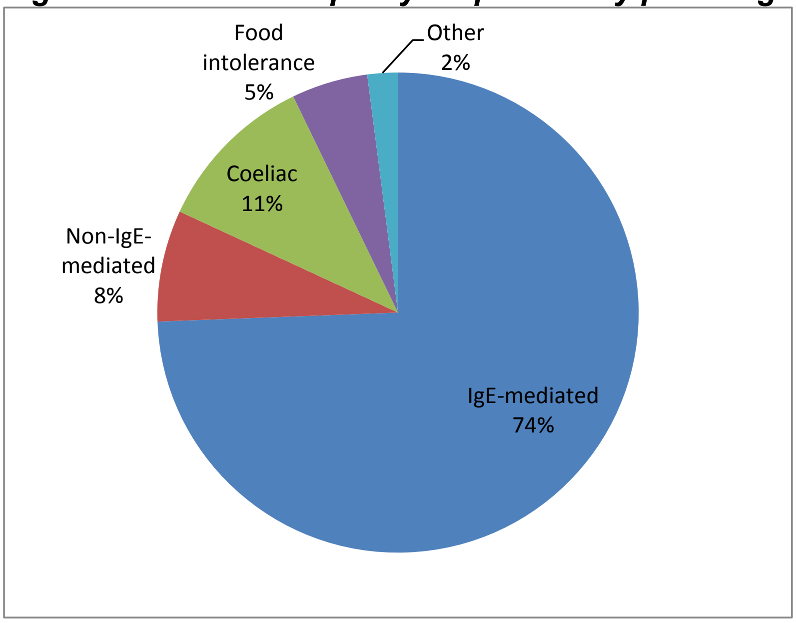


Figure 2. Survey respondents by age

Figure 2a. Adults (n=649)

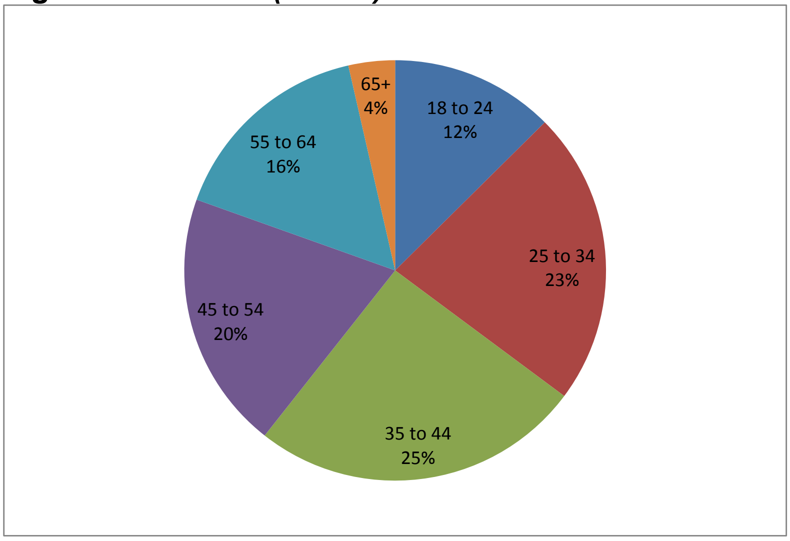


Figure 2b. Children – proxy responses by parent/ guardian (n=291)

