Estimating Quality Adjusted Life Years and Willingness to Pay Values for Microbiological Foodborne Disease (Phase 2)

Final Report

For the Food Standards Agency (FSA)
and Food Standards Scotland (FSS)

March 2017

eftec
73-75 Mortimer Street
London W1W 7SQ
tel: 44(0)2075805383
fax: 44(0)2075805385
eftec@eftec.co.uk

This document has been prepared for the Food Standards Agency (FSA) and Food Standards Scotland (FSS) by Economics for the Environment Consultancy Ltd (eftec) in association with the University of Manchester and University of Liverpool.

Study team:
University of Manchester: Dan Rigby; Michael Burton; Katherine Payne; and Stuart Wright.
University of Liverpool: Sarah O'Brien and Jo Hardstaff
eftec: Ece Ozdemiroglu, Erin Gianferrera and Rohit Mistry

Reviewer(s) provided by the team:
Ece Ozdemiroglu (eftec); Diane Dupont (University of British Columbia); Andrew Jarvis (ICF) and Louise Longworth (University of Brunel).

Reviews from the FSA, the steering group and external reviewers:
Alice John, Paul Cook, Nicholas Daniel, Darren Holland, Abdul Khaled, and Rowlando Morgan.

Reviews from the project Steering Group:
David Allen (Public Health England); John Coia (NHS Greater Glasgow and Clyde); John Henderson (Department of Health); Sandra Hoffman (USDA); Rick Holliman (St George's University of London); Paul Hunter (University of East Anglia); Miren Iturriza-Gomara (University of Liverpool); Jason March (Australian Food Standards Agency); and Michael Zand (Health and Safety Executive).

External Reviewers:
Vic Adamowicz (University of Alberta), Helen Mason (Glasgow Caledonian University), and Brecht Devleeschauwer.

Document evolution

Version 1	06/12/2016	Reviewed by Ece Ozdemiroglu
Version 2	21/03/2017	Reviewed by Ece Ozdemiroglu

PROJECT SUMMARY

This study has estimated the value of the pain and suffering associated with microbiological foodborne disease for the UK using both Quality Adjusted Life Year (QALY) and monetary (Willingness to Pay (WTP)) metrics.

QALYs are derived from the Integrate study (Wellcome Trust and Department of Health grant HICF-T5-354), systematic review of the literature and expert opinion. The QALY burden of illness was calculated using Markov Transition Models to represent the short and lifetime experiences of patients with each foodborne pathogen.

The causes of the greatest burden of foodborne illness in terms of QALY are *Campylobacter* spp. and Norovirus, primarily due to the large number of individuals who are infected by these pathogens each year. *Campylobacter* spp. and Norovirus are also associated with the greatest burden when assessed in monetary terms. The pathogen with the most severe impact, in terms of expected QALY loss per case, was *Listeria monocytogenes* due to the high death rate from this bacterium.

Giardia lamblia accounts for relatively few foodborne cases but is ranked third in terms of aggregate QALY burden (6% of the total QALY loss), and fourth in terms of WTP due to the relatively high probability of developing Irritable Bowel Syndrome (IBS) as a result of infection.

IBS is the primary driver of burden, dominating even losses associated with death. This is because of its high incidence, long duration and the high loss of quality of life by patients experiencing the condition. The large share of burden associated with IBS applies to the analyses using both QALY and monetary metrics.

Although children and elderly are more at risk of severe outcomes, for the main contributors of overall burden (*Campylobacter* spp. and Norovirus); it is the adult group (16-64 year olds) who suffer the majority of the burden. This is because they are the largest population group most likely to suffer from IBS as a sequela of infection, and have a longer life span over which the impacts can accrue.

Monetary estimates are expressed in terms of respondents' WTP to avoid pain and suffering associated with foodborne disease (FBD) (among both adults and children). FBDs were represented using (i) vignettes (descriptions of symptoms) and (ii) the EuroQol 5 dimension, 3 level health questionnaire (EQ-5D-3L). A UK sample (representative of UK population in terms of gender, age and income) were asked for their WTP to avoid the described symptoms for themselves and for their children. In total, 4397 usable surveys were completed. The results indicate an absence of large scale protest responses to the valuation scenario.

Asking respondents to trade off illness (defined through the EQ-5D-3L), length of life and income allows derivation of the monetary value of a QALY, which is estimated to range between £6,100 and £61,500 for those with annual incomes between £10,000 and £100,000 respectively. For median income the QALY value is estimated to be £19,456.

For individual symptoms and duration of these, WTP to avoid pain and suffering are presented for adults, and for parents (on behalf of their children). Look up tables (Appendix O) are produced to allow the user to create a combination of symptoms to estimate the WTP for an individual case. The Markov Transition Models are built in Excel with the user able to adjust underlying values and assumptions in order to assess changes in aggregate burden, in QALY and monetary terms, by pathogen.

The QALY and monetary metric estimates can be used in impact assessments and economic evaluation (post implementation review) for strategic priorities and policy options to reduce FBD risks; preparing briefings and food chain analyses, and supporting Finance & Strategic Planning in developing appropriate Key Performance Indicators. Appendix O is created to help with such uses. Uncertainties are reflected in the confidence intervals for both QALY and WTP estimates throughout the report.

LIST OF ABBREVIATIONS

CEA	Cost Effectiveness Analysis
CRF	Chronic Renal Failure
CV	Contingent Valuation
DALY	Disability Adjusted Life Year
DCE	Discrete Choice Experiment
DOT	Disease Outcome Tree
DV	Diarrhoea & Vomiting
DW	Disability Weights
EQ5D	EuroQol Five Dimensions Questionnaire
EQ5D-3L	EuroQol Five Dimensions Questionnaire Three Levels of Severity
ESRD	End Stage Renal Disease
FBD	Food Borne Disease
FSA	Food Standards Agency
FSS	Food Standards Scotland
GBD	Global Burden of Disease
GBS	Guillain–Barré Syndrome
GP	General Practitioner
HRQoL	Health-Related Quality of Life
HSE	Health & Safety Executive
HUS	Hemolytic Uremic Syndrome
IBS	Irritable Bowel Syndrome
ICU	Intensive Care Unit
IID	Infectious Intestinal Disease
MA	Mesenteric Adenitis
MTM	Markov Transition Model
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
PICO	Patient, problem or population - Intervention - Comparison, control or comparator – Outcome
PSA	Probabilistic Sensitivity Analysis
PTO	Person Trade Off
QALY	Quality Adjusted Life Year
RA	Reactive Arthritis
SP	Stated Preference

TTO	Time Trade Off
TTP	Thrombotic Thrombocytopenic Purpura
VAS	Visual Analog Scale
VTEC	Vero cytotoxin-producing Escherichia Coli
WHO	World Health Organisation
WTP	Willingness to Pay

GLOSSARY

Censored Variables	"Censored" refers to the fact that the outcome variable (utility score) is constrained to lie between 0 and 1.
Conditional Logit Model	a model designed to explain how respondent make choices in a choice experiment. The probability of choosing a given option is selected is explained in terms of the characteristics of the alternatives rather than attributes of the individuals (as in the multinominal logit model).
Contingent Valuation	a stated preference approach to valuing non-market goods and services where individuals are asked what they are willing to pay (or accept) for a change in provision of a non-market good or service.
Cost Benefit Analysis	a decision-making tool that compares costs and benefits of a proposed policy or project in monetary terms.
Cost Effectiveness Analysis	An analysis aimed to find the least cost option for achieving an objective, or to generate the highest benefits per unit of money spent
Cost Utility Analysis	the use of generalised measures of quality and length of life gains in the economic evaluation of health care interventions
Dichotomous Choice Experiment	a stated preference method and form of choice modelling in which respondents are presented with a series of alternatives and asked to choose their most preferred.
Disease Outcome Tree	an approach to describing an illness by severity, with branches of the tree (diagram) describing disease progression resulting in recovery, death, or long-term sequelae
EQ-5D-3L	descriptive system of health-related quality of life states consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) each of which can take one of three responses. The responses record three levels of severity (no problems/some or moderate problems/extreme problems) within a particular EQ5D dimension.

Foodborne Disease	any illness resulting from the food spoilage of contaminated food, pathogenic bacteria, viruses or parasites that contaminate food, as well as chemical or natural toxins such as poisonous mushrooms and various species of beans that have not been boiled for at least 10 minutes. Terms like 'food poisoning' and 'food related disease' are also used interchangeably to mean foodborne disease. In this study, the focus is on the foodborne diseases caused by microbiological pathogens.
Markov Transition Model	a stochastic model used to model randomly changing systems where it is assumed that future states depend only on the current state not on the events that occurred before it. Generally, this assumption enables reasoning and computation with the model that would otherwise be intractable. For this reason, in the fields of predictive modelling and probabilistic forecasting, it is desirable for a given model to exhibit the Markov property.
Multinominal Logit Model	a model designed to explain how respondent make choices in a choice experiment. In the usual multinomial logit model, the probability of choosing an option is explained in terms of the characteristics of the individuals.
Pseudo Confidence Intervals	confidence intervals produced from a Monte Carlo simulation of a data sample
S-efficient Design	A design criterion for constructing DCE experiments that minimises sample size needed to identify parameters, given their priors.
Sequelae	a condition which is the consequence of a previous disease or injury
Tobit Model	The model supposes that there is a latent (i.e. unobservable) variable. This variable linearly depends on x_i via a parameter (vector) ß, which determines the relationship between the independent variable (or vector) x_i and the latent variable (just as in a linear model). In addition, there is a normally distributed error term to capture random influences on this relationship. The observable variable is defined to be equal to the latent variable whenever the latent variable is above zero and zero otherwise.
Willingness To Pay	The monetary measure of the value of obtaining a gain in the provision of good or service or avoiding a loss.

CONTENTS

LIST OF TABLES

LIST OF FIGURES

EXECUTIVE SUMMARY

Food Standards Agency (FSA) uses health and monetary metrics to estimate the costs and benefits of policy options for reducing this disease burden. The objective of this project is to provide new estimates of pain and suffering imposed by foodborne diseases (FBD) for the following 10 pathogens[1] deemed to be the most material for FSA and FSS in terms of (i) the extent of FBD by the pathogen; (ii) the severity of the FBD and (iii) the cost of the FBD to the UK. The pain and suffering associated with these pathogens are estimated using two metrics: QALYs and money.

- *Campylobacter* spp.*,
- *Clostridium perfringens,*
- *Cryptosporidium parvum,*
- *Giardia lamblia,*
- Hepatitis E
- *Listeria monocytogenes,*
- Norovirus*,
- *Salmonella* (non-typhoidal)*,
- *Shigella* spp.
- VTEC O157*

*: Age differentiated models were estimated for these pathogens.

Quality Adjusted Life Years (QALY) – approach and results

The project conceptualises, using expert opinion, Markov State Transition Models (MTMs) for each pathogen. These models are parameterised to estimate the burden of disease using QALYs. MTMs represent the flow of a defined cohort of people through the various health states which characterise FDB for each of the 10 selected pathogens. For *Campylobacter* spp., for example, the MTM includes separate states for: healthy; uncomplicated diarrhoea/vomiting; hospitalising diarrhoea; febrile convulsions; mesenteric adenitis; septicaemia; Guillain-Barre Syndrome (GBS), Irritable Bowel Syndrome (IBS); reactive arthritis; and death. The models are parameterised with values for the transition probabilities between states and the utility losses associated with being in those states relative to being healthy. The values for the transition probabilities and utility losses are identified from a systematic literature review (see Appendices B and C). The variation in these identified values produces substantial uncertainty in the results which is reported. Fully executable models are provided for a decision-maker to use their own model input parameter values, which allows exploration of the impact of each identified input value (see Appendix O).

The parameterised models are used to determine the burden of disease for the UK by subtracting the total QALYs accrued by the population from the QALYs that would have been accrued by the population if there had been no disease caused by the pathogen. The disease burden is estimated for: (i) the short term burden of disease – over a single year in which new infections occur, and (ii) the long term burden of disease – in which the total burden of illness associated with those new infections is estimated over 100 years. QALYs lost in future years are discounted at a rate of 3.5% in line with the NICE reference case.

Campylobacter spp. and Norovirus dominate the overall QALY burden, accounting for 52% and 36% of the overall burden of the 10 pathogens considered (QALY loss

[1] Enteroaggregative *Escherichia coli* was also considered but had to be abandoned due to lack of sufficient data.

of 140 000). Although *Giardia lamblia* has a relatively lower prevalence, a relatively high number of the cases translate into long term sequelae, leading to a relatively high burden (6% of total burden) which is greater than that caused by far more prevalent *Salmonella*. *Listeria monocytogenes* generates by far the greatest QALY loss per case: 4.03 compared to 0.67 for Norovirus and 0.26 for *Campylobacter* spp. IBS dominates the QALY loss associated with sequelae because of the long-term nature of this sequela. The predicted burden per case for each pathogen, and the confidence intervals for these estimates, are shown in Table ES.1.

Table ES.1: Total lifetime QALYs lost due to infections from 10 foodborne pathogens falling in a given year in order from largest to smallest burden of illness

Pathogen	Deterministic Burden (QALYs)	Mean Probabilistic Burden (QALYs)	Lower Pseudo Confidence Interval[1]	Upper Pseudo Confidence Interval[1]
Campylobacter spp.	72,911	69,108	39,284	108,238
Norovirus	49,877	48,068	26,738	72,777
Giardia lamblia	7,916	6,634	3,602	10,641
Salmonella (non-typhoidal)	7,023	6,924	4,100	10,652
Listeria monocytogenes	734	672	628	716
VTEC O157	588	537	440	651
Clostridium perfringens	317	305	174	485
Hepatitis E	76	51	44	60
Cryptosporidium parvum	63	59	36	89
Shigella spp.	32	29	19	42

An exploratory analysis of the burden by age stratification indicates that for *Campylobacter* spp., Norovirus and *Salmonella*, the aggregate burden of disease falling mainly on the adult group (aged 16-64), as does the burden per case. This pattern is not universal, with the opposite pattern for VTEC O157, with children and the elderly bearing the greatest burden.

Willingness to Pay (WTP) – approach and results

The second approach to estimating the burden of FBD used monetary values. A stated preference survey is designed and employed to elicit WTP measures to avoid short term and long term symptoms and diseases (or 'conditions' for short) caused by the 10 pathogens.

The short term and long term conditions are represented in two forms in parallel approaches:

Vignette descriptions

- A nationally representative sample of 1040 adults regarding themselves being ill
- 592 adults - parents regarding their children aged 2-17 being ill

EuroQol 5 dimension, 3 level health questionnaire (EQ5D-3L)

- A nationally representative sample of 2097 adults
- 668 parents of children aged 2-17

In total, 4397 usable surveys were completed across the UK. There are no national population statistics for parents of children aged 2-17, but age and income descriptors show close to national statistics.

The questionnaires are presented in Appendices I - K. Vignettes are described using medical definition of symptoms. EQ-5D-3L are described using the approach's definitions of: five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) and three levels of severity (no problems/some or moderate problems/extreme problems).

In both versions, a sub-sample of parents was interviewed specifically relating to their children because children cannot identify such values for themselves. The questionnaire used two design approaches:

- The Discrete Choice Experiment (DCE) was used for short and long term conditions in the EQ-5D-3L WTP study. In the vignette WTP study a DCE was used for short term conditions, with the attributes and their levels embedded within the descriptions of illness, and
- The Dichotomous Choice Contingent Valuation (CV) was used for the long term conditions such as IBS or GBS.

Extensive testing of the SP questionnaire in six focus groups, a series of cognitive interviews, and a pilot survey indicated that respondents understood and were able to complete the task of trading off money (WTP) with experiencing a condition. Protest behaviour, for example caused by relating this task to the context of NHS provision of healthcare free at the point of use, was not a problem. Very few respondents objected to paying to avoid the conditions, and they were removed from the sample (3.2% vignette sample, 3.7% EQ-5D-3L sample)[2].

Another measure of the validity of the responses is the proportion of respondents who found the questionnaire too difficult. For this survey, very few reported that the short term vignette based questions were "very difficult" to understand (2% of adults and 4% of parents), with the equivalent figures for the long term vignette illness.

In the EQ-5D valuation instrument, ill health was represented by 3 levels of 5 dimensions of health. Very few respondents reported that the short term EQ-5D-3L valuation questions were "very difficult" to understand (2% of adults, 5% of parents), with equivalent figures for the long term EQ-5D-3L questions (4% and 8% respectively).

For short term conditions affecting adults we find models estimated on the DCE vignette choice data yield intuitive and plausible results. The attributes are significant and of the expected sign: the disutility of illness increases with duration and severity of symptoms. Economically intuitive results are found that (i) the WTP increases with respondents' income level, and (ii) the WTP to avoid additional days of illness increases with the costs respondents report they incur from being too ill to work. However, the proportion of WTP that is due to the cost of work days lost is very small

[2] If the "Other" responses are included in the sample (ie not counted as protest), the protest rates go down to 2.7% and 2.4%, respectively.

and possible to isolate from the key results we are interested in, i.e. WTP to avoid pain and suffering alone.

This study is one of a small number to integrate EQ-5D representations of health within an economic valuation instrument – combining health states with durations and cost. For the adult sample, models estimated on the DCE choice data, for both short and long term conditions, yield intuitive results with attributes significant and of the expected sign. The same holds true to a large extent for the parental sample making choices regarding short term episodes of child ill health. This breaks down for the models of long term child ill health, with little attention paid to the health attributes. Asking respondents to trade off illness (defined through the EQ-5D-3L), length of life and income allows derivation of the monetary value of a QALY, which is estimated to range between £6,100 and £61,500 for those with annual incomes between £10,000 and £100,000 respectively. For median income the QALY value is estimated to be £19,456.

As a result of using vignettes that describe symptoms, WTP to avoid varying illnesses constructed of composite attributes can be estimated. For example, an adult on median household income is predicted to be willing to pay £69 to avoid a 3-day illness involving 'a high temperature, with aching muscles and chills, diarrhoea and vomiting'. They would be willing to pay £93 to avoid a 5 day illness involving a high temperature, with aching muscles and chills, diarrhoea and blood in their stools necessitating a visit to the doctor.

The short term models for children's illness also generate intuitive results, with parents' choices affected by the duration and nature of the child's illness but also the cost, with that cost effect again moderated by their income. WTP to avoid varying illnesses constructed from composite attributes can be estimated for children's illness, too. For example, a parent on median household income is predicted to be willing to pay £148 to avoid a 5 day illness in which their child experiences a high temperature with diarrhoea and vomiting.

Far larger WTP estimates are derived for the 11 long term conditions that adults may suffer as a result of FBD. For example, WTP to avoid pain and suffering due to a year's experience of GBS is valued at £7,581, while someone aged 40 is willing to pay £13,653 to avoid the pain and suffering due to acquiring lifelong IBS. The equivalent values to avoid Septicaemia and Chronic Renal Failure are £19,869 and £45,804, respectively.

As one might expect, the values parents are willing to pay for their child to avoid serious complications from FBD far exceed what they would pay to avoid the conditions themselves. For example, they would pay £22,744 to avoid the pain and suffering of their child acquiring lifelong IBS. The equivalent values to avoid Septicaemia and Chronic Renal Failure are £98,074 and £146,296 respectively.

Uses of results

These individual WTP values can be aggregated to national values when combined with the MTMs which estimate the numbers experiencing each health state in a given year. For *Campylobacter* spp. the aggregate WTP to avoid the pain and suffering from all 280,000 foodborne cases that occur in a year is estimated to be

£424m. This value incorporates the discounted, long term burden from sequelae associated with *Campylobacter* spp. and, in this case, is dominated by IBS. Table ES.2 shows the aggregated WTP to avoid pain and suffering associated with aggregate burden per pathogen.

Table ES.2: Aggregated monetary value of avoiding pain and suffering associated with aggregate foodborne disease burden, by pathogen

	Burden £ million	**95% Confidence Intervals**
Campylobacter spp.	424.2	(308.2-540.3)
Clostridium perfringens	9	(7.6 - 10.4)
Cryptosporidium parvum	0.8	(0.6 - 1)
Giardia lamblia	40	(27.8 - 52.2)
Hepatitis E	12.5	(9.2-15.8)
Listeria monocytogenes	18.5	(10.8 - 26.2)
Norovirus	248.5	(164.9 - 332.1)
Salmonella (Non-Typhoidal)	143.9	(119.1 – 168.7)
Shigella spp.	7.7	(5.8 - 9.7)
VTEC O157	38.4	(31.9 – 45.0)
Total	**943.6**	

These values are based on foodborne cases attributable to the named pathogens. The microbial cause of FBD is not always identified and this diagnostic gap means that the values reported are likely to underestimate the value of pain and suffering caused by each of the 10 pathogens.

This study provides new estimates of the number of FBD cases and the consequent burden of disease. For individual symptoms and their duration, WTP to avoid pain and suffering are presented for adults and for parents (on behalf of their children) in the look up tables (Appendix O). These allow the user to create combinations of symptoms to estimate the WTP for an individual case. The Markov Transition Models are built in Excel with these look up tables enabling the user to adjust underlying values and assumptions in order to assess changes in aggregate burden, in QALY and monetary terms, by pathogen.

1 INTRODUCTION

1.1 Background / policy context

Actions to reduce the burden are likely to involve costs and hence their evaluation should include estimates of both the costs and benefits, the latter being the value of averted disease. The FSA analysis uses existing estimates for medical and productivity costs. This project is commissioned to estimate the value of the pain and suffering caused by microbiological foodborne disease (FBD). This is done using both QALY and monetary metrics.

1.2 Project scope

The geographical scope of the project is the UK. The costs considered are the pain and suffering associated with FBD caused by 10 pathogens. These pathogens were selected as the most material for FSA and FSS in terms of (i) the extent of FBD by the pathogen; (ii) the severity of the FBD and (iii) the cost of the FBD to the UK.

- *Campylobacter* spp.*,
- *Clostridium perfringens,*
- *Cryptosporidium parvum,*
- *Giardia lamblia,*
- Hepatitis E
- *Listeria monocytogenes,*
- Norovirus*,*
- *Salmonella* (non-typhoidal)*,
- *Shigella* spp.
- VTEC O157*

*: Age differentiated models were estimated for these pathogens. Enteroaggregative *Escherichia coli* was initially considered. An absence of suitable data means that only a partial analysis of this pathogen is possible, with no burden estimates generated.

The project considers the burden of all cases arising in a single year. The diseases are defined in terms of short and long term symptoms and conditions – the latter continue after the initial year as a result of sequelae.

1.3 Objectives of this study

The objectives of the study are to:

- develop Markov State Transition Models (MTMs) for a set of foodborne pathogens and their sequelae
- revise preliminary QALY values for the disease states within the MTMs using a combination of literature, expert opinion and patient values
- produce QALY estimates for sequelae relevant to the set of foodborne pathogens such as Guillain–Barré Syndrome (GBS), Reactive Arthritis (RA), Irritable Bowel Syndrome (IBS), Hemolytic Uremic Syndrome (HUS) etc.
- establish how the age of onset of a patient impacts the QALY loss associated with a set of foodborne pathogens
- conduct primary research using a stated preference design to elicit individual WTP values to avoid microbiological FBD pertaining specifically to the selected pathogens and their sequelae

- use the EuroQol 5 dimension, 3 level health questionnaire (EQ-5D-3L) within a stated preference valuation instrument to estimate the monetary value of a QALY gain
- aggregate the QALY and monetary value estimates to the national level for the set of pathogens.

1.4 Report structure

The report contains six Sections:

- Section 2 provides a brief overview of the project's approach;
- Section 3 provides an overview of the use of QALYs;
- Section 4 reports the use of Markov State Transition Models (MTMs) to derive estimates of QALY burden, by pathogen;
- Section 5 gives details of the stated preference survey component of the project; and
- Section 6 provides monetary values are reported for short and long term effects and aggregated to national level using the value of a QALY derived within the study, and using the vignettes approach to WTP.

The report also contains 15 Appendixes:

A. Markov transition models
B. Systematic review of the clinical literature
C. Systematic review of primary health weights used in burden of illness studies of foodborne pathogens
D. Parameter values and references for the MTMs
E. Integrate data and validation of MTM utility values
F. Examples of valuation questions – adult & child disease, short and long term
G. Long term illness (including sequelae) valuation – design information
H. Vignette survey (adults)
I. Vignette survey (parents)
J. EQ-5D-3L survey (adults)
K. EQ-5D-3L survey (parents)
L. Data analysis (Vignette survey)
M. Data analysis (EQ-5D-3L survey)
N. Aggregation of willingness to avoid foodborne diseases – *Campylobacter* spp.
O. Separate Excel files presenting the 'look up' tables allowing the users to update QALY and WTP estimates using new data on disease burden.

2 OVERVIEW OF THE PROJECT METHOD

The project uses Markov State Transition Models (MTMs) to analyse the flow of people through the various health states which characterise FBD for a set of pathogens. These models are parameterised and validated using both secondary and primary data. These MTMs include short, mild and long term conditions associated with all the modelled pathogens.

The MTMs are used to estimate the QALY losses associated with all cases associated with each pathogen in a year. The estimates are calculated for that current year, and over the duration of patients' lives, with QALY losses projected to occur in the future being discounted to convert into their equivalent 'present value'.

A stated preference (SP) survey is designed and employed to elicit WTP measures to avoid illness caused by the set of foodborne pathogens.

The short term and long term conditions are represented in two forms in parallel approaches:

Vignette descriptions

- A nationally representative sample of 1040 adults regarding themselves being ill
- 592 adults - parents regarding their children aged 2-17 being ill

EuroQol 5 dimension, 3 level health questionnaire (EQ5D-3L)

- A nationally representative sample of 2097 adults
- 668 parents of children aged 2-17

Note: the questionnaires are presented in Appendix H - K. There are no national population statistics for parents of children aged 2-17, but age and income descriptors show close to national statistics.

Vignettes are described using medical definition of symptoms. EQ-5D-3L are described using the approach's definitions of: five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) and three levels of severity (no problems/some or moderate problems/extreme problems). Both versions use both long and short term illnesses associated with those pathogens.

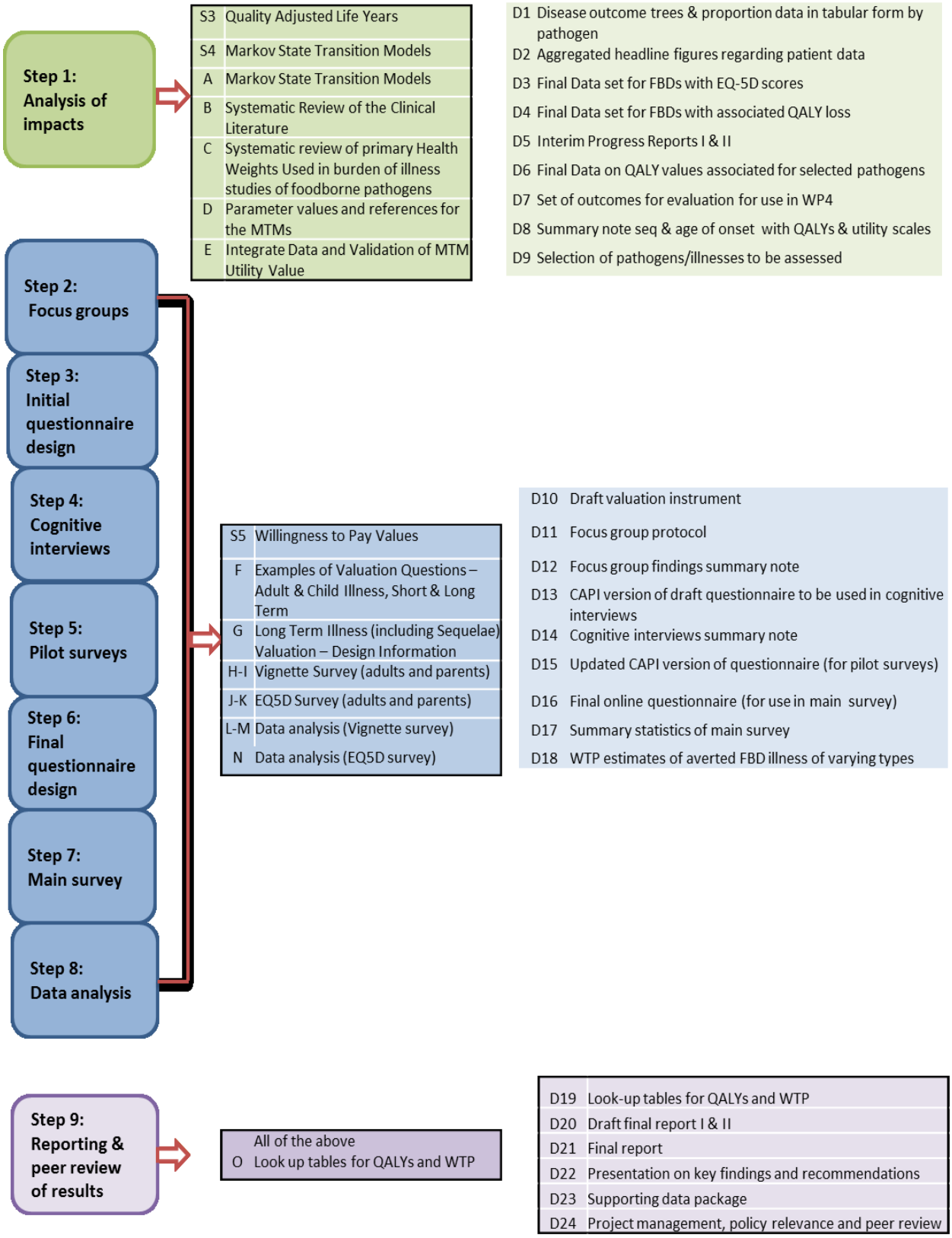
The questionnaire uses two design approaches:

- the Discrete Choice Experiment (DCE) was used for short and long term conditions in the EQ-5D-3L WTP study. In the vignette WTP study a DCE was used for short term conditions, with the attributes and their levels embedded within the descriptions of illness, and
- the Dichotomous Choice Contingent Valuation (CV) was used for the long term conditions such as IBS or GBS.

The use of the EQ-5D-3L allows estimation of the monetary value of QALY losses and gains. These values are aggregated by modifying the MTMs to accumulate monetary losses, rather than utility decrements, caused by a pathogen over a year. The project generates estimates of QALY and monetary losses for each considered pathogen, accounting for sequelae.

Figure 1 shows the study methodology, deliverables submitted throughout the project and the relevant Sections and Appendixes.

Figure 1: Project methodology showing deliverables with links to sections and appendixes



3 QUALITY ADJUSTED LIFE YEARS

3.1 What are QALYs?

The QALY is a composite measure of health status and length of life used to measure the impact of healthcare interventions on patients (Drummond, 2005). The focus is on the health status, generally measured using a generic measure such as the EQ-5D (which has three or five level versions (EuroQol, 2016, Herdman et al., 2011) rather than clinical outcomes. This helps decision makers allocate healthcare resources by facilitating the comparison of the relative cost-effectiveness of interventions in different areas of health. For example, the impact of a cancer treatment can be compared with that of an intervention for a person with a mental health related condition. The use of such measures of generalised quality and length of life gains in the economic evaluation of health care interventions is known as cost-utility analysis.

The use of QALYs is underpinned by the extra-welfarist view and as such is not consistent, and moves away from, cost-benefit analysis which has become the standard economic evaluation technique used in public sectors other than health (HM Treasury, 2011). The welfarist paradigm has been argued to be at odds with the aims of the NHS, particularly to provide equitable healthcare. Many of these arguments focus on how the relevant impacts are identified (Brouwer et al., 2008, Brouwer et al., 2000), measured and valued. For example, improved health may enable individuals to engage in the workforce, become more productive, earn more money and pay more taxes. Whilst these consequences are important, their inclusion in an economic evaluation may introduce bias into decision making, penalising treatments for conditions which are more likely to affect the economically disadvantaged, women (due to the pay gap) or the elderly. Using willingness to pay (WTP), it has been argued to depend on individuals' ability to pay, again favouring treatments for the affluent. The very existence of a publicly funded healthcare system indicates a societal preference for a more equitable distribution of healthcare. Using cost-benefit evaluation based on WTP in a system where patients are not required to pay for healthcare is therefore somewhat counterintuitive. Instead, an extra-welfarist paradigm using Cost Effectiveness Analysis (CEA) is used in the UK to value new healthcare interventions. However, this is not consistent with other public sectors. The use of QALYs is consistent with NICE methods for technology appraisal and other NICE programmes (NICE, 2013).

Disability Adjusted Life Years (DALYs) are endorsed by the World Health Organisation (WHO, 2016a). The WHO global burden of disease (GBD) measures burden of disease using DALY. This time-based measure combines years of life lost due to premature mortality and years of life lost due to time lived in states of less than full health (WHO, 2016b). The DALY metric was developed in the original GBD 1990 study to assess the burden of disease consistently across diseases, risk factors and regions (Murray and Lopez, 1996). The WHO endorses the use of DALYs in preference to QALYs to estimate the burden of FBD. For example, the WHO published a report estimating the global burden of FBD (WHO, 2015) which includes estimates of the burden of FBD caused by 31 bacteria, viruses, parasites, toxins and chemicals. The estimates are based on the best available data at the time of reporting, and identified data gaps were filled using imputation, assumptions and other methods.

In principle, DALYs are also a measure of health adjusted life years but importantly they vary in how they are measured and valued and have been shown to produce different values to QALYs (Sassi, 2006). DALYs are framed as years lost from a global ideal length and quality of life whereas QALYs lost are framed against the QALYs that would have been achieved by the population of interest.

DALYs are weighted in favour of adults in view of the fact that they support children and the elderly, whilst QALYs account for age in the average healthy utility value of the population (Sassi, 2010). Finally, with regards to the weights applied to the years lived differ in DALYs and QALYs: DALYs use disability weights, a measure of the severity of disease bounded between 1 for full health and 0 for death. It is not possible to exist in a state worse than death. Disability weights do not reflect the wider quality of life impacts of disease, such as impact on daily activities and mental health. The method of valuing severity also differs for disability weights. Generally, a 'person trade off approach' is used and this has typically been based on the opinion of experts rather than patients and the public (Murray and Lopez, 1996). Such values are therefore not compatible with the estimation of QALYs which require a preference based valuation of generalised Health-related quality of life (HRQoL).

3.2 How can QALYs be used for FBDs?

QALYs were the measure of choice in the terms of reference for this project. The relevant decision problem posed was: what is the burden of illness of selected foodborne pathogens valued using QALYs? The use of QALY adjusted life years allows the FSA and FSS to align with NICE and the NHS in their valuation of interventions to promote generalised health. The use of QALYs also allows the FSA and FSS to compare interventions in diverse areas. The burden of illness estimates will allow the FSA and FSS to determine priorities for interventions in FBD by showing the total QALY burden caused by each pathogen as well as the burden caused per case.

To calculate the total burden of disease caused by a foodborne pathogen it is necessary to estimate the number of cases, the progression of symptoms experienced by cases, the severity of those symptoms and the number of cases who die as a result of their disease. Traditionally, the burden of FBD has been modelled with the use of Disease Outcome Trees (DOTs) which illustrate the proportion of cases suffering from different symptoms. However, the duration of symptoms were rarely taken into account in such models. In reality, patients who suffer symptoms for longer time periods experience a greater burden of disease.

Furthermore, DOTs are linear and do not allow the movement of patients back into previous health states. For example, it is possible for a case to become healthy and then become re-infected, thus becoming an additional new case, within a given time period. Failure to account for such cases may lead to burden being underestimated. The use of Markov State Transition Models (MTMs) mitigates these problems. This is why MTMs have been used to estimate QALY in this study – as reported in the next section.

4 MARKOV STATE TRANSITION MODELS

This section is supported by Appendix A which sets out the decision-analytic model structures derived for this study.

4.1 What are MTMs

In the UK, the National Institute for Health and Care Excellence (NICE) has defined a set of decision-making processes and methods to inform whether, for example, technologies (as part of the NICE Technology Appraisal Programme), diagnostics (as part of the NICE Diagnostic Assessment Programme) or public health interventions (as part of the NICE Public Health Programme) are an effective use of a fixed budget for healthcare service provision. Method guides have been produced to inform NICE processes and set out how to develop the required evidence base including epidemiological, clinical and economic data. The first method guide developed informed the NICE Technology Appraisal programme, which has become the core guide referred to as the 'NICE Reference Case' (NICE, 2013). This suggests the use of decision-analytic model based cost-effectiveness analysis as the main mechanism to assimilate all available information and produce an estimate of the incremental costs (healthcare resource use) and benefits (QALYs) of the technology under appraisal compared with current practice. Decision analytic models can take a number of forms (Brennan et al., 2006) but the most commonly used type of model in NICE appraisals are Markov State Transition Models.

Brennan et al. (2006) produced a useful taxonomy of model types with an extended catalogue of 14 techniques including those that are not commonly used in economic evaluation of healthcare interventions. The types of models are differentiated in terms of the definition for the model population as either cohort or individual and whether interaction between individuals is permitted within the model. Cohort models are those defined as representing a proportion of patients that share common characteristics, whereas individual models can be defined as those accounting for each patient separately with different characteristics. Interaction is defined as the assumption of independence or not between individuals within a model such as infectious disease transmission or service capacity constraints.

MTMs are cohort models. In a Markov model, a population travels through different health states in a given time period. A probability is associated with moving from each state to a new state. Cases also have a probability of remaining in the same state, allowing the duration of symptoms to be taken into account. Each state has a health utility value associated with it, indicating the severity of being in that state. Health utility is accrued by the population based on the number of cases in each health state in each time period. To determine the burden of disease, the total QALYs accrued by the population is subtracted from the QALYs that would have been accrued by the population if there had been no disease caused by the issue of interest, in this case foodborne pathogens.

There are some weaknesses associated with using Markov models to capture the health loss from foodborne pathogens. Markov models are "memoryless" as they operate at a cohort level. For example, the probability of a case developing severe complications could not depend on their previous experience of the disease as it is

impossible to identify the pathways followed by individual cases. Similarly, an individual cannot have a higher likelihood of developing a FBD if they have previously had a disease in the same year.

The parameters included in such cohort models are based on population averages. Demographic factors such as age and co-morbidity may impact on different individuals' experience of FBD in terms of their likelihood of developing complications or sequelae, their duration of illness, or its severity. A Markov model cannot capture these individual level factors and their impact on burden of disease. However, the population can be broken down into sub-groups who form a new population with their own parameter values. For each of these sub-groups, a new Markov model is required. This approach has been used in this study to determine how age of onset may impact the burden of disease caused by FBDs.

Another assumption of Markov models is that all health states occur independently of another. For example, if a model for FBD included complications for uncomplicated diarrhoea and vomiting, a patient could not be in both of these states at once. In order to model such a combined health state, an additional state would need to be added to the model, adding a significant number of new parameters. This may make the identification of relevant data significantly more difficult. For example, with one uncomplicated state, the incidence of a FBD could be used as the probability of moving from healthy to uncomplicated in a year. With three uncomplicated states detailed above, three transition probabilities would be required, breaking down the aggregate incidence into different symptoms. As such, in the models used in this study, one generic uncomplicated state is used to represent uncomplicated diarrhoea with or without vomiting.

The analysis was designed to answer the following three research questions:

- What is annual burden of foodborne illness caused by the selected 10 foodborne pathogens in the UK in terms of the QALYs lost due to infection?
- What proportion of the burden of foodborne illness is due to long term burden associated with the sequelae of infection?
- Does burden of foodborne disease per case in four key pathogens differ amongst age groups? (*Campylobacter* spp*.,* Norovirus*, Salmonella* (non-typhoidal) and VTEC O157)

The approach taken in this project was structured around the stated decision problem (see Table 1 and further detail in Appendix A).

Table 1: Decision problem and approach overview

Decision problem	What is annual burden of illness caused by 10 foodborne pathogens in the UK in terms of the QALYs lost due to infection? The 10 foodborne pathogens were: *Campylobacter* spp*., Clostridium perfringens, Cryptosporidium parvum, Giardia lamblia,* Hepatitis E*, Listeria monocytogene*s, Norovirus, *Salmonella* (non-typhoidal), *Shigella* spp. and VTEC O157. Enteroaggregative *Escherichia coli* was also considered. An absence of suitable data means that only a partial analysis of this pathogen is possible, with no burden estimates generated.
Comparators	The health of the UK population in the absence of any of the 10 foodborne pathogens. A utility for full health of 0.856 was used (Janssen and Szende, 2013), representing the average utility of an individual in full health across all age groups.
Model type	Pathogen specific Markov state transition models
Population	The 2014 UK population (n=64,596,800). The median age is assumed to be 40 years old.
Perspective	Costs: health service perspective Consequences (QALYs): (i) adults - the impact on the person with the FBD (ii) children- parent of the person with the FBD
Time Horizon	Each model is separated into two phases i) short term and ii) long term. The short term phase takes place over a period of one year and incorporates the short term symptoms and complications of infection with a foodborne pathogen. The long term phase has a time horizon of 100 years and only incorporates the long term sequelae of infection alongside sequelae specific and all-cause mortality.
Burden of Illness	QALYs lost due to short term symptoms and complications and the long term sequelae resulting from infection in a specific year.
Discounting	No discounting is applied in the short term phase as this takes place over a period of one year. A discount rate of 3.5% is applied to QALYs lost due to sequelae occurring in the long term model.