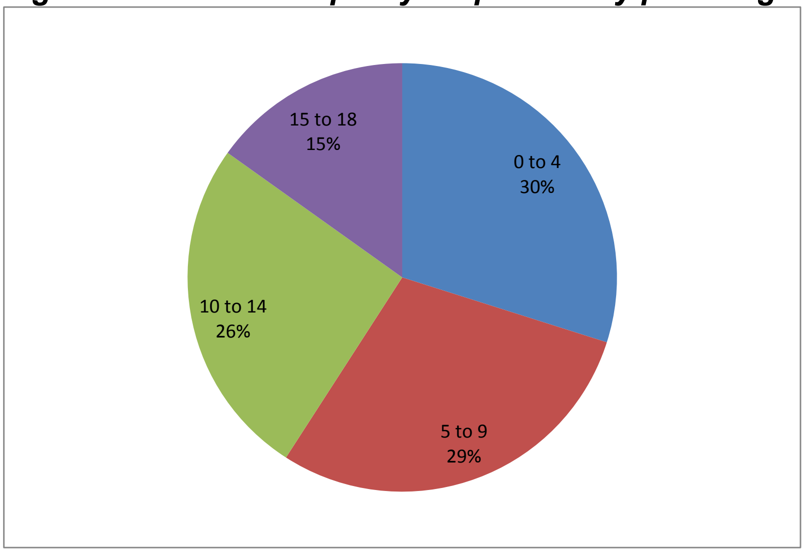
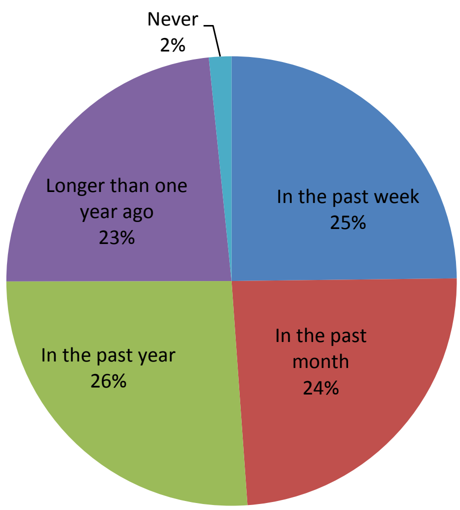
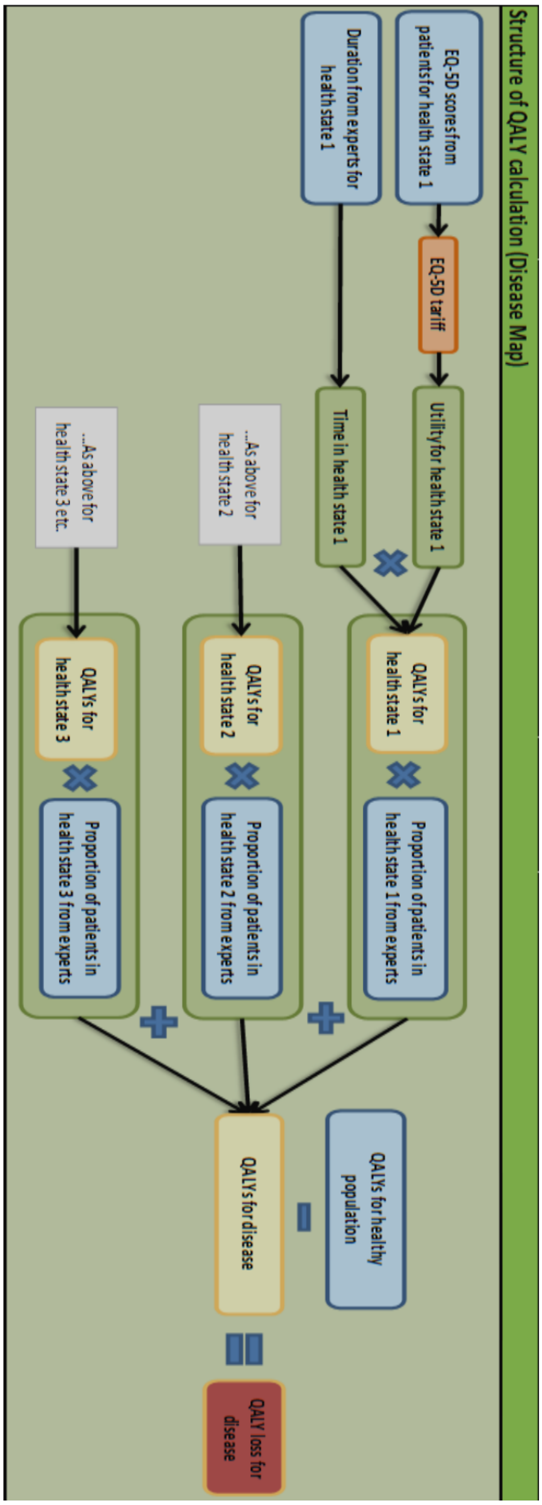


Figure 3. Survey respondents by time of last reaction (n=931)



Technical Annexe 4: Schematic approach to calculating QALY burden



Technical Annexe 5: Initially proposed list of FBD and food hypersensitivity types.

List of FBDs	
Campylobacter	***Giardia lamblia***
Listeria (*Listeria monocytogenes*)	***Staphylococcus aureus (foodborne)***
Salmonella (Non-typhoidal)	***Yersinia enterocolitica (causes foodborne yersinosis)***
Enteropathogenic Escherichia coli	***Cryptosporidium parvum***
Enteroaggregative Escherichia coli	***Shigella***
Norovirus	**Adenovirus**
Hepatitis A (few foodborne sources)	**Astrovirus**
Hepatitis E	**Rotavirus**
Clostridium perfringens	**Sapovirus (SRSV)**
Clostridium botulinium	**Cyclospora spp**
Bacillus cereus	
List of Food Hypersensitivity Types	
Milk	**Eggs**
Lactose	**Fish**
Cereals containing gluten (wheat, barley, rye, oats)	**Soya**
Gluten	**Celery**
Peanuts	**Mustard**
Tree nuts (almonds, hazelnuts, cashew nuts)	**Sulphur dioxide**
Lupin	**Sesame**
Molluscs	**Crustaceans**

Technical Annexe 6: Health state descriptions, proportions and durations elicited from experts

Figure 5a. Food hypersensitivity

Food hypersensitivity	Health state	Av. duration of episode (days)	% patients (of all episoodes in population)	Description of symptoms	Comments
IgE-mediated	Symptom-free	-	60.000%	*Quality of life issues associated with symptom-free. However these will be considered in phase 2*	
	Mild	2	28.899%	Pruritus, erythema, rhinoconjuctivitis, rhinitis, oral symptoms (itching and tingling)	
	Moderate	5	10.000%	Chest tightness, vomiting, angioedema, urticaria, diarrhoea, chest tightness	
	Severe	5	1.000%	Stridor, severe vomiting, wheezing shortness of breath and lightheadedness, marked throat tightness, choking sensation	
	Life-threatening	5	0.100%	Hypoxia, hypotension, stridor, loss of consciousness	
	Dead	-	0.001%	-	
			100.000%		
Non-IgE-mediated e.g. FPIES, EoE, eczema flare in absence of IgE symptoms	Symptom-free	-	40.000%	*Quality of life issues associated with symptom-free. However these will be considered in phase 2*	
	Mild	5	40.000%	Reflux, decreased appetite, itchy skin, nausea, mild abdominal pain	
	Moderate	5	15.000%	Vomiting, poor weight gain,marked abdominal pain, eczema flare, diarrhoea, eczema flare, mild dysphagia	
	Severe	5	4.000%	Persistent vomiting inc. haematemesis, severe diarrhoea inc. bloody diarrhoea, poor growth, severe eczema flare not responding to topical corticosteroids, severe dysphagia	
	Life-threatening	5	1.000%	Dehydration, shock, food impaction, perforation	
	Dead	-	0.000%	-	
			100.000%		
Coeliac	Symptom-free	-	50.000%	*Quality of life issues associated with symptom-free. However these will be considered in phase 2*	
	Mild	7	25.000%	Mild abdominal pain, bloating, excess wind, lethargy, itchy skin, mouth ulcerss	
	Moderate	7	15.000%	Diarrhoea, vomiting, weight loss, dermatitis herpetiformis flare, fatigue	
	Severe	7	5.500%	Chronic diarrhoea, failure to thrive or faltering growth, persistent gastrointestinal symptoms including nausea and vomiting, prolonged fatigue, recurrent abdominal pain, cramping or distension, sudden or unexpected weight loss, unexplained iron-deficiency anaemia, ataxia, neuropathy, epilepsy, diabetes, severe dermatitis herpetiformis	
	Life-threatening	N/A	3.000%	Bowel cancer, non responsive CD	
	Dead	-	1.500%	-	
			100.000%		
Other conditions perceived as "food intolerence" not listed above	Symptom-free	-	28.000%	*Quality of life issues associated with symptom-free. However these will be considered in phase 2*	
	Mild	7	40.000%	Mild abdominal pain, bloating, excess wind, lethargy, rash, nausea, pruritus, headache, sinus symptoms, thrush	
	Moderate	7	20.000%	Abdominal pain, myalgia, arthralgia, fatigue, decreased appetite, heartburn, chest tightness, persistent wheeze, moderate pruritus, tachycardia , space out	
	Severe	7	10.000%	Excessive abdominal pain, chronic fatigue, chronic pruritus, chronic diarrhoea, persistent vomiting, severe fatigue	
	Life-threatening	5	2.000%	Severe asthmatic reaction, anaphylaxis	Treated quickly: event is shorter but more severe
	Dead	-	0.000%	-	
			100.000%		