4.2 Results

The final model structures are shown in Appendix A. The model input values are available in the submitted adaptable Excel spreadsheets (and available from the authors on request). The estimated number of annual cases of symptoms relating from the 10 exemplar foodborne pathogens are presented in Table 2.

Burden of illness estimates could not be calculated for Enteroaggregative *Escheriicha coli* due to a lack of data in the literature. Outbreaks of this bacteria in the developed world have been rare. Furthermore, the one major outbreak which occurred in Germany in 2011 was atypical as the pathogen had developed a shiga toxin resulting in high rates of haemolytic uremic syndrome and deaths (Buchholz et al., 2011). As such it was deemed that accurate and representative burden of illness estimates could not be estimated.

Table 2: Predicted number of symptom cases for 10 foodborne pathogens per year

	Mild symptoms[1]	Hospitalising complications[2]	Long term sequelae[3]	Deaths
Campylobacter spp.	279,899	3505	26,051	34
Clostridium perfringens	79,219	184	0	2
Cryptosporidium parvum	2,759	120	14	0
Giardia lamblia	7,838	93	2,479	0
Hepatitis E	282	63	0	4
Listeria monocytogenes	182	126	0	40
Norovirus	73,763	373	15,545	14
Salmonella (Non-Typhoidal)	32,973	3,796	2,288	17
Shigella spp.	1,198	140	7	0
VTEC O157	9,838	2,261	62	8

[1] Uncomplicated diarrhoea and/or vomiting, flu-like illness or uncomplicated jaundice
[2] Hospitalising diarrhoea, febrile convulsions, mesenteric adenitis, septicaemia, osteomyelitis, haemolytic uremic syndrome, thrombotic thrombocytopenic purpura or complicated jaundice
[3] Guillain-Barre Syndrome, Irritable Bowel Syndrome, Reactive Arthritis, renal failure or neurological damage

4.2.1 Base case analysis: number of cases

The annual number of cases varied significantly by pathogen. *Campylobacter* spp. was widespread estimated to affect a large number of individuals (n=279,899) when compared with the rarer *Listeria monocytogenes* (n=182). The number of hospitalisations due to complications was generally low, with the exception of: *Campylobacter* spp. (n=3,505); *Salmonella* (n=3,796): and VTEC O157 (n=2,261). Despite having the lowest number of annual cases, *Listeria monocytogenes* caused the most deaths (n=40). For three pathogens (*Cryptosporidium parvum*, *Giardia lambia* and *Shigella* spp.), no deaths were expected in a given year.

4.2.2 Base case analysis: Burden of Illness

Table 3 presents the estimated total number of QALYs lost, when compared with a healthy population (QALY burden) due to the selected foodborne pathogens in a given year. The pathogens are reported in order of total QALY burden from largest to smallest. The largest burden of illness was attributable to *Campylobacter* spp. (72,911 QALYs) and Norovirus (49,877 QALYs) whilst *Shigella* spp. had the lowest burden (32 QALYs).

The expected QALY loss for a single case of FBD, by pathogen, is shown in Table 4. *Listeria monocytogenes* had the largest burden per case with an expected loss of 4.03 QALYs per case. This was four times the size of the expected burden of *Giardia lamblia* which has the second highest burden per case (1.01 QALYs). *Clostridium perfringens* was the least severe pathogen, with an expected QALY loss of 0.004 per case, while *Cryptosporidium parvum* (0.023 QALYs lost per case) and *Shigella* spp. (0.027 QALYs lost per case) also had low burden of illness per case.

4.2.3 Probabilistic sensitivity analysis

The probabilistic sensitivity analysis allowed uncertainty in the model parameters to be incorporated into the results, providing 95% pseudo confidence intervals around the

QALY burden estimates. Table 3 shows the average total burden predicted for each pathogen along with the confidence intervals around this estimate. The predicted burden per case for each pathogen, and the confidence intervals for these estimates, are shown in Table 4.

Table 3: Total lifetime QALYs lost due to infections from 10 foodborne pathogens falling in a given year in order from largest to smallest burden of illness

Pathogen	Deterministic Burden (QALYs)	Mean Probabilistic Burden (QALYs)[1]	Lower Pseudo Confidence Interval[1]	Upper Pseudo Confidence Interval[1]
Campylobacter spp.	72,911	69,108	39,284	108,238
Norovirus	49,877	48,068	26,738	72,777
Giardia lamblia	7,916	6,634	3,602	10,641
Salmonella (non-typhoidal)	7,023	6,924	4,100	10,652
Listeria monocytogenes	734	672	628	716
VTEC O157	588	537	440	651
Clostridium perfringens	317	305	174	485
Hepatitis E	76	51	44	60
Cryptosporidium parvum	63	59	36	89
Shigella spp.	32	29	19	42

[1] Probabilistic burden is the result of the probabilistic sensitivity analysis and allows for uncertainty in the parameters of the deterministic model to be incorporated in the analysis. This provides pseudo confidence intervals from a Monte Carlo simulation of a data sample.

Table 4: Expected lifetime burden of illness per case for 10 foodborne pathogens in order from largest to smallest

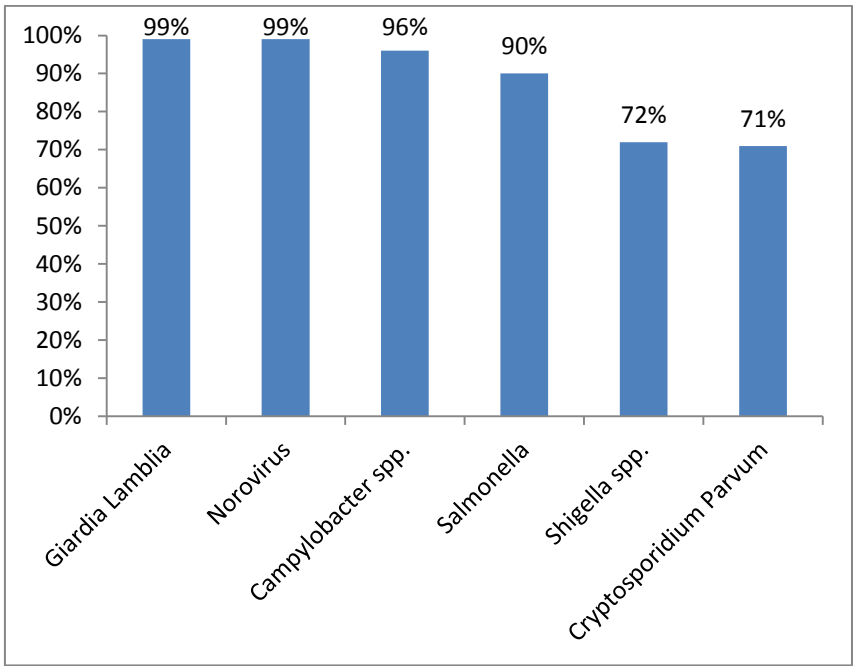
Pathogen	Deterministic Burden per Case (QALYs)	Mean Probabilistic Burden per Case (QALYs)	Lower Pseudo Confidence Interval	Upper Pseudo Confidence Interval
Listeria monocytogenes	4.031	3.690	3.449	3.932
Giardia lamblia	1.010	0.846	0.460	1.358
Norovirus	0.673	0.652	0.362	0.987
Hepatitis E	0.269	0.181	0.156	0.213
Campylobacter spp.	0.260	0.247	0.140	0.387
Salmonella (non-typhoidal)	0.212	0.210	0.124	0.323
VTEC O157	0.060	0.055	0.045	0.065
Shigella spp.	0.027	0.024	0.016	0.035
Cryptosporidium parvum	0.023	0.021	0.013	0.032
Clostridium perfringens	0.004	0.004	0.002	0.006

4.2.4 Proportion of Burden of Illness Attributable to Sequelae

Sequelae

The impact of the long term sequelae of infection is shown by their significant contribution to overall burden. Where such sequelae were included, their contribution to the overall burden of illness eclipsed that of all over symptoms combined. In particular, IBS contributed over 70% of the burden of illness resulting from the six models in which it was included. On average the burden of illness from IBS was 87.8%. Figure 2 shows the proportion of burden attributable to IBS for each pathogen.

Figure 2: Proportion of Total Burden of Illness Attributable to IBS



While it may seem surprising that the 96% of the burden of illness from pathogens such as *Campylobacter* spp. derives from IBS, this can be explained by the difference between the immediate and short term effects and the experiencing of a long term chronic disease. For example, of the predicted 279,899 cases of *Campylobacter* spp., approximately 250,000 will only suffer from mild diarrhoea. With a disutility of 0.092 per case and a mean duration of 0.78 weeks, the typical *Campylobacter* spp. sufferer will only experience a QALY loss of 0.001 QALYs. However, for the 7.6% of patients who experience IBS, their condition has a mean duration of 50 years. Coupled with a disutility of 0.18, this means that a patient with IBS will expect to lose approximately 9 QALYs over their life time. Whilst discounting significantly reduces the present value of this value, in the first year of experiencing IBS after the year of infection, a patient would expect to lose 9,000 times the number of QALYs as a typical *Campylobacter* spp. sufferer only experiencing mild diarrhoea. Even if the disutility from IBS took the lowest identified value in the literature (0.014), patients would still expect to experience a loss of 0.7 undiscounted QALYS: 700 times that of a typical suffer. While there is variation in the IBS disutility reported in the literature, it will remain the key driver of foodborne burden of disease due to its chronic, long lasting nature.

As the sequelae Guillain-Barré Syndrome (GBS) and Reactive Arthritis (RA) only appear in models where IBS is also a sequelae, their relative contribution to burden of

illness appears small. This is due to the ability of patients to recover from these sequelae in a much shorter timeframe than IBS, which often lasts for the rest of a patient's life. However, as these conditions can still last for many years, their burden again dominates that of a typical case with mild diarrhoea and/or vomiting. It is for this reason that even though a much smaller number of cases suffer GBS (n=198) and RA (4,359) than mild and/or vomiting alone (n~250,000), their burden is still sizeable. In fact the burden of illness contributed by RA cases is 5% larger (mean=881 QALYs) than that contributed by those with mild diarrhoea (mean= 833 QALYs): a population approximately 57 times larger. For VTEC O157, the sequelae of renal failure and neurological damage show a similar domination of the burden of illness estimates, contributing 91% of QALY loss despite only comprising 0.62% of cases.

4.2.5 Age stratification

The burden of illness falling across four selected age groups was calculated for *Campylobacter* spp., Norovirus, *Salmonella* and VTEC O157 (Tables 5 and 6).

Table 5: Total lifetime QALYs lost due to infections from 4 foodborne pathogens falling in a given year in the UK, stratified by age group

	Age Group			
Pathogen	**0 to 4 (n=4,026,270)**	**5 to 15 (n=8,126,951)**	**16 to 64 (n=41,036,710)**	**65+ (n=11,406,821)**
Campylobacter spp.	785	3433	59200	11109
Norovirus	396	2147	40469	7422
Salmonella (non-typhoidal)	159	393	5679	1139
VTEC O157	146	147	84	283

Table 6: Expected lifetime QALYs lost per case for 4 foodborne pathogens, stratified by age group

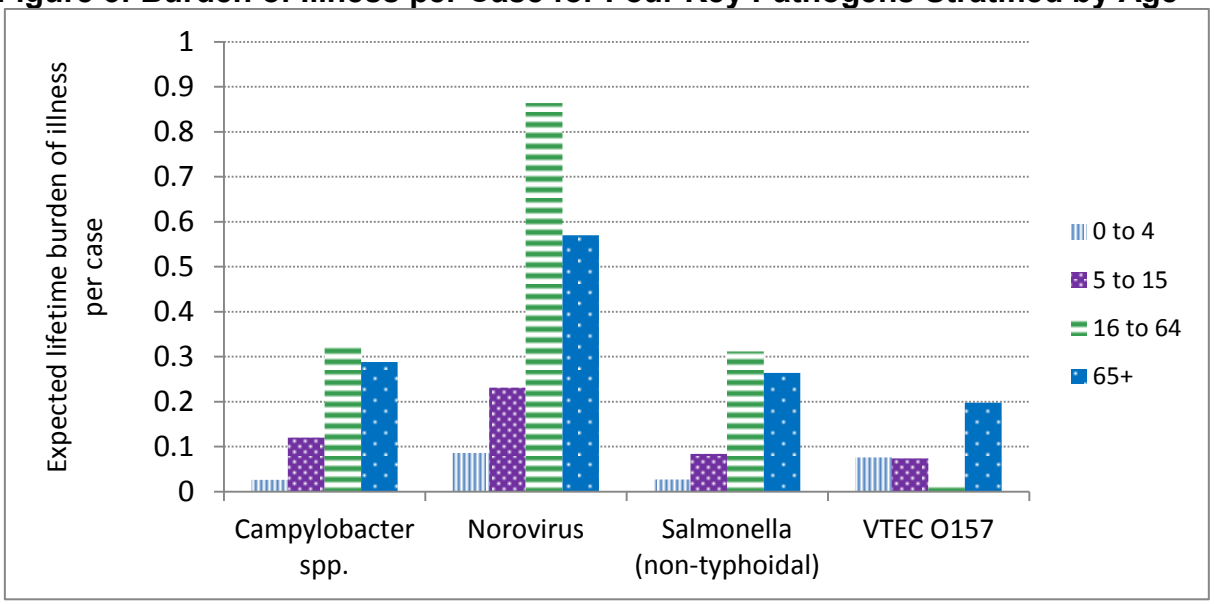
	Age Group			
Pathogen	**0 to 4**	**5 to 15**	**16 to 64**	**65+**
Campylobacter spp.	0.026	0.120	0.323	0.288
Norovirus	0.086	0.231	0.864	0.570
Salmonella (non-typhoidal)	0.027	0.084	0.312	0.264
VTEC O157	0.076	0.074	0.019	0.198

For *Campylobacter* spp., Norovirus and *Salmonella*, the distribution of burden of disease was similar, with the largest burden falling on the adult group and the second highest burden falling on the elderly group (see Figure 3). While the number of individuals in these adult groups are larger than the smaller age groups representing children, the similar patterns observed in the burden per case estimates over these age groups suggests that adults contracting these foodborne pathogens experience more severe illness. This is particularly true for adults who contract Norovirus who have significantly higher burden of illness per case than any other age group.

The pattern of burden of illness per case is reversed for VTEC O157 where individuals over the age of 65 experience the most severe disease followed by children of all

ages. This is due to the fact that it was assumed in the model that the sequelae of renal failure and neurological damage did not occur in the adult population. For each pathogen, the most severe illness was experienced by the age group who were most likely to experience the sequelae of infection with the pathogen.

Figure 3: Burden of Illness per Case for Four Key Pathogens Stratified by Age



The distribution of burden of illness was reversed for VTEC O157 with children (0 to 4 years: QALYS lost=146, 5 to 15 years: QALYs lost=147), and particularly the elderly (QALYs lost=282), facing a higher burden of illness that adults (QALYs lost=84). This was also reflected in the burden per case where the expected QALY loss per case of VTEC O157 for an individual over 65 years (QALYs lost=0.198) is ten times greater than an individual who is between 16 and 64 years (QALYs lost=0.019).

5 WILLINGNESS TO PAY VALUES

5.1 Study Design

The monetary valuation component of the project estimated the economic value of (averted) FBD burden. These values are presented at the individual level and aggregated to the national level. The stated preference survey used two approaches to defining FBDs from the 10 pathogens

Table 7: Willingness to Pay study design parameters

Description of health states due to FBD	**EQ5D**: The estimates derived provide a monetary value per QALY, which means that an aggregate value can be generated by from the aggregate QALY burden estimates. **Vignettes**: The vignette health states that featured in the WTP study are mapped on to the Markov Transition Models (MTMs) health states through which people suffering illness from the pathogens of interest pass. This enables aggregation to the national level because the MTMs include estimates of the numbers of people passing through each disease state within a year.
Severity of FBD	**Short term** or uncomplicated (e.g. lasting up to 14 days) that may be widespread but have a relatively low impact on people. **Long term** or more severe consequences and sequelae. These may affect patients for months or years and may cause disability or even death.
Population	Adults to avoid experiencing FBD themselves. Parents (or guardians) to avoid their children experiencing FBD (children aged between 2 – 17 years, focusing on one child if the person has more than one) Disease burden between adults and children distinguished through the MTM and QALY work.
Willingness to Pay (WTP) elicitation format	**Discrete choice experiments (DCEs)**: respondents were asked to choose their most preferred choice. Attributes of the choice were several symptoms (described as vignettes or through EQ5D, duration and cost). However, the representation was modified to make it feel more intuitive to respondents. **Contingent valuation (CV)**: respondents were asked for their WTP to avoid the long term conditions such as IBS or GBS.

Further details about the survey design can be found in Appendixes F-M.

5.1.1 Description of FBD and design of the WTP elicitation questions

In the EQ5D-3L version, respondents choose between spending time in competing health states described using the generic EQ-5D-3L. In the vignette version, FBD is described using a textual vignette. The EQ-5D-3L approach is entirely generic and potentially values all possible EQ-5D states. The disadvantage of the EQ-5D representation, evident in the focus groups, is that they are less intuitive than the vignettes. This was especially so for short term and mild illnesses.

For each disease state within the MTMs, a description of that state (e.g. in terms of length and nature of symptoms) was generated in conjunction with the project's clinical lead (Professor O'Brien) and used as the basis for vignettes presented to respondents within the valuation process.

The vignette approach allows direct valuation of the outcome of interest. Also such a vignette provides an intuitive representation of an illness episode to respondents – this means the illness could be described in terms of specific symptoms (diarrhoea, vomiting, stomach cramps, blood in stools etc.) unlike the generic EQ-5D-3L representations.

The vignette approach could require the valuation exercise to include each 'state' within the MTMs: a potentially large set (See Appendix A). The number of illness episodes requiring valuation is reduced by recognising the patient experiences symptoms, not pathogens, and in most cases there will be no clinical identification of the pathogen causing the symptoms. In the focus groups, the possibility of naming the pathogens in the questionnaire was considered. This might have caused different responses and valuations for the same set of symptoms (perhaps because of a 'dread' factor associated with certain pathogen names). The discussions in the focus groups did not suggest that naming the pathogen was important to respondents: they were concerned with symptoms and long term complications rather than labels. This 'sharing' of symptoms in the vignette descriptions applies to "uncomplicated diarrhoea and/or vomiting" across many pathogens and also to many of the sequelae caused by FBD.

Both Vignettes and EQ-5D designs had four different versions, which are described in the rest of this section:

- Adults – short term, uncomplicated, foodborne illness
- Adults – long term, complicated, foodborne illness
- Parents (for Children) – short term, uncomplicated, foodborne illness
- Parents (for Children) – long term, complicated, foodborne illness

A concern with the stated preference approach is that it may lead to overstatement of values, because the costs are not consequential. In the development of the survey design we developed materials to remind people of their fixed budgets, of the other things their money could be spent on and that illness was part of normal life. They were also reminded to think only about the (value of) averted pain and suffering not the costs of childcare, lost wages etc. This reminder featured in all versions of the questionnaire.

Vignette Design – Adults: Short Term

The vignettes had the following common foundation (to which specific attributes were added according to an efficient experimental design) (see Table 8):

"*You develop a high temperature, with aching muscles and chills. You have little energy and no appetite. You develop diarrhoea*…"

The resulting description of the illness was presented as a paragraph (Figure F.1 in Appendix F) rather than the more usual discrete choice experiment form in which the attributes are separated. The respondents given the choice to experience the option A

(e.g. the lower level of vomiting is added, stomach cramps, two doctor visits in an illness lasting seven days) or Option B (to avoid it at a cost). Costs are not tied to a particular solution (e.g. a pill) or an institution (e.g. NHS) to avoid influencing the responses through uncertainties about the efficacy of a pill or the political discussions surrounding the institutions. This neutral presentation of costs (and other options) was tested in focus groups (Appendix F).

Table 8: Attributes and levels used in the dichotomous choice experiment (vignettes - short term illness)

Attribute	Levels
Vomiting	none
	"…and vomiting"
	"you experience uncontrolled and frequent vomiting for 2 days - you aren't always able to make it to the toilet/sink before being violently sick"
Stomach cramps	none
	"*..and strong stomach cramps*"
Blood in stools	none
	"*..and have blood in your stools (poo)"*
GP visits	none
	"you visit your GP once, who tells you to rest, drink plenty of fluids and take paracetamol."
	"you visit your GP twice, who tells you to rest, drink plenty of fluids and take paracetamol."
Duration	"*the illness lasts for 'x' days*." (x=1,2,4,7,10,14 days)
Cost	£5, £20, £50, £100, £150 or £250

Twenty four such choice sets were constructed, with the combination of illness symptoms and durations being determined by an efficient experimental design (Rose et al 2012; Scarpa and Rose, 2008). Plausibility required some combinations were prohibited in the design. For example, two doctors' visits were only allowed if the duration was seven days or more, and at least one doctors visit was required if blood in the stools featured in the illness.

DCEs often feature an opt-out option – whether it is a 'none of these' or a 'status quo'/'current' option. The design here did not include this option since this would dominate ("no illness - no cost" would always be preferable). Whether either Option A or Option B represents a status quo is debatable. Option A represents the status quo in the sense that if the person does nothing they will become ill. Option B represents the status quo in the sense that (if the person pays) they will stay in their current health. Strictly neither option represents the current position (health or income is different in either option) and hence the DCE design could be regarded as a 'forced choice' design. A design decision like this is made to make sure the questionnaire fits the context of the valuation and is an acceptable good practice.

Vignette Design – Children: Short Term

The analysis of short term conditions relating to children was similar in design and analysis as for the adult sample. The attributes were the same even though the

phrasing around them was modified to reflect that illness concerned a child. An example choice set question is shown in Figure F.2 in Appendix F.

Vignette Design – Adults: Long Term

The design of the long term vignettes was different. Rather than using a DCE design in which illnesses were constructed from attributes, a series of long term named conditions were described. These mapped on to the complicated, long term conditions associated with the 10 pathogens which were modelled as discrete disease states in the MTMs. The long term condition vignettes were defined in collaboration with the project clinical lead, Professor O'Brien:

Guillain-Barre Syndrome (GBS)
Irritable Bowel Syndrome (IBS)
Reactive Arthritis (RA)
Mesenteric Adenitis (MA)
Septicaemia
Jaundice
Osteomyelitis
Thrombotic thrombocytopenic purpura (TTP)
Chronic Renal Failure (CRF)
Meningitis
Brain damage

Of these 11 conditions, the duration of the illness was varied for eight. For the other three (IBS, MA, Brain damage) variations in duration were not considered clinically appropriate, as they were either too short or lifelong conditions. More detail is given in Appendix G.

The design included six cost levels with the cost levels seen conditioned on the respondent's reported household income. Full details are given in Appendix G. An example of a choice question is given in Figure F.3 in Appendix F.

Vignette Design – Children: Long Term

The analysis of the WTP to avoid long term illness in children followed the same approach as in the Adult study. Descriptions were modified and some illnesses were added or removed to include all illnesses relevant to children: HUS and febrile convulsions were added, and TTP was removed.

EQ5D Design – Adults: Short Term

In the short run DCE design the attributes were the EQ-5D-3L levels (specified as dummies), cost and duration of illness. Duration entered the utility function multiplicatively i.e. the utility function in the design recognised that illness would last for the duration specified, as well as a separate variable, so that it would be possible to identify a separate duration effect to account for e.g. a marginal cost of time irrespective of the severity of the illness.

The cost attribute took six levels: £5, £20, £50, £100, £150, £250.
The durations of the illness were set at 1, 2, 4, 7, 10 and 14 days.

The S-efficient design was generated using Ngene (Choicemetrics, 2014) specified 48 choice sets, blocked into six groups of eight: each respondent saw eight choice-sets comprising two alternatives. Alternative A involved a specified duration of ill health before returning to current health, Alternative B meant remaining in current health but at a cost (see Figure F.5 in Appendix F). The respondents' "current health", self–assessed earlier in the survey, was piped into the DCE sets. A Dynamic Design was implemented to ensure that the "ill health" represented in Alternative A was never

better than the current health in Alternative B - the levels in Alternative A were set to those of the efficient design, or the current state, whichever was worse. The cognitive efficiency of the "current health" was deemed to outweigh the small statistical cost (assessed via simulation) of deviating from a full health design.

Additional design elements were used to reduce the cognitive burden for respondents in all EQ-5D instruments. The hierarchy of levels within each of the five health dimensions were represented visually via background shading within the sets (see Figures F.5 and F.6 in Appendix F which show the darker shading for the worse health levels). This also aided comparison between the two alternatives since if a health attribute took the same level in both options, the identical shading could help the respondent discard the attribute as irrelevant in that set.

EQ5D Design – Adults: Long Term

In the long run DCE design the health attributes were EQ-5D-3L levels (specified as dummies). Rather than choosing between current health and a temporary period of ill health at a cost, the two options comprised alternative life paths, of differing durations and differing incomes. In each case, the specified life span (of given health, income and duration) was followed by death (see Figure F.7 in Appendix F). This allowed estimation of the value of a QALY.

EQ5D Design – Parents: Short Term

The child illness design followed the same structure as for adult illness with parents making choices between a reduced health state, and their child's current health at a cost, for a nominated child (see Figure F.6 in Appendix F).

EQ5D Design – Parents: Long Term

The design of the EQ-5D DCE for long term child ill health took the same form as the short term DCE. The parents chose between (i) ill health for their child for a fixed duration followed by a return to current health and (ii) a current health option with a cost. The durations and costs were much greater in the long term DCE.

The cost attribute took 6 levels in the design: £5k, £20k, £50k, £100k, £150k, £250k. The 'number of years duration of the illness' were set at 1, 2, 4, 7, 10 and 14 years. Because of the seriousness of the illness, and the duration, the costs were set to be substantial values. However, in the presentation to respondents these values were pivoted off their income level.

5.1.2 The overall questionnaire structure

The questionnaire and the materials included within it were subject to extensive testing and revision before the main samples were recruited. Six focus groups were held in Manchester, Cardiff and London, with materials refined after each. In addition, 20 cognitive interviews were held using the draft questionnaire and feedback from them led to the final questionnaire used in the surveys. Focus group and cognitive interview summary reports are presented in Appendix F.

PDFs of the questionnaires used are in Appendix H (adult illness, vignette), Appendix I (child illness, vignette), Appendix J (adult illness, EQ-5D-3L) and Appendix K (child illness, EQ-5D-3L). A summary structure for the questionnaires is provided in Table 9.

Table 9: Questionnaire structure

Vignette Questionnaire Structure	EQ-5D-3L Questionnaire Structure
i. demographics (gender, age, occupation, income)	i. demographics (gender, age, occupation, income)
ii. history of diarrhoea, stomach upsets, vomiting and food poisoning in family in past year	ii. history of diarrhoea, stomach upsets, vomiting and food poisoning in family in past year
iii. review some descriptions of food poisoning	iii. review some descriptions of food poisoning
iv. recall & describe a food poisoning episode and give WTP to avoid	iv. recall & describe a food poisoning episode and give WTP to avoid
v. indicate various costs of being off work (1 day, 5 days)	v. indicate various costs of being off work due to food poisoning (1 day, 5 days)
vi. rate their (child's) health using EQ-5D-3L	vi. a practice vignette DCE set
vii. explain the short term valuation tasks, and a practice choice set	vii. explanation of EQ-5D-3L
viii. 'cheap talk' script*	viii. rate own (child's) health using EQ-5D-3L
ix. 8 short term valuation choice sets	ix. given a FBD vignette - rate their (child's) health using EQ-5D-3L if they had that illness
x. debrief questions on task difficulty & protest behaviour (always paid, never paid)	x. a practice EQ-5D DCE set
xi. explain the long term food poisoning conditions	xi. cheap talk script*
xii. explain the long term valuation tasks, and a practice choice set	xii. eight short term EQ-5D DCE sets
xiii. 10 long term valuation questions	xiii. debrief questions on task difficulty & protest behaviour (always paid, never paid)
xiv. debrief questions on task difficulty & protest behaviour (always paid, never paid)	xiv. explain the long term food poisoning conditions
xv. rate how their (child's) health would be, using EQ-5D-3L, if they had a FBD (drawn from the set of vignettes). Repeated.	xv. explain the long term valuation tasks
xvi. demographics (region, ethnicity, education, medical training, experience of named conditions)	xvi. eight long term EQ-5D DCE sets
	xvii. debrief questions on task difficulty & choice behaviour (always paid, never paid)
	viii. rate how their (child's) health would be, using EQ-5D-3L, if they had a food poisoning illness (drawn from the set of vignettes). Repeated.
	xix. demographics (region, ethnicity, education, medical training, experience of named conditions)

Note: * 'cheap talk' scripts are designed to reduce hypothetical bias. Respondents are reminded that they had limited income and that illness and temporary discomfort are part of normal life. The parent version of the questionnaire also included some additional cheap talk script concerning the unusual nature of them (not) paying to alleviate their child's pain and suffering.

5.1.3 Sample Recruitment & Descriptive Statistics

The samples for Adult and Child illness valuation were collected via an online market research panel (panel by Research Now) between October 2016 and January 2017. For the Adult sample, the specification was for a UK representative sample of adults. For the parents, the sample size required was demanding and required them to

approach all the parents of children aged 2+ whom they held in their panel. A full report of descriptive statistics for the samples is available in Appendices L (vignette samples) and M (EQ-5D-3L samples). Table 10 summarises the population characteristics.

The explanatory information and valuation questions were cognitively demanding, especially so for the long term conditions (hence the time and resources assigned to their development and testing). The ability of respondents to process and incorporate that information in their choices is partially revealed by statistical analysis of the valuation choice data.

Additional insights are available from debrief questions. In the Adult-Vignette sample, 2% and 8% described the short term sets as 'very difficult' and 'difficult' respectively. The rates in long term sets were 4% and 9%, respectively, a higher but still very small percentage. In the Parent-Vignette sample, 4% and 8% described the short term sets as 'very difficult' and 'difficult', respectively. The rates in long term sets were 6% and 11%, respectively. The numbers reporting the short term EQ-5D valuation questions as being "very difficult" to understand was low (2% adults, 5% parents) with equivalent figures for the long term EQ-5D questions of 4% and 8% respectively. These rates are very low and hence a factor confirming the validity of the responses.

Sections 5.2 and 5.3 present the results of the Vignette and EQ-5D-3L versions of the questionnaire. Since the data analysis for these two designs require different approaches, results are grouped into these versions. Within each section, results for short and long term conditions and for adults and parents (for their child) are reported separately, where possible. Details of the analysis are presented in Appendix L for vignette design and Appendix M for EQ-5D-3L design.

The results are presented here in terms of unit estimates with the median household income. The look up tables presented in Appendix O aim to help the user to define the combination of symptoms and durations associated with a given pathogen to estimate the relevant WTP to avoid pain and suffering. The tables also allow the user to estimate WTP to avoid pain and suffering at different levels of gross median household income.

Table 10: Sample characteristics

Sample name	Size*	Female – male (%)	Geographical distribution (England, Scotland, Wales, NI)	Median gross household income
Adult - Vignette	1189 (1040)	53-47	83.7% - 8.2% - 5% - 3.1%	£25-35,000
Adult – EQ-5D-3L	2211(2097)	52-48	83.2% - 9.3% - 5.3% - 2.2%	£25-35,000
Parent - Vignette	653 (592)	60-40	84.9% - 7.8% - 3.7% - 3.6%	£35-45,000
Parent – EQ-5D-3L	720 (668)	50-50	84% - 8% - 6% - 2%	£35-45,000
Total sample	**4773 (4397)**			

*Figure in brackets is the usable sample once those completing the survey excessively quickly were removed. Geographical distributions were close to the true population proportions. Median household income for the UK is £31,655 is the gross income adjusted from £26,400 disposable income estimate for 2015/16 in [3].

[3] https://www.ons.gov.uk/peoplepopulationandcommunity/personalandhouseholdfinances/incomeandwealth/bulletins/nowcastinghouseholdincomeintheuk/2015to2016

5.2 WTP Results – Vignettes

More details on Vignette results are provided in Appendix L which show statistically significant models and individual variables. Here the key points for adult and parent samples are presented for short and long term conditions, Sections 5.2.1 and 5.2.2 separately.

5.2.1 Short term Conditions

Adults

WTP measures for each element of illness are reported in Table 11 based on the significant attributes. These are displayed based on median household income and with zero costs from being too ill to work (since the objective is to estimate WTP for pain and suffering). These results are presented for each symptom per unit duration, except for doctors' visit which the analysis showed was insignificantly different between one or two visits. There is also a fixed component of the WTP to avoid the pain and suffering of FBD regardless of the duration of the symptoms.

Table 11: WTP to avoid the pain and suffering of short term FBD conditions: adult

	WTP (£)*	95% CI	
Fixed diarrhoeal illness effect**	43.19	32.10	54.29
For each day of diarrhoea	3.98	3.068	4.88
For each day of vomiting	1.68	0.53	2.83
2 days of extreme vomiting	26.76	15.66	37.86
For each day of with blood in stools	2.96	1.30	4.62
Doctor visited	17.35	9.63	25.07

*Evaluated at gross household income level of £31 655

**This is the value of the illness episode, irrespective of duration and characteristics.

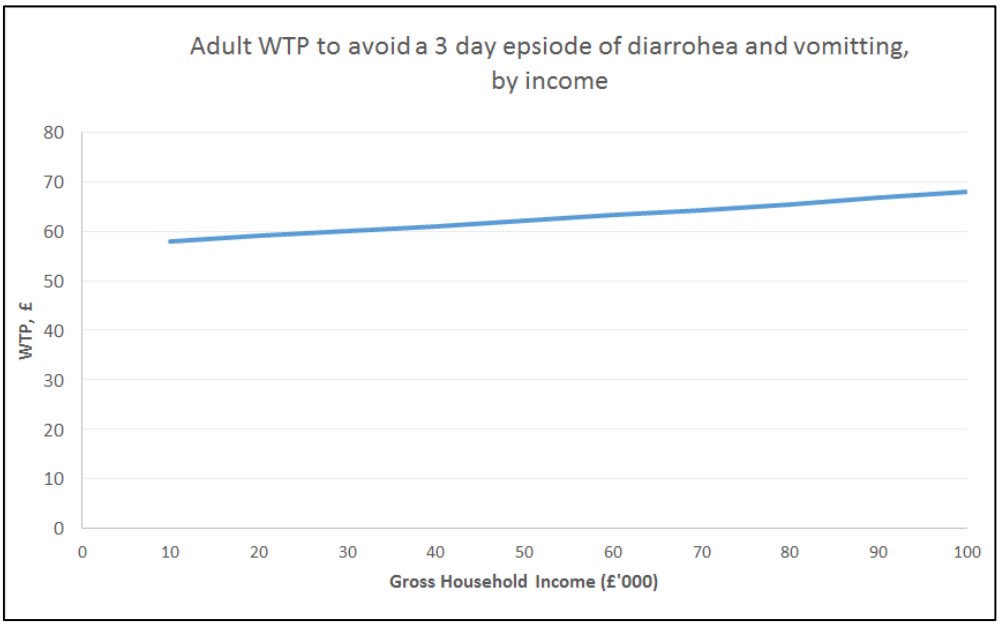
The unit estimates in Table 11 can be used to estimate different symptom combinations. For example, the WTP to the pain and suffering from avoid a 3-day illness involving a high temperature, with aching muscles and chills, diarrhoea and vomiting is:

£60.17= £43.19 + (3 x £3.98) + (3 x £1.68)

If the illness also involved two days of extreme vomiting (as might be associated with Norovirus), the WTP would increase by £26.76.

The role of income in moderating the WTP to avoid short term foodborne illness is evident in Figure 4 which shows an increase in WTP of 13% between those with gross household income of £30,000 and £100,000.

Figure 4: Income effect on WTP to avoid a 3 day adult illness with a high temperature, aching muscles and chills and diarrhoea and vomiting - adults



Parents

The analysis of short term conditions relating to children followed the approach described for adults – starting with estimation of a conditional logit model (reported in Appendix L). WTP estimates are reported in Table 12 for the statistically significant attributes. There is a much larger estimate for the 'fixed' effect: the amount parents are willing to avoid the baseline illness (high temperature, aching muscles and chills, little energy and no appetite with diarrhoea), irrespective of additional characteristics compared to the value for adults (compared £43.19, Table 11). This is to be expected. The marginal effects are broadly similar.

Table 12: WTP to avoid the pain and suffering of short term FBD conditions: parent

	WTP (£)*	95% CI	
Fixed effect**	£125.73	111.43	140.02
For each day of diarrhoea / vomiting	£4.87	3.80	5.93
2 days of extreme vomiting	£17.41	5.30	29.53
For each day of with blood in stools	£5.04	3.06	7.02

*: Evaluated at household income level of £31,655
**: This is the value of the illness episode, irrespective of duration and characteristics

The unit estimates in Table 12 can be used to estimate different symptom combinations. For example, WTP to avoid the pain and suffering from a 3 day illness for their child involving a high temperature, with aching muscles and chills and diarrhoea is:

£140.34 = £125.73 + 3*£4.87

If the illness also involved blood in the child's stools the WTP would increase to £155.46.

5.2.2 Long term Conditions

Adults

Analysis of the long term conditions requires a logit model which provides results in terms of the median WTP: the value at which 50% of the sample will pay to avoid the illness. These values are reported in Table 13, evaluated for someone aged 40 (the age of the representative respondent used in the MTMs) and at the median household income of £31,655.

As with the short term illness results, there is also a 'fixed effect' for the long term conditions, which is the sum they are willing to pay irrespective of the duration of the illness. There is also a marginal effect, which is the additional contribution to the WTP to avoid pain and suffering for each additional year of illness.

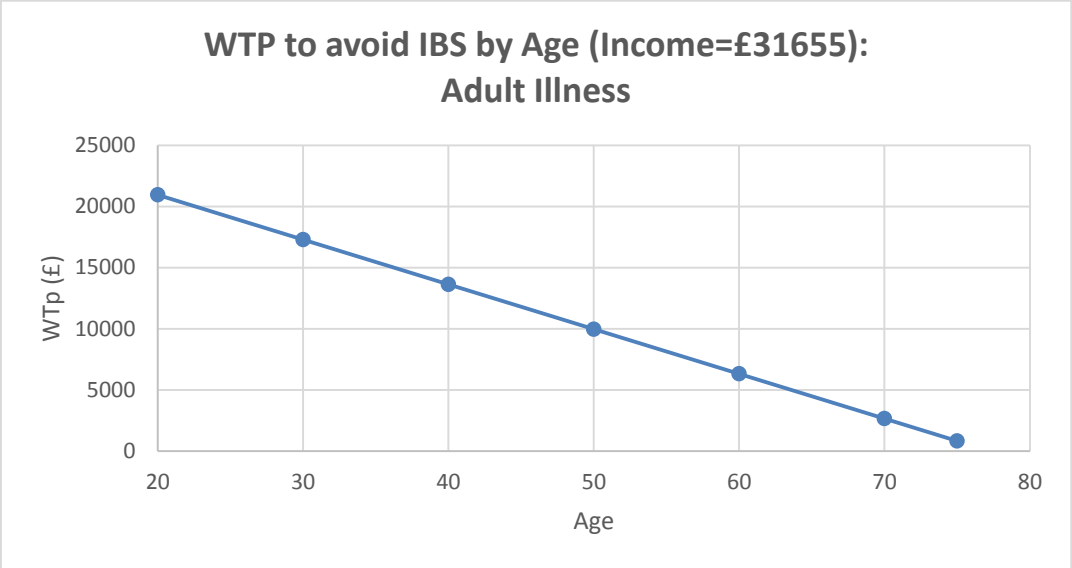
The scale of the age-duration interaction effect is evident in Figure 5. Holding income at the median level, the plot shows how WTP to avoid pain and suffering due to lifelong IBS declines with the age of the respondent. The WTP of £2,666 at age 70 is 85% lower than the value at age 30 (£17,286).