Figure 5b. Food-borne disease

Pathogen	Health state	Av. duration (days)	% cases	Description of symptoms	Comments
Campylobacter (Campylobacter jejuni the main cause of Foodborne Disease. C.coli also common)	Mild	2	50%	Mild diarrhoea with slight abdominal pains	14% of cases present to GPs (IID2 study)
	Moderate	5	33%	Diarrhoea, abdominal pains, fever and headache	
	Severe	14	17%	Bloody diarrhoea, severe abdominal pains, fever and headaches	Small % of cases develop Guillain-Barre syndrome which leads to long term neurological symptoms.
	Dead	-	0%	-	Estimated case fatality rate 0.02% (from outbreaks)
			100%		
Listeria (Listeria monocytogenes)	Mild	14	19%	Mild gastroenteritis, flu like symptoms	National enhanced surveillance data
	Moderate	21	38%	Gastroenteritis and septicaemia	
	Severe	180	18%	Meningitis with or without septicaemia or gastroenteritis	
	Dead	-	25%	-	
			100%		
Salmonella (Non-typhoidal)	Mild	4	67%	Mild diarrhoea with slight stomach pains	33% of cases present to GPs (IID2 study)
	Moderate	7	27%	Diarrhoea, abdominal pains, fever and headache	
	Severe	21	5%	Prolonged diarrhoea, abdominal pains, fever and headaches	A small proportion of cases develop reactive arthritis following infection
	Dead	-	1%	-	Estimated case fatality rate 0.3% (from outbreaks)
			100%		
Salmonella (Typhoidal)	Mild	14	20%	Fever, malaise and diarrhoea	
	Moderate	28	75%	Fever, myalgia, diarrhoea, vomiting, confusion	
	Severe	72	4%	Intestinal perforation, haemorrhage, meningitis, renal failure	
	Dead	-	1%	-	Less than 1% but greater than 0
			100%		
Enteropathogenic Escherichia coli - includes whole family of virulent cytotoxin strains (O157:H7 is a common strain)	Mild	4	36%	Diarrhoea and abdominal pains	National enhanced surveillance data
	Moderate	14	56%	Bloody diarrhoea, severe abdominal pains, fever	
	Severe	28	6%	Haemolytic uraemic syndrome	
	Dead	-	2%	-	
			100%		