Table 13: WTP to avoid the pain and suffering of long term FBD conditions: adult (£, evaluated at median income (£31 655), age of 40)

	Fixed effect £ per case	Marginal effect £ per year
GBS	ns	7,581 (4,686-10,476)
IBS	13,653 (8,186-19,119)	na
RA	ns	1,584 (1,121-2,046)
MA	0	na
Septicaemia	19,869 (10,062-29,675)	ns
Osteomyelitis	-4,005 (-8,784-774)	8076 (4,382-11,770)
TTP	6,034 (605-11,462)	5,264 (1,635-8894)
CRF	45,804 (21,056-70,552)	ns
Meningitis	ns	5,108 (2,615-7,602)
Jaundice	26,700 (15,457-37,944)	5,112 (-130-10,355)
Brain damage	223,871 (155,409-292,333)	na

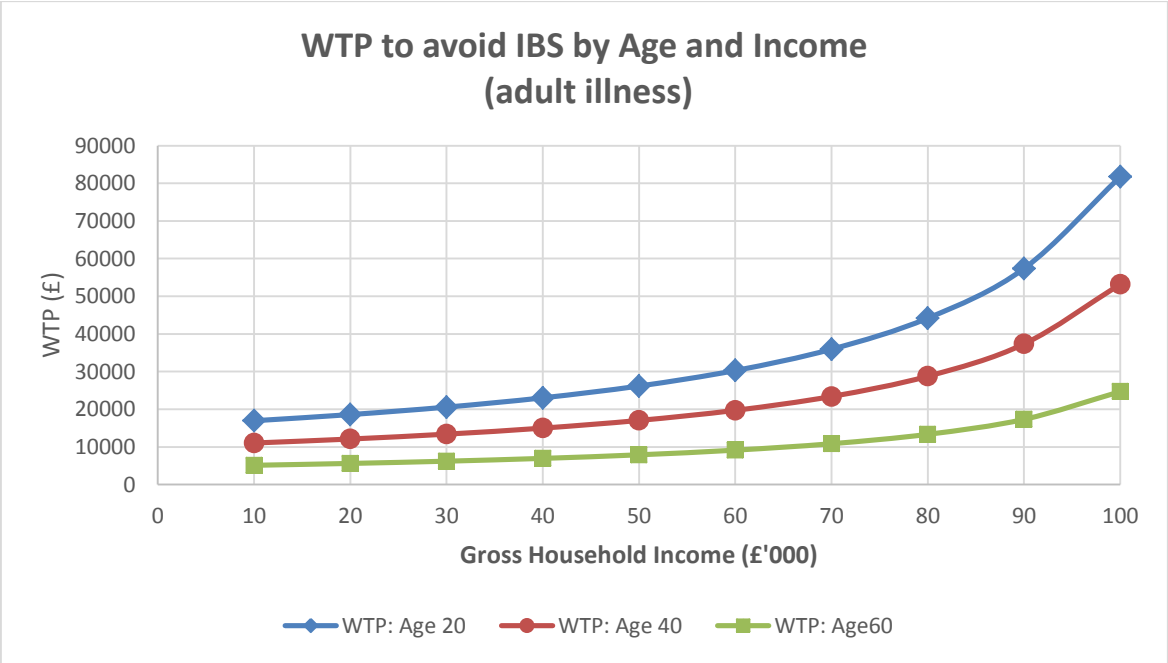
(95% CI in parenthesis)
na: length of illness not included for the condition
ns: length of illness was included but not significant & dropped from the model

Figure 5: Effect of the age of onset on adults' WTP to avoid pain and suffering due to lifelong IBS



The WTP is moderated by income as well as age as shown in Figure 6 which shows (for three age levels: 20, 40, 60) how WTP to avoid pain and suffering due to lifelong IBS increases with gross household income levels.

Figure 6: Age and Income effect on adults' WTP to avoid pain and suffering due to lifelong IBS



Parents

Table 14 reports the implied median WTP to avoid pain and suffering due to each of the long term conditions. Although there is limited sensitivity to duration of illness within some conditions, there does seem to be a reasonable sensitivity across conditions. The most extreme illness (brain damage, HUS, CRF and Jaundice, which

involves a liver transplant – see Appendix G for illness descriptions) all have values in excess of £100,000, while MA and Osteomyelitis are much lower.

Table 14: WTP to avoid the pain and suffering of long term FBD conditions: parent (£, evaluated at median income (£31 655))

	Fixed effect £ per case	Marginal effect £ per year
GBS	63,923 (28,161-99,686)	7072 (-550-14,694)
IBS	22,744 (14,185-31,303)	na
RA	17,030 (12,008-22,052)	2,222 (628-3,815)
MA	1,747 (909-2,586)	na
Septicaemia	98,074 (63,475-132,674)	ns
Osteomyelitis	8,869 (4,489-13,249)	5,766 (-169-11,701)
HUS	173,263 (122,056-224,470)	ns
CRF	146,296 (110,152-182,440)	ns
Meningitis	57,625 (41,846-73,403)	ns
Jaundice involving a liver transplant	117,132 (85,102-149,163)	na
Brain damage	352,412 (257,302-447,520)	na
Febrile convulsions	7,979 (3340-12,618)	na

(95% CI in parenthesis)
na: length of illness not included for the condition
ns: length of illness was included but not significant & dropped from the model except for Osteomyelitis which was only very marginally not significant

5.3 WTP Results – EQ-5D

More details on EQ-5D results are provided in Appendix M which shows statistically significant models and individual variables. Here the key points for adult and parent samples are presented for short and long term conditions, Sections 5.3.1 and 5.3.2 separately.

5.3.1 Short term Conditions

Adults

Because the marginal utility of money varies with gross household income levels, in Table 15 three values are reported: for median gross household income (£31,655) and at a lower (£10,000) and higher (£100,000) value.

Table 15: WTP to avoid pain and suffering associated with 1 day of reduced health, relative to full health, £/day

	Low Income £10,000	Median Income £31,655	High Income £100,000
mobility_D2	-1.36	-1.47	-1.95
mobility_D3	-3.52	-3.81	-5.17
selfcare_D2	-2.25	-2.43	-3.30
selfcare_D3	-6.67	-7.23	-9.80
usualactivities_D2	-1.45	-1.57	-2.12
usualactivities_D3	-3.30	-3.58	-4.85
pain_D2	-1.83	-1.99	-2.69
pain_D3	-8.00	-8.67	-11.75
anxiety_D2	-0.40*	-0.43*	-0.59*
anxiety_D3	-5.49	-5.95	-8.06
T	-4.85	-5.25	-7.12
T x LE	-0.002	-0.002	-0.002
Ill	-21.91	-23.73	-32.17

All estimates significantly different from zero at p<0.001, unless indicated. * not significantly different from zero. Negative WTP values correspond to a decline in utility from the base category. Mobility, self care, performing usual activities, pain / discomfort, anxiety/depression are the five dimensions of EQ-5D. The three levels apply to each of these five dimensions in terms of Level D1: "no problems", D2: "some problems" and D3: "the worst case" (confined to bed, unable to self-care, unable to perform usual activities, extreme pain and extremely anxious or depressed). T: the length of the illness, irrespective of health state. LE: self-reported lost earnings per day (LE). ILL: an individual specific Alternative Specific Constant (ASC) coded as 1 for the illness option and 0 otherwise.

The 'fixed effects' imply that a respondent with median income is willing to pay £23.73 to avoid pain and suffering due to illness, and an additional £5.25 per day of illness, irrespective of the health state. Although significant, the effect of lost earnings is negligible: for every £ per day in lost earnings expected, their WTP increases by 0.2 pence, i.e. someone with expected lost earnings per day of £100 will place a value on avoiding day of illness of £5.30, compared to £5.10 for someone with zero lost earnings.

The WTP to avoid pain and suffering due to a period of ill health can be aggregated from its elements – as shown in Appendix O. For example, an illness that last for 5 days and reduces mobility to being confined to bed, and involves extreme pain or discomfort, would be valued at:

£112.38 = £23.73 + 5 * (5.25 + 8.67 + 3.81)

A more minor illness: 3 days of moderate pain or discomfort would be valued at:

£45.45 = £23.73 + 3 * (5.25 + 1.99)

Those on higher incomes are willing to pay more to avoid the illness but the effect is not proportional to income: moving from £32,000 to £100,000 of income leads to a 36% increase in values.

Parents

Because the marginal utility of money varies with income level, Table 16 reports three values: for gross median income (£31,655) and at lower (£10,000) and higher (£100,000) income levels.

Table 16: Parents' WTP to avoid pain and suffering associated with 1 day of child's ill health, relative to full health, £/day

	Income £10,000	Median income £31,655	Income £100,000
mobility_D2	-1.76	-1.86	-2.26
mobility_D3	-2.63	-2.78	-3.39
selfcare_D2	0.65*	0.69*	0.84*
selfcare_D3	-2.90	-3.07	-3.73
usualactivities_D2	-1.53	-1.62	-1.97
usualactivities_D3	-4.47	-4.72	-5.75
pain_D2	-3.71	-3.92	-4.77
pain_D3	-9.16	-9.68	-11.78
anxiety_D2	0.65*	0.69*	0.84*
anxiety_D3	-4.63	-4.89	-5.95
T	-3.94	-4.16	-5.07

All estimates significantly different from zero at p<0.001, unless indicated. * not significantly different from zero
Negative WTP values correspond to a decline in utility from the base category. Mobility, selfcare, performing usual activities, pain / discomfort, anxiety/depression are the five dimensions of EQ-5D. The three levels apply to each of these five dimensions in terms of Level D1: "no problems", D2: "some problems" and D3: "the worst case" (confined to bed, unable to self-care, unable to perform usual activities, extreme pain and extremely anxious or depressed). T: the length of the illness, irrespective of health state,

The results from the Parent EQ-5D study for short term child ill health have largely 'worked', as judged by the sign and significance of terms and the plausibility of the WTP values presented in Table 16.

5.3.2 Long term Conditions

Adults

Table 17 reports estimates of the marginal willingness to pay per year to avoid pain and suffering due to each of the 10 health states below full health.

For the higher level (level 3) illness states, the WTP to avoid a year in that state are relatively high proportions of income: up to 94% to avoid being confined to bed for one year and 86% to avoid a year of extreme pain.

Table 17: WTP to avoid year in a health state, as proportions of current income

variable	WTP	SE	Z
mobility_D2	0.49	0.09	5.41
mobility_D3	0.94	0.04	23.97
selfcare_D2	0.30	0.095	3.16
selfcare_D3	0.86	0.06	13.25
usualactivities_D2	0.32	0.08	4.01
usualactivities_D3	0.63	0.09	7.02
pain_D2	0.45	0.09	4.94
pain_D3	0.86	0.06	14.05
anxiety_D2	0.48	0.09	5.22
anxiety_D3	0.84	0.07	11.82

Mobility, selfcare, performing usual activities, pain / discomfort, anxiety/depression are the five dimensions of EQ-5D. The three levels apply to each of these five dimensions in terms of Level D1: “no problems”, D2: “some problems” and D3: “the worst case” (confined to bed, unable to self-care, unable to perform usual activities,

Parents

The analysis reported in Appendix M indicates that respondents paid very little attention to the EQ-5D-3L health attribute levels when making their choices – most parameter estimates are insignificant. However, the respondents did take account of the duration of the illness and the cost to avoid illness. Further, there was a significant effect of income on what people would pay to avoid their child’s pain and suffering due to illness. Although these results indicate that parents are willing to pay to avoid long term illness for their children, they are of little use as the choices. Hence any WTP values derived from them are not differentiated by the severity of the illness experienced by the child.

5.3.3 Monetary Value of a QALY

The model estimated for the responses to the EQ-5D version of the questionnaire (Appendix M) can be used to estimate the value of obtaining an additional year of full health i.e. the WTP to acquire a QALY. Conceptually this identifies the reduction in income that would exactly offset the increase in utility associated with the length of life being extended by one year at full health.

Analysis of the choice data indicated that respondents were not discounting. An assumption has to be made as to whether additional income is earned when the additional year of life is gained. Both no additional income and additional median income assumptions are tested (Appendix M).

To illustrate the effect of household income and the number of life years remaining (T), Table 18 reports the values for a QALY for three different income levels, and for an initial T of 1 and 10.

Table 18: WTP for a QALY, by income level, and number of years of life remaining (£)

	Gross Median Household Income		
	£10,000	**£31,655**	**£100,000**
T=1	6,100 (3,400-8,90)	19,456 (10,700-28,200)	61,500 (33,900-89,100)
T=10	12,300 (3,600-20,900)	38,900 (11,600-66,200)	122,900 (36,500-209,200)

T: expected life span. (95% confidence intervals in the brackets).

As expected, the WTP increases in proportion to income. If one takes the median income of £31,655 then the WTP for a QALY would be £19,456 for a year gained immediately.

These results assume that there is no rate of time preference. As the additional year of life occurs at the end of the period, then discounting with a positive discount rate will reduce the WTP.

These results are based on the assumption that the additional year of life does not affect wealth, i.e. that consumption in that year has to be met by reallocating consumption from other years. An alternative assumption is that the earning capacity of the individual was the same in that additional year. This changes the fundamental object being valued: it is now an additional year of life, plus an addition to wealth of Y. WTP for a QALY increases simply by the amount of annual income. Thus, WTP for a QALY for an individual at median income, under these assumptions, would be £31,655 + £19,456 = £51,111 per year. Similarly, all other estimates simply need to be updated by the value of annual income.

5.4 Aggregation of WTP to avoid foodborne illness

The WTP estimates reported in Section 5.3 are at the level of the individual (adult, child, short term, long term). In this Section, aggregated results are presented for vignette and EQ-5D versions of the questionnaire.

Going forward the WTP results could be updated with respect to

- Any changes in the sensitivity to FBD and hence WTP to avoid it (this would require new update surveys which would not be necessary on an annual basis unless there is significant change in the health evidence)
- Inflation – best through changes in real income to address the income effect on WTP. HM Green Book advice should be followed for this.
- Population changes (perhaps not annually but to reflect any significant changes in the number and composition of the population). ONS population statistics can be used for this.

5.4.1 Aggregation - Vignettes

The MTMs provide the foundation for the monetary aggregation based on vignette WTPs. They define the health states people move through, the numbers doing so and

the utility decrement associated with that state. Aggregate WTP estimates of burden involve replacement of the QALY disutility of the states with the estimated WTP to avoid the pain and suffering associated with those states. There are however complications in doing so regarding:

Duration & WTP

For some conditions (such as septicaemia) respondents were not sensitive to long term duration meaning only a "fixed effect" WTP is available. Such duration-invariant WTPs are accommodated within the WTP aggregation by multiplying the estimated monetary fixed effect by the number of UK cases simulated by the model.

For conditions for which there is both a fixed and marginal effect, both a WTP value associated with the number of cases, and a value associated with the duration of those cases are included.

Death

The vignette WTP study does not provide a value for death. We designed the valuation question in terms of certain outcomes instead of risks of any given ill health state occurring. Therefore, the survey would not ask respondents about their WTP to avoid their certain death. To address this gap we use the value of a QALY reported in Section 5.3.3 of £19,456.

We report this process of aggregation in detail for *Campylobacter* spp., before presenting results for the full set of 10 pathogens.

Table 19 reports WTP values estimated for the marginal value for a year in each state, and any fixed effects. Note that these values are weighted averages of the adult and child illness values, to reflect that the aggregate number of cases include both adults and children. For *Campylobacter* spp.*, Salmonella,* Norovirus and VTEC O157, the age weightings were taken from the age stratified MTMs developed in the study. For Hepatitis E all cases were assumed to occur in adults and for the remaining five pathogens the proportional split between adults and child cases was taken from data provided by Public Health England (private correspondence). The weightings are in each of the MTM Excel look up tables in Appendix O.

Table 19: Values used in estimating aggregate WTP to avoid disease – Conditions relevant to *Campylobacter* spp. only

	Fixed effect (£'000 per case)	Marginal effect (£'000 per year)
Uncomplicated Diarrhoea /vomiting	0.060	2.006
Hospitalizing Diarrhoea /vomiting	0.084	3.313
Febrile Convulsions	7.978	0
Mesenteric Adenitis	1.747	0
Septicaemia	35.98	0
GBS	6.83	7.581
IBS	14.05	0
RA	6.51	1.584
Dead	--	19.5

The values in Table 19 are multiplied by the number of person episodes spent in each state from Section 4. Table 20 reports these values generated using the two monetisation approaches.

For *Campylobacter* spp. the magnitude of the monetary values is quite different between the vignette WTP study (£429m) and that from monetising the QALY burden using a value of £19,456 per QALY (£1,419m). A large part of the difference in total burden is due to the difference in the monetary value assigned to IBS: vignette WTP to avoid pain and suffering due to IBS is 14,050 per case, while the monetary value of a QALY is £60,093. The large number of cases of IBS (21,500) associated with *Campylobacter* spp., and their long duration, means this difference in £/case leads to substantial differences in the aggregate monetary burden.

Table 20: Estimates of monetary burden from pain and suffering arising from an annual caseload of *Campylobacter* spp.

	WTP (£'000)	
Total	**424,244**	**(308,244 - 540,264)**
Uncomplicated Diarrhoea	34,939	(30,900 - 38,900)
Hospitalizing Diarrhoea	472	(427 - 518)
Febrile Convulsions	339	(138 - 540)
Mesenteric Adenitis	426	(218 - 635)
Septicaemia	22,515	(15,700 – 29,300)
GBS	6,855	(4,800 - 8,900)
IBS	302,071	(187,160 - 417,00)
RA	41,972	(29,800 – 54,100)
Dead (from all of at the above)	**14,654**	**(7,900 - 21,400)**

The aggregation process reported for *Campylobacter* spp. is repeated for the other nine pathogens, generating the values reported in Table 21.

Table 21: Aggregated monetary value of avoiding pain and suffering associated with aggregate foodborne disease burden, by pathogen

	Burden £ million	95% Conf Intervals
Campylobacter spp.	424.2	(308.2-540.3)
Clostridium perfringens	9	(7.6 - 10.4)
Cryptosporidium parvum	0.8	(0.6 - 1)
Giardia lamblia	40	(27.8 - 52.2)
Hepatitis E	12.5	(9.2-15.8)
Listeria monocytogenes	18.5	(10.8 - 26.2)
Norovirus	248.5	(164.9 - 332.1)
Salmonella (Non-Typhoidal)	143.9	(119.1 – 168.7)
Shigella spp.	7.7	(5.8 - 9.7)
VTEC O157	38.4	(31.9 – 45.0)
Total	**943.6**	

The monetary value of the FBD burden is considerably lower from the aggregation of vignette based WTP values than from the monetisation of the QALY losses: £921.7m based on vignette WTP values against £2715m from monetising the QALY burden at a value of £19 456 per QALY. As discussed with respect to *Campylobacter* spp., a large part of this difference is due to the monetary value assigned to IBS between the two approaches.

5.4.2 Aggregation - EQ5D

Assuming the loss of the QALY occurs at T=1, the value of £19,456 (from Section 5.3) is applied to the estimated QALY losses reported in Table 3, giving values reported in Table 22.

Table 22: Aggregated monetary value of disease burden QALY losses, by pathogen

	QALY loss	£ / QALY	Burden, £m	95% Confidence Interval
Campylobacter spp.	72,911	19,456	1418.6	(730.6-2106.6)
Norovirus	49,877	19,456	970.4	(492.1-1448.6
Giardia lamblia	7,916	19,456	154.0	(85.8-222.2
Salmonella (non-typhoidal)	7,023	19,456	136.6	(69.1-204.1
Listeria monocytogenes	734	19,456	14.3	(8.3-20.30
VTEC O157	588	19,456	11.4	(6.5-16.3)
Clostridium perfringens	317	19,456	6.2	(3.3-9.1)
Hepatitis E	76	19,456	1.5	(1.0-1.9)
Cryptosporidium parvum	63	19,456	1.2	(0.6-1.8)
Shigella spp.	32	19,456	0.6	(0.3-0.9)
TOTAL			**2714.8**	(2159.3-3270.3)

6 SUMMARY AND RECOMMENDATIONS

This study has produced 10 Markov State Transition Models that are used to estimate the QALY burden of selected foodborne pathogens over two time frames, one-year and a life-time. The life-time horizon incorporates the burden of illness as a result of sequelae from the foodborne pathogen.

Published data were used to populate these decision-analytic models but the spreadsheet lookup templates developed (Appendix O) allow users to use their own data sources to adjust the model input parameters and derive new estimates of burden.

The utility values identified in the published literature for selected health states were cross checked against current UK values derived from the in-progress Integrate study. Utility values for uncomplicated and complicated (hospitalising) illness estimated on a sample of c.300 patients from Integrate were found to be similar to the utility values in the literature and used in the MTMs.

Using the MTMs, the estimated annual number of cases varies significantly by pathogen. *Campylobacter* spp. has the biggest impact in terms of the number of cases compared with the rarer *Listeria monocytogenes*. The estimated number of annual deaths from *Campylobacter* spp. (34) is fewer than commonly reported[4].

The number of hospitalisations due to complications is generally low, with the exception of: *Campylobacter* spp., *Salmonella* and VTEC O157. Despite having the lowest number of annual cases, *Listeria monocytogenes* causes the most deaths.

The largest QALY burden of illness is attributable to *Campylobacter* spp. whilst *Shigella* spp. has the lowest burden. *Listeria monocytogenes* has the largest burden per case. This is four times the size of the expected burden of the next most severe pathogen *Giardia lamblia*.

Probabilistic sensitivity analysis allowed uncertainty in the model parameters to be incorporated into the results and showed substantial variation around the mean QALY burden estimates as reported in Section 4.

Results from an age-disaggregated analysis indicate that for *Campylobacter* spp., Norovirus and *Salmonella*, the age profile of the burden of illness was similar across four age groups (0-4, 5-15, 16-64 and 65+). For those pathogens the largest burden fell on the adult group (16-64) with the second highest burden falling on the elderly group (65+). In contrast, for VTEC O157 the highest burden was associated with the elderly, followed by children (5-15).

Giardia lamblia accounts for relatively few cases but is ranked the third in terms of overall QALY burden per pathogen (6% total QALY loss). This is largely a result of the relatively high probability of developing Irritable Bowel Syndrome (IBS). IBS accounts

[4] See https://www.food.gov.uk/sites/default/files/multimedia/pdfs/campylobacterstrategy.pdf

for a very large proportion of the aggregate burden from microbiological FBD. It dominates QALY losses associated with death. This is because of its relatively high incidence, long duration and the high disutility placed upon the condition. The large share of burden associated with IBS applies to both QALY and monetary analyses but to a lesser extent.

Turning to the monetary analysis, the study has involved the development and testing of stated preference valuation instruments concerning the value of pain and suffering associated with FBD. These instruments have used vignette and EQ-5D-3L representations of illness. The EQ-5D component is one of very few studies which have sought to include a payment vehicle alongside EQ-5D attributes and a duration term. Thus, this project was a test case for this approach. An attraction of such an approach is the possibility of estimating the monetary value of a QALY.

The results indicate that it is possible to successfully implement Stated Preference surveys concerning the value of pain and suffering associated with FBD. Rates of protest behaviour, such as rejection of the scenario in which one is asked to pay to avoid illness, were low. The magnitude of estimated WTP values was plausible with little evidence of extreme 'yea saying', or overstatement of values.

There were differences between the experience of using vignette and EQ-5D-3L approaches. The former approach 'worked' when implemented with respect to both adult and child illness, for short and long term conditions. The EQ-5D-3L valuation approach resulted in significant parameter estimates, of the anticipated sign, and WTP results in plausible ranges for adult illness. For the parent sample concerned with child illness this was true only for short term ill health, but not long term conditions. In these latter results many EQ-5D-3L health parameter estimates were insignificant. The results suggest that the duration of the long term conditions was, to a large degree, driving choices rather than the specific health states. The 'success' of the Vignette – WTP study for long term conditions in children implies that this is not caused by a wholesale rejection of the valuation scenario by parents. Rather it was the specifics of the EQ5D-3L approach that caused the disregarding of health attribute levels.

We note that because the long term child EQ-5D did not include choices between lives of differing length for the child, measures of the WTP for a QALY could never be derived from such choice data. The WTP for a QALY is derived from the Adult version in which people chose between two lives of differing incomes, health states and durations.

The WTP estimates for a QALY for someone on median gross household income of £31,655 ranged between £19,456 and £38,900 depending on the number of years of life remaining prior to the additional year being obtained (1 and 10 years respectively for the values reported).

The WTP values estimated at the individual level are aggregated to national values by combining the stated preference estimates with the predicted numbers experiencing each health state in a given year derived from the MTMs.

For *Campylobacter* spp. the aggregate WTP to avoid the pain and suffering from all 280,000 cases that occur in a year is estimated to be £424m. Norovirus is estimated to

generate the next greatest burden (£249m) followed by *Salmonella* (£144m). The burden from IBS contributes a very high proportion of these values.

The total monetary value of the burden of pain and suffering from the 10 pathogens is predicted to be £943.6m. This is markedly lower than the value (£2,715m) derived from monetising the estimated QALY loss, with the difference resulting in large part from the valuation of IBS between the two methods. Aggregate value to avoid pain and suffering associated with the aggregate burden for each pathogen is reported in Table 21 (Section 5).

The key recommendations based on this research include the following:

- the results can be used for impact assessments and evaluations by the FSA and FSS
- FSA and FSS could consider commissioning work on the utility decrements associated with IBS given the high disease burden it poses
- FSA and FSS could consider revisiting its priorities in light of the finding that Norovirus and Giardia have relatively high disease burdens.

In terms of which results to use for impact assessments and evaluations, both QALY and WTP results are available as the project intended to produce. One option could be to work entirely in terms of QALYs and then use the single £ per QALY value to monetise that. However, it is clear that respondents do not value (in monetary terms) illness in the same relative manner as the QALY values suggest. If one places any credence in the patient derived WTP for different illnesses, then using the uniform £/QALY estimate will misrepresent the relative burden across pathogens, as well as the aggregate value of the burden for the population. In addition, £ per QALY does not feature children at all – the estimate comes from the adult respondents choosing two alternative life paths for themselves (like the time trade off studies which the QALY literature works with). Therefore the best practice would be to use both QALY and WTP results, and being transparent about assumptions and coverage of each.

REFERENCES

Agreus L, Svardsudd K, Talley NJ, Jones MP, Tibblin G. 2001. Natural History of Gastroesophageal Reflux Disease and Functional Abdominal Disorders: A Population-Based Study. *The American Journal of Gastroenterology*. 96(10); 2905–2914. Available at: papers://5aecfcca-9729-4def-92fe-c46e5cd7cc81/Paper/p52884

Aherfi, S. et al., 2014. Liver transplantation for acute liver failure related to autochthonous genotype 3 Hepatitis E virus infection. Clinics and Research in Hepatology and Gastroenterology, 38(1), pp.24–31. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24462173 [Accessed January 27, 2017].

Aldabe, B. et al., 2011. Household transmission of haemolytic uraemic syndrome associated with Escherichia coli O104:H4, south-western France, June 2011. *Eurosurveillance*, 16(31). Available at: www.eurosurveillance.org [Accessed January 27, 2017].

Altman, R.L. et al., 1994. Hip joint infection caused by Shigella sonnei in a one-year-old boy. The *Pediatric infectious disease journal*, 13(12), pp.1156–8. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7892094 [Accessed January 27, 2017].

Ariza-Ariza, R. et al., 2006. Assessing utility values in rheumatoid arthritis: A comparison between time trade-off and the EuroQol. *Arthritis & Rheumatism*, 55(5), pp.751–756. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17013822 [Accessed January 30, 2017].

Arslan, F. et al., 2015. The clinical features, diagnosis, treatment, and prognosis of neuroinvasive listeriosis: a multinational study. European Journal of Clinical Microbiology & Infectious Diseases, 34(6), pp.1213–1221. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25698311 [Accessed January 27, 2017].

Aureli, P. et al., 2000. An Outbreak of Febrile Gastroenteritis Associated with Corn Contaminated by Listeria monocytogenes. New England Journal of Medicine, 342(17), pp.1236–1241. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10781619 [Accessed January 27, 2017].

Baka, S. et al., 2013. Symptomatic Shigella sonnei urinary tract infection in pregnancy. *Clinical and experimental obstetrics & gynecology*, 40(1), pp.116–7. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23724523 [Accessed January 27, 2017].

Bakir, M. et al., 2013. Estimating and comparing the clinical and economic impact of paediatric rotavirus vaccination in Turkey using a simple versus an advanced model. *Vaccine*, 31(6), pp.979–986.

Batz M, Hoffmann S, Morris JG. 2014. Disease-Outcome Trees, EQ-5D Scores, and Estimated Annual Losses of Quality-Adjusted Life Years (QALYs) for 14 Foodborne Pathogens in the United States. *Foodborne Pathogens and Disease*. 11(5); 395-402.

Beigelman, A., Leibovitz, E. & Sofer, S., 2002. Septic shock associated with Shigella flexneri dysentery. *Scandinavian journal of infectious diseases*, 34(9), pp.692–3. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12374365 [Accessed January 27, 2017].

Bersano, A. et al., 2006. Long term disability and social status change after Guillain–Barré syndrome. Journal of Neurology, 253(2), pp.214–218. Available at: http://link.springer.com/10.1007/s00415-005-0958-x [Accessed January 27, 2017].

Berthelot, E. et al., 2012. Unusual Pseudotumoral Right Atrial Involvement in Listeria monocytogenes Septicemia. Circulation, 126(6), pp.e66–e68. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22869861 [Accessed January 27, 2017].

Beusterien, K.M. et al., 2009. Societal preference values for advanced melanoma health states in the United Kingdom and Australia. *British Journal of Cancer*, 101(3), pp.387–389. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19603025 [Accessed January 30, 2017].

Beusterien, K.M. et al., 2010. Population preference values for treatment outcomes in chronic lymphocytic leukaemia: a cross-sectional utility study. *Health and Quality of Life Outcomes*, 8(1), p.50. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20482804 [Accessed January 30, 2017].

Bleichrodt and Quiggin (1999) 'QALYs and consumer demand for health care', *Journal of Health Economics*18, 681-708..

Bowles, C., Ancker, M. & Triadafilopoulos, G., 2011. Gastrointestinal Dysfunction Following Hemolytic Uremic Syndrome. D*igestive Diseases and Sciences*, 56(8), pp.2241–2243. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21559739 [Accessed January 27, 2017].

Bracco, A. et al., 2007. Economic Evaluation of Tegaserod vs. Placebo in the Treatment of Patients with Irritable Bowel Syndrome: An Analysis of the TENOR Study. *Value in Health*, 10(4), pp.238–246.

Brazier, J. et al., 2006. Does the whole equal the sum of the parts? Patient-assigned utility scores for IBS-related health states and profiles. *Health Economics*, 15(6), pp.543–551. Available at: http://doi.wiley.com/10.1002/hec.1074 [Accessed January 30, 2017].

Bremell, T., Bjelle, A. & Svedhem, A., 1991. Rheumatic symptoms following an outbreak of campylobacter enteritis: a five year follow up. *Annals of the Rheumatic Diseases,* 50(12), pp.934–8. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1768164 [Accessed January 27, 2017].

Brennan A, Chick SE, Davies R. 2006. A taxonomy of model structures for economic evaluation of health technologies. *Health Economics*, 15(12), pp.1295–1310.

Brouwer WB, Culyer AJ, van Exel NJ, Rutten FFH. 2008. Welfarism vs, extra welfarism, *Journal of Health Economics,* 27(2): 325-38.

Brouwer WBF, Koopmanschap MA. 2000. On the economic foundations of CEA: Ladies and gentlemen, take your positions!, *Journal of Health Economics*, 19:439-59.

Bruffaerts, R. et al., 2015. Acute ataxic neuropathy associated with Hepatitis E virus infection. Muscle & Nerve, 52(3), pp.464–465. Available at: http://doi.wiley.com/10.1002/mus.24676 [Accessed January 27, 2017].

Bruyère, O. et al., 2009. Impact of chondroitin sulphate on health utility in patients with knee osteoarthritis: towards economic analysis. *Journal of Medical Economics*, 12(4), pp.356–360. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19900070 [Accessed January 30, 2017].

Buchholz U, Bernard H, Werber D, Bohmer MM, Remschmidt C, Wilking H, Delere Y, an der Heiden M, Adlhoch C, Dreesman J, Ehlers J, Ethelberg J, Faber M, Frank C, Fricke G, Greiner M, Hohle M, Ivarsson S, Jark U, Kirchner M, Koch J, Krause G, Luber P, Rosner B, Stark K, Kuhne M. 2011. German Outbreak of Escherichia coli O104:H4 Associated with Sprouts. *The New England Journal of Medicine*. 365:1763-1770.

Byrne, L. et al., 2015. The epidemiology, microbiology and clinical impact of Shiga toxin-producing Escherichia coli in England, 2009–2012. *Epidemiology and Infection*, 143(16), pp.3475–3487. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25920912 [Accessed January 27, 2017].

Calvert, N. et al., 2007. A hotel-based outbreak of Salmonella enterica subsp. Enterica serovar Enteritidis (Salmonella Enteritidis) in the United Kingdom, 2006. Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin, 12(3), p.222. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17439807 [Accessed January 27, 2017].

Canavan, C., West, J. & Card, T., 2015. Change in Quality of Life for Patients with Irritable Bowel Syndrome following Referral to a Gastroenterologist: A Cohort Study D. S. Courvoisier, ed. *PLOS ONE*, 10(10), p.e0139389. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26431458 [Accessed January 30, 2017].

Cantey, P.T. et al., 2011. Study of non-outbreak giardiasis: novel findings and implications for research. The American journal of medicine, 124(12), p.1175.e1-8. Available at: http://linkinghub.elsevier.com/retrieve/pii/S0002934311005432 [Accessed January 27, 2017].

Centre for Disease Control (CDC), 2008. Norovirus Outbreaks on Three College Campuses --- California, Michigan, and Wisconsin, 2008. Morbidity and Mortality Weekly Report. Available at: https://www.cdc.gov/Mmwr/preview/mmwrhtml/mm5839a2.htm [Accessed January 27, 2017].

Chan, C.V. et al., 2011. Norovirus as cause of benign convulsion associated with gastro-enteritis. Journal of Paediatrics and Child Health, 47(6), pp.373–377. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21309881 [Accessed January 27, 2017].

Chen, S. et al., 2009. Norovirus Infection as a Cause of Diarrhoea-Associated Benign Infantile Seizures. Clinical Infectious Diseases, 48(7), pp.849–855. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19239351 [Accessed January 27, 2017].

Cheung, M. et al., 2012. Hepatitis E – an unexpected problem at home. Scandinavian Journal of Gastroenterology, 47(2), pp.253–253. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22229940 [Accessed January 27, 2017].

Chit, A. et al., 2015. Expected cost effectiveness of high-dose trivalent influenza vaccine in US seniors. *Vaccine*, 33(5), pp.734–741.

Chmelík, V. et al., 1998. Clinical features of diarrhoea in children caused by Cryptosporidium parvum. Folia parasitologica, 45(2), pp.170–2. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9684327 [Accessed January 27, 2017].

Choicemetrics, 2014. Ngene experiment Design Software. http://www.choice-metrics.com

Chyongchiou, J.L., Zimmerman & Smith, 2013. Cost-Effectiveness of Pneumococcal and Influenza Vaccination Standing Order Programs. *American Journal of Managed Care*, 19(January 2013 1).

Coffey, J.T. et al., 2002. Valuing health-related quality of life in diabetes. *Diabetes care*, 25(12), pp.2238–43. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12453967 [Accessed January 30, 2017].

Colson, P. et al., 2008. Severe thrombocytopenia associated with acute Hepatitis E virus infection. Journal of clinical microbiology, 46(7), pp.2450–2. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18480231 [Accessed January 27, 2017].

Cronin, S. et al., 2011. Anti-glycolipid GM2-positive Guillain–Barre syndrome due to Hepatitis E infection. Irish Journal of Medical Science, 180(1), pp.255–257. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21063804 [Accessed January 27, 2017].

Dalton, H. et al., 2007. Locally acquired Hepatitis E in chronic liver disease. The Lancet, 369(9569), p.1260. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17434400 [Accessed January 27, 2017].

Dalton, H.R. et al., 2008. Autochthonous Hepatitis E in Southwest England: natural history, complications and seasonal variation, and Hepatitis E virus IgG seroprevalence in blood donors, the elderly and patients with chronic liver disease. European Journal of Gastroenterology & Hepatology, 20(8), pp.784–790. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18617784 [Accessed January 27, 2017].

Dalton, C.B. et al., 1997. An Outbreak of Gastroenteritis and Fever Due to Listeria monocytogenes in Milk. New England Journal of Medicine, 336(2), pp.100–106. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8988887 [Accessed January 27, 2017].

Dave, J. et al., 2015. Enteric fever and its impact on returning travellers. International Health, 7(3), pp.163–168. Available at: https://academic.oup.com/inthealth/article-lookup/doi/10.1093/inthealth/ihv018 [Accessed January 27, 2017].

Delmas, Y. et al., 2014. Outbreak of Escherichia coli O104:H4 haemolytic uraemic syndrome in France: outcome with eculizumab. *Nephrology Dialysis Transplantation*, 29(3), pp.565–572. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24293658 [Accessed January 27, 2017].

Deroux, A. et al., 2014. Association between Hepatitis E and neurological disorders: Two case studies and literature review. Journal of Clinical Virology, 60(1), pp.60–62. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24583064 [Accessed January 27, 2017].

Despierres, L.-A., 2011. Neurologic Disorders and Hepatitis E, France, 2010. Emerging Infectious Diseases. Available at: http://wwwnc.cdc.gov/eid/article/17/8/10-2028_article.htm [Accessed January 27, 2017].

Brecht Devleesschauwer, Juanita A. Haagsma, Frederick J. Angulo, David C. Bellinger, Dana Cole, Dörte Döpfer, Aamir Fazil, Eric M. Fèvre, Herman J. Gibb, Tine Hald, Martyn D. Kirk, Robin J. Lake, Charline Maertens de Noordhout, Colin D. Mathers, Scott A. McDonald, Sara M. Pires, Niko Speybroeck, M. Kate Thomas, Paul R. Torgerson, Felicia Wu, Arie H. Havelaar, Nicolas Praet (2015) Methodological framework for World Health Organization estimates of the global burden of foodborne disease. PLoS ONE, 10(12), pp.1–20.

Dhawan, V.K. et al., 1986. Campylobacter jejuni septicaemia--epidemiology, clinical features and outcome. *The Western Journal of Medicine*, 144(3), pp.324–8. Available at: http://www.ncbi.nlm.nih.gov/pubmed/3962297 [Accessed January 27, 2017].

Dolan P, Gudex C, Kind P, Williams A. 1995. *A Social Tariff for EuroQol: Results from a UK General Population Survey*. York: University of York Discussion Paper 138.

Dornonville de la Cour, C. & Jakobsen, J., 2005. Residual neuropathy in long-term population-based follow-up of Guillain-Barré syndrome. Neurology, 64(2), pp.246–53. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15668421 [Accessed January 27, 2017].

Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. 2005. *Methods for the economic evaluation of health care programmes*, Oxford University Press Inc: New York.

Dundas, S. et al., 2001. The Central Scotland Escherichia coli O157:H7 Outbreak: Risk Factors for the Hemolytic Uremic Syndrome and Death among Hospitalized Patients. Clinical Infectious Diseases, 33(7), pp.923–931. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11528561 [Accessed January 27, 2017].

Duff, S.B. et al., 2003. Cost-effectiveness of a targeted disinfection program in household kitchens to prevent foodborne illnesses in the United States, Canada, and the United Kingdom. *Journal of food protection*, 66(11), pp.2103–15. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14627290 [Accessed January 30, 2017].

Dworkin, M.S. et al., 2001. Reactive Arthritis and Reiter's Syndrome Following an Outbreak of Gastroenteritis Caused by Salmonella enteritidis. Clinical Infectious Diseases, 33(7), pp.1010–1014. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11528573 [Accessed January 27, 2017].

Edwards, D.S. et al., 2014. Campylobacteriosis outbreak associated with consumption of undercooked chicken liver pâté in the East of England, September 2011: identification of a dose–response risk. *Epidemiology and Infection,* 142(2), pp.352–357. Available at: http://www.journals.cambridge.org/abstract_S0950268813001222 [Accessed January 27, 2017].

EuroQol Group 1990. EuroQol- a new facility for the measurement of health-related quality of life. *Health Policy* 16: 199-208

EuroQol. 2016. The EQ-5D. http://www.euroqol.org/about-eq-5d.html [Accessed 03 December 2016]

Feng Y, Devlin N and Herdman M., 2015. Assessing the health of the general population in England: how do the three- and five-level versions of EQ-5D compare? *Health and Quality of Life Outcomes*, 13: 171.

Forbes, R.B. et al., 2003. Cost-utility analysis of vagus nerve stimulators for adults with medically refractory epilepsy. *Seizure*, 12(5), pp.249–256.

Fowler, R.A. et al., 2003. Cost-effectiveness of recombinant human activated protein C and the influence of severity of illness in the treatment of patients with severe sepsis. *Journal of Critical Care*, 18(3), pp.181–191.

Frost, J.A. et al., 1995. An Outbreak of Shigella sonnei Infection Associated with Consumption of Iceberg Lettuce. *Emerging Infectious Diseases*, 1(1), pp.26–29. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8903151 [Accessed January 27, 2017].

Giraudon, I. et al., 2009. Large outbreak of salmonella phage type 1 infection with high infection rate and severe illness associated with fast food premises. Public Health, 123(6), pp.444–447. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19464715 [Accessed January 27, 2017].

Givney, R., Darzenos, J. & Davos, D., 1998. Shigella at a wake in Adelaide, June 1998. *Communicable diseases intelligence*, 22(13), p.297. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9893341 [Accessed January 27, 2017].

Goh, S. et al., 2002. Outbreak in North Cumbria associated with pasteurized milk. *Epidemiologic reviews*, 129, pp.451–457.

Gomez, J. et al., 2013. Cost-effectiveness and cost utility analysis of three pneumococcal conjugate vaccines in children of Peru. *BMC Public Health*, 13. Available at: http://www.biomedcentral.com/1471-2458/13/1025 [Accessed January 30, 2017].

Goulet, V. et al., 2008. Increasing incidence of listeriosis in France and other European countries. Emerging infectious diseases, 14(5), pp.734–40. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18439354 [Accessed January 27, 2017].

Griffin, P.M. & Tauxe, R. V, 1991. The epidemiology of infections caused by Escherichia coli O157:H7, other enterohemorrhagic E. coli, and the associated hemolytic uremic syndrome. *Epidemiologic reviews*, 13, pp.60–98. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1765120 [Accessed January 27, 2017].

Guillois, Y. et al., 2016. High Proportion of Asymptomatic Infections in an Outbreak of Hepatitis E Associated With a Spit-Roasted Piglet, France, 2013. Clinical Infectious Diseases, 62(3), pp.351–357. Available at: https://academic.oup.com/cid/article-lookup/doi/10.1093/cid/civ862 [Accessed January 27, 2017].

Haacke, C. et al., 2006. Long-Term Outcome After Stroke: Evaluating Health-Related Quality of Life Using Utility Measurements. *Stroke*, 37(1), pp.193–198. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16339458 [Accessed January 30, 2017].

Haagsma, J. A et al., 2008. Disability adjusted life years and minimal disease: application of a preference-based relevance criterion to rank enteric pathogens. Population health metrics, 6, p.7. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2655281&tool=pmcentrez&rendertype=abstract.

Haagsma, J.A. et al., 2015. Assessing disability weights based on the responses of 30,660 people from four European countries. Population Health Metrics, 13(1), p.10.

Hanevik, K. et al., 2009. Development of functional gastrointestinal disorders after Giardia lamblia infection. *BMC Gastroenterology*, 9(27).

Hanevik, K. et al., 2014. Irritable Bowel Syndrome and Chronic Fatigue 6 Years After Giardia Infection: A Controlled Prospective Cohort Study. Clinical Infectious Diseases, 59(10), pp.1394–1400. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25115874 [Accessed January 27, 2017].

Hannu, T. et al., 2002. Campylobacter-triggered reactive arthritis: a population-based study. *Rheumatology*, 41(3), pp.312–318. Available at: https://academic.oup.com/rheumatology/article-lookup/doi/10.1093/rheumatology/41.3.312 [Accessed January 27, 2017].

Havelaar, A.H. et al., 2000a. Health burden in the Netherlands due to infection with thermophilic Campylobacter spp. Epidemiology and infection, 125(3), pp.505–22. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2869634&tool=pmcentrez&rendertype=abstract.

Havelaar, A.H. et al., 2000b. Balancing the risks and benefits of drinking water disinfection: Disability adjusted life-years on the scale. Environmental Health Perspectives, 108(4), pp.315–321.

Havelaar, A.H. et al., 2004. Disease burden in The Netherlands due to infections with Shiga toxin-producing Escherichia coli O157. *Epidemiology and infection*, 132(3), pp.467–84. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15188716 [Accessed January 27, 2017].

Health and Social Care Information Centre. 2015. Hospital Episode Statistics, Admitted Patient Care – England, 2014-15: Diagnosis. [Dataset]. Available at: http://content.digital.nhs.uk/searchcatalogue?productid=19420&q=title%3a%22Hospital+Episode+Statistics%2c+Admitted+patient+care+-+England%22&sort=Relevance&size=10&page=1#top [Accessed: 27 January 2017]

Helmers, S.L. et al., 2012. Clinical outcomes, quality of life, and costs associated with implantation of vagus nerve stimulation therapy in pediatric patients with drug-resistant epilepsy. *European Journal of Paediatric Neurology*, 16(5), pp.449–458.

Helms, M., Simonsen, J. & Molbak, K., 2006. Foodborne Bacterial Infection and Hospitalization: A Registry-Based Study. *Clinical Infectious Diseases*, 42(4), pp.498–506. Available at: https://academic.oup.com/cid/article-lookup/doi/10.1086/499813 [Accessed January 27, 2017].

Hensher D, Rose J, Greene W. 2005. Applied choice analysis: a primer. Cambridge University Press, Cambridge.

Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, Bonsel G, Badia X. 2011. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L), *Quality of Life Research*, 20(10): 1727–1736.

Hershcovici, T. et al., 2010. Cost effectiveness of mass screening for celiac disease is determined by time-delay to diagnosis and quality of life on a gluten free diet. *Alimentary Pharmacology & Therapeutics*, 31(8), pp.901–10. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20096017 [Accessed January 30, 2017].

Herwaldt, B.L. et al., 1991. Waterborne-disease outbreaks, 1989-1990. MMWR. CDC surveillance summaries: Morbidity and mortality weekly report. *CDC surveillance summaries*, 40(3), pp.1–21. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1770924 [Accessed January 27, 2017].

HM Treasury. 2011. *The Green Book*. London: TSO. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/220541/green_book_complete.pdf [Accessed: 03 December 2016]

Houdouin, V. et al., 2004. A Pediatric Cluster of Shigella dysenteriae Serotype 1 Diarrhea with Hemolytic Uremic Syndrome in 2 Families from France. *Clinical Infectious Diseases*, 38(9), pp.e96–e99. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15127361 [Accessed January 27, 2017].

Hsu, P.C. et al., 2012. Health utilities and psychometric quality of life in patients with early- and late-stage Hepatitis C virus infection. *Journal of Gastroenterology and Hepatology*, 27(1), pp.149–157. Available at: http://doi.wiley.com/10.1111/j.1440-1746.2011.06813.x [Accessed January 30, 2017].

Huang, E.S. et al., 2007. Patient Perceptions of Quality of Life With Diabetes-Related Complications and Treatments. *Diabetes Care*, 30(10), pp.2478–2483. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17623824 [Accessed January 30, 2017].

Huang, H. et al., 2015. Economic evaluation of linaclotide for the treatment of adult patients with irritable bowel syndrome with constipation in the United States. *Journal of Medical Economics*, 18(4), pp.283–294. Available at: http://www.tandfonline.com/doi/full/10.3111/13696998.2014.979291 [Accessed January 30, 2017].

Inman, R.D. et al., 1988. Postdysenteric reactive arthritis. A clinical and immunogenetic study following an outbreak of salmonellosis. Arthritis and rheumatism, 31(11), pp.1377–83. Available at: http://www.ncbi.nlm.nih.gov/pubmed/3190782 [Accessed January 27, 2017].

Insulander, M. et al., 2013. Molecular epidemiology and clinical manifestations of human cryptosporidiosis in Sweden. *Epidemiology and Infection*, 141(5), pp.1009–1020. Available at: http://www.ncbi.nlm.nih.gov/pubmed/2287756 2 [Accessed January 27, 2017].

Ispahani, P. & Slack, R.C., 2000. Enteric fever and other extraintestinal salmonellosis in University Hospital, Nottingham, UK, between 1980 and 1997. *European journal of clinical microbiology & infectious diseases*: official publication of the European Society of Clinical Microbiology, 19(9), pp.679–87. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11057501 [Accessed January 27, 2017].

Janssen B, Szende A. 2013. Population Norms for the Eq-5D. In: Szende A, Janssen B, Cabases J. Eds. *Self-Reported Population Health: An International Perspective based on EQ-5D*. The Netherlands: Springer

Janssen B, Szende A. 2013. Population Norms for the Eq-5D. In: Szende A, Janssen B, Cabases J. Eds. *Self-Reported Population Health: An International Perspective based on EQ-5D*. The Netherlands: Springer

Johner, A., Raymakers, A. & Wiseman, S.M., 2013. Cost utility of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. *Surgical Endoscopy*, 27(1), pp.256–262. Available at: http://link.springer.com/10.1007/s00464-012-2430-1 [Accessed January 30, 2017].

Jokopii, L., Pohjola, S. & Jokipii, A.M.M., 1983. Cryptosporidium: A Frequent Finding In Patients With Gastrointestinal Symptoms. T*he Lancet*, 322(8346), pp.358–361. Available at: http://linkinghub.elsevier.com/retrieve/pii/S0140673683903410 [Accessed January 27, 2017].

Jones, P.H. et al., 1981. Campylobacter enteritis associated with the consumption of free school milk. *The Journal of Hygiene*, 87(2), pp.155–62. Available at: http://www.ncbi.nlm.nih.gov/pubmed/6895230 [Accessed January 27, 2017].

Kang, H.-J. et al., 2014. The utility score of epilepsy with partial seizure measured by TTO, VAS, and EQ-5D in the general Korean population. *Epilepsy Research*, 108(5), pp.963–971. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24679945 [Accessed January 30, 2017].

Kemmeren, J.M. et al., 2013. Priority setting of foodborne pathogens. Journal of Chemical Information and Modeling, 53(9), pp.1689–1699.

Kitterer, D. et al., 2014. Gas gangrene caused by clostridium perfringens involving the liver, spleen, and heart in a man 20 years after an orthotopic liver transplant: a case report. *Experimental and clinical transplantation*: Official journal of the Middle East Society for Organ Transplantation, 12(2), pp.165–8. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23962047 [Accessed January 27, 2017].

Koch, J. & Stark, K., 2006. Significant increase of listeriosis in Germany--epidemiological patterns 2001-2005. Euro surveillance: bulletin Europeen sur les maladies transmissibles, *European communicable disease bulletin*, 11(6), pp.85–8. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16801695 [Accessed January 27, 2017].

Koeppen, S. et al., 2006. Long-Term Outcome of Guillain-Barré Syndrome. *Neurocritical Care*, 5(3), pp.235–242. Available at: http://link.springer.com/10.1385/NCC:5:3:235 [Accessed January 27, 2017].

Kramer, M.H. et al., 1996. Surveillance for Waterborne-Disease Outbreaks -- United States, 1993-1994. *Morbidity and Mortality Weekly Report*. Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/00040818.htm [Accessed January 27, 2017].

Krogvold, L. et al., 2011. Clinical aspects of a nationwide epidemic of severe haemolytic uremic syndrome (HUS) in children. Scandinavian journal of trauma, resuscitation and emergency medicine, 19, p.44. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21798000 [Accessed January 27, 2017].

Kuchuk, I. et al., 2013. Preference weights for chemotherapy side effects from the perspective of women with breast cancer. *Breast Cancer Research and Treatment*, 142(1), pp.101–107. Available at: http://link.springer.com/10.1007/s10549-013-2727-3 [Accessed January 30, 2017].

Lai, T., Habicht, J. & Kiivet, R.A., 2009. Measuring burden of disease in Estonia to support public health policy. European Journal of Public Health, 19(5), pp.541–547.

Larson, H.E., 1988. Infectious Diarrhea Due to Clostridium perfringens. *The Journal Of Infectious Diseases*·, 157(2·).

Launders, N. et al., 2016. A large Great Britain-wide outbreak of STEC O157 phage type 8 linked to handling of raw leeks and potatoes. *Epidemiology and Infection*, 144(1), pp.171–181. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26041509 [Accessed January 27, 2017].

Lavelle, T.A., Uyeki, T.M. & Prosser, L.A., 2012. Cost-Effectiveness of Oseltamivir Treatment for Children with Uncomplicated Seasonal Influenza. *The Journal of Pediatrics*, 160(1), p.67–73.e6.

Lee, J.M. et al., 1997 Escherichia coli O157:H7--two case reports. *Irish journal of medical sci*ence, 166(1), pp.20–2. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9057426 [Accessed January 27, 2017].

Lee, B.Y. et al., 2010. Universal methicillin-resistant Staphylococcus aureus (MRSA) surveillance for adults at hospital admission: an economic model and analysis. *Infection control and hospital epidemiology*, 31(6), pp.598–606. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20402588 [Accessed January 30, 2017].

Lee, B.Y. et al., 2011. The economic value of screening haemodialysis patients for methicillin-resistant Staphylococcus aureus in the USA. *Clinical Microbiology and Infection*, 17(11), pp.1717–1726

Lee, D. et al., 2013. The Cost Effectiveness of Licensed Oromucosal Midazolam (Buccolam®) for the Treatment of Children Experiencing Acute Epileptic Seizures: An Approach When Trial Evidence is Limited. *Pediatric Drugs*, 15(2), pp.151–162. Available at: http://link.springer.com/10.1007/s40272-013-0009-5 [Accessed January 30, 2017].

Levine, W.C., Stephenson, W.T. & Craun, G.F., 1990. Waterborne Disease Outbreaks, 1986-1988. Morbidity and Mortality Weekly Report. Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/00001596.htm [Accessed January 27, 2017].

Lewis, H.C. et al., 2009. Outbreaks of Shigella sonnei infections in Denmark and Australia linked to consumption of imported raw baby corn. *Epidemiology and Infection*, 137(3), p.326. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19134229 [Accessed January 27, 2017].

Ljaz, S. et al., 2014. Indigenous Hepatitis E in England and Wales From 2003 to 2012: Evidence of an Emerging Novel Phylotype of Viruses. *Journal of Infectious Diseases*, 209(8), pp.1212–1218. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24273173 [Accessed January 27, 2017].

Lung, T.W.C. et al., 2011. A meta-analysis of health state valuations for people with diabetes: explaining the variation across methods and implications for economic evaluation. *Quality of Life Research*, 20(10), pp.1669–1678. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21472392 [Accessed January 30, 2017].

Lyytikäinen, O. et al., 2006. Surveillance of listeriosis in Finland during 1995-2004. Euro surveillance : bulletin Europeen sur les maladies transmissibles, *European communicable disease bulletin*, 11(6), pp.82–5. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16801696 [Accessed January 27, 2017].

Mangen, M.-J.J., Havelaar, A.H. & De Wit, G.A., 2004. Campylobacteriosis and sequelae in the Netherlands: Estimating the disease burden and cost-of-illness. , pp.1–108.

Maniadakis, N. et al., 2013. Economic evaluation of agomelatine relative to other antidepressants for treatment of major depressive disorders in Greece. *BMC Health Services Research*, 13(173).

Mangen, M.-J.J. et al., 2015. Cost-of-illness and disease burden of food-related pathogens in the Netherlands, 2011. *International Journal of Food Microbiology*, 196, pp.84–93.

Marra, C.A. et al., 2004. A comparison of four indirect methods of assessing utility values in rheumatoid arthritis. *Medical care*, 42(11), pp.1125–31. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15586840 [Accessed January 30, 2017].

Matheson, N. et al., 2010. Ten years' experience of Salmonella infections in Cambridge, UK. *Journal of Infection*, 60(1), pp.21–25.

McCarthy, N. & Giesecke, J., 2001. Incidence of Guillain-Barré syndrome following infection with Campylobacter jejuni. *American journal of epidemiology*, 153(6), pp.610–4. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11257070 [Accessed January 27, 2017].

McComb, M.N. & Collins, C.D., 2014. Comparative Cost-effectiveness of Alternative Empiric Antimicrobial Treatment Options for Suspected Enterococcal Bacteremia. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, 34(6), pp.537–544. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24390863 [Accessed January 30, 2017].

Melegaro, A. & Edmunds, W.J., 2004. Cost-effectiveness analysis of pneumococcal conjugate vaccination in England and Wales. *Vaccine*, 22(31), pp.4203–4214.

Melliez, H. et al., 2008. Cost and cost-effectiveness of childhood vaccination against rotavirus in France. *Vaccine*, 26(5), pp.706–715.

Messori, A. et al., 1998. Adjunctive lamotrigine therapy in patients with refractory seizures: a lifetime cost-utility analysis. *European Journal of Clinical Pharmacology*, 53(6), pp.421–427. Available at: http://link.springer.com/10.1007/s002280050402 [Accessed January 30, 2017].

Miettinen, M.K. et al., 1999. Molecular epidemiology of an outbreak of febrile gastroenteritis caused by Listeria monocytogenes in cold-smoked rainbow trout. *Journal of clinical microbiology*, 37(7), pp.2358–60. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10364616 [Accessed January 27, 2017].

Michaud, C.M. et al., 2006. The burden of disease and injury in the United States 1996, Available at: http://www.ncbi.nlm.nih.gov/pubmed/17049081.

Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA, PRISMA-P Group. 2015. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews*. 4(1).

Morgan, C.L. et al., 2006. Characterization and comparison of health-related utility in people with diabetes with various single and multiple vascular complications. *Diabetic Medicine*, 23(10), pp.1100–1105. Available at: http://doi.wiley.com/10.1111/j.1464-5491.2006.01936.x [Accessed January 30, 2017].

Mpamugo, O., Donovan, T. & Brett, M.M., 1995. Enterotoxigenic Clostridium perfringens as a cause of sporadic cases of diarrhoea. *Journal of Medical Microbiology*, 43(6), pp.442–445. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7473678 [Accessed January 27, 2017].

Murray CJL and Lopez AD. 1996. *The Global Burden of Disease*. Harvard Press. Cambridge, MA.

Myers, E.R., Misurski, D.A. & Swamy, G.K., 2011. Influence of timing of seasonal influenza vaccination on effectiveness and cost-effectiveness in pregnancy. *American Journal of Obstetrics and Gynecology*, 204(6), pp.S128–S140.

Nafees, B. et al., 2008. Health state utilities for non-small cell lung cancer. *Health and Quality of Life Outcomes*, 6(1), p.84. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18939982 [Accessed January 30, 2017].

Nelson, A.M. et al., 2012. Disruption of the Human Gut Microbiota following Norovirus Infection Y. Sanz, ed. *PLoS ONE*, 7(10), p.e48224. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23118957 [Accessed January 27, 2017].

Newall, A.T. et al., 2013. Understanding the Cost-Effectiveness of Influenza Vaccination in Children: Methodological Choices and Seasonal Variability. *Pharmaco Economics*, 31(8), pp.693–702. Available at: http://link.springer.com/10.1007/s40273-013-0060-7 [Accessed January 30, 2017].

NICE. 2013. *Guide to the methods of technology appraisal. London: National Institute for Health and Care Excellence*. Available at: https://www.nice.org.uk/process/pmg9/resources/guide-to-the-methods-of-technology-appraisal-2013-pdf-2007975843781 [Accessed: 03 December 2016]

Nielsen, H.L. et al., 2012. Short-term and medium-term clinical outcomes of Campylobacter concisus infection. *Clinical Microbiology and Infection*, 18(11), pp.E459–E465.

Nordstrom, D.C., 1996. Reactive arthritis, diagnosis and treatment: a review. Acta orthopaedica Scandinavica, 67(2), pp.196–201. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8623582 [Accessed January 27, 2017].

Office for National Statistics. 2014. MYE2: Population Estimates by single year of age and sex for local authorities in the UK, mid-2014. [Dataset]

Olesen, B. et al., 2005. Etiology of diarrhea in young children in Denmark: a case-control study. *Journal of clinical microbiology,* 43(8), pp.3636–41. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16081890 [Accessed January 27, 2017].

Papasian, C.J., Enna-Kifer, S. & Garrison, B., 1995. Symptomatic Shigella sonnei urinary tract infection. *Journal of clinical microbiology,* 33(8), pp.2222–3. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7559987 [Accessed January 27, 2017].

Paré, P.. et al., 2006. Health-related quality of life, work productivity, and health care resource utilization of subjects with irritable bowel syndrome: Baseline results from logic (longitudinal outcomes study of gastrointestinal symptoms in Canada), a naturalistic study. Clinical Therapeutics, 28(10), pp.1726–1735. Available at: http://www.scopus.com/inward/record.url?eid=2-s2.0-33751574668&partnerID=40&md5=4b6f6a94f9bcd1c2af4ba25cda91007c.

Paul, M.L. et al., 1994. Listeriosis--a review of eighty-four cases. *The Medical journal of Australia*, 160(8), pp.489–93. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8170424 [Accessed January 27, 2017].

Peasgood, T., Ward, S. & Brazier, J., 2010. A Review and Meta Analysis of Health State Utility Values in Breast Cancer, Discussion Paper. (Unpublished)

Pelegrín, I. et al., 2014. Listeria monocytogenes meningoencephalitis in adults: analysis of factors related to unfavourable outcome. *Infection*, 42(5), pp.817–827. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24902522 [Accessed January 27, 2017].

Pennington TH. 2014. E.coli O157 outbreaks in the United Kingdom: past, present, and future. *Infection and Drug Resistance*. 7, 211-222

Petta, S. et al., 2014. Cost-effectiveness of sofosbuvir-based triple therapy for untreated patients with genotype 1 chronic Hepatitis C. *Hepatology*, 59(5), pp.1692–1705. Available at: http://doi.wiley.com/10.1002/hep.27010 [Accessed January 30, 2017].

Phillips, A.D., Thomas, A.G. & Walker-Smith, J.A., 1992. Cryptosporidium, chronic diarrhoea and the proximal small intestinal mucosa. *Gut,* 33(8), pp.1057–61. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1398230 [Accessed January 27, 2017].

Pickard, A.S. et al., 2004. Agreement Between Patient and Proxy Assessments of Health-Related Quality of Life After Stroke Using the EQ-5D and Health Utilities Index. *Stroke*, 35(2), pp.607–612. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14726549 [Accessed January 30, 2017].

Pitman, R.J., Nagy, L.D. & Sculpher, M.J., 2013. Cost-effectiveness of childhood influenza vaccination in England and Wales: Results from a dynamic transmission model. *Vaccine*, 31(6), pp.927–942.

Porter, C.K. et al., 2015. Establishment of Health Utility Indices for Post-Infectious Functional Gastrointestinal Disorders in Active Duty Us Military. *Journal of Travel Medicine*, 22(4), pp.237–241. Available at: https://academic.oup.com/jtm/article-lookup/doi/10.1111/jtm.12200 [Accessed January 30, 2017].

Prosser, L.A. et al., 2011. Effects of Adverse Events on the Projected Population Benefits and Cost-effectiveness of Using Live Attenuated Influenza Vaccine in Children Aged 6 Months to 4 Years. *Archives of Pediatrics & Adolescent Medicine*, 165(2), pp.685–696. Available at: http://archpedi.jamanetwork.com/article.aspx?doi=10.1001/archpediatrics.2010.182 [Accessed January 30, 2017].

Public Health Laboratory Service Study Group. 1990. Cryptosporidiosis in England and Wales: prevalence and clinical and epidemiological features. *BMJ*, 300.

Ramos-Goñi, J.M. and O. Rivero-Ariaseq 2011 eq5d: A command to calculate index values for the EQ-5D quality-of-life instrument *The Stata Journal* Volume 11 Number 1: pp. 120-125

Ravel, A. et al., Epidemiological and clinical description of the top three reportable parasitic diseases in a Canadian community. Epidemiology and Infection. 141(2). PP.431-442

Rees, J.H. et al., 1995. Campylobacter jejuni Infection and Guillain–Barré Syndrome. *New England Journal of Medicine*, 333(21), pp.1374–1379. Available at: http://www.nejm.org/doi/abs/10.1056/NEJM199511233332102 [Accessed January 27, 2017].

Roberts M, Russell LB, Paltiel AD, Chambers M, McEwan P, Krahn M, on behalf of the ISPOR-SMDM Modeling Good Research Practice Task Force. 2012. Conceptualizing a model: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force-2. *Value in Health*. **32,** 678–89.

Rodríguez, L.A.G. & Ruigómez, A., 1999. Increased risk of irritable bowel syndrome after bacterial gastroenteritis: cohort study. *BMJ*, 318(7183).

Rose J, Collins A, Bliemer M, Hensher D. 2012. Ngene 1.1.1. Statistical Software.

Rowe, P.C. et al., 1998. Risk of hemolytic uremic syndrome after sporadic Escherichia coli O157:H7 infection: results of a Canadian collaborative study. Investigators of the Canadian Pediatric Kidney Disease Research Center. *The Journal of Pediatrics*, 132(5), pp.777–82. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9602185 [Accessed January 27, 2017].

Rudwaleit, M. et al., 2001. Low incidence of reactive arthritis in children following a salmonella outbreak. *Annals of the rheumatic diseases*, 60(11), pp.1055–7. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11602478 [Accessed January 27, 2017].

Ruzante, J.M. et al., 2011. Hospitalization and deaths for select enteric illnesses and associated sequelae in Canada, 2001–2004. *Epidemiology and Infection*, 139(6), pp.937–945. Available at: http://www.journals.cambridge.org/abstract_S0950268810001883 [Accessed January 27, 2017].

Ryen, L. and Svensson, M. 2015. The Willingness to Pay for a QALY: A Review of the Empirical Literature, *Health Economics*, 24: 1289-1301.

Saab, S. et al., 2014. Cost-effectiveness analysis of sofosbuvir plus peginterferon/ribavirin in the treatment of chronic Hepatitis C virus genotype 1 infection. *Alimentary Pharmacology & Therapeutics*, 40(6), pp.657–675. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25065960 [Accessed January 30, 2017].

Salomon, J.A. et al., 2012. Common values in assessing health outcomes from disease and injury: Disability weights measurement study for the Global Burden of Disease Study 2010. The Lancet, 380(9859), pp.2129–2143.

Salomon, J.A. et al., 2015. Disability weights for the Global Burden of Disease 2013 study. The Lancet Global Health, 3(11), pp.e712–e723.

Samp, J.C. et al., 2015. Patient health utility, work productivity, and lifestyle impairment in chronic Hepatitis C patients in France. *Clinics and Research in Hepatology and Gastroenterology*, 39(3), pp.307–314.

Sanz, M.A. et al., 2011. Analysis of EQ-5D scores from two phase 3 clinical trials of romiplostim in the treatment of immune thrombocytopenia (ITP). *Value in Health*, 14(1), pp.90–96. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21211490 [Accessed January 30, 2017].

Sassi F. 2006. Calculating QALYs, comparing QALY and DALY calculations. Health Policy and Planning. 21(5); 402-408.

Sassi, F. 2010. Calculating QALYs and DALYs: Methods and Applications to Fatal and Non-Fatal Conditions. In: Preedy VR, Watson RR. Eds. *Handbook of Disease Burdens and Quality of Life Measures*. Springer. New York, NY.

Scallan, E. et al., 2011. Foodborne illness acquired in the United States--major pathogens. Emerging infectious diseases, 17(1), pp.7–15. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21192848 [Accessed January 27, 2017].

Scarpa R, Ferrini S, Willis KG. 2006. Performance of error component models for status-quo effects in choice experiments. Pages 247-274 in Scarpa R, Alberini A, editors. Applications of simulation methods in environmental and resource economics. Springer, Netherlands.

Scarpa R an Rose JM. 2008. Design efficiency for non-market valuation with choice modelling: how to measure it, what to report and why. *The Australian Journal of Agricultural and Resource Economics* 52: 253-282.

Scharn, N. et al., 2014. Guillain–Barré syndrome associated with autochthonous infection by Hepatitis E virus subgenotype 3c. Infection, 42(1), pp.171–173. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23512540 [Accessed January 27, 2017].

Shadick, N.A. et al., 2001. The Cost-effectiveness of Vaccination Against Lyme Disease. *Archives of Internal Medicine*, 161(4), p.554. Available at: http://archinte.jamanetwork.com/article.aspx?doi=10.1001/archinte.161.4.554 [Accessed January 30, 2017].

Shimizu, T. & Tokuda, Y., 2012. Miller Fisher syndrome linked to Norovirus infection. *Case Reports*, 2012 (dec14 1), p.bcr2012007776-bcr2012007776. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23242098 [Accessed January 27, 2017].

Shiroiwa, T., Fukuda, T. & Tsutani, K., 2009. Health utility scores of colorectal cancer based on societal preference in Japan. *Quality of Life Research*, 18(8), pp.1095–1103. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19626462 [Accessed January 30, 2017].

Skedgel, C. et al., 2011. An incremental economic evaluation of targeted and universal influenza vaccination in pregnant women. *Canadian journal of public health = Revue canadienne de sante publique*, 102(6), pp.445–50. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22164556 [Accessed January 30, 2017].

Song, Y. et al., 2012. The potential economic value of a Staphylococcus aureus vaccine among hemodialysis patients. *Vaccine*, 30(24), pp.3675–3682.

Spiegel, B. et al., 2009. Developing Valid and Reliable Health Utilities in Irritable Bowel Syndrome: Results From the IBS PROOF Cohort. *The American Journal of Gastroenterology*, 104(8), pp.1984–1991. Available at: http://www.nature.com/doifinder/10.1038/ajg.2009.232 [Accessed January 30, 2017].

Statacorp 2013, Stata/IC 13.1, Statistical Software.

Stepanova, M. et al., 2014. Patients' preferences and health utility assessment with SF-6D and EQ-5D in patients with chronic Hepatitis C treated with sofosbuvir regimens. *Alimentary Pharmacology & Therapeutics*, 40(6), pp.676–685. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25040192 [Accessed January 30, 2017].

Stevenson, S.M. et al., 2014. Cost-effectiveness of neoadjuvant chemotherapy before radical cystectomy for muscle-invasive bladder cancer. *Urologic Oncology: Seminars and Original Investigations*, 32(8), pp.1172–1177.

Stouthard, M.E.A. et al., 1997. Disability weights for diseases in the Netherlands, Available at: http://dare.uva.nl/document/174853.

Stamuli, E. et al., 2012. Cost-effectiveness of acupuncture for irritable bowel syndrome: findings from an economic evaluation conducted alongside a pragmatic randomised controlled trial in primary care. *BMC gastroenterology*, 12, p.149. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23095351 [Accessed January 30, 2017].

Szende, A., M. Oppe, and N.Devlin, ed. 2007 *EQ5D value sets: Inventory, Comparative Review and User Guide.* Dordrecht: Springer.

Szende, A. et al., 2009. Valuation of transfusion-free living in MDS: results of health utility interviews with patients. *BMC Health and Quality of Life Outcomes*, 7(81).

Szende, A. et al., 2010. Measurement of utility values in the UK for health states related to immune thrombocytopenic purpura. *Current Medical Research and Opinion*, 26(8), pp.1893–1903. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20553121 [Accessed January 30, 2017].

Tam, C. C., & O'Brien, S. J. 2016. Economic Cost of Campylobacter, Norovirus and Rotavirus Disease in the United Kingdom. *PLOS ONE*, 11(2).

Tam CC, Larose T, O'Brien, IID2 Study Group. 2014. Costed extension to the Second Study of Infectious Intestinal Disease in the Community: Identifying the proportion of foodborne disease in the UK and attributing foodborne disease by food commodity. Food Standards Agency. Available at: https://www.food.gov.uk/sites/default/files/IID2%20extension%20report%20-%20FINAL%2025%20March%202014_0.pdf [Accessed: 03 December 2016]

Tarride, J.-E. et al., 2012. Cost-effectiveness analysis of intranasal live attenuated vaccine (LAIV) versus injectable inactivated influenza vaccine (TIV) for Canadian children and adolescents. *ClinicoEconomics and outcomes research : CEOR*, 4, pp.287–98. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23055756 [Accessed January 30, 2017].

Thomas, M.K. et al., 2015. Estimates of Foodborne Illness–Related Hospitalizations and Deaths in Canada for 30 Specified Pathogens and Unspecified Agents. *Foodborne Pathogens and Disease*, 12(10), pp.820–827. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26259128 [Accessed January 27, 2017].

Toljander, J. et al., 2012. Public health burden due to infections by verocytotoxin-producing Escherichia coli (VTEC) and Campylobacter spp. as estimated by cost of illness and different approaches to model disability-adjusted life years. *Scandinavian Journal of Public Health*, 40(3), pp.294–302. Available at: http://sjp.sagepub.com/cgi/doi/10.1177/1403494811435495 [Accessed January 27, 2017].

Torrance, G.W. et al., 2004. Improvement in health utility among patients with rheumatoid arthritis treated with adalimumab (a human anti-TNF monoclonal antibody) plus methotrexate. *Rheumatology*, 43(6), pp.712–718. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15039494 [Accessed January 30, 2017].

Tu, H.A.T. et al., 2014. Economic evaluation of meningococcal serogroup B childhood vaccination in Ontario, Canada. *Vaccine*, 32(42), pp.5436–5446.

Tufts Medical Center. 2016. *Cost-Effectiveness Analysis Registry*. Available at: http://healtheconomics.tuftsmedicalcenter.org/cear4/Home.aspx [Accessed: 03 December 2016]

van Lier, E.A. & Havelaar, A.H., 2007. Disease Burden of Infectious Disease : A Pilot Study. RIVM report 215011001/2007. Bilthoven: RIVM, Centre for Infectious Disease Control Netherlands

Vedeler, C.A., Wik, E. & Nyland, H., 1997. The long-term prognosis of Guillain-Barré syndrome. Evaluation of prognostic factors including plasma exchange. *Acta Neurologica Scandinavica*, 95(5), pp.298–302. Available at: http://doi.wiley.com/10.1111/j.1600-0404.1997.tb00214.x [Accessed January 27, 2017].

Vera-Llonch, M., Brandenburg, N.A. & Oster, G., 2008. Cost-effectiveness of Add-on Therapy with Pregabalin in Patients with Refractory Partial Epilepsy. *Epilepsia*, 49(3), pp.431–437. Available at: http://doi.wiley.com/10.1111/j.1528-1167.2007.01279.x [Accessed January 30, 2017].

Wan, M.J. et al., 2009. Acute Appendicitis in Young Children: Cost-effectiveness of US versus CT in Diagnosis—A Markov Decision Analytic Model. *Radiology*, 250(2), pp.378–386. Available at: http://pubs.rsna.org/doi/10.1148/radiol.2502080100 [Accessed January 30, 2017].

Werber, D. et al., 2013. Years of potential life lost for six major enteric pathogens, Germany, 2004–2008. *Epidemiology and Infection*, 141(5), pp.961–968. Available at: http://www.journals.cambridge.org/abstract_S0950268812001550 [Accessed January 27, 2017].

Westwood, M. et al., 2015. Procalcitonin testing to guide antibiotic therapy for the treatment of sepsis in intensive care settings and for suspected bacterial infection in emergency department settings: a systematic review and cost-effectiveness analysis. *Health Technology Assessment*, 19(96), pp.1–236. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26569153 [Accessed January 30, 2017].

Wielage, R.C. et al., 2013. Cost-Utility Analysis of Duloxetine in Osteoarthritis: A US Private Payer Perspective. *Applied Health Economics and Health Policy*, 11(3), pp.219–236. Available at: http://link.springer.com/10.1007/s40258-013-0031-3 [Accessed January 30, 2017].

Williams, R. et al., 1985. Diarrhoea due to enterotoxigenic Clostridium perfringens: clinical features and management of a cluster of ten cases. *Age and ageing*, 14(5), pp.296–302. Available at: http://www.ncbi.nlm.nih.gov/pubmed/2864815 [Accessed January 27, 2017].

World Health Organisation. 2015. *WHO Estimates of the Global Burden of Foodborne Disease*. Available at: http://apps.who.int/iris/bitstream/10665/199350/1/9789241565165_eng.pdf?ua=1 [Accessed: 25 November 2016]

World Health Organisation. 2016a. *Disability-adjusted life years (DALYs*). Available at: http://www.who.int/gho/mortality_burden_disease/daly_rates/text/en/ [Accessed: 25 November 2016]

World Health Organisation. 2016b. *Metrics: Disability-Adjusted Life Year (DALY).* Available at: http://www.who.int/healthinfo/global_burden_disease/metrics_daly/en/ [Accessed: 25 November 2016]

Wu, J.X. et al., 2015. Cost effectiveness of nonoperative management versus laparoscopic appendectomy for acute uncomplicated appendicitis. *Surgery*, 158(3), pp.712–721.

Zanini, B. et al., 2012. Incidence of Post-Infectious Irritable Bowel Syndrome and Functional Intestinal Disorders Following a Water-Borne Viral Gastroenteritis Outbreak. *The American Journal of Gastroenterology*, 107(6), pp.891–899. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22525306 [Accessed January 27, 2017].

Zhang, P. et al., 2012. Health utility scores for people with type 2 diabetes in U.S. managed care health plans: results from Translating Research Into Action for Diabetes (TRIAD). *Diabetes care*, 35(11), pp.2250–6. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22837369 [Accessed January 30, 2017]

APPENDIX A – MARKOV TRANSITION MODELS

This appendix sets out each of the MTMs derived for this study. They are presented in the following sub-sections.

A.1 Overview of the models

Table below reproduces Table 1 from the main report. The rest of this section provides further information on each element of the approach.

Table A.1: Decision problem and approach overview

Decision problem	What is annual burden of illness caused by 10 foodborne pathogens in the UK in terms of the QALYs lost due to infection? The 10 foodborne pathogens were: *Campylobacter* spp.*, Clostridium perfringens, Cryptosporidium parvum, Giardia lamblia,* Hepatitis E*, Listeria monocytogene*s, Norovirus, *Salmonella* (non-typhoidal), *Shigella* spp. and VTEC O157. Enteroaggregative *Escherichia coli* was also considered. An absence of suitable data means that only a partial analysis of this pathogen is possible, with no burden estimates generated.
Comparators	The health of the UK population in the absence of any of the 10 foodborne pathogens. A utility for full health of 0.856 was used (Janssen and Szende, 2013), representing the average utility of an individual in full health across all age groups.
Model type	Pathogen specific Markov state transition models
Population	The 2014 UK population (n=64,596,800). The median age is assumed to be 40 years old.
Perspective	Costs: health service perspective Consequences (QALYs): (i) adults - the impact on the person with the FBD (ii) children- parent of the person with the FBD
Time Horizon	Each model is separated into two phases i) short term and ii) long term. The short term phase takes place over a period of one year and incorporates the short term symptoms and complications of infection with a foodborne pathogen. The long term phase has a time horizon of 100 years and only incorporates the long term sequelae of infection alongside sequelae specific and all-cause mortality.
Burden of Illness	QALYs lost due to short term symptoms and complications and the long term sequelae resulting from infection in a specific year.
Discounting	No discounting is applied in the short term phase as this takes place over a period of one year. A discount rate of 3.5% is applied to QALYs lost due to sequelae occurring in the long term model.

Decision-analytic Model Conceptualisation

The first stage in creating a decision-analytic model, suitable to inform resource allocation decisions, is to define the scope of the decision problem. This is a formal stage included in NICE methods guide (NICE, 2013). The process of defining the

decision problem includes defining clearly the: relevant study perspective (e.g. health system; public-sector; or societal); population (e.g. patients with a specific condition; general public); time horizon for the analysis (e.g. one-year; life-time). The process of model conceptualisation is an integral part of making sure the decision problem can be addressed using the decision-analytic model. A number of best practice guidelines are now established within health economics that describe the importance of model conceptualisation (Roberts et al., 2012). When conceptualising a decision-analytic model it is important to have input from all relevant experts and stakeholders. In the case of foodborne pathogens we used a clinical expert (Professor O'Brien) to ratify the model conceptualisation process and agree on the final model structures.

Building the decision-analytic model

A separate decision-analytic model, each with two time frames, was built for each of the 10 pathogens. The models were built in Excel. Each Excel file includes instructions for using the model alongside details of its structure and tables for storing (adaptable) parameter input values (available from the authors on request). These files also summarise the data sources for each parameter input value.

Populating the model

Three types of input parameter were needed to populate each model: state transition probabilities, durations of symptoms and utility values for each health state. The point estimates of the parameters and full list of sources for transition probabilities, durations and utility values are available in Appendix D.

State transition probabilities

To identify the transition probabilities and durations for the model, a systematic review of the clinical literature was conducted. The review aimed to identify epidemiological studies describing the experiences of patients with each type of foodborne pathogen and the number of cases experiencing different symptoms. This review followed published guidelines (Moher et al., 2015) and was conducted in February 2016.

Five electronic databases (PubMed, MEDLINE, Science Direct, EMBASE, Biosis Previews) were searched in April 2016 using a structured search strategy (Appendix B) by one reviewer (Jo Hardstaff). As the required parameter evidence was broad and given that the PICO approach did not apply well to the study question, broad terms were used in the search strategy with no specific study types targeted. To be considered for inclusion studies had to focus on a diagnosed, confirmed pathogen and could not include cases infected with multiple pathogens. Studies conducted in developing countries were excluded as the experience of patients was believed to be different in these countries. To be included in this study, papers had to be available in English language.