Pathogen	Health state	Av. duration (days)	% cases	Description of symptoms	Comments
Enteroaggregative Escherichia coli	Mild	2	96%	Mild diarrhoea, sometimes with vomiting	4% of cases present to GPs (IID2 study)
	Moderate	4	3%	Watery diarrhoea, abdominal pains and sometimes vomiting	
	Severe	10	1%	Bloody diarrhoea, severe abdominal pains	Epidemiology is poorly understood
	Dead	-	0%	-	
			100%		
Norovirus	Mild	1	95%	Mild diarrhoea and vomiting	4.4% of cases present to GPs (IID2 study)
	Moderate	2	4%	Diarrhoea and violent vomiting	
	Severe	7	1%	Diarrhoea, violent vomiting and fever	
	Dead	-	0%	-	
			100%		
Hepatitis A (few foodborne sources)	Mild	21	30%	Nausea, vomiting, malaise, diarrhoea	
	Moderate	28	54%	Jaundice, fever, nausea, vomiting, malaise, diarrhoea	
	Severe	180	15%	Liver inflammation, jaundice, etc	
	Dead	-	1%	-	
			100%		
Hepatitis E	Mild	14	70%	Nausea, vomiting, malaise, diarrhoea	
	Moderate	28	19%	Jaundice, fever, nausea, vomiting, malaise, diarrhoea	
	Severe	42	10%	Prolonged to chronic disease	
	Dead	-	1%	-	
			100%		
Clostridium perfringens	Mild	1	84%	Abdominal pains and mild diarrhoea	16% of cases present to GPs (IID2 study)
	Moderate	1	12%	Abdominal pains and diarrhoea	
	Severe	2	4%	Abdominal pains and longer lasting diarrhoea	
	Dead	-	0%	-	Estimated case fatality 0.1% (from outbreaks)
			100%		

Pathogen	Health state	Av. duration (days)	% cases	Description of symptoms	Comments
Clostridium botulinium	Mild	2	30%	Blurred vision, difficulty swallowing, muscle weakness	
	Moderate	10	40%	Muscle paralysis, blurred vision etc	
	Severe	28	20%	Generalised paralysis including limbs, trunk and respiratory muscles	
	Dead	-	10%	-	
			100%		
Bacillus cereus	Mild	1	20%	Nausea	Data from IID1Study
	Moderate	1	40%	Nausea and vomiting	
	Severe	1	40%	Nausea, vomiting and diarrhoea	
	Dead	-	0%	-	
			100%		
Giardia lamblia	Mild	7	94%	Diarrhoea	5.5% of cases present to GPs (IID2 study)
	Moderate	14	4%	Diarrhoea, abdominal pains, fever and malaise	
	Severe	60	2%	Prolonged diarrhoea, malabsorption and weight loss.	
	Dead	-	0%	-	
			100%		
Staphylococcus aureus (foodborne)	Mild	1	15%	Nausea	Data from IID1Study
	Moderate	2	80%	Nausea, vomiting and diarrhoea	
	Severe	3	5%	Nausea, vomiting and diarrhoea lasting for a longer period	
	Dead	-		-	
			100%		
Yersinia enterocolitica (causes foodborne yersinosis)	Mild	2	22%	Watery diarrhoea	Data from IID1Study
	Moderate	5	64%	Watery diarrhoea with fever	
	Severe	9	14%	Bloody diarrhoea with fever followed by arthritis	
	Dead	-	0%	-	
			100%		

Pathogen	Health state	Av. duration (days)	% cases	Description of symptoms	Comments
Cryptosporidium parvum	Mild	7	60%	Watery diarrhoea	29% of cases present to GPs (IID2 study)
	Moderate	14	30%	Watery diarrhoea, abdominal pains and fever	
	Severe	30	10%	Prolonged watery diarrhoea, abdominal pains, fever leading to weight loss	Symptoms last longer in immunocompromised people
	Dead	-	0%	-	Estimated case fatality 0.14% (from outbreaks)
			100%		
Shigella	Mild	2	50%	Mild diarrhoea	
	Moderate	7	40%	Watery diarrhoea, vomiting, fever, abdominal pains and malaise	
	Severe	30	10%	Bloody diarrhoea, vomiting, fever, toxic megacolon, haemoytic uraemic syndrome	
	Dead	-	0%	-	Estimated case fatality 0.05% (England and Wales outbreaks)
			100%		
Rotavirus	Mild	3	30%	Watery diarrhoea	
	Moderate	5	60%	Watery diarrhoea with vomiting and abdominal pains	
	Severe	8	10%	Watery diarrhoea with vomiting, fever and abdominal pains	
	Dead	-	0%	-	
			100%		
Other Viruses	Mild	4	20%	Diarrhoea	Mainly sapovirus, data from IID1 Study
	Moderate	8	54%	Diarrhoea and vomiting	
	Severe	10	26%	Diarrhoea, vomiting and fever	
	Dead	-	0%	-	
			100%		