Where estimates could not be found using this general search strategy, specific targeted searches were made for each pathogen by combining symptom and pathogen specific terms, for example "*Salmonella* AND hospital*" to find specific evidence of patients' experience of hospitalising *Salmonella*. Data from the studies was extracted into a data extraction form in Microsoft Excel. Key data items included: pathogen identified, type of study, year of study, country of study, number of individuals with pathogen, number of individuals with each symptom and duration of symptoms. Due to the limited nature of the evidence, no critical appraisal of the

included studies was attempted. The published extension to the IID2 study (Tam et al., 2014) was identified as the best source of incidence estimates for the UK and therefore the probability that a healthy individual would become a case was taken exclusively from this source where available. Incidence estimates for Hepatitis E were identified in the literature.

The probability that a case would develop a complication or sequelae was calculated using case estimates identified in the systematic review. For the purpose of calculation, it is assumed that individuals described in the literature followed the same clinical experience as described by the model structure. As such, the occurrence of specific complications and sequelae are assumed to be mutually exclusive from the occurrence of all other complications and sequelae. While this is not strictly true in practice, it would be impossible to add health states for all possible interactions of symptoms and to identify the data to populate these states. For example, cases of septicaemia are assumed to have arisen directly from uncomplicated cases. Cases were aggregated as though they were from one study before each probability was estimated. This gives an advantage over averaging the implied probabilities from individual studies in that larger studies are given a larger weight in the calculation of the transition probability.

Duration of symptoms

To generate a QALY it is necessary to understand how long each symptom will last. Median durations of illness for each symptom were also identified in the systematic review. Estimates of the medians were averaged across sources and then these means were used to calculate the probability of an individual remaining in the same state for the next stage of the model. This calculation relied on the fact that at the median duration, half of the individuals suffering from a symptom would have recovered, died or experienced a different symptom whilst half would continue to suffer. Equation 1 was used to calculate the transition probability required for a one week period such that half of the individuals with a symptom will have recovered by the median duration.

$$\mathrm{P}(S_{i,t+1}|S_{i,t}) = \sqrt[\tilde{x}_i]{0.5} \qquad (1)$$

Where $S_{i,t}$ is a case in a state in a given time period, $S_{i,t+1}$ is the same case in the same state in the next time period and x_i is the median duration a case stays in the health state S.

Utilities: published values

Utility values are then combined with the duration of symptoms to generate a burden of illness using a QALY. The primary analysis used a rapid review to identify studies which had valued the health impact of symptoms relating to foodborne infection. In total, 19 studies which presented primary estimates of health utility were identified (Appendix C). In all but one of these studies, the health outcome used was the disability adjusted life year (DALY). As such, these studies included disability weights for symptoms rather than utilities or disutilities. Such weights are inappropriate in the context of the UK health service and would not integrate with the current paradigm as: states cannot be worse than death; they are generally determined by experts rather than patient or health system user preferences and; severity in terms of the extent of disability is not the same as lost quality of life.

As such, a new, pragmatic search was conducted to identify generic utilities for each of the symptoms. This search began by utilising the Tufts database of economic evaluations which can be searched for utility estimates for specific conditions and symptoms (Tufts Medical Center, 2016). Each symptom was searched for using the utility values search in the database. Where available, disutilities for each symptom were recorded along with study details. Disutilities were calculated by subtracting the utility of a symptom related health state from the utility of full health used in each study. In some cases, where limited data was available for a specific symptom, a proxy was used instead. For example, only one study was identified for febrile convulsions and none for mesenteric adenitis so epileptic seizures and appendicitis were used as proxy conditions. For haemolytic uremic syndrome and thrombotic thrombocytopenic purpura where no values were found, specific searches were made in the EMBASE database for studies which had valued the relevant health states. This was accomplished by combining the clinical term (and different spellings of these), with terms for health state utility including: “health state”, “utility”, “quality of life”, “time trade off” and “standard gamble”.

The studies and values identified within them are reported in Appendix D. The results of this search are shown in Table A.2. As it is possible that studies used different values for full health, the implied disutilities of health states were recorded. This allowed the estimates to be subtracted from the utility for normal health used in this study. This value, 0.856, was taken from published population norms for the UK using time trade off methods to value EQ-5D states (Janssen and Szende, 2013). This value represents the average utility of normal health in the absence of foodborne disease across the age spectrum of the study population.

Table A.2: Symptom related disutilities

Symptom	Disutility
Flu-like Illness	-0.026
Uncomplicated Diarrhoea and/or Vomiting	-0.092
Mild Jaundice	-0.109
Febrile Convulsions	-0.140
Hospitalising Diarrhoea	-0.167
Irritable Bowel Syndrome	-0.181
Severe Jaundice	-0.246
Mesenteric Adenitis	-0.385
Reactive Arthritis	-0.388
Thrombotic Thrombocytopenic Purpura	-0.403
Neurological Damage	-0.436
Osteomyelitis	-0.448
Guillain-Barré Syndrome	-0.497
Renal Failure	-0.587
Septicaemia	-0.606
Meningitis	-0.827
Haemolytic Uremic Syndrome	-0.840

Utilities: from Integrate study

Utility data were also potentially available from the Integrate study, which collected individual patient-level data (http://www.integrateproject.org.uk/). A sample of patients were recruited into the Integrate study when they presented at their GPs with diarrhoea and vomiting and asked to complete EQ-5D-3L surveys and record symptoms and answer questions on basic demographic details. In some cases, patients also provided stool samples to allow for the pathogen causing the illness to be identified. Patients then completed a second questionnaire around two to three weeks later. Questions concern symptoms, contact with medical services and whether they are still ill or the duration of the illness and the EQ-5D-3L. These data provided the basis for an analysis of the impact of their illness on self-reported EQ-5D-3L health state. These data can be transformed into utility values using the published population EQ-5D 3 level tariff (Dolan et al., 1995). More detail on how these data compared with the published utility values is shown in Appendix E.

Taking account of sequelae

Two timeframes were used to generate estimates of the burden of foodborne illness using QALYs. The short term time horizon reflects the burden over one year and incorporates the short term symptoms and complications of infection with a foodborne pathogen. A cohort of the UK population entered the Markov model in week 0. They then proceeded through the model, with cases suffering infection, over an initial period of 52 weeks.

The long term time horizon reflects the lifetime horizon, and lasts a maximum of 100 years and only incorporates the long term sequelae of infection alongside sequelae specific and all-cause mortality (based on a population with an average age of 40). The long term health impact was modelled over 100 years to account for the impact of sequelae. For every week and year in which a member of the cohort remained in a non-healthy state, they suffered a reduction in utility.

The sequelae of foodborne infections have been identified as a significant cause of long term burden (Batz et al., 2014). A structured search of published literature was undertaken to characterise the clinical effect of each pathogen.

Table A.3: Sequelae of Foodborne Pathogens Included in this Study

Pathogen	Sequelae
Campylobacter spp.	Guillain-Barré syndrome Irritable Bowel Syndrome Reactive Arthritis
Cryptosporidium parvum	Irritable Bowel Syndrome
Giardia lamblia	Irritable Bowel Syndrome
Norovirus	Irritable Bowel Syndrome
Salmonella (Non-typhoidal)	Irritable Bowel Syndrome Reactive Arthritis
Shigella spp.	Irritable Bowel Syndrome
VTEC O157	Acute Renal Failure Neurological Damage

Little long term information was found regarding IBS. However, Agréus et al. (2001) found that in their study, 86.4% of individuals still exhibited symptoms 10 years after diagnosis. This value was used to inform the duration of illness estimates for IBS in the long term model. When applying this value to the short term model, the probability

that a case would return to the healthy state was minimal and as such it was assumed to be 0. It is assumed that individuals with IBS are no more likely to die than healthy individuals. In the sensitivity analysis, this value was varied by adding a distribution to the number of individuals still experiencing symptoms after 10 years and then converting each sampled value into a duration.

Reactive arthritis (RA) is a condition in which a proportion of individuals go on to develop chronic disease. It is also possible for cases which have apparently resolved to relapse. To incorporate these effects a pool of chronic RA cases and a pool of "relapsable", previous, RA cases were created. The total number of cases in each year was then calculated as the number of chronic cases added to the number of "relapsable" cases multiplied by the relapse rate. Nordstrom et al. (1996) place the probability of developing chronic RA as 5-30% and the probability of relapsing at 15-50%. The analysis in this paper uses the midpoint values of these intervals. Cases of relapsed RA were assumed to return to resolve again within a year, re-entering the "relapsable" RA pool. It is assumed that individuals with RA are no more likely to die than healthy individuals.

Guillain–Barré Syndrome (GBS) is highly heterogeneous with varying levels of severity and duration. In the short term, the condition can be extremely severe, with the individual's breathing inhibited. This can be fatal and as such, a GBS specific death rate is included in the Markov transition models. The duration of symptoms can also vary to a great extent. As such, while a point estimate is used in the models, synthesising information from four studies, the probabilistic sensitivity analysis provides a better representation of variability in the sequelae.

With regards to the sequelae of VTEC O157, more specifically the experience of haemolytic uremic syndrome following infection with VTEC O157, neurological damage was assumed to be permanent, meaning that patients could not return to the healthy state. Renal failure is associated with a range of potential outcomes assuming dialysis, renal transplant and death. As data on this sequelae were limited, a fixed duration of 0.76 years was used. This was derived from research which showed that 4 of 10 individuals with renal failure still suffered from impaired renal functioning one year post infection (Pennington, 2014).

Data Analysis

In the first stage of data analysis, point values were estimated for the burden of disease caused by each pathogen measured in QALYs (base case analysis). Single, aggregated values were used for the transition probabilities, durations and utilities.

The total utility experienced by the cohort in the initial year and following 100 years was calculated. An identical cohort was then entered into a model with only healthy and dead states, linked by all-cause mortality. This allowed the calculation of the baseline number of QALYs which would have been experienced by the cohort in the absence of disease. The total number of QALYs experienced by the cohort in the presence of disease was subtracted from the number of QALYs experienced in the absence of disease to determine a point estimate for the QALY burden of disease caused by each pathogen.

Probabilistic sensitivity analysis (PSA)

Uncertainty in the parameter estimates was incorporated into the analysis using probabilistic sensitivity analysis. Each parameter estimate was assigned a distribution in the model, taking a new value for each week within the short term model or year in the long term model. For each pathogen, 1000 Monte Carlo simulations were conducted, with new parameter estimates being drawn in each. The total QALY burden was calculated for each iteration and used to create a mean value with confidence intervals representing the uncertainty in the estimates.

Two types of distribution were used in the PSA: beta distributions and gamma distributions. Beta distributions were used for transition probabilities between states and were created by aggregating estimates of the number of cases of each symptom. Gamma distributions were used for duration related transition probabilities and disutilities. The distributions for symptom durations were created by taking the average and variance of the reported median durations in the literature. Whilst this averaging of averages potentially overestimates the uncertainty in the duration estimates, no individual level duration estimates were available. Similarly, for the disutilities, the mean and variance of the reported mean disutilities were used (See Appendix D for details).

Stratification by age

The severity of a FBD and distribution of disease burden may depend on the age of a cohort. For example, children and the elderly have weaker immune systems which means such individuals may be more susceptible to being infected. Furthermore, such individuals may have a higher probability of suffering from more severe complications. Finally, the age of onset of sequelae will impact on the burden that can accrue to individuals. Children will suffer from sequelae for a large number of years but the burden experienced in future years will become heavily discounted. The elderly may be more likely to die from other causes, reducing the burden that can accrue due to sequelae. Understanding how different age groups experience FBD may aid in the prioritisation of interventions to prevent the spread of such pathogens.

However, stratifying the model based on estimates of FBD is data intensive. A completely new set of parameter inputs are required for each age band for each pathogen. Furthermore, evidence identifying the demographic characteristics of cases is limited in the literature. Within this project the age stratified models were developed for four key pathogens: *Campylobacter* spp., Norovirus, *Salmonella* (non-typhoidal) and VTEC O157.

Four key age bands of interest were identified by the researchers; 0-4 (babies and toddlers), 5-15 (children), 16-64 (adults) and 65+ (the elderly). Information regarding the stratification of burden by age was identified in the systematic review which was used to identify the original probability and duration estimates. This information generally took the form of a breakdown of case numbers by age for a specific symptom of a pathogen. These numbers were converted into proportions and then these were applied to the estimates of the number of cases of each symptom produced from the aggregated models.

Age band specific transition probabilities were then calculated from these case numbers. It was assumed that the duration of illness for each symptom was constant across age bands and that the disutility of the symptoms was the same. However, the

utility of the healthy population was varied according to population estimates and as such the absolute utility levels of each health state varied. Furthermore, age specific all-cause mortality was applied to each sample and this increased as the cohort aged.

A.1 *Campylobacter* spp.

Figure A.1 presents the Markov Transition Model (MTM) for *Campylobacter* spp. The starting point is the healthy state, whereby upon suffering from the FBD, the patient can move within and between states (with a step period of one week). In the case of *Campylobacter* spp., a patient can, for example, stay within their health state, or go from a healthy state to either uncomplicated diarrhoea and/or vomiting or death. In the case of uncomplicated diarrhoea, a patient could continue to have uncomplicated diarrhoea and/or vomiting for more than 1 week, return to a healthy state or move to diarrhoea with complications (see Figure A.2) or result in Sequelae (see Figure A.3). With the exception of death, it would be anticipated that a patient would eventually return to a healthy state, although with Sequelae (see Figure A.3), the length of time before that occurs could be substantial depending on the transition probabilities.

Figure A.1: Campylobacter *spp*.

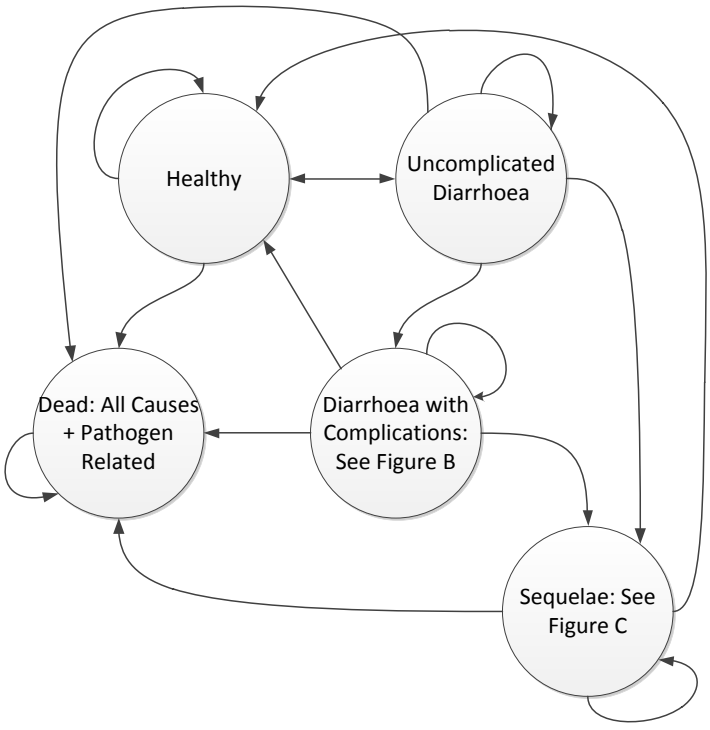


Figure A.2 shows the four types of complications possible with *Campylobacter* spp. such as febrile convulsions or septicaemia. As illustrated it is possible for a patient to remain with this complication for more than one week, eventually return to a healthy state, result in sequelae (see Figure A.3), or death.

Figure A.2: *Campylobacter* spp. Complications (figure B)

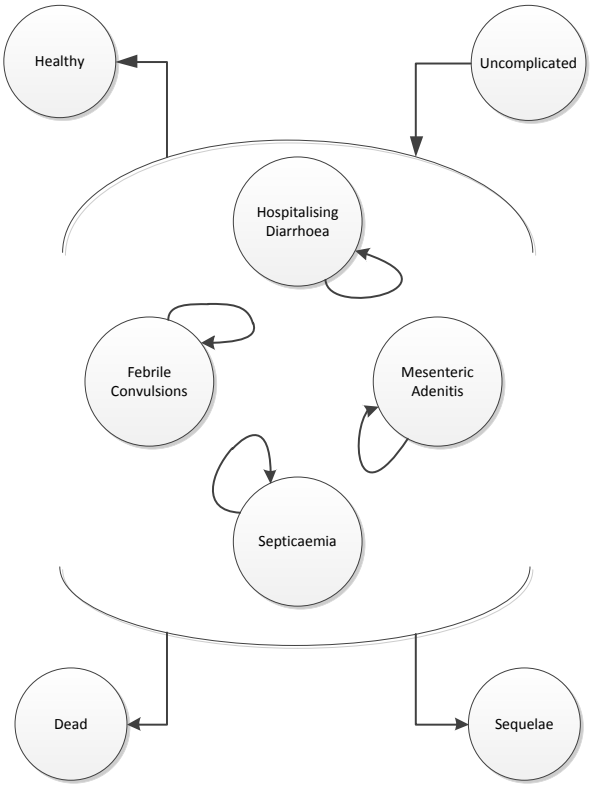
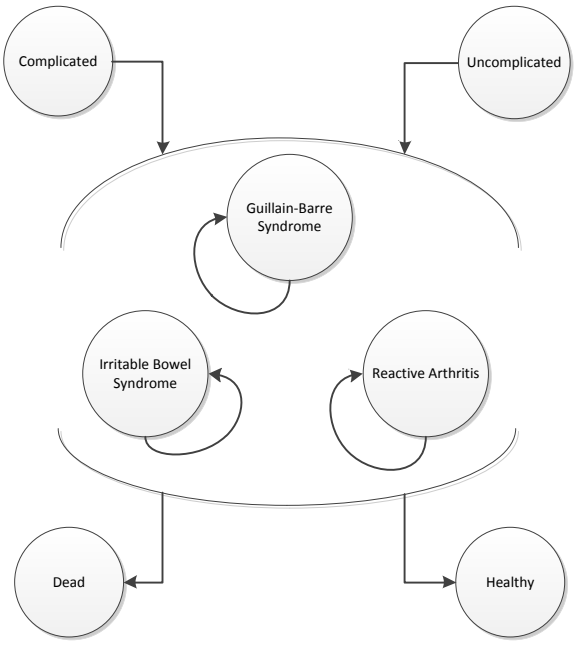


Figure A.3 illustrates the three possible types of sequelae possible with *Campylobacter* spp.; Guillain-Barre Syndrome (GBS), Irritable Bowel Syndrome (IBS) and Reactive Arthritis (RA). As illustrated it is possible for a patient to remain with the sequelae for more than one week, eventually return to a healthy state, or result in death.

Figure A.3: *Campylobacter* spp. sequelae (figure C)



A.2 *Clostridium perfringens*

Figure A.4 presents the Markov Transition Model (MTM) for *Clostridium perfringens*. The starting point is the healthy state, whereby upon suffering from the FBD, the patient can move within and between states (with a step period of one week). In the case of *Clostridium perfringens*, a patient can, for example, stay within their health state, or go from a healthy state to either uncomplicated diarrhoea and/or vomiting or death. In the case of uncomplicated diarrhoea and/or vomiting, a patient could continue to have uncomplicated diarrhoea and/or vomiting for more than one week, return to a health state, or diarrhoea with complications (see Figure A.5). With *Clostridium perfringens* a patient is not expected to suffer from long term sequelae.

Figure A.5 shows the two types of complications possible with *Clostridium perfringens*; such as hospitalising diarrhoea or febrile convulsions. As illustrated it is possible for a patient to remain with this complication for more than one week, eventually return to a healthy state, or result in death.

Figure A.4: *Clostridium perfringens* (figure B)

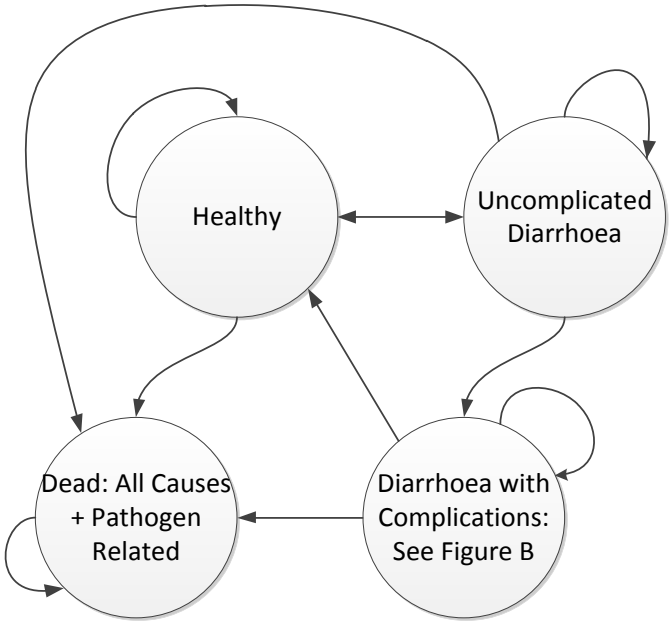
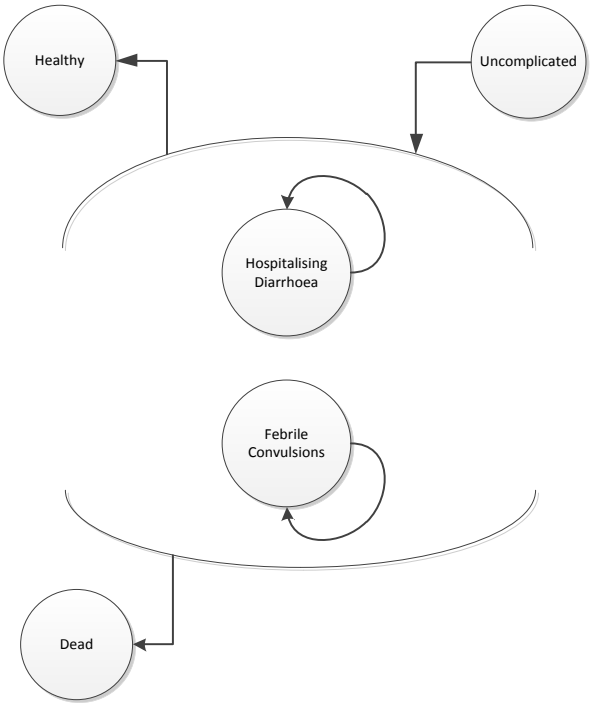


Figure A.5: *Clostridium perfringens* complications (figure C)



A.3 *Cryptosporidium parvum*

Figure A.6 presents the Markov Transition Model (MTM) for *Cryptosporidium parvum*. With *Cryptosporidium parvum* it is possible for a patient to suffer from diarrhoea with complications (See Figure A.7) and/or Sequelae (see Figure A.8).

Figure A.6: *Cryptosporidium parvum*

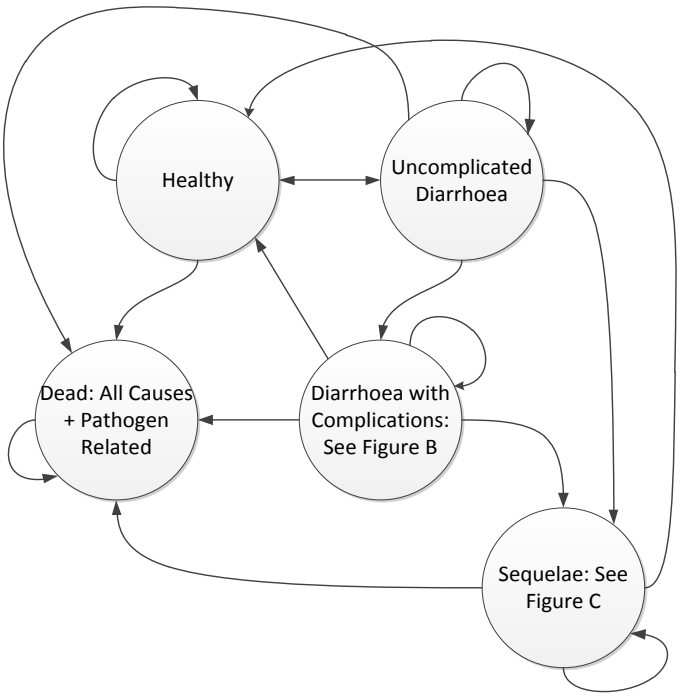


Figure A.7: *Cryptosporidium parvum* complications (figure B)

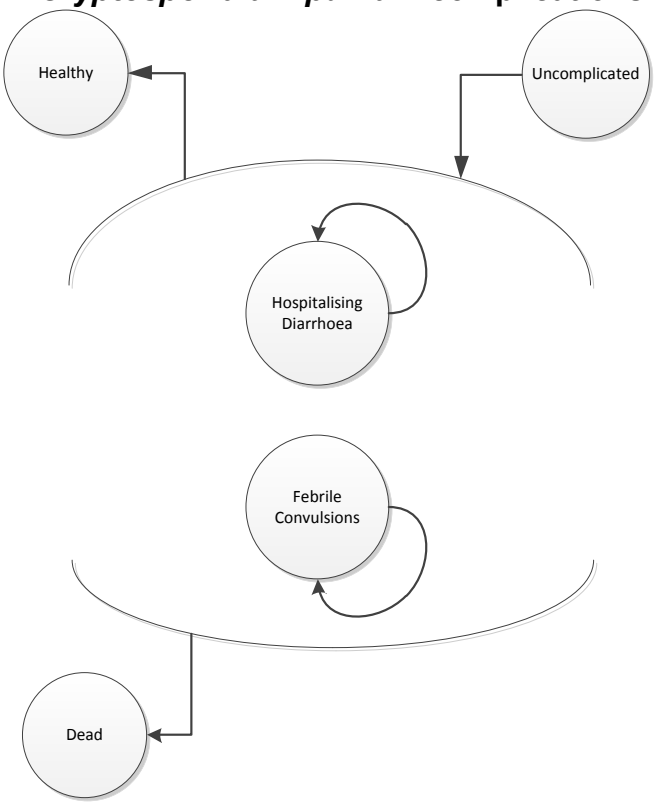
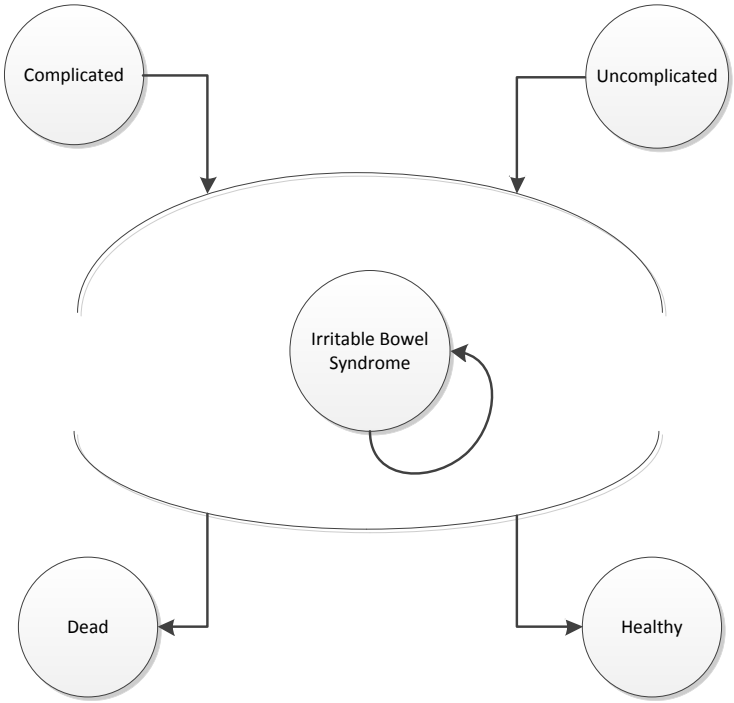


Figure A.8: *Cryptosporidium parvum* sequelae (figure C)



A.4 Enteroaggregative *Escherichia coli*

Figure A.**9** presents the Markov Transition Model (MTM) for Enteroaggregative *Escherichia coli.* With Enteroaggregative *Escherichia coli* it is possible for a patient to suffer from diarrhoea with complications (See Figure A.10) and/or Sequelae (see Figure A.11).

Figure A.9: Enteroaggregative *Escherichia coli*

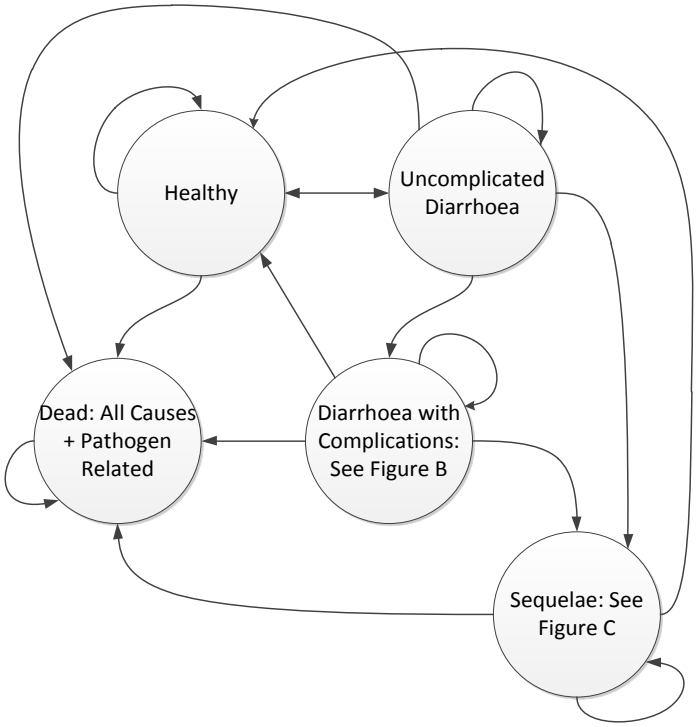


Figure A.10: Enteroaggregative *Escherichia coli* complications (figure B)

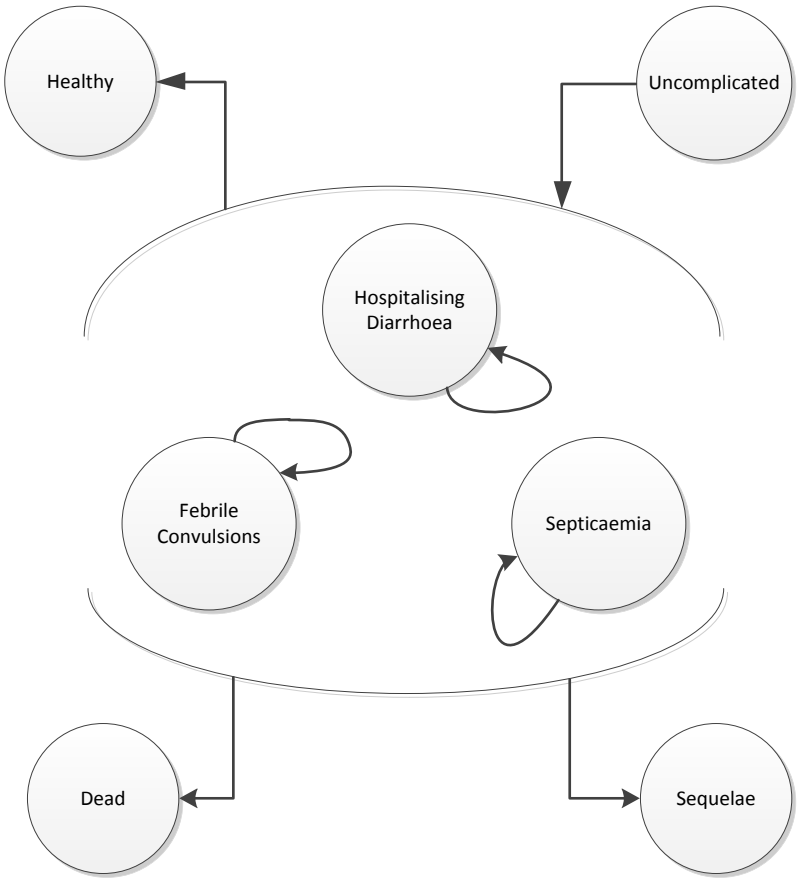
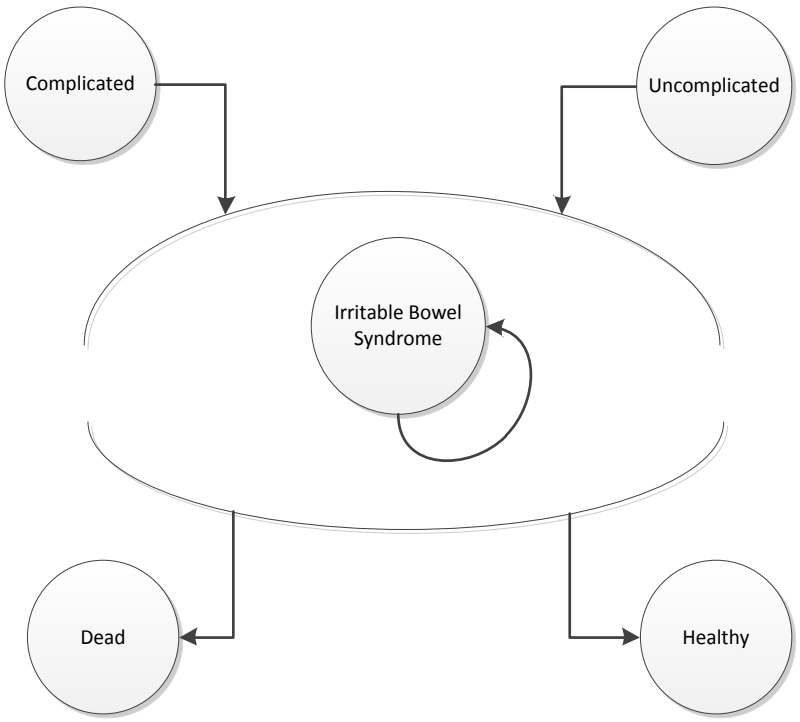


Figure A.11: Enteroaggregative *Escherichia coli* sequelae (figure C)



A.5 *Giardia lamblia*

Figure A.12 presents the Markov Transition Model (MTM) for *Giardia lamblia*. With *Giardia lamblia* it is possible for a patient to suffer from diarrhoea with complications (See Figure A.13) and/or Sequelae (see Figure A.14).

Figure A.12: *Giardia lamblia*

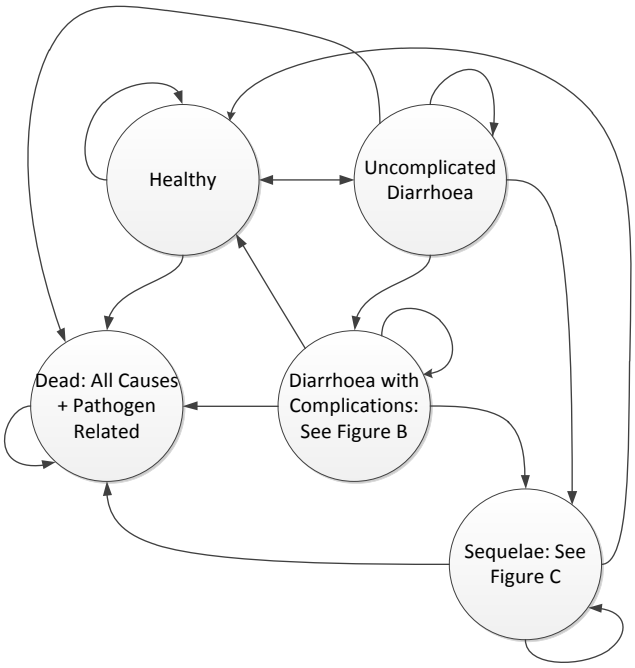


Figure A.13: *Giardia lamblia* complications (figure B)

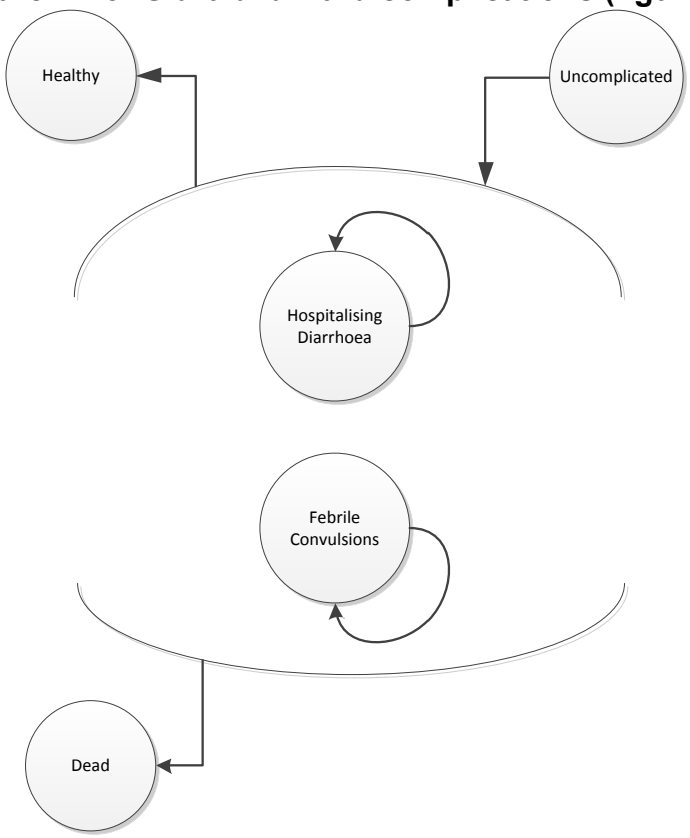
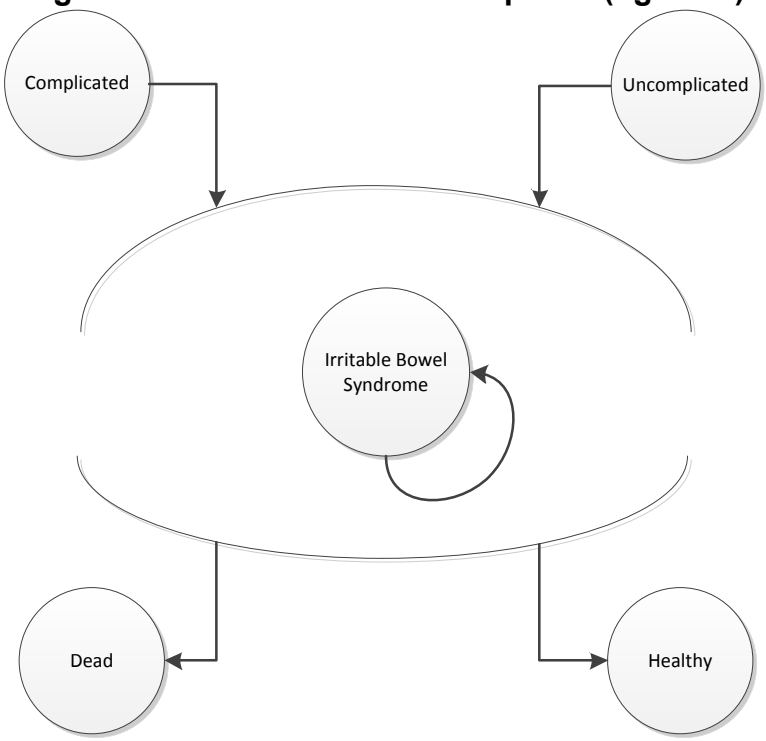


Figure A.14: *Giardia lamblia* sequelae (figure C)



A.6 Hepatitis E

Figure A.15 presents the Markov Transition Model (MTM) for Hepatitis E. With Hepatitis E it is possible for a patient to suffer from complicated jaundice (See Figure A.16) but it is not expected to result in any long term sequelae.

Figure A.15: Hepatitis E

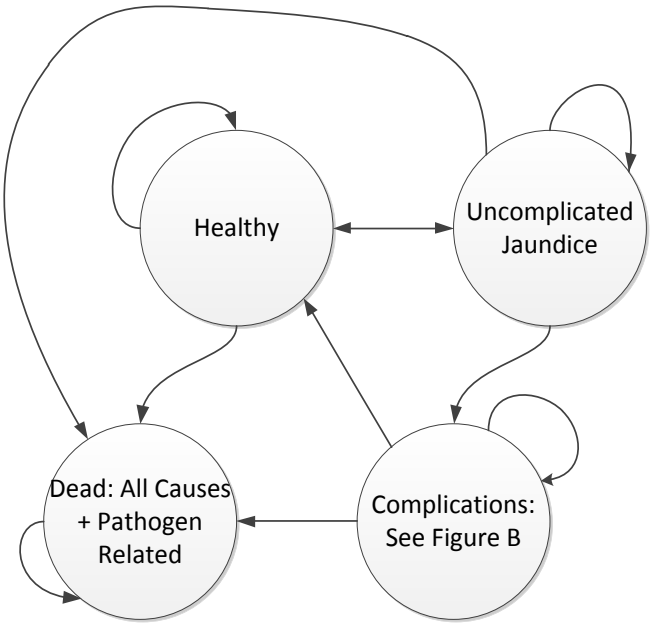
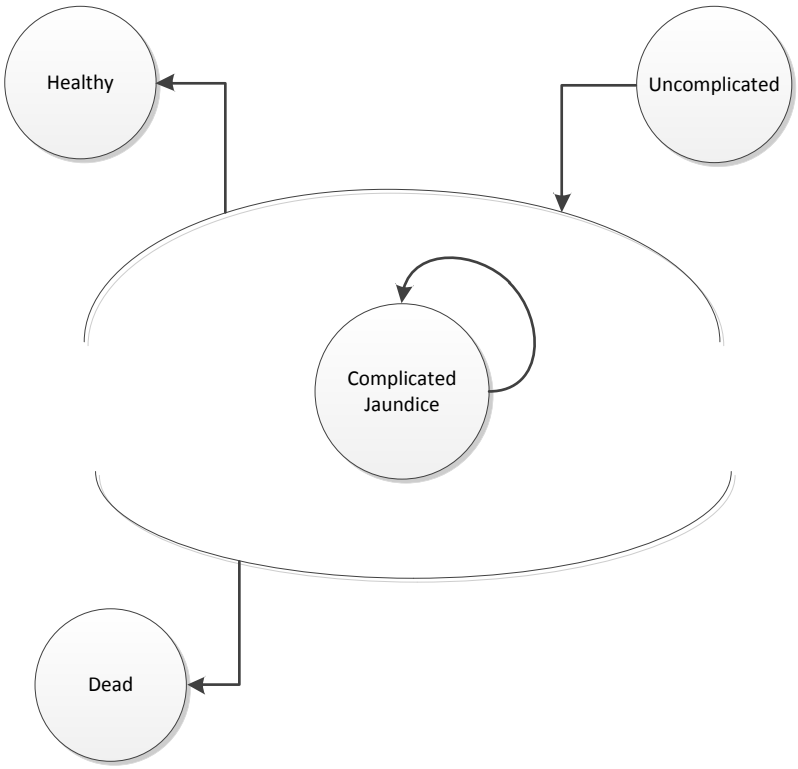


Figure A.16: Hepatitis E complications (figure B)



A.7 *Listeria monocytogenes*

Figure A.17 presents the Markov Transition Model (MTM) for Listeria Monocytogenes. With *Listeria monocytogenes* it is possible for a patient to suffer from complications (See Figure A18) but not expected to result in any long term sequelae.

Figure A.17: *Listeria monocytogenes*

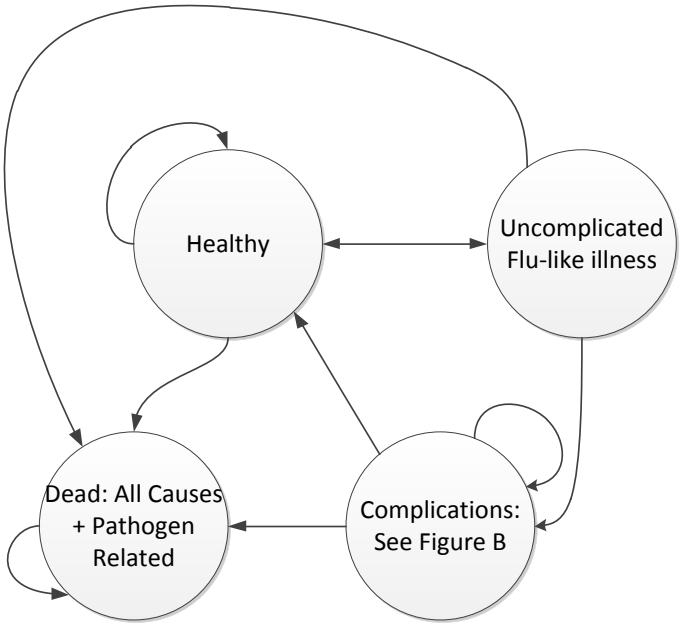
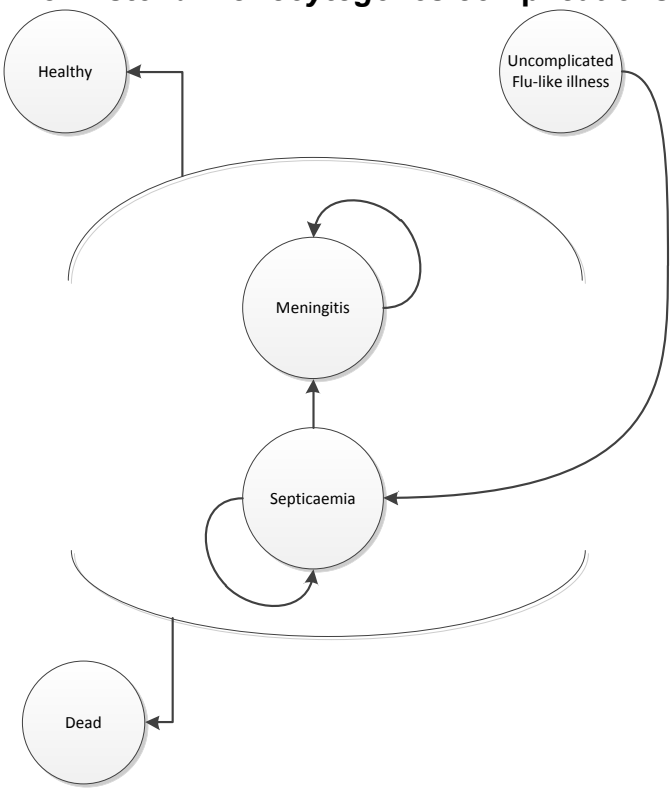


Figure A.18: *Listeria monocytogenes* complications (figure B)



A.8 Norovirus

). It is important to note here, as discussed in report that “uncomplicated diarrhoea” refers to “uncomplicated diarrhoea and/or vomiting”

Figure **A.19** presents the Markov Transition Model (MTM) for Norovirus. With Norovirus it is possible for a patient to suffer from complications (See Figure A.20) and/or Sequelae (see Figure A.21). It is important to note here, as discussed in report that “uncomplicated diarrhoea” refers to “uncomplicated diarrhoea and/or vomiting”

Figure A.19: Norovirus

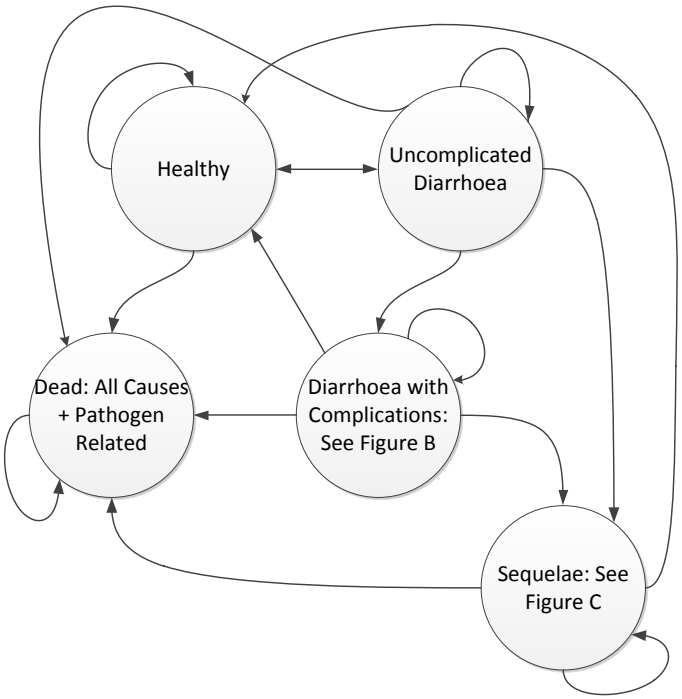


Figure A.20: Norovirus complications (figure B)

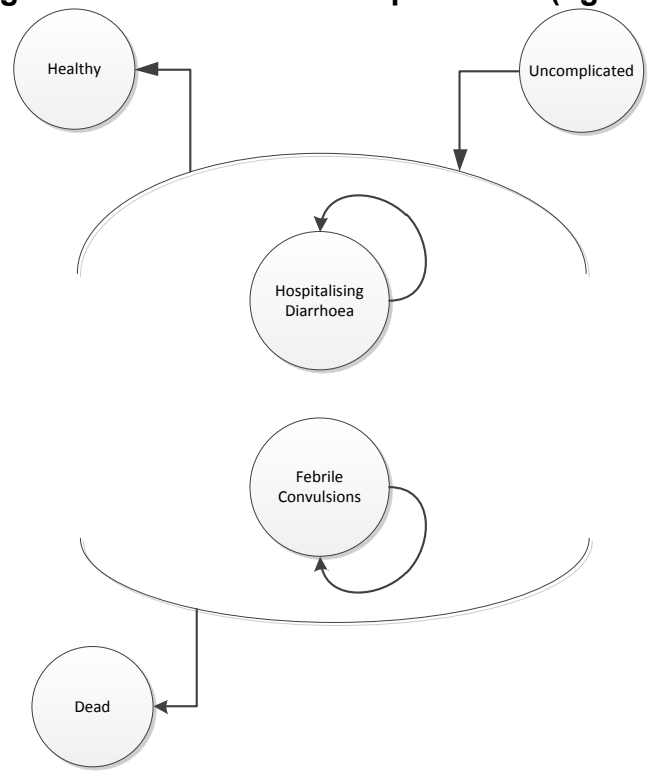
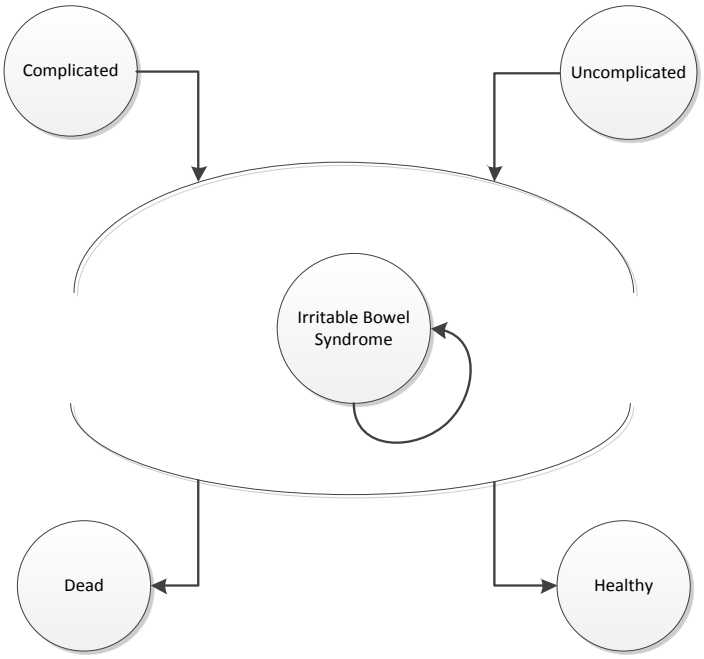


Figure A.21: Norovirus sequelae (figure C)



A.9 *Salmonella* (Non-Typhoidal)

Figure A.22 presents the Markov Transition Model (MTM) for *Salmonella* (Non-Typhoidal). With *Salmonella* (Non-Typhoidal) it is possible for a patient to suffer from diarrhoea with complications (See Figure A.23) and/or Sequelae (see Figure A.24).

Figure A.22: *Salmonella* (Non-Typhoidal)

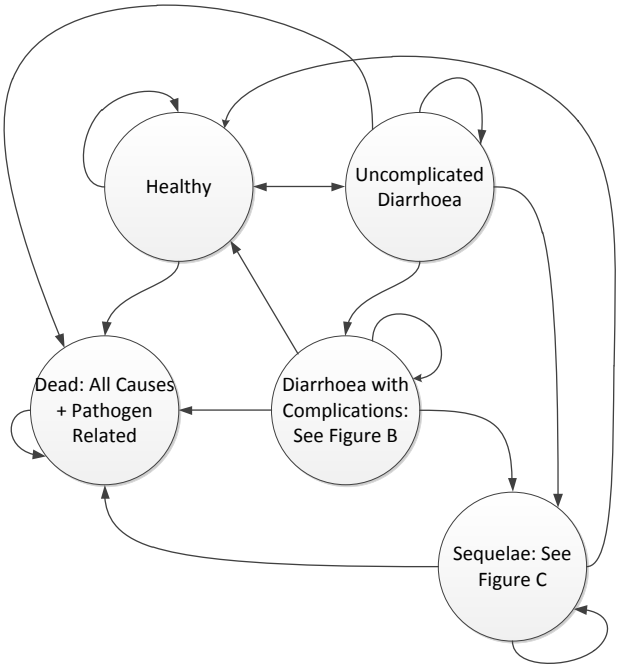


Figure A.23: *Salmonella* (Non-Typhoidal) complications (figure B)

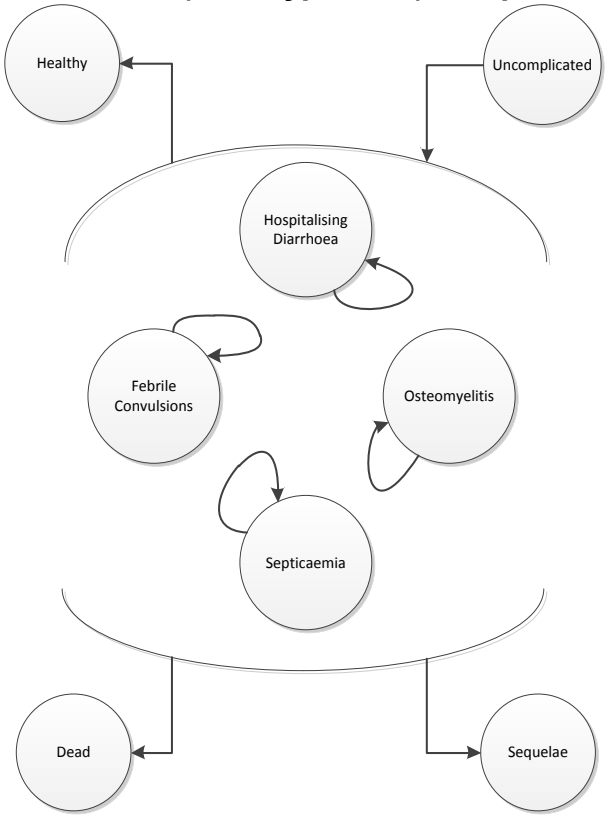
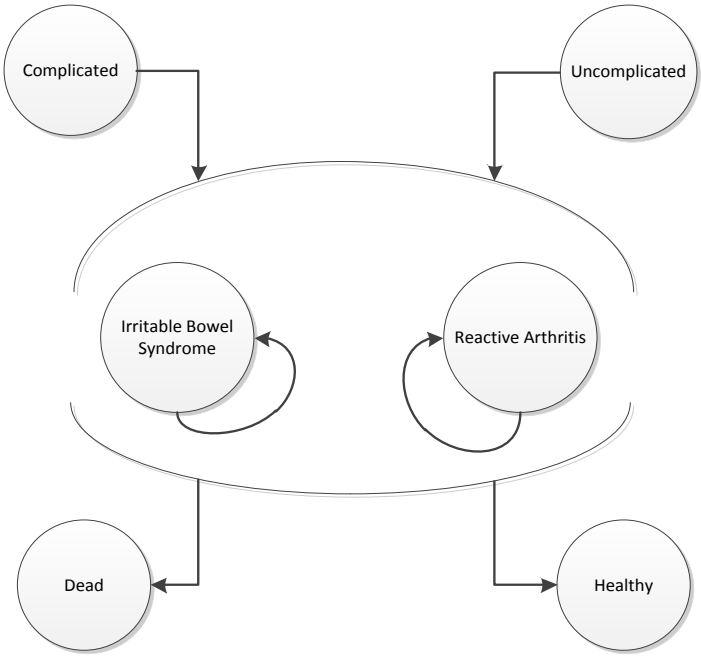


Figure A.24: *Salmonella* (Non-Typhoidal) sequelae (figure C)



A.10 *Shigella* spp.

Figure A.25 presents the Markov Transition Model (MTM) for *Shigella* spp. With *Shigella* spp. it is possible for a patient to suffer from diarrhoea with complications (See Figure A.26) and/or Sequelae (see Figure A.27).

Figure A.25: *Shigella* spp.

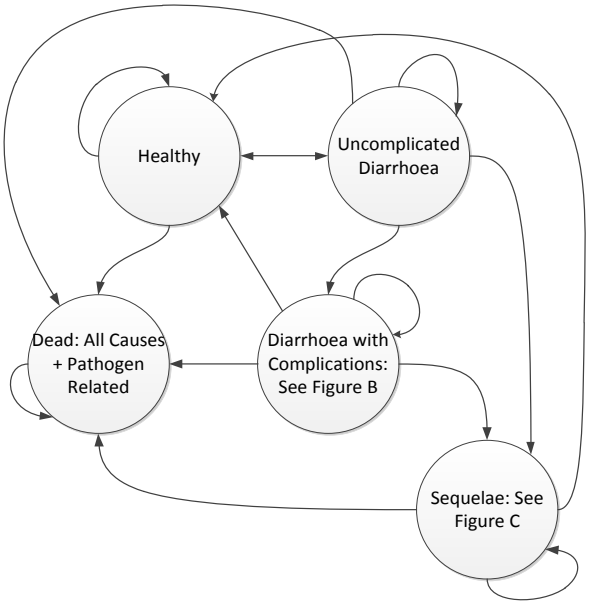


Figure A.26: *Shigella* spp. complications (figure B)

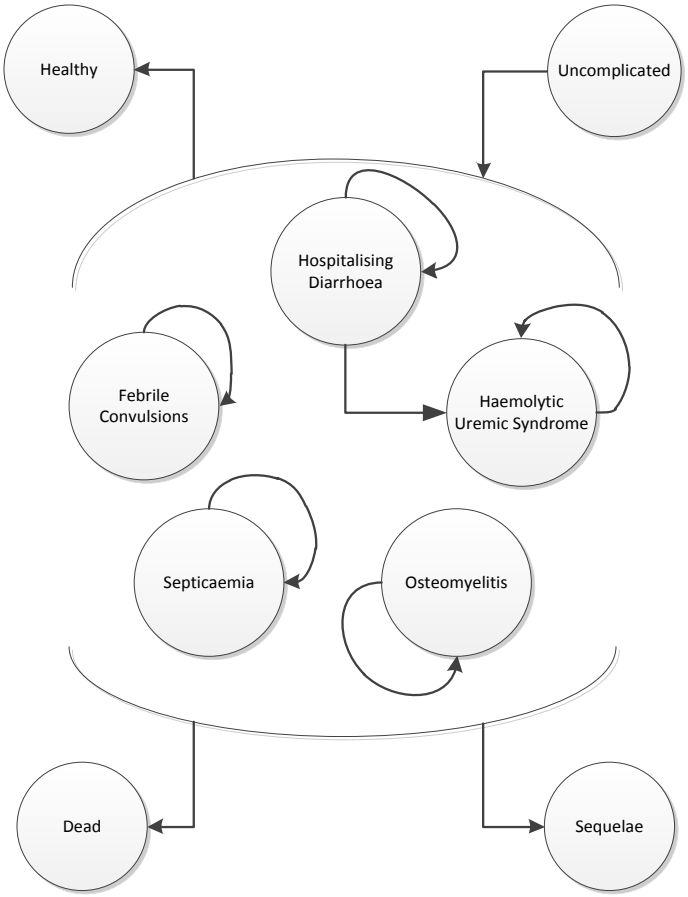
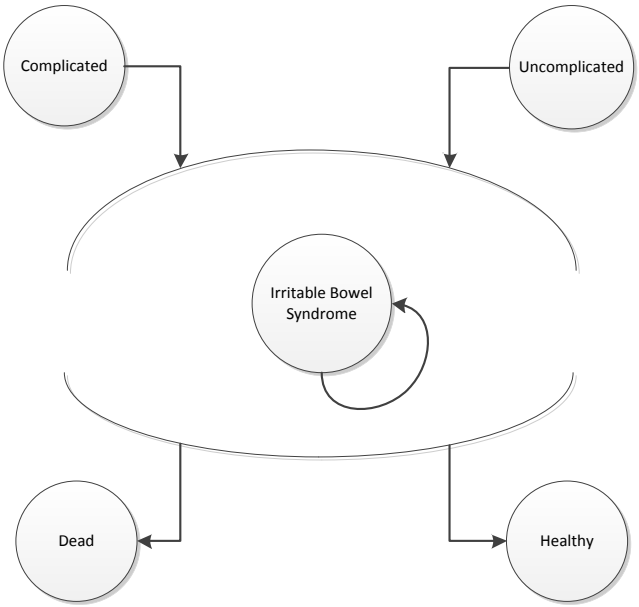


Figure A.27: *Shigella* spp. sequelae (figure C)



A.11 VTEC O157

Figure A.28 presents the Markov Transition Model (MTM) for VTEC O157. With VTEC O157 it is possible for a patient to suffer from diarrhoea with complications (See Figure A.29) and/or Sequelae (see Figure A.30).

Figure A.28: VTEC O157

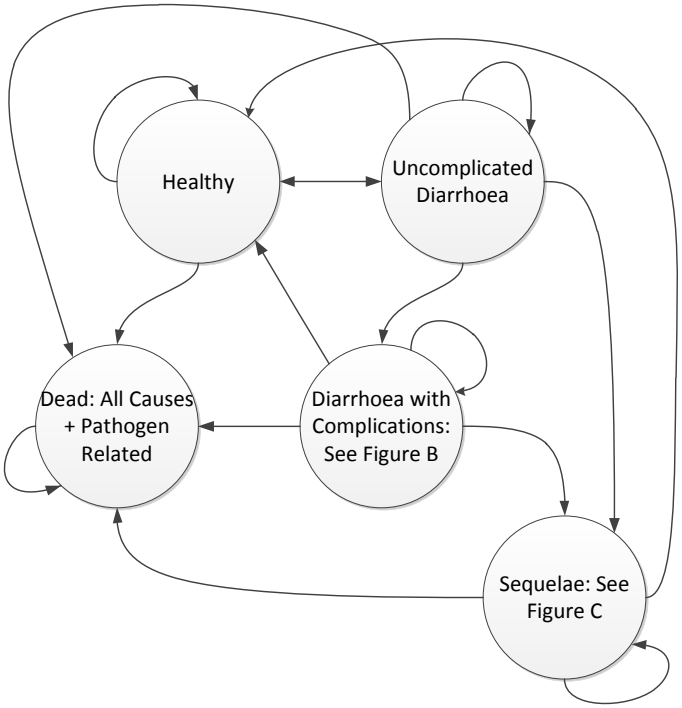


Figure A.29: VTEC O157 complications (figure B)

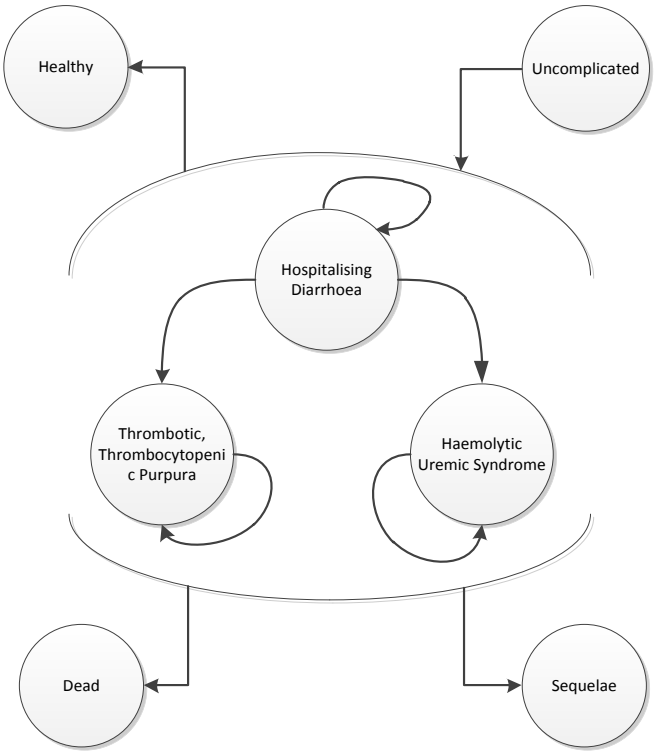
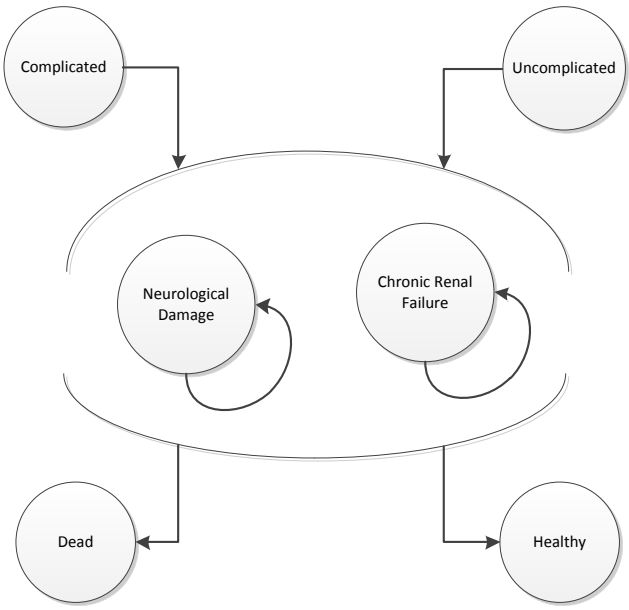


Figure A.30: VTEC O157 sequelae (figure C)



APPENDIX B: SYSTEMATIC REVIEW OF THE CLINICAL LITERATURE

This supporting appendix shows the search terms used in the systematic review of the clinical literature which informed the transition probabilities and durations included in the Markov Transition Models.

"sequelae and pathogen", "sequelae and illness", "side effects or complications or long-term and pathogen or illness", "sequelae from gastrointestinal infections"

OR

"*Campylobacter* OR Campylobacteriosis AND sequelae OR side effects OR complications OR long-term"

OR

"Norovirus AND sequelae OR side effects OR complications OR long-term"

OR

"Hepatitis E AND sequelae OR side effects OR complications OR long-term"

OR

"*Listeria* OR Listeriosis AND sequelae OR side effects OR complications OR long-term"

OR

"*Salmonella* OR Salmonellosis AND sequelae OR side effects OR complications OR long-term"

OR

"*Shigella* OR Shigellosis AND sequelae OR side effects OR complications OR long-term"

OR

"Cryptosporidium OR Cryptosporidiosis AND sequelae OR side effects OR complications OR long-term"

OR

"Giardia OR Giardiasis AND sequelae OR side effects OR complications OR long-term"

OR

"*Clostridium perfringens* AND sequelae OR side effects OR complications OR long-term"

OR

"Enteroaggregative *E. coli* AND sequelae OR side effects OR complications OR long-term"

OR

"*E.coli* O157 AND sequelae OR side effects OR complications OR long-term"

APPENDIX C: SYSTEMATIC REVIEW OF PRIMARY HEALTH WEIGHTS USED IN BURDEN OF ILLNESS STUDIES OF FOODBORNE PATHOGENS

Author (Year)	Country	Type of Utility Elicited	Valuation Method	Pathogen Specific Symptom Utilities Elicited	Generic Symptom Utilities Elicited
Batz et al., (2014)	USA	Health-related quality of life (HRQoL) for use in Quality Adjusted Life Years (QALYS)	The authors created EQ-5D-3L profiles describing the health states resulting from infection resulting from 14 different pathogens. These were validated by experts and then converted to utilities using a US preference tariff (Shaw et al., 2015)	*Campylobacter* spp. Acute illness: No doctor visit – 0.8270 (EQ-5D: 11121) Visit doctor – 0.7080 (EQ-5D: 21222) Hospitalised, severe – 0.4370 (EQ-5D: 22322) Recovery after hospitalisation – 0.8600 (EQ-5D: 11211) Chronic: Guillain-Barré Syndrome Hospitalised, no ventilator, intensive care - -0.1090 (EQ-5D: 33333) Hospitalised, ventilator, intensive care - -0.1090 (EQ-5d: 33333) Hospitalised, no ventilator, post intensive care – 0.4370 (EQ-5D: 22322) Hospitalised, ventilator, post intensive care – 0.2160 (EQ-5D: 32322) Recovery, no ventilator, in hospital – 0.7080 (EQ-5D: 21222) Recovery, ventilator, in hospital – 0.7080 (EQ-5D: 21222) Chronic, do not resume work – 0.5080 (EQ-5D: 22321)	-

				Clostridium perfringens No doctor visit – 0.8160 (EQ-5D: 11221) Visit doctor – 0.7780 (EQ-5D: 21221) Hospitalised, severe – 0.4370 (EQ-5D: 22322) Recovery after hospitalisation – 1 (EQ-5D: 11111) *Cryptosporidium parvum* No doctor visit – 0.8270 (EQ-5D: 11121) Visit doctor – 0.8160 (EQ-5D: 11221) Hospitalised, severe – 0.4370 (EQ-5D: 22322) Recovery after hospitalisation – 0.8600 (EQ-5D: 11211) Diarrhoea relapse – 0.8270 (EQ-5D: 11121) *STEC non-0157* (analogous to VTEC) Acute Illness: No doctor visit – 0.8160 (EQ-5D: 11221) Visit doctor (not lab confirmed) – 0.7080 (EQ-5D: 21222) Visit doctor (lab confirmed) – 0.7080 (EQ-5D: 21222) Hospitalised, non-haemolytic uremic syndrome – 0.4370 (EQ-5D: 22322) Recovery, after non- haemolytic	

				uremic syndrome – 0.8160 (EQ-5D: 11221) Hospitalised, haemolytic uremic syndrome – -0.1090 (EQ-5D: 33333) Recovery, after haemolytic uremic syndrome – 0.7780 (EQ-5D: 21221) End Stage Renal Disease: Hemodialysis – 0.5920 (EQ-5D: 21312) Peritoneal dialysis – 0.8270 (EQ-5D: 21112) Transplant surgery – 0.0300 (EQ-5D: 33323) Post-transplant therapy – 0.8440 (EQ-5D: 1112) *Listeria monocytogenes* Acute illness: No doctor visit – 0.8160 (EQ-5D: 11221) Visit doctor – 0.7080 (EQ-5D: 21222) Hospitalised, pregnant - 0.3330 (EQ-5D: 22323) Recovery after hospitalisation, pregnant – 0.8600 (EQ-5D: 11211) Hospitalised, moderate - 0.4370 (EQ-5D: 22322) Recovery after hospitalisation, moderate – 0.8600 (EQ-5D: 11211) Hospitalised, severe, intensive care - -0.1090 (EQ-5D: 33333) Hospitalised, severe, post	

				intensive care – 0.2160 (EQ-5D: 32322) Recovery after hospitalisation, severe – 0.8330 (EQ-5D: 11212) <u>Norovirus</u> No doctor visit – 0.8160 (EQ-5D: 11221) Visit doctor – 0.7780 (EQ-5D: 21221) Hospitalised, severe – 0.4370 (EQ-5D: 22322) Recovery after hospitalisation – 1(EQ-5D: 11111) <u>*Salmonella* (non-typhoidal)</u> No doctor visit – 0.8270 (EQ-5D: 11121) Visit doctor – 0.7780 (EQ-5D: 21221) Hospitalised, severe – 0.4370 (EQ-5D: 22322) Recovery after hospitalisation – 0.8600 (EQ-5D: 11211) <u>*Shigella* spp.</u> No doctor visit – 0.8160 (EQ-5D: 11221) Visit doctor – 0.7080 (EQ-5D: 21222) Hospitalised, severe – 0.3330 (EQ-5D: 22323) Recovery after hospitalisation – 0.8600 (EQ-5D: 11211) <u>*Yersinia enterocolitica*</u>	

				No doctor visit – 0.8270 (EQ-5D: 11121) Visit doctor – 0.7780 (EQ-5D: 21221) Hospitalised, sepsis – 0.1670 (EQ-5D: 22333) Recovery after hospitalisation, sepsis – 0.8160 (EQ-5D: 11221) Hospitalised, non-septic – 0.3330 (EQ-5D: 22323) Recovery after hospitalisation, non-septic – 0.8600 (EQ-5D: 11211) Hospitalised, appendectomy – 0.3330 (EQ-5D: 22323) Recovery after appendectomy – 0.7780 (EQ-5D: 21221)	
Devleeschauwer et al., (2015)	Worldwide	Disability weights (DW) for use in Disability Adjusted Life Year (DALY) calculation	Expert adjustment of Global Burden of Disease estimates to account for varying severity of symptoms by pathogen	Norovirus Diarrheal disease - 0.074 *Campylobacter* spp Diarrheal disease - 0.101 Guillain-Barré syndrome – 0.445 Shiga toxin-producing *E.coli* (analogous to VTEC) Diarrheal disease - 0.091 Hemoyltic uremic syndrome – 0.210 End-stage renal disease – 0.573 *Salmonella* (non-typhoidal) Diarrheal disease - 0.101 Invasive salmonellosis – 0.210 *Shigella* spp.	Hepatitis (for Hepatitis A) – 0.108

				Diarrheal disease - 0.101 *Cryptosporidium* spp Diarrheal disease - 0.074 *Giardia* spp Diarrheal disease - 0.074 *Listeria monocytogenes* Sepsis – 0.210 Central nervous system infection – 0.426 Neurological sequelae – 0.292	
Haagsma et al., (2008)	The Netherlands	DWs for DALYs	The authors created 20 health states representing the symptoms of 5 pathogens. These were presented in vignettes containing a disease label, clinical description and a representation of the health state as an EQ-5D profile. A sample of the public (n=107) valued the health states using visual analogue scales (VAS) and the time trade off (TTO) approach.	-	Gastroenteritis, mild, 1 day – 0.036 (VAS), 0.002 (TTO) Gastroenteritis, mild, 5 days – 0.102 (VAS), 0.010 (TTO) Gastroenteritis, moderate, 10 days – 0.130 (VAS), 0.015 (TTO) Gastroenteritis, severe, 7 days – 0.231 (VAS), 0.025 (TTO) Gastroenteritis, severe, 14 days – 0.295 (VAS), 0.041 (TTO) Gastroenteritis, chronic, 6 months – 0.368 (VAS), 0.099 (TTO) See Havelaar et al.,

					(2000a) for details of GBS severity levels) GBS, F1, whole year – 0.185 (VAS), 0.044 (TTO) GBS, F2, whole year – 0.420 (VAS), 0.137 (TTO) GBS, F3, whole year – 0.545 (VAS), 0.215 (TTO) GBS, F4, whole year – 0.700 (VAS), 0.367 (TTO) GBS, F5, whole year – 0.722 (VAS), 0.460 (TTO) Reactive arthritis, mild, 1 week – 0.107 (VAS), 0.004 (TTO) Reactive arthritis, mild, 6 weeks – 0.197 (VAS), 0.023 (TTO) Reactive arthritis, moderate, 6 months – 0.447 (VAS), 0.115 (TTO) Reactive arthritis, severe, 6 months – 0.503 (VAS), 0.186 (TTO) Hemolytic uremic syndrome (HUS), moderate, 1 month – 0.279 (VAS), 0.056 (TTO) HUS, severe, 1 month

					– 0.481 (VAS), 0.110 (TTO) Renal failure, whole year – 0.628 (VAS), 0.328 (TTO) Crohn's disease, 6 months – 0.347 (VAS), 0.105 (TTO)
Haagsma et al., (2015)	Hungary, Italy, The Netherlands, Sweden	DWs for DALYs	Description for health symptoms created for lay audience using less than 70 words. Health professionals were involved in design of these descriptions. 255 health states were evaluated. A discrete choice experiment (DCE) was used to value the health states. 30,660 respondents completed the DCE, each answering 15 questions. The results were analysed using a probit regression.		The weights presented below are mean values across all four countries. Infectious disease, acute episode, mild – 0.007 Infectious disease, acute episode, moderate – 0.051 Infectious disease, acute episode, severe – 0.125 Infectious disease, post-acute consequences – 0.217 Diarrhoea, mild – 0.073 Diarrhoea, moderate – 0.149 Diarrhoea, severe – 0.239 Thrombocytopenic purpura – 0.167 Chronic kidney illness (stage IV) – 0.108 End-stage renal

					disease, on dialysis – 0.487 End-stage renal disease, with kidney transplant – 0.030 Irritable bowel syndrome – 0.062 Intellectual disability, borderline – 0.014 Intellectual disability, mild – 0.053 Intellectual disability, moderate – 0.123 Intellectual disability, severe – 0.213 Intellectual disability, profound – 0.213 Osteomyelitis – 0.053
Havelaar et al 2000a	The Netherlands	DWs for DALYs	The authors created short clinical descriptions for health states not available in the Global Burden of Disease study. These were also described with EQ-5D profiles. These health states were then valued by asking a panel of experts (24 physicians and 11 environment epidemiologists) to rank their severity relative to health states with existing values.	*Campylobacter* spp. Severe gastroenteritis (requiring general practitioner visit) – 0.368 GBS F1 – Completely recovered from an episode of GBS but having problems with insomnia, fatigue and related emotional constraints – 0.10 GBS F2 – Muscle weakness in legs and arms. Able to walk at least 10m without walking aid but cannot run – 0.30 GBS F3 – Muscle weakness in legs and arms and only able to walk at least 10m with a walking aid – 0.44	

				GBS F4 – Severe muscle weakness in legs and arms, not able to walk, bedridden or in a wheelchair – 0.80 GBS F5 – Severe muscle weakness in legs and arms, not able to walk, bedridden and need artificial ventilation for at least part of the day – 0.94	
Havelaar et al., (2000b)	The Netherlands	DWs for DALYs	No previous estimates available for the authors so they use assumption that reactive arthritis has the same disutility as mild rheumatoid arthritis. They took this disutility from a previous Dutch study which is not available in English.	*Campylobacter* spp Reactive arthritis – 0.21	-
Havelaar et al., (2004)	The Netherlands	DWs for DALYs	Experts used the EQ-5D questionnaire to describe the health status of patients with HUS. This was converted to a utility score using the values in Dolan et al., (2004). To determine values for end stage renal disease (ESRD) the authors identified EQ-5D profiles representing various levels of severity from existing literature (De Wit et al., 1998) and converted these to	Shiga toxin-producing *Escherichia Coli* 0157 (analogous to VTEC) HUS -0.93 Dialysis for ESRD – 0.18 Transplantation for ESRD – 0.18 Functioning graft for ESRD – 0.12	

			utility score using the above method.		
Janssen et al., (2008)	The Netherlands	HRQoL for QALYs	A population panel, general practitioners (n=9), medical advisers (n=22), lay people (n=105) and a panel of the Dutch Consumers Association (n=622) valued vignettes for 46 disease stages using the visual analog scale (VAS) and time tradeoff (TTO) methods. Vignettes contained disease-specific information, a generic description (EQ-6D5L), a description of the disease course over time, and a visual representation of the disease.		Results from Dutch Consumers Association panel Irritable bowel syndrome – 0.906 (TTO) Irritable bowel syndrome, yearly recurrent – 0.913 (TTO)
Kemmerman et al., (2006)	The Netherlands	DW for DALYs	The values presented in this paper are not original values. However, the source paper from which the values are taken is only available in Dutch (Melse et al., 1998).	*Listeria monocytogenes* Listeriosis, mild symptoms – 0.01 Listeriosis, severe symptoms – 0.11	Meningitis – 0.32 Neurological disorders – 0.25 Reactive arthritis, not visiting gp – 0.127 Reactive arthritis, visiting gp – 0.21 Reactive arthritis, hospitalised – 0.37 Sepsis – 0.93
Lai et al., (2009)	Estonia	DWs for DALYs	A panel of 25 experts with a medical background valued 26		Diarrhoeal infectious diseases – 0.011

			indicator states using a person trade off (PTO) approach. 257 additional states were then plotted to a VAS, using the initial indicator states as a reference.		Other intestinal infections – 0.119 Viral Hepatitis – 0.282 Childhood infections – 0.119 Mental retardation – 0.242 Meningitis – 0.597 Inflammatory disease of stomach – 0.177 Osteomyelitis – 0.416 Acute conditions in kidney – 0.340 Severe chronic kidney disease – 0.300
Mangen et al., (2004)	The Netherlands	DWs for DALYs	For reactive arthritis the authors assumed an EQ-5d state for very mild arthritis based on the belief that previous estimates (Stouthard et al., 1997) were too high. For inflammatory bowel disease, the authors required a singular DW so averaged the weights for different severities, weighting for the duration that patients spend in those	*Campylobacter* spp Reactive arthritis, no visiting GP – 0.127 Inflammatory bowel disease – 0.26	

			severities.		
Michaud et al., (2006)	Atlanta, USA	DWs for DALYs	Person trade off based on Global Burden of Disease methodology (see Murray et al., 1996)		Watery diarrhoea – 0.06
Murray and Lopez (1996)	Global	DWs for DALYs	A panel of world health organisation (WHO) experts were asked to value 22 indicator conditions using a PTO approach. These were validated against the results of nine additional experiments (number of participants unclear).		Watery diarrhoea - 0.066 Age specific values are available for the symptoms below (15-44 presented) Diarrhoeal disease, episodes – 0.086 Bacterial meningitis, episodes – 0.613 Mental retardation – 0.483 Hepatitis B/C, episodes (analogous to Hepatitis E) – 0.209
Pare et al., (2006)	Canada	HRQoL	Baseline EQ-5D based utility scores for IBS patients (n=1555) in a clinical trial. Valuation based Dolan et al., (1997) regression model.		IBS – 0.641
Salomon et al., (2012)	Bangladesh, Indonesia, Peru, Tanzania, USA	DW for DALYs	DCE where participants (n=30,230) compare patients in different described health states and choose which they		Infectious disease, acute episode, mild – 0.005 Infectious disease, acute episode,

			think if the healthiest. Results analysed using probit regression.		moderate – 0.053 Infectious disease, acute episode, severe – 0.210 Infectious disease, post-acute consequences – 0.254 Diarrhoea, mild – 0.061 Diarrhoea, moderate – 0.202 Diarrhoea, severe – 0.281 ESRD with kidney transplant – 0.027 ESRD on dialysis – 0.573 Intellectual disability, mild – 0.031 Intellectual disability, moderate – 0.080 Intellectual disability, severe – 0.126 Intellectual disability, profound – 0.157 Abdominopelvic problem, mild – 0.012 Abdominopelvic problem, moderate – 0.123 Abdominopelvic problem, severe – 0.326
Salomon et al., (2015)	Hungray, Italy, Netherlands,	DW for DALYs	This study presents aggregated estimates based on Salomon et		Infectious disease, acute episode, mild – 0.006

	Sweden, Bangladesh, Indonesia, Peru, Tanzania, USA		al., (2012) and Haagsma et al., (2015)		Infectious disease, acute episode, moderate – 0.051 Infectious disease, acute episode, severe – 0.133 Infectious disease, post-acute consequences – 0.219 Diarrhoea, mild – 0.074 Diarrhoea, moderate – 0.188 Diarrhoea, severe – 0.247 Chronic kidney disease (Stage 4) – 0.104 ESRD with kidney transplant – 0.024 ESRD on dialysis – 0.571 Intellectual disability, mild – 0.043 Intellectual disability, moderate – 0.100 Intellectual disability, severe – 0.160 Intellectual disability, profound – 0.200 Abdominopelvic problem, mild – 0.011 Abdominopelvic problem, moderate – 0.114 Abdominopelvic problem, severe –

					0.324 Thrombocytopenic purpura – 0.159
Stouthard et al., (1997)	The Netherlands	DW for DALYs (note, the values are presented in a fashion more akin to HRQoL values, i.e. 1 is perfect health and 0 is dead.	A set of indicator values were valued by a panel of health experts using a PTO approach. Health states were described and accompanied by a representative EQ-5D state. 175 alternative health states were then position on a VAS containing utility values representing those elicited for the indicator states.		Digestive tract infection, uncomplicated course (duration 2 weeks) – 0.99 Digestive tract infection, complicated course (duration 2-4 weeks) – 0.97 Permanent locomotor impairment after bacterial meningitis – 0.83 Permanent cognitive impairment after bacterial meningitis – 0.75 Permanent locomotor and cognitive impairment after bacterial meningitis – 0.24 Mild mental handicap – 0.71 Moderate mental handicap – 0.57 Severe mental handicap – 0.18 Extreme mental handicap – 0.24 Mental retardation – 0.91 Inflammatory bowel

					disease, active exacerbation – 0.60 Inflammatory bowel disease, in remission – 0.82
Maertens de Noordhout et al.,., (2014)	Belgium	DW for DALYs	Expert elicitation with eight members of the Belgian Association of Neurology. A Las Vegas method was used whereby the experts distributed 100 points over the different outcomes to determine the DWs	*Listeria monocytogenes* Central nervous system infection – 0.426 Neurological sequelae – 0.292	
Van Lier et al., (2007)	The Netherlands	DWs for DALYs	Creation of mean severity weights by weighting severity specific weights by proportion of patients experiencing those states.	*Campylobacter* spp Reactive arthritis – 0.14 GBS, first year – 0.25 GBS, long term – 0.16 *Salmonella* Reactive arthritis – 0.15	

APPENDIX D: PARAMETER VALUES AND REFERENCES FOR THE MARKOV TRANSITION MODELS

Campylobacter spp.

Transition Probability	Point Estimate Value	Sources and assumptions
Healthy to uncomplicated diarrhoea	0.004328	IID2 (Tam et al 2014)
Uncomplicated diarrhoea to uncomplicated diarrhoea	0.409421	Helms (2002) (2006), Ruzante (2011), Edwards (2014)
Uncomplicated diarrhoea to hospitalising diarrhoea	0.009429	Oleson, Ruzante (2011), Toljander (2012), Edwards (2014), Nielsen (2012), IID2, HES
Uncomplicated diarrhoea to febrile convulsions	0.000155	Jones (1981)
Uncomplicated diarrhoea to mesenteric adenitis	0.000889	Based on generic GI complications, Helms (2002)
Uncomplicated diarrhoea to septicaemia	0.002279	Based on generic extraintestinal infection, Helms (2002)
Uncomplicated diarrhoea to GBS	0.000711	Helms (2002), Mangen (2015), Toljander (2012), McCarthy (2001)
Uncomplicated diarrhoea to IBS	0.07615	Mangen (2015), Helms (2002), Nielsen (2012)
Uncomplicated diarrhoea to RA	0.015637	Mangen (2015), Helms (2002), Toljander (2012), Hannu, Bremell (1991)
Hospitalising diarrhoea to hospitalising diarrhoea	0.361350	Helms (2002), Ruzante (2011), HSCIC (2015)
Hospitalising diarrhoea to GBS	0.000711	Helms (2002), Mangen (2015), Toljander (2012), McCarthy (2001)
Hospitalising diarrhoea to IBS	0.076150	Mangen (2015), Helms (2002), Nielsen (2012)
Hospitalising diarrhoea to RA	0.015637	Mangen (2015), Helms (2002), Toljander (2012), Hannu (2002), Bremell (1991)
Febrile convulsions to febrile convulsions	2.673E-51	Assumption, see Norovirus
Febrile convulsions to GBS	0.000711	Helms (2002), Mangen (2015), Toljander (2012), McCarthy (2001)
Febrile convulsions to IBS	0.076150	Mangen (2015), Helms (2002), Nielsen (2012)
Febrile convulsions to RA	0.015637	Mangen (2015), Helms (2002), Toljander (2012), Hannu (2002), Bremell (1991)
Mesenteric adenitis to mesenteric adenitis	0.500000	Based on generic GI complication length, Helms (2002), Hospital episode statistics
Mesenteric adenitis to GBS	0.000711	Helms (2002), Mangen (2015), Toljander (2012), McCarthy

Mesenteric adenitis to IBS	0.076150	Mangen (2015), Helms (2002), Nielsen (2012)
Mesenteric adenitis to RA	0.015637	Mangen (2015), Helms (2002), Toljander (2012), Hannu, Bremell (1991)
Septicaemia to septicaemia	0.574349	Helms (2002), Dawan (1986)
Septicaemia to GBS	0.000711	Helms (2002), Mangen (2015), Toljander (2012), McCarthy
Septicaemia to IBS	0.076150	Mangen (2015), Helms (2002), Nielsen (2012)
Septicaemia to RA	0.015637	Mangen (2015), Helms (2002), Toljander (2012), Hannu, Bremell (1991)
GBS to GBS	0.945451	Helms (2002), Rees (1995)
IBS to IBS	0.999976	Agreus et al (2001)
RA to RA	0.912168	Hannu (2002), Bremell (1991)
Death rate, uncomplicated diarrhoea	9.92E-05	Werber, Ruzante (2011), Mangen (2015), Toljander (2012), Scallan (2011)
Death rate, hospitalising diarrhoea	9.92E-05	Werber, Ruzante (2011), Mangen (2015), Toljander (2012), Scallan (2011)
Death rate febrile convulsions	9.92E-05	Werber, Ruzante (2011), Mangen (2015), Toljander (2012), Scallan (2011)
Death rate mesenteric adenitis	9.92E-05	Werber, Ruzante (2011), Mangen (2015), Toljander (2012), Scallan (2011)
Death rate septicaemia	9.92E-05	Werber, Ruzante (2011), Mangen (2015), Toljander (2012), Scallan (2011)
Death rate GBS	0.031930	Mangen (2015), Toljander (2012), Rees (1995)
UK All Cause Mortality	0.001229	ONS Life Tables, 40 year olds (2014)

Clostridium perfringens

Transition Probability	Point Estimate Value	Sources and Assumptions
Healthy to uncomplicated diarrhoea	0.001233058	IID2 (Tam et al 2014)
Uncomplicated diarrhoea to uncomplicated diarrhoea	0.508099691	Williams (1985), Mpamugo (1995), Larson (1988)
Uncomplicated diarrhoea to hospitalising diarrhoea	0.002343041	IID2 (Tam et al 2014)
Uncomplicated diarrhoea to febrile convulsions	0.017512726	Lack of data, see Norovirus
Hospitalising diarrhoea to hospitalising diarrhoea	0.143587294	Batz (2014), Kitterer (2014)
Febrile convulsions to febrile convulsions	2.67276E-51	Assumption, 1 hour
Uncomplicated death rate	2.72657E-05	Mangen (2015), Scallan (2011)
Hospitalising diarrhoea death rate	2.72657E-05	Mangen (2015), Scallan (2011)
Febrile convulsions death Rate	2.72657E-05	Mangen (2015), Scallan (2011)
All cause mortality	0.001229	ONS Life Tables, 40 year olds (2014)

Cryptosporidium parvum

Transition Probabilities	Point Estimate Value	Sources and Assumptions
Healthy to uncomplicated diarrhoea	4.29699E-05	IID2 (Tam et al 2014)
Uncomplicated diarrhoea to uncomplicated diarrhoea	0.62528276	Jokipii (1983), PHLS (1990), Phillips (1992)
Uncomplicated diarrhoea to hospitalising diarrhoea	0.043299739	IID2, HES (2015)
Uncomplicated diarrhoea to febrile convulsions	0.017512726	See Norovirus
Uncomplicated diarrhoea to IBS	0.005102041	Insulander
Hospitalising diarrhoea to hospitalising diarrhoea	0.259814807	Chmelik (1998), HSCIC (2015)
Hospitalising diarrhoea to IBS	0.005102041	Insulander (2013)
Febrile convulsions to febrile convulsions	2.67276E-51	See Norovirus
Febrile convulsions to IBS	0.005102041	Insulander (2013)
IBS to IBS	0.986758694	Agreus (2001)
Uncomplicated diarrhoea death rate	7.00804E-05	Mangen (2015), Scallan (2011)
Hospitalising diarrhoea death rate	7.00804E-05	Mangen (2015), Scallan (2011)
Febrile convulsions death rate	7.00804E-05	Mangen (2015), Scallan (2011)
All cause mortality	0.001229	ONS Life Tables, 40 year olds (2014)

Giardia lamblia

Transition probability	Point Estimate Value	Sources and Assumptions
Healthy to uncomplicated diarrhoea	0.000122062	IID2 (Tam et al 2014)
Uncomplicated diarrhoea to uncomplicated diarrhoea	0.873909358	Jokipii, Ravel
Uncomplicated diarrhoea to hospitalising diarrhoea	0.001754317	IID2 (Tam et al 2014), HES (2015)
Uncomplicated diarrhoea to febrile convulsions	0.002565252	Lack of data, see Norovirus
Uncomplicated diarrhoea to IBS	0.046512024	Hannevik (2009), Hannevik (2014), Rodriguez (1999)
Hospitalising diarrhoea to hospitalising diarrhoea	0.378929142	Cantey (2011), HES (2015)
Hospitalising diarrhoea to IBS	0.186309597	Hannevik (2009), Hannevik (2014), Rodriguez (1999)
Febrile convulsions to febrile convulsions	2.67276E-51	Lack of data, see Norovirus
Febrile convulsions to IBS	0.279359431	Hannevik (2009), Hannevik (2014), Rrodriguez (1999)
IBS to IBS	0.999804414	Agreus (2001)
Uncomplicated diarrhoea death rate	2.8401E-05	Mangen (2015), Scallan (2011)
Hospitalising diarrhoea death rate	2.8401E-05	Mangen (2015), Scallan (2011)
Febrile convulsions death rate	2.8401E-05	Mangen (2015), Scallan (2011)
All cause mortality	0.001229	ONS Life Tables, 40 year olds (2014)

Hepatitis E

Transition Probability	Point Estimate Value	Sources and Assumptions
Healthy to uncomplicated jaundice	4.37036E-06	Ljaz (2014), Mangen (2015) (World Bank used for population)
Uncomplicated jaundice to uncomplicated jaundice	0.629960525	Colson (2008), Bruffaerts (2015), Dalton (2007, 2008), Deroux (2014), Cronin (2011), Sharn
Uncomplicated jaundice to complicated jaundice	0.210674157	Dalton (2007, 2008), Guillois (2016), HSCIC (2015)
Complicated jaundice to complicated jaundice	0.85415108	Aherfi (2014), Bruffaerts (2015), Cheung (2012), Colson (2008), Deroux (2014), Despierre (2011), Cronin (2011), Sharn (2014)
Death rate for uncomplicated jaundice	0.011764706	Mangen (2015), Dalton (2007, 2008)
Death rate for complicated jaundice	0.011764706	Mangen (2015), Dalton (2007, 2008)
All cause mortality	0.001229	Office of National Statistics Life Tables, 40 year olds (2014)

Listeria monocytogenes

Transition Probabilities	Point Estimate Value	Sources and Assumptions
From healthy to flu-like illness	2.83573E-06	IID2 (Tam et al 2014)
From flu-like illness to flu-like illness	0.361992425	Arslan (2015), Berthelot (2012), Dalton (1997), Miettenen (1999)
From flu-like illness to septicaemia	0.302215123	Mangen (2015), Goulet (2008), Koch (2006), Paul (1994), HSCIC (2015)
From septicaemia to septicaemia	0.629069827	Arslan (2015), Berthelot (2012), Aureli (2000), Pelegrin (2014), HSCIC (2015)
From septicaemia to meningitis	0.192752166	Mangen (2015), Goulet (2008), Paul (1994), HSCIC (2015)
From meningitis to meningitis	0.629069827	Lack of data, assumed same as Septicaemia
From flu-like illness to death	0.129390018	Mangen (2015), Werber (2013), Arslan (2015), Lyytikäinen (2006), Paul (1994), Pelegrin (2014), Scallan (2011)
From septicaemia to death	0.129390018	Mangen (2015), Werber (2013), Arslan (2015), Lyytikäinen (2006), Paul (1994), Pelegrin (2014), Scallan (2011)
From meningitis to death	0.129390018	Mangen (2015), Werber (2013), Arslan (2015), Lyytikäinen (2006), Paul (1994), Pelegrin (2014), Scallan (2011)
All cause mortality	0.001229	ONS Life Tables, 40 year olds (2014)

Norovirus

Transition Probability	Point Estimate Value	Sources and assumptions
Healthy to uncomplicated diarrhoea	0.00114829	IID2 (Tam et al 2014)
Uncomplicated diarrhoea to uncomplicated diarrhoea	0.165787465	Shimizu (2012), MMWR Morb Mortal Wkly Rep
Uncomplicated diarrhoea to febrile convulsions	0.014686392	Chen (2009), Chan (2011), NB adjusetd to account for UK population aged 0-9
Uncomplicated diarrhoea to hospitalising diarrhoea	0.004259443	Zanini (2012), CDC (2008), Olesen (2005), IID2 (Tam et al 2014)
Uncomplicated to IBS	0.178979444	Zanini (2012), Nelson (2012)
Hospitalising diarrhoea to hospitalising diarrhoea	0.595704605	Shimizu (2012), Chen (2009), Chan (2011)
Hospitalising diarrhoea to IBS	0.093398318	Zanini (2012), Nelson (2012)
Febrile convulsions to febrile convulsions	2.67276E-51	Assumption, 1 day
Febrile convulsions to IBS	0.209821429	Zanini (2012), Nelson (2012)
IBS to IBS	0.999804414	Agreus (2001)
Death rate uncomplicated diarrhoea	0.000195968	Werber (2013), Mangen (2015)
Death rate hospitalising diarrhoea	0.000195968	Werber (2013), Mangen (2015)
Death rate febrile convulsions	0.000195968	Werber (2013), Mangen (2015)
All cause mortality	0.001229	ONS Life Tables, 40 year olds (2014)

Salmonella

Transition Probability	Point Estimate Value	Sources and assumptions
Healthy to Uncomplicated	0.000513285	From IID2 (Tam et al 2014)
Uncomplicated diarrhoea to uncomplicated diarrhoea	0.359311513	Dworkin (2001), Giraudon (2009), Helms (2006)
Uncomplicated diarrhoea to hospitalising diarrhoea	0.041047459	Kramer (1996), Dworkin (2001), Olesen (2005), Ruzante (2011), Giraudon (2009), IID2 (Tam et al 2014), HSCIC (2015)
Uncomplicated diarrhoea to febrile convulsions	0.011377269	Lack of data, see Norovirus
Uncomplicated diarrhoea to osteomyelitis	0.022948092	Ispahani (2000)
Uncomplicated diarrhoea to septicaemia	0.011568465	Matheson (2010), Helms (2006)
Uncomplicated diarrhoea to IBS	0.035372065	Mangen (2015), Helms (2006)
Uncomplicated diarrhoea to RA	0.005699558	Mangen (2015), Inman (1988), Rudwaleit (2001), Helms (2006)
Hospitalising diarrrhoea to hospitalising diarrhoea	0.41387664	Dave (2015), HSCIC (2015)
Hospitalising diarrhoea to IBS	0.032512234	Mangen (2015), Helms (2006)
Hospitalising diarrhoea to RA	0.005232272	Mangen (2015), Inman (1988), Rudwaleit (2001), Helms (2006)
Febrile convulsions to febrile convulsions	2.67276E-51	See Norovirus
Febrile convulsions to IBS	0.054088205	Mangen (2015), Helms (2006)
Febrile convulsions to RA	0.008786804	Mangen (2015), Inman (1988), Rudwaleit (2001), Helms (2006)
Osteomyelitis to osteomyelitis	0.738413045	Helms (2006)
Osteomyelitis to IBS	0.015286587	Mangen (2015), Helms (2006)
Osteomyelitis to RA	0.002441997	Mangen (2015), Inman (1988), Rudwaleit (2001), Helms (2006)
Septicaemia to septicaemia	0.738413045	Helms (2006)
Septicaemia to IBS	0.015286587	Mangen (2015), Helms (2006)
Septicaemia to RA	0.002441997	Mangen (2015), Inman (1988), Rudwaleit (2001), Helms (2006)
IBS to IBS	0.999804414	Agreus (2001)
RA to RA	0.896291883	Helms (2006), Inman (1988)
Uncomplicated diarrhoea death rate	0.00046833	Mangen (2015), Calvert (2007), Kramer (1996), Werber (2013), Ruzante (2011), Scallan (2011)

Hospitalising diarrhoea death rate	0.00046833	Mangen (2015), Calvert (2007), Kramer (1996), Werber (2013), Ruzante (2011), Scallan (2011)
Febrile convulsions death rate	0.00046833	Mangen (2015), Calvert (2007), Kramer (1996), Werber (2013), Ruzante (2011), Scallan (2011)
Ostemyelitis death rate	0.00046833	Mangen (2015), Calvert (2007), Kramer (1996), Werber (2013), Ruzante (2011), Scallan (2011)
Septicaemia death rate	0.00046833	Mangen (2015), Calvert (2007), Kramer (1996), Werber (2013), Ruzante (2011), Scallan (2011)
All cause mortality	0.001229	ONS Life Tables, 40 year olds (2014)

Shigella spp.

Transition probability	Point Estimate Value	Sources and Assumptions
Health to uncomplicated diarrhoea	1.86387E-05	IID2 (Tam et al 2014)
Uncomplicated diarrhoea to uncomplicated diarrhoea	0.502464018	Givney (1998)
Uncomplicated diarrhoea to hospitalising diarrhoea	0.031019031	Levine (1990), Frost (1995), Papasian (1995), Helms (2006), IID2 (Tam et al 2014), HSCIC (2015)
Uncomplicated diarrhoea to febrile convulsions	0.008924349	No data, see Norovirus
Uncomplicated diarrhoea to osteomyelitis	0.001257447	Helms (2006), Lewis (2009)
Uncomplicated diarrhoea to septicaemia	0.012081616	Helms (2006)
Uncomplicated diarrhoea to IBS	0.002831421	Helms (2006)
Hospitalising diarrhoea to hospitalising diarrhoea	0.531063588	Baka (2013), Helms (2006), HSCIC (2015)
Hospitalising diarrhoea to HUS	0.252352667	Houdoin (2004)
Hospitalising diarrhoea to IBS	0.002677694	Helms (2006)
Febrile convulsions to febrile convulsions	2.67276E-51	No data, see Norovirus
Febrile convulsions to IBS	0.005572755	Helms (2006)
Osteomyelitis to osteomyelitis	0.731224897	Helms (2006), Altman (1994)
Osteomyelitis to IBS	0.001587147	Helms (2006)
Septicaemia to septicaemia	0.430059654	Helms (2006), Beigelm (2002)
Septicaemia to IBS	0.003228583	Helms (2006)

HUS to HUS	0.731224897	Houdoin (2004), Helms (2006) (from diarrheagenic e.coli)
HUS to IBS	0.001591224	Helms (2006)
IBS to IBS	0.999804414	Agreus (2001)
Uncomplicated diarrhoea death Rate	7.64131E-05	Thomas (2015), Scallan (2011)
Hospitalising diarrhoea death rate	7.64131E-05	Thomas (2015), Scallan (2011)
Febrile convulsions death rate	7.64131E-05	Thomas (2015), Scallan (2011)
Osteomyelitis death rate	7.64131E-05	Thomas (2015), Scallan (2011)
Septicaemia death rate	7.64131E-05	Thomas (2015), Scallan (2011)
HUS death rate	7.64131E-05	Thomas (2015), Scallan (2011)
All cause mortality	0.001229	ONS Life Tables (2014), 40 year olds

VTEC O157

Transition Probabilities	Point Estimate Value	Sources and Assumptions
Healthy to uncomplicated diarrhoea	0.000153162	IID2 (Tam et al 2014)
Uncomplicated diarrhoea to uncomplicated diarrhoea	0.323557276	Goh (2002), Aldabe (2011), Byrne (2015), Havelaar (2004), Lee (1997)
Uncomplicated diarrhoea to hospitalising diarrhoea	0.146219897	Herwaldt (1991), Ruzante (2011), Goh (2002), Byrne (2015), Dundas (2001), Launders (2016), Toljander (2012), IID2 (Tam et al 2014)
Hospitalising diarrhoea to hospitalising diarrhoea	0.323557276	Byrne (2015), Havelaar (2004)
Hospitalising diarrhoea to HUS	0.037024071	Herwaldt (1991), Mangen (2015), Goh (2002), Byrne (2015), Dundas (2001), Launders (2016), Rowe (1998), Toljander (2012)
Hospitalising diarrhoea to TTP	0.028638338	Griffin (1991)
HUS to HUS	0.53684001	Aldabe (2011), Delmas (2014), Bowles (2011)
HUS to renal failure	0.067181344	Mangen (2015)
HUS to neurological damage	0.204329484	Dundas (2001)
TTP to TTP	0.53684001	Assumed same as HUS
Renal failure to renal failure	0.974654609	Krogvold (2011)

Neurological damage to neurological damage	0.997033908	Assumption, permanent damage
Uncomplicated diarrhoea death rate	0.000680992	Herwaldt (1991), Mangen (2015), Byrne (2015), Dundas (2001), Launders (2016), Toljander (2012), Scallan (2011)
Hospitalising diarrhoea death rate	0.000680992	Herwaldt (1991), Mangen (2015), Byrne (2015), Dundas (2001), Launders (2016), Toljander (2012), Scallan (2011)
HUS death rate	0.000680992	Herwaldt (1991), Mangen (2015), Byrne (2015), Dundas (2001), Launders (2016), Toljander (2012), Scallan (2011)
TTP death rate	0.000680992	Herwaldt (1991), Mangen (2015), Byrne (2015), Dundas (2001), Launders (2016), Toljander (2012), Scallan (2011)
Renal failure death rate	0.000680992	Herwaldt (1991), Mangen (2015), Byrne (2015), Dundas (2001), Launders (2016), Toljander (2012), Scallan (2011)
Neurological damage death rate	0.000680992	Herwaldt (1991), Mangen (2015), Byrne (2015), Dundas (2001), Launders (2016), Toljander (2012), Scallan (2011)
All cause mortality	0.001229	ONS Life Tables (2014), 40 year olds

Long Term Sequelae

Transition Probability	Point Estimate Value	Sources
GBS to GBS	0.945451367	Vedeler (1997), Dornonville de la Cour (2005), Bersano (2006), Koeppen (2006)
RA recurrence rate	0.275	Nordstrom (1996)
Rate of chronic RA	0.175	Nordstrom (1996)

Utility Values

Symptom	Disutility	Clinical Sources of Symptom or Proxy Symptom	Sources
Flu-like Illness	-0.026	Cancer drug side effect, flu vaccination	Beusterien (2009), Chit (2015), Newall (2013), Chyongchiou (2015), Tarride (2012), Pitman (2013), Lavelle (2012)
Uncomplicated Diarrhoea	-0.092	Cancer drug side effect, gastro-intestinal infection, anti-depressant side effect, osteoarthritis drug side effect, rotavirus vaccination, rotavirus infection	Beusterien (2009), Beusterien (2010), Nafees (2008), Kuchuk (2013), Maniadakis (2013), Wielage, Bakir (2013), Melliez (2008), Peasgood (2010)
Mild Jaundice	-0.109	Hepatitis C, Choleycystitis	Samp (2015), Johner (2013)
Febrile Convulsions	-0.140	Epilepsy, refractory seizures, meningitis B vaccination	Kang (2014), Lee (2013), Helmers (2012), Vera-Llonch (2013), Forbes (2003), Messori (1998), Tu (2014)
Hospitalising Diarrhoea	-0.167	Cancer drug side effects, rotavirus infection	Shiroiwa (2001), Kuchuk (2013), Melliez (2008)
Irritable Bowel Syndrome	-0.181	IBS, coeliac disease	Canavan (2015), Huang (2015), Stamuli (2012), Bracco (2007), Brazier (2006), Porter (2015), Spiegel (2009), Hershcovivi (2010)
Severe Jaundice	-0.246	Hepatitis C	Samp (2015), Stepanova (2014), Hsu (2012), Petta (2014), Saab (2014)
Mesenteric Adenitis	-0.385	Appendicitis	Wu (2015), Wan (2009)
Reactive Arthritis	-0.388	Rheumatoid arthritis, osteoarthritis, reactive arthritis	Ariza-Ariza (2006), Marra (2004), Bruyere (2009), Torrance (2004), Duff (2003)
Thrombotic Thrombocytopenic Purpura	-0.403	Immune thrombocytopenic purpura, myelodysplastic syndrom	Szende (2009), Szende (2010), Sanz (2011)
Neurological Damage	-0.436	Stroke	Pickard (2004), Haacke (2006)
Osteomyelitis	-0.448	Chemotherapy side effect, *Staphylococcus* vaccination, screening for *Staphylococcus*, surveillance for S*taphylococcus*	Stevenson (2014), Song (2012), Lee (2010), Lee (2011)
Guillain-Barré Syndrome	-0.497	C. Difficile prevention, influenza vaccine	Duff (2003), Skedgel (2011), Myers (2011), Prosser (2011)

Renal Failure	-0.587	Diabetes	Huang (2007), Morgan (2006), Lung (2011), Zhang (2012), Coffey (2002)
Septicaemia	-0.606	Cancer complications, bacterial infection, cancer drug side effects, sepsis, *Staphylococcus* vaccination, surveillance for *Staphylococcus*	Peasgood (2010), Westwood, Fowler (2003), Stevenson (2014), McComb (2014), Song (2012), Lee (2010)
Meningitis	-0.827	Influenza vaccination, lyme disease	Gomez (2013), Melegaro (2004), Shadick (2001)
Haemolytic Uremic Syndrome	-0.840	Prevention of foodborne illness, E.Coli 0157	Duff (2003), Batz (2014)

APPENDIX E: INTEGRATE DATA AND VALIDATION OF MTM UTILITY VALUES

The project used patient completed health ratings, during and after an episode of diarrhoea and vomiting (D&V) to validate the utility values used in the Markov Transition Models (MTMs) developed in the project. The data came from the on-going Integrate project (http://www.integrateproject.org.uk/ - HICF-T5-354); a study funded by the Department of Health (DoH) and the Wellcome Trust which samples from the North West of England, an area containing 1/7 of the population.

The data comes from questionnaires completed by patients presenting FBD symptoms with their GP. The patients were recruited into the Integrate study when they present at their GPs with incidents of diarrhoea and vomiting (D&V). As well as providing stool samples which allow, in some cases, for the pathogen causing the illness to be identified, the patients complete a questionnaire initially (survey 1) which includes information about them (demographics) and asks them to rate their health using the EQ-5D-3L. In most cases this will be completed when they are ill[5] (more details below).

Patients are also invited to complete a second questionnaire initially (survey 2) 2-3 weeks later. Questions concern their symptoms, contact with medical services and whether they are still ill or the duration of the illness. They again rate their health using the EQ-5D-3L format. In most cases this will be completed when they are no longer ill (more details below).

These data provide the basis for an analysis of the impact of their illness on self-reported EQ-5D-3L health state, and hence, their Utility. This involves mapping from the EQ5D scores to Utility scores and analysing the impact of the presence of the illness on that Utility.

The Markov Transition Models (MTMs) used within this project estimate QALY burden estimates of FBD for the UK, based on utility scores from literature and experts. Many of the literature derived parameter values are from patients' own assessment of health impacts, but many come from non–UK studies. The contemporaneously reported, UK-based, data from Integrate allows a cross-check with the Utility scores (and hence QALY values) in the MTMs.

E.1 Summary statistics

The Integrate data set was extracted on 7/11/2016 with the data collected between September 2015 and October 2016. It contained 384 observations, not all of which were complete, or suitable for analysis. 321 respondents (patients) completed EQ5D scores for Survey 1, and 340 patients completed EQ5D scores for Survey 2. 308 completed both survey 1 and 2.

[5] For our purposes 'ill' refers to the presence of symptoms related to the diarrhoeal illness which caused them to be recruited into the study.

A core sample of 280 was retained after children and people with missing data were excluded. 88% were ill at the point of completing the first survey (ills1=1), and 31% (87 out of 280 respondents) were still ill at the second survey (which is carried out 2-3 weeks later). A relatively small number (2%) were not ill at survey 1 but were so at survey 2 (i.e. 6 of out of 280 respondents).

Table E.1: Respondent or carer (n=280)

	Ill at survey 2		
Ill at survey 1		No	Yes
	No	27	6
	Yes	160	87

Respondents reported in the Survey 1 the symptoms experienced during the illness. Only a few (5/280) did not report diarrhoea, 19% reported having experienced vomiting and 9% had had blood in their stools.

The number of people reporting each of these symptoms in Survey 1 is shown in Table E.2.

Table E.2: Reported symptoms of illness (n=280)

	N	%
Diarrhoea	275	98.2
Blood in stools	25	8.9
Vomiting	54	19.3

There was some data on patients' contact with medical services (e.g. GP, hospitals). These are reported as the number of contacts for each category. There are significant numbers of missing values for these variables. Categorical variables are also created for they attended A&E or hospital or not (0/1). These categorical variables are be used in analysis below.

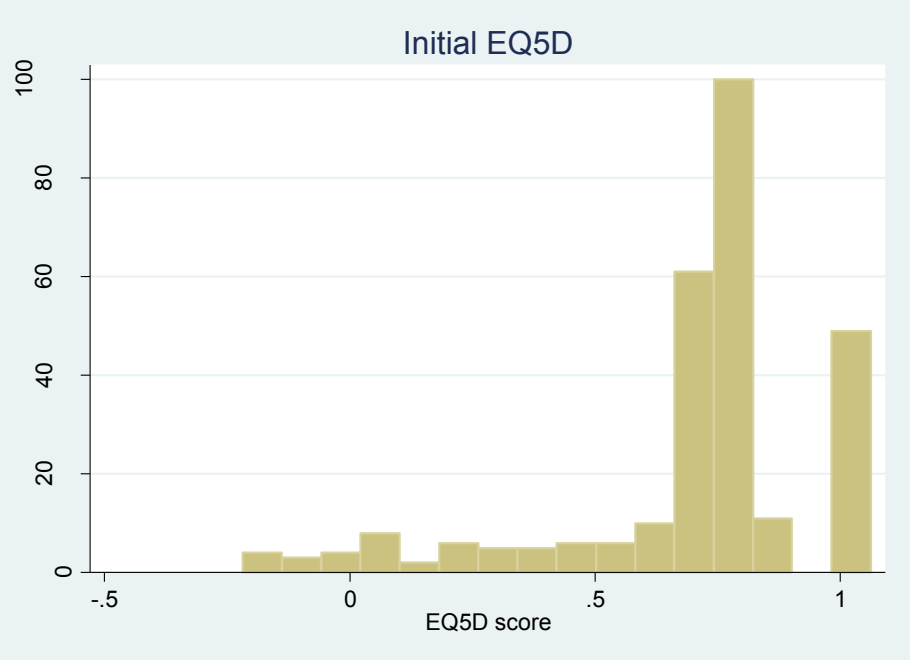
Table E.3: Descriptive Statistics - contact with medical services

	n	mean	st.dev	min	max
N°. of visits or phone calls to GPs	278	1.759	1.326	0	10
N°. of consultations GP out of hours surgery	257	0.093	0.374	0	3
N°. of GP visits at home	255	0.054	0.315	0	3
N°. of times speaking with GP on phone	265	0.777	1.016	0	7
N°. of times attending A&E	257	0.101	0.683	0	10
N°. of nights staying in hospital	257	0.221	1.417	0	13
N°. of visits to NHS walk-in-centre	256	0.043	0.269	0	3
N°. of consultations with community pharmacist	259	0.185	0.547	0	3
N°. of times dialled 999	256	0.043	0.479	0	7
N°. of times dialled 111	256	0.070	0.324	0	3
N°. of times requiring home care	254	0.004	0.063	0	1
Have *any* attendance at A&E (0/1)	257	0.054	0.227	0	1
Have *any* nights in hospital (0/1)	257	0.031	0.174	0	1

Note: Not all respondents completed these question: non-completion was treated as missing, rather than a zero.

Respondents reported their current health status using the EQ-5D-3L framework. These are converted to a Utility Score using the Great Britain tariff, as programmed within the Stata *eq5d* command (Ramos-Goñi, J.M. and O. Rivero-Ariaseq 2011). Figure 1 is a histogram of Utility Scores from Survey 1. Only 17% report have a score of 1 (scoring 1 on all 5 dimensions of health), whereas in a general sample of the population this would be closer to 55% (Feng, Y., Devlin, N. and Herdman, M., 2015).

Figure E.1: Histogram of EQ5D scores, Survey 1. N=280



In Survey 2 (see Figure E.2), the EQ5D has a higher proportion at full health (48%). Of those who report that they no longer have symptoms, 60% have an EQ5D score of 11111.

It is possible to scatter the two EQ5D scores against each other (Figure E.3). One would anticipate that most respondents would lie below the 45^0 line, ie that their status improved over the period. This is largely true, and it is notable the large number who shifted from <1 to 1 (full health).

Those who still had symptoms at the second survey are marked with a circle, and it is notable that this group makes up the majority of respondents who lie above the line, ie who report a worse state at the second survey.

One can summarise the EQ5D scores by status in the two surveys as presented in Table E.4.

Figure E.2: Histogram of EQ5D scores, Survey 2. N=280

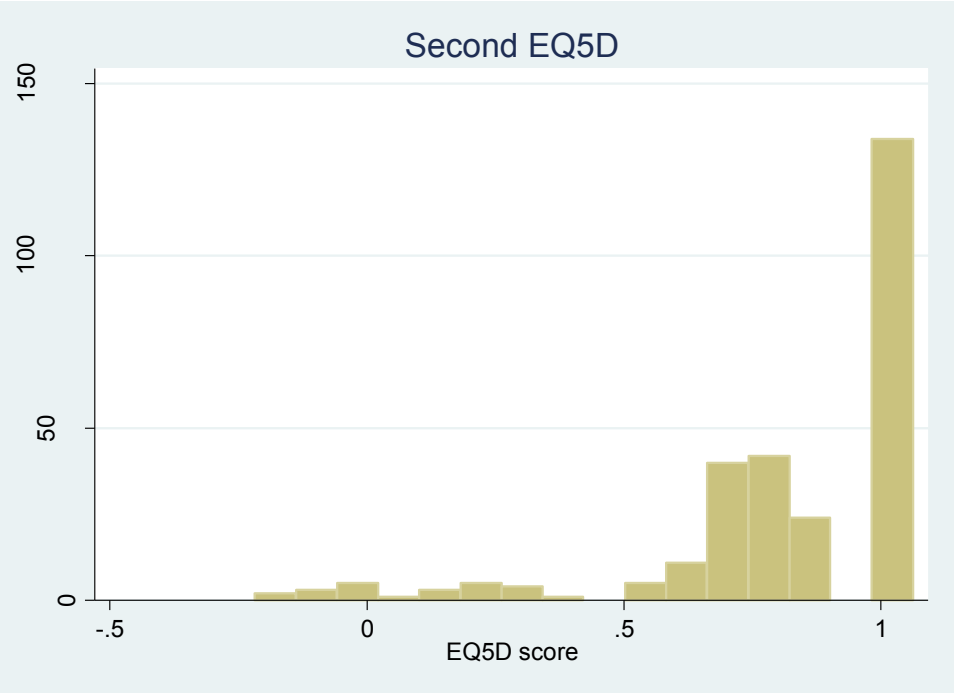


Figure E.3: Scatter plot of EQ5D scores across two survey points (jitter applied). N=280

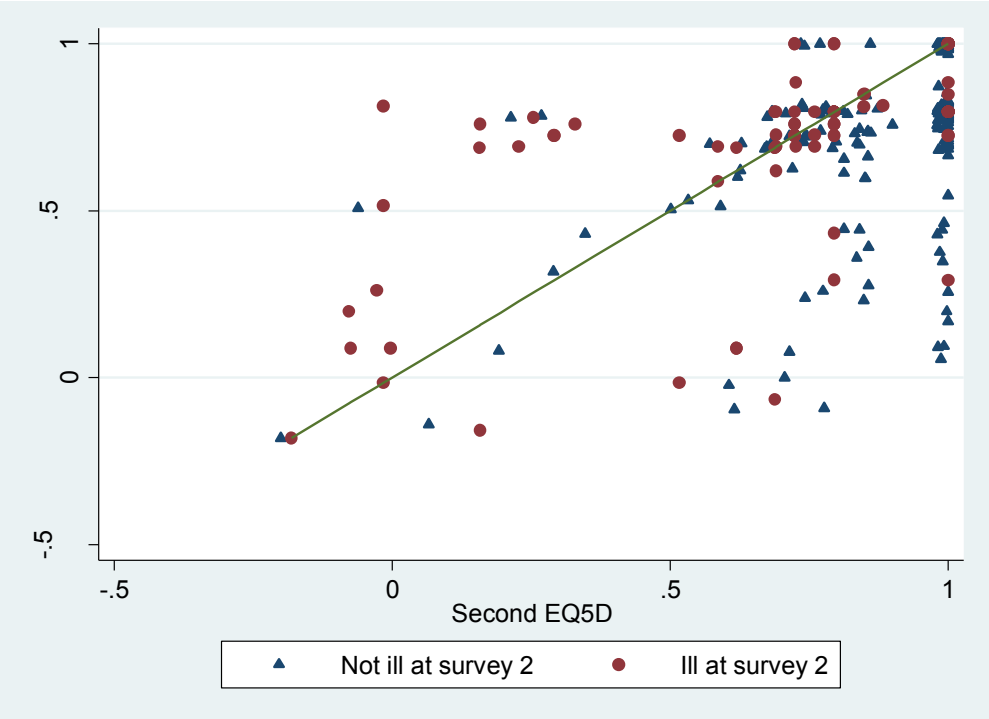


Table E.4: Change in EQ5D utility score (Survey 1-Survey 2)

	n	Mean	Std.dev
All sample	280	-0.109	0.260
Ill in Survey 1, well in survey 2	160	-0.183	0.249
Ill in Survey 1, ill in survey 2	87	0.001	0.256

The aggregate decrement is 0.1 across all, 0.18 for those that are ill in survey 1 but get better. And zero for those who were ill in both. What is notable is the wide range of values, including some whose scores improved. But this does not take account of other conditions which might affect self-reported health.

E.2 Modelling utility scores

To control for this, we conduct a simple statistical analysis: estimating a double bounded Tobit model. Because of definition of EQ5D there is an upper limit of 1, and a gap between that and the next lowest value (0.883). Here we use a Tobit model and define it as having an upper limit for any value >= 0.884, to overcome the issue of modelling the gap. A lower limit of -0.594 is applied (generated if an EQ5D assessment of 33333 is given) although no one in the sample reports this value.

We assume that the primary explanation of the underlying EQ5D utility score in survey 1 will be the respondents 'normal' EQ5D score, which we assume is recorded in the second survey. The illness then causes deviations from that 'normal' level. We expect that respondents who are well at the time of the first survey to not deviate from the score in the second survey (as they are required to describe their illness on the day of the survey, not recall their state during illness).

We include an interaction for whether they are currently ill and have blood in stools (we would expect that it is only significant for those who are ill at time of survey). We also include a number of interactions based on the two illness states:

- ill at the first survey, but well at the second (which we expect to generate the maximal effect);
- well at the first survey and well at the second (which we would expect to see generate no impact);
- ill at the second but not at the first (where one may expect to see the EQ5D score in survey 1 to be higher than that in survey 2).

We estimate two models, one using alternative indicators of a severe case: A. blood in stools (Table E.5) and B. attendance at A&E (Table E.6). Demographic and other symptom variables such as vomiting, gender, age etc were included in the model but were not significant.

Table E.5: Tobit Model - Survey1 EQ5D Scores, using 'blood in stools' as indicator of severity – N= 280

eq5d1	Coef.	Std. Err.	t	P>t	[95% Conf. Interval]	
EQ5D Survey2	0.570	0.060	9.56	0	0.452	0.687
Not ill Survey1:blood	0.177	0.207	0.85	0.394	-0.231	0.584
Ill Survey1: blood	-0.088	0.052	-1.68	0.093	-0.190	0.015
Ill Survey1: not ill Survey2	-0.174	0.055	-3.15	0.002	-0.283	-0.066
Ill Survey1: ill Survey 2	-0.060	0.059	-1.01	0.315	-0.177	0.057
Not ill Survey1: ill Survey2	-0.111	0.118	-0.94	0.347	-0.344	0.121
_cons	0.378	0.074	5.1	0	0.232	0.523
/sigma	0.233	0.011			0.212	0.255
Log likelihood = -29.647383						

0 left-censored observations; 231 uncensored observations; 49 right-censored observations at eq5d1 >= .884

As expected:

- There is a strong relationship between the EQ5D score reported in the second survey, and the first: this will account for any individual specific idiosyncrasies in health state.
- The impact of blood in stools causes a reduction in score only for those who are ill at the time of the first survey: -0.088 (although only marginally significant).
- Those who are ill at the first survey but well at the second show a significant deviation from their second survey EQ5D score: a coefficient of -0.174.
- Those who were ill at both survey dates, or who were will at the second but not the first, show no additional impact (NB the base line case are those who are not ill at either survey).

The raw parameters reported above cannot be taken as the impact of being ill, as the Tobit model is non-linear, with censoring, and this influences the expected value of a respondent's utility scores.

There are a variety of marginal effects that can be estimated: we report the marginal effects on the expected value of the censored outcome (i.e. accounting for the censoring in the Tobit model). These marginal effects vary according to the point in the distribution they are measured at: conditioning on points close to the censoring points reduces the marginal effect. We report values conditioned at a value of EQ5D=1 in the second survey.

The estimated reduction in EQ5D utility score from being ill (with no further complications) is -0.11 (Std.err=0.03), while the additional effect of having blood in stools is -0.053 (Std.err=0.03). The second model uses whether the respondent presented to A&E as an indication of severity. This leads to some reduction in sample due to missing values, but the estimated effect is more significant than for blood in stools (the two are correlated and cannot be included in the same model).

As all who reported attending A&E were still ill at the time of the first survey, there are no interaction effects on this variable. Other effects are very similar.

Table E.6: Tobit Model - Survey1 EQ5D Scores, using A&E attendance as indicator of severity N= 257

eq5d1	Coef.	Std. Err.	t	P>t	[95% Conf. Interval]	
EQ5D Survey2	0.568	0.061	9.33	0	0.448	0.687
Attend A&E	-0.135	0.065	-2.07	0.04	-0.263	-0.006
Ill Survey1: not ill Survey2	-0.193	0.056	-3.44	0.001	-0.303	-0.082
Ill Survey1: ill Survey 2	-0.065	0.060	-1.08	0.282	-0.183	0.053
Not ill Survey1: ill Survey2	-0.132	0.119	-1.11	0.268	-0.366	0.102
_cons	0.391	0.075	5.22	0	0.244	0.538
/sigma	0.231	0.011			0.208	0.254
Log likelihood = 25.160443						

0 left-censored observations; 212 uncensored observations; 45 right-censored observations at eq5d1 >= .884

Calculating the marginal effects, as above gives estimates of -0.12 (Std.err=0.03) and -0.08 (Std err. =0.04), suggesting that the A&E presentation represents a more significant illness state than reporting 'blood in stools'.

E.3 Comparison with Markov Transition models

We find significant effects of being ill on respondent's EQ5D Utility Scores, controlling for individual level effects. There is no effect of demographics (age, gender) on those illness-utility impacts. Vomiting does not generate additional utility decrements over and above that of the baseline condition of diarrhoea. The presence of blood in the patient's stools does have a significant impact on utility, as does them having attended A&E. Of these 2 definitions of more serious cases, attendance at A&E fits better with the MTMs which use hospital attendance to delineate uncomplicated D&V from more serious illness.

As reported in the Introduction, the Markov Transition Models used within this project estimate QALY burdens, based on utility scores from literature and experts with the former comprising studies from around the world.

The analysis reported here using Integrate project data provides a UK cross check with the Utility scores (and hence QALY values) in the Markov Transition Models. Table 7 compares the estimated Integrate utility impacts with the estimates in the MTMs.

Table E. 7: Comparison of EQ5D Utility Impacts between Tobit Models estimated on Integrate study data and MTM parameterised in this study

	MTM	Integrate Data Models	
		Model A "Blood in stools" as indicator of severe case	**Model B "A&E" as indicator of severe case**
Mild	-0.092 (0.057)	-0.105 (0.033)	-0.117 (0.030)
Additional Severity		-0.053 (0.032)	-0.081 (0.040)
Severe	-0.167 (0.079)	***-0.158***	***-0.198***

st. errors reported in parentheses

The utility decrements based on Tobit models estimated on Integrate data for mild and severe diarrhoeal illness are close to those values being used in the MTMs developed in the project, which are derived from many, international, studies.

APPENDIX F: WTP SURVEY: FOCUS GROUPS, COGNITIVE INTERVIEWS AND EXAMPLES OF VALUATION QUESTIONS – ADULT & CHILD ILLNESS, SHORT & LONG TERM

F.1 Focus Groups

This section summarises the key elements of and findings from the focus groups. Focus groups are semi-structured discussion groups led by a moderator in which participants are presented with cues and prompts about the topic of interest. The main aim of the focus groups, in this case, was to help ensure that the proposed wording of the key parts of the main survey instrument was clear to participants. They were also an opportunity to test how participants could be encouraged to think about pain, grief and suffering in isolation of the other attributes FBDsuch as loss of income, cost of alternative child care, and so on.

Group details	Focus Groups 1 & 2	Focus Groups 3 & 4	Focus Groups 5 & 6
City	Manchester	London	Cardiff
Date	11 May 2016	17 May 2016	24 May 2016
Time	5.30pm-7.30pm and 7.45pm-9.45pm	5.30pm-7.30pm and 7.45pm-9.45pm	5.30pm-7.30pm and 7.45pm-9.45pm
Viewers	Dan Rigby and Michael Burton from University of Manchester	Michael Burton from University of Manchester, Ece Ozdemiroglu from eftec and Nicholas Daniel and Alice John from the FSA	None

In each location, the first group was with adults to discuss FBD risk to their own health, and the second group was with adults to discuss FBD risk to their children (not babies). Six groups were deemed to be sufficient, and this was evidenced as new learning started to decline.

Focus group participants were selected to achieve a mix of both socio-economic groups and answers to the following questions:

1. Have you or any member of your family or close friends been employed in any of the following roles?
2. Note gender
3. What was your age at your last birthday?
4. Do you have any children?
5. Can you tell me how many children you have in each of the following age groups? Pl*ease note that the parent group in particular need to be made aware that there may be some sensitive materials shown and sensitive discussions about the impact of these diseases on children*

6. Which of the following best describes your ethnic background?

Potential participants were also asked how many focus groups they had previously participated in, and when they had last participated in a focus group. Participants were selected amongst the group with low (1-3 groups) and past participation (more than 6 months ago).

On the whole the six groups covered a fair combination of the possibilities, and socio-economic and age groups were kept together to ensure that each group was harmonious in these respects.

The recruitment of participants, moderation of the groups, video and voice recording, and subsequent transcription of the group discussions were undertaken by Facts UK.

The adults–own risk and adults–parents groups followed the same protocol. The only difference was that risks to adults were described in the former, and risks to children (participants' own children) were described in the latter.

The protocols on all six groups followed the same structure, but the wording and focus on specific issues were tested then changed after each pair: the learning in each pair was reflected in the next protocol.

All the focus groups tested both understanding of short term mild cases versus long term more serious cases, and WTPfor risks to their own health and to the health of their children.

The focus groups started with the moderator explaining the topic and purpose of the research. It was made particularly clear that the research was for the FSA and not for a private medical or pharmaceutical company. Participants were also reassured that there were no right or wrong answers and that their responses would help the research team to improve the questionnaire for a national survey. Finally, participants were told that the groups would be audio and video recorded, and in the case of Manchester and London, also viewed. However, confidentiality was guaranteed, therefore the transcripts are included in the Annexes to this report but the video recordings are not.

The first section of the protocol covered what is involved in **food poisoning**. The purpose was to warm up the participants and help them recall and share their experience and knowledge about food poisoning. The moderator was instructed to prompt if the discussion did not progress or an important aspect that expected someone to mention was not mentioned.

The second section of the protocol involved testing the concept and wording of **vignettes**. Vignettes listed descriptions of a series of different symptoms of food poisoning, including whether the person would feel the need to visit a doctor. The discussion about whether the wording was clear was followed by a few willingness to pay (WTP) questions. Again, testing to ensure questions were clear to the participants was more important than their actual answers. A dichotomous contingent valuation approach was used, whereby participants answered on their

own (on paper) whether they would be willing to pay £x, if yes, they were directed to a WTP question with double £x; if no, they were directed to an amount half £x. They were also asked what their maximum WTP was.

While answering both WTP questions, participants were encouraged to think about precisely what they were being asked to pay: pain, grief and suffering. They were asked not to think about their loss earnings, cost of alternative child care and so on.

The next section of the protocol used the EQ5D scale to describe the health state of the participant and also similar wording was used to describe the health state with food poisoning. In this approach we asked respondents to make choices which allow direct valuation of generic EQ-5D states (for appropriate durations) and then use those value components to construct the value of particular pathogen/severity states as required.

In the next section of the protocol, participants were told about some likely long term symptoms or illnesses from food poisoning. Once the clarity of these descriptions was established, they were then asked to respond to a dichotomous contingent valuation question about these illnesses. Again both vignettes and EQ5D presentations were tested.

Key Findings

Participants in all six groups had previously experienced varying degrees of food poisoning. They were much less aware of the more serious sequelae of FBD.

What was being asked was also clear: trading off money vs. a case of food poisoning with described symptoms, or trading off money (and life years) vs. a case of food poisoning and sequelae. Even those who could not decide on the amount they would be willing to pay were clear what they were being asked about. Even in the parents groups, risks to children's health could be discussed, and trade-off could be made – in particular participants had different reactions to short term mild cases vs. long term serious symptoms.

On the whole participants found the vignette approach more intuitive. EQ5D were found to be too general. The exercise of taking participants through an EQ5D survey before asking their WTP to avoid an option described using EQ5D was also confusing, partly because EQ5D asks about how the participant feels on that day, whereas WTP is asked about a hypothetical time. Participants found it particularly difficult to link EQ5D to food poisoning when considering short term and mild cases.

Mentioning the names of pathogens did not make a difference to participants' consideration of health impacts.

The likelihood of the presence of the following biases in responses were tested through the focus groups:

- **Hypothetical bias** – when respondents do not take the trade-off questionnaire seriously

Participants were sufficiently aware of FBD– for ease of identification called 'food poisoning' during the group discussions and materials. The task of trading off money and symptoms was clear and participants engaged in this trade off.

They were also observed to engage in the exercise realistically. Even in the parents groups, although the discussion started with paying anything for the health of their child, it then moved on to considering the severity of the illness and WTP for mild illnesses was lower than that for severe illnesses.

How the different symptoms of FBD could be linked to EQ5D was less clear. But the task of expressing willingness to pay to avoid FBD was clear. EQ5D scores for risks to children's health was also found confusing as it had severe symptoms like difficulty washing and getting dressed etc.

In some groups, participants were offered a pill to make the symptoms to go away. There was a lot of discussion about what this pill would contain, any side effects, how and when and from where it could be obtained. Therefore, it added to the hypothetical nature of the valuation scenario and it was removed from the questionnaire.

Finally, the 'cheap talk' presented to the group participants seem to have worked reminding them that there are other risks to protect from and limited funds. The maximum WTP (open ended) question did not result in unrealistically high numbers.

- **Protest responses** – when respondents give an answer that does not reflect their true preference (e.g. zero, no WTP response to protest being asked to trade off not because they do not value what they are being asked to trade off).

At the start of focus groups protocols, the trade-off context was set as for the policy analysis of the FSA, and not for a private medical or pharmaceutical company. This seemed to make the context less prone to protest answers.

Participants were, on the whole, not familiar with the more severe illnesses that could be caused by food poisoning. They were reassured that the information provided was real. The main questionnaire needs to be clear that such severe cases could occur, even if they are unlikely.

- **Embedding (part-whole bias)** – this part of the discussion tested whether participants could isolate, and focus on, pain and suffering associated with FBD.

The participants were able to identify other impacts of FBD like loss of income, work days lost, medical expenses, extra childcare expenses and so on. Once these were identified, they could think of pain and suffering in isolation. In the parents groups, participants mentioned that there is also cost and stress to them from anxiety and worry, but also sleepless nights and so on.

F.2 Cognitive Interviews

This section presents the main findings from the cognitive testing interviews carried out from 29 June – 1 July 2016 as part of the design phase for the main valuation questionnaires. The cognitive testing interviews were conducted on a sample of ten: five adults considering risks to their own health and five adults considering (as parents) risks to the health of their child. The draft questionnaire was administered to respondents in a Computer Assisted Personal Interview (CAPI) and this was then followed by a separate set of debriefing questions. The debriefing permits the testing of a number of issues concerning the design of the questionnaire, including respondent comprehension and retrieval of information (eg questions and other survey materials, such as showcards) and respondent decision processes (eg mental effort, motivations behind choices, truth telling). Cognitive interviews are therefore highly useful in evaluating the validity of questionnaires, especially when the questions and issues presented to respondents are complex.

The debriefing questions and summary of responses are provided below. Text to be read out loud is in bold. Some questions are worded differently depending on the version of the questionnaire.

DQ0. *Please record any observations you have made during the CAPI part of the interview, such as any signs of difficulty, hesitation, speeding up (not reading) responds showed. If possible record where in the questionnaire you observed such signs.*

Please also record any questions the respondent asked you during the CAPI part of the interviews. Please answer ***"The researchers would like you to answer the questions as best you as without further information or clarification at this stage. So please continue and we can discuss the details after you completed the survey"***

- Most respondents had little difficulty with the questionnaire overall. A couple of respondents (2/10) asked about the frequency of the payments, or whether they were one-off payments.

I now want to ask you about the questions you have just answered and what you thought of them. There are no right or wrong answers and your responses will be used to help us improve the survey.

DQ1. First, please could you tell me in your own words what you were asked to do in this questionnaire?

- Nearly all respondents (8/10) understood that they were being asked to make a trade-off between "different amounts of money" and avoiding illness as described in "different scenarios". Two respondents seemed to interpret the purpose of the exercise as being to "put a value on preventative measures" and "potential treatment costs for myself and my child". The purpose behind the survey will be made more explicit in further iterations of the CAPI survey.

DQ2. The main part of the survey asked you about food poisoning and its impacts on health. How clear / unclear were the descriptions?

- Most respondents (8/10) found the survey clear and "straightforward". Two respondents explained that the long-term illness descriptions were more difficult to understand.

DQ3. Did you think, on the whole, the description of the health impacts was realistic or not?

NOTE TO INTERVIEWER: Here we mean the symptoms (common to both Vignette and EQ5D versions of the questionnaire): both short term like vomiting, diarrhoea and long term like the GBS, IBS, reactive arthritis, chronic renal failure, meningitis, septicaemia.

PROBE: for both short term and long term symptoms. Refer to the relevant pages where necessary. Please note if reminding the symptoms has been necessary.

- Most respondents (7/10) found the descriptions realistic. Three respondents commented that health issues are not as "cut and dry" as the descriptions suggest. One respondent suggested that the idea that a person would return to their current state of health after a long-term illness was unrealistic.

DQ4. ADULT VERSION When making choices, did you think you could possibly suffer the symptoms described? In other words, did you think "this could happen to me"?

DQ4. PARENT VERSION When making choices, did you think your child could possibly suffer the symptoms described? In other words, did you think "this could happen to him or her"?

NOTE TO INTERVIEWER: Here we mean the symptoms (common to both Vignette and EQ5D versions of the questionnaire): both short term like vomiting, diarrhoea and long term like the GBS, IBS, reactive arthritis, chronic renal failure, meningitis, septicaemia.

PROBE: for both short term and long term symptoms

- Nearly all (9/10) respondents reported that the symptoms described could happen to them.

DQ5. What did you think you were being asked to pay for?

NOTE TO INTERVIEWER: They should have mentioned this in DQ1 but still ask them to repeat. PROBE: Did you think about how paying this amount would avoid the food poisoning? Did you think about to whom you'd pay and so on?

- Most respondents understood that they were being asked to avoid pain and suffering as described in the scenarios presented. Some respondents thought about the question more generally, while others thought more specifically about what they were paying for such as "drugs" or "immunisation".

DQ6. Did you think this was a one-off payment or an annual payment?

- Nearly all respondents (9/10) thought the payment was a one-off payment, although a few respondents (3/10) commented that they found this confusing and couldn't be certain. The payment frequency will be addressed more explicitly in further iterations of the CAPI questionnaires.

DQ7. When did you think you would make this payment? Now or in the future? If future when?

- Most respondents (8/10) thought that they would make the payment now or "immediately". One respondent was unsure and another thought the payment would be "in the future, after the remedy".

DQ8. Did you state the £ payment on your behalf or on behalf of your household?

- Most respondents (6/10) stated the payment on their behalf.

DQ9. How do you think other people like you would answer these questions about paying to avoid the health impacts of food poisoning?

- Most respondents (7/10) indicated that they believed other people like them would answer in a similar way.

DQ10. ADULTS VERSION

When making choices about paying to avoid the health impacts of food poisoning, did you also consider how much it would cost you to take sick leave; to pay for extra child care and for the medical expenses?

DQ10. PARENTS VERSION

When we asked you about your child having food poisoning, did you think you'd also be ill at the same time or did you think you'd be healthy? Did you include the possibility that you may need to take time off work to look after your child into account?

PROBE if the answer is no: We did not want you to think about these. We wanted you to focus only on the 'pain and suffering'. What was it that made this clear to you?

PROBE if the answer is yes: We did not want you to think about these. We wanted you to focus only on the 'pain and suffering'. How could we have made this clearer?

- Three of the 'adult version' respondents did not think about taking time off from work while the other two are retired and so this question was not applicable. Most of the parent respondents (4/5) indicated that they did not think they would be ill and that they did not include time off work in their decisions.

DQ11. FOR ADULT_EQ5D VERSION ONLY: What did you think about the questions about your current general health state?

DQ11. FOR PARENT EQ5D VERSION ONLY: What did you think about the questions about your child's current general health state?

NOTE TO INTERVIEWER: This is the set of questions about 'walking about, self-care, usual activities, pain / discomfort, anxiety / depression'. This is the page that that starts with the 'EQ5D explain' box.

PROBE: How easy / difficult / specific / general?

- Most respondents (8/10) found the questions "general" and "straightforward".

DQ12. FOR EQ5D VERSION ONLY: How relevant did you think these questions were in general? How relevant did you think they were in relation to food poisoning?

- Most respondents (6/10) thought the questions were relevant while four respondents did not answer the question.

DQ13. VIGNETTES VERSION:

When making choices about the <u>short term illnesses</u> that can be caused because of food poisoning, could you give a short description of the thought processes that you used to make the decision?

PROBE: See if all types of information are mentioned, if not probe to make sure we know what they thought of all the following (even if they did not consider them). Description of the symptoms? Number of days? Number of days spent in bed? Whether you felt the need to visit the GP or not? The amount of money you were being asked to pay?

Parents should answer about the choices they made thinking of their child.

DQ13. EQ5D VERSION:

Did you recognise that what was being shown as 'current' health was the answers you had given earlier to the health rating question?

Parents should answer about the choices they made thinking of their child.

- Only three vignette version respondents provided adequate answers to this question, of which two thought about the short term illness in terms of "how long they could cope with those symptoms", and the remaining respondent's thought process was based on "on available medication like ibuprofen. How much would I pay to have a cure all, my own money circumstances came into it". Only three EQ5D respondents answered this question, two

recognising that their 'current' health was based on their answers to health questions, while one did not know.

DQ14. How certain are you of the choices you made about the short term health impacts of food poisoning?

1: Very certain, 2: Certain, 3: Not sure, 4: Uncertain, 5: Very uncertain

- Most respondents (6/10) were 'certain' about their choices, one respondent was 'very certain', one respondent was 'uncertain', one respondent was 'not sure' and one respondent answered that they "did not know".

DQ15. VIGNETTES VERSION

When making choices about the long term illnesses that can be caused because of food poisoning, could you give a short description of the thought processes that you used to make the decision?
PROBE: See if all types of information are mentioned, if not probe to make sure we know what they thought of all the of following (even if they did not consider them) Description of the symptoms? Number of days? Number of days spent in bed? Whether you felt the need to visit the GP or not? The cost to avoid the illness? Parents should answer about the choices they made thinking of their child.

- Two vignette version respondents described the thought process as being "quick" and "obvious". The other three respondents mentioned the "impact on external family members", "work and living standards", and "education" as being part of their thought process.

DQ16. EQ5D VERSION

When making choices about the long term illnesses that can be caused because of food poisoning, could you give a short description of the thought processes that you used to make the decision?
PROBE: See if all types of information are mentioned, if not probe to make sure we know what they thought of all the following (even if they did not consider them) descriptions of the health state (walking about, self-care, usual activities, pain or discomfort, anxiety or depression)? The number of months / years you'd have the illness? The number of years you will have current health state in Life A (with illness)? The number of years you will have current health state in Life B (without illness)? The average yearly income until death in Life A? The average yearly income until death in Life B?
Show a copy of the DECLongIntro page
Parents should answer about the choices they made thinking of their child.

- The five EQ5D respondents listed "length of time" and "severity" of illness as being weighted against the cost. One respondent also mentioned a prior illness and not wanting "to have long term illness for any considerable period of time". Another respondent highlighted that "if you are in pain (your child) no amount of time would be relevant you would want to prevent it".

DQ17. How certain are you of the choices you made about <u>the long term</u> illnesses that can be caused because of food poisoning?

1: Very certain, 2: Certain, 3: Not sure, 4: Uncertain, 5: Very uncertain

- Of the eight responses to this question, most (5/8) were certain about their choices, while two were not sure and one was uncertain.

DQ18. If you said yes to at least one £ amount in the many choices you made, what were the main reasons for doing this? Why were you willing to pay to the amount(s) given?

PROBE: please get them to say as many reasons as possible and record all verbatim.

- Most adult respondents answered that they were willing to pay certain amounts because it was worth not experiencing the pain or symptoms described. All parent respondents (5/10) indicated payment was worth it to avoid their child from being in any pain.

DQ19. Overall, would you say that you were presented with enough information to make the choices you were asked to make?

PROBE: Was there too much to take in? Was it relevant? Was anything missing? Was it too detailed? Not detailed enough?

- Nearly all respondents (9/10) reported that they were presented with enough information to make the choices, while one respondent thought there was too much information given.

DQ20. Were there any other issues that influenced your any of your answers to the survey in any way at all?

- Of the five respondents that answered this question, three responded that their income and "ability to pay" influenced their choices, with the remaining two respondents answering "the fact I have already paid into NHS my working life" and "the amount of days ill and the amount of days that you would be healthy for" respectively.

<u>INTERVIEWER DEBRIEFING:</u> *Any other observations / suggestions you wish to share with us?*

- Of the three interviewers who answered, one noted that the questionnaire "worked quite well" was "challenging" and "not obvious, which not good". Another answered that "health is not black and white" while the remaining interviewer found the exercise "interesting".

F.3 Examples of Valuation Questions – adult & child illness, short & long term

Figure F.1: Example of an adult illness short term choice question

Imagine that you experience the illness caused by food poisoning shown in Option A below.

After the illness you will return to your current state of health, as you reported in the earlier form.

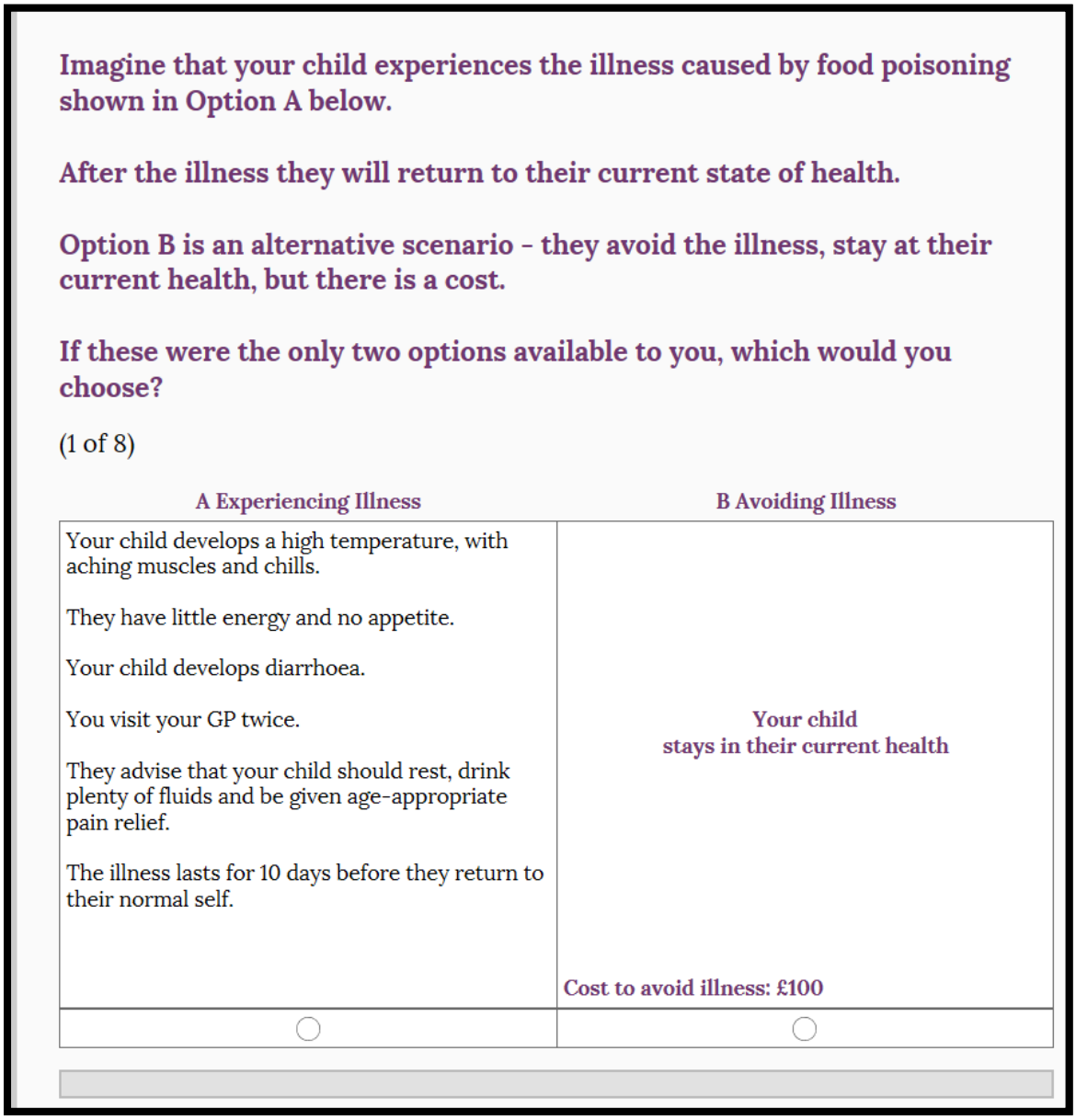
Option B is an alternative scenario - you avoid the illness, stay at your current health, but there is a cost.

If these were the only two options available to you, which would you choose?

(2 of 8)

A Experiencing Illness	B Avoiding Illness
You develop a high temperature, with aching muscles and chills. You have little energy and no appetite. You develop diarrhoea and vomiting and strong stomach cramps. You visit your GP twice, who tells you to rest, drink plenty of fluids and take paracetamol. The illness lasts for 7 days before you return to your normal self.	Staying in your current health Cost to avoid illness: £150
○	○

Figure F.2: Example of a child illness short term choice question



Imagine that your child experiences the illness caused by food poisoning shown in Option A below.

After the illness they will return to their current state of health.

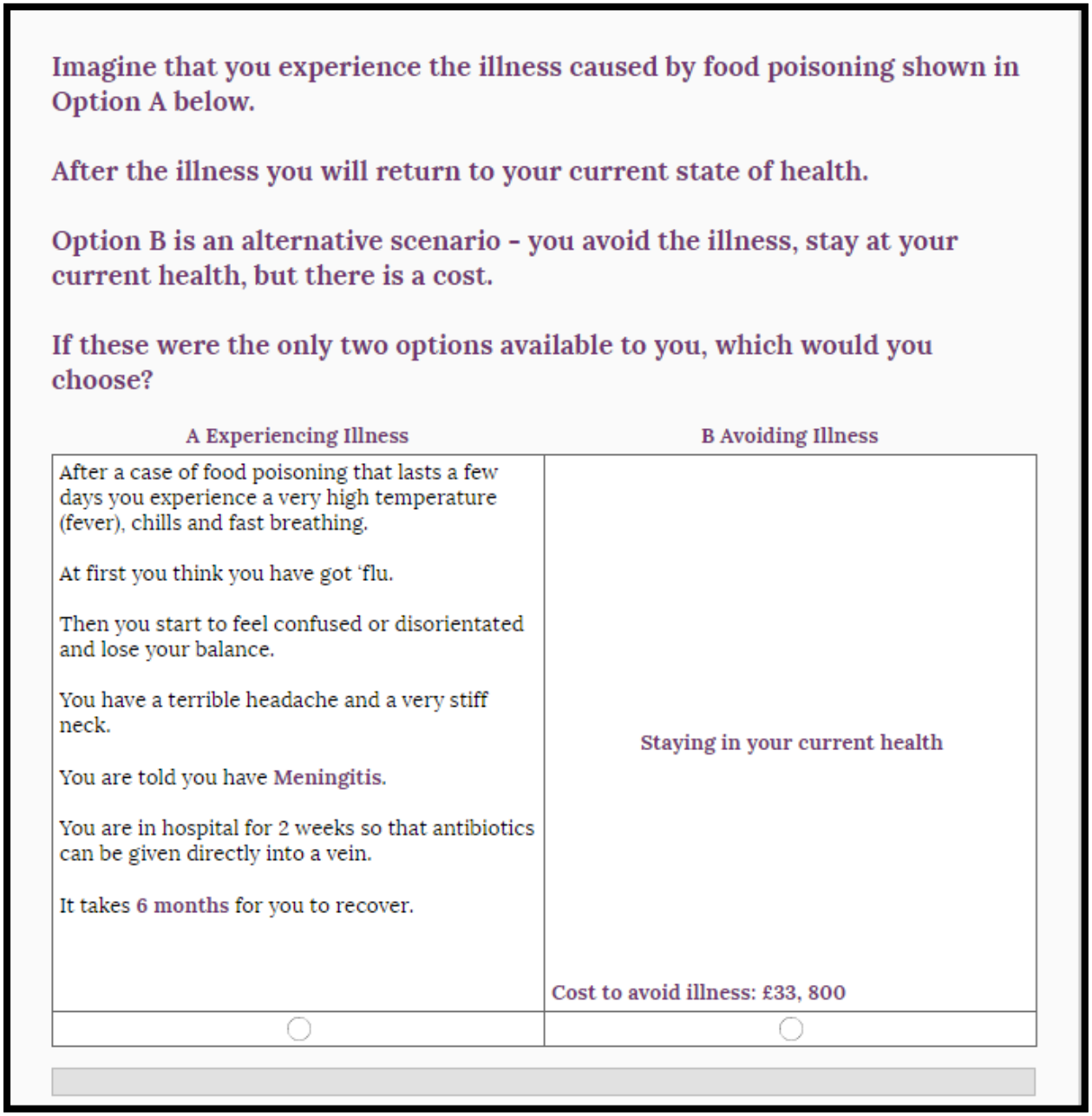
Option B is an alternative scenario - they avoid the illness, stay at their current health, but there is a cost.

If these were the only two options available to you, which would you choose?

(1 of 8)

A Experiencing Illness	B Avoiding Illness
Your child develops a high temperature, with aching muscles and chills. They have little energy and no appetite. Your child develops diarrhoea. You visit your GP twice. They advise that your child should rest, drink plenty of fluids and be given age-appropriate pain relief. The illness lasts for 10 days before they return to their normal self.	**Your child stays in their current health** **Cost to avoid illness: £100**
○	○

Figure F.3: Example of a long term vignette for adult illness: meningitis



Imagine that you experience the illness caused by food poisoning shown in Option A below.

After the illness you will return to your current state of health.

Option B is an alternative scenario - you avoid the illness, stay at your current health, but there is a cost.

If these were the only two options available to you, which would you choose?

A Experiencing Illness	B Avoiding Illness
After a case of food poisoning that lasts a few days you experience a very high temperature (fever), chills and fast breathing. At first you think you have got 'flu. Then you start to feel confused or disorientated and lose your balance. You have a terrible headache and a very stiff neck. You are told you have Meningitis. You are in hospital for 2 weeks so that antibiotics can be given directly into a vein. It takes 6 months for you to recover.	Staying in your current health Cost to avoid illness: £33, 800
○	○

Figure F.4: Example of a long term vignette for child illness: meningitis

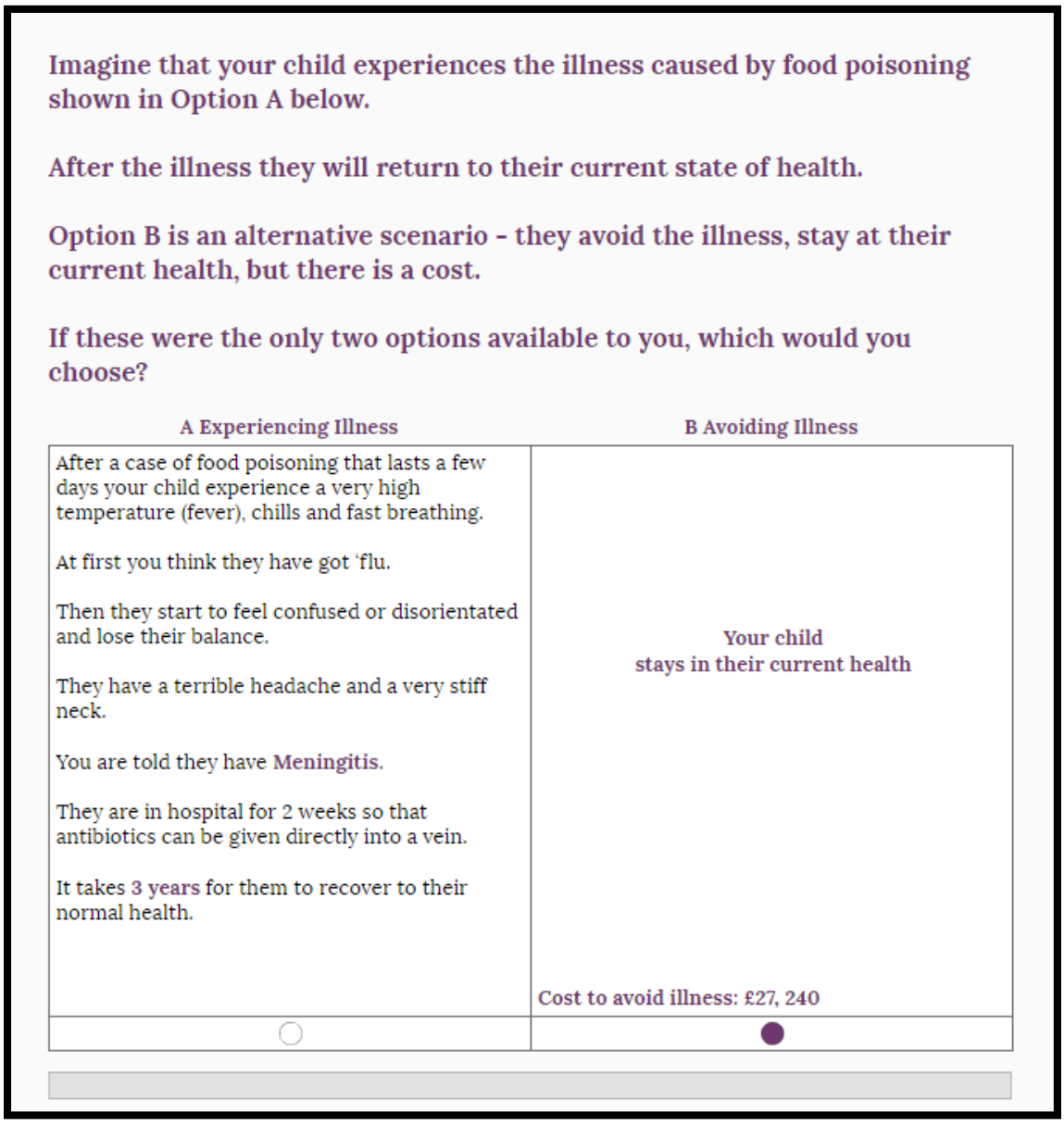


Figure F.5: Example of an EQ-5D-3L short term adult illness choice question

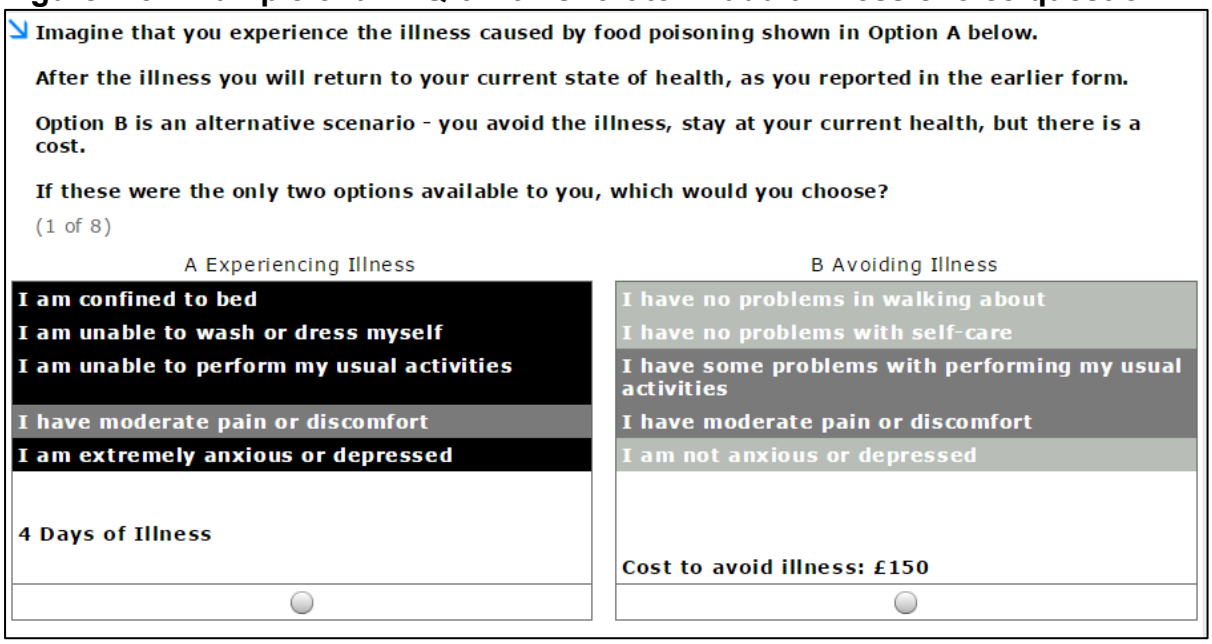


Figure F.6: Example of an EQ-5D-3L short term child illness choice question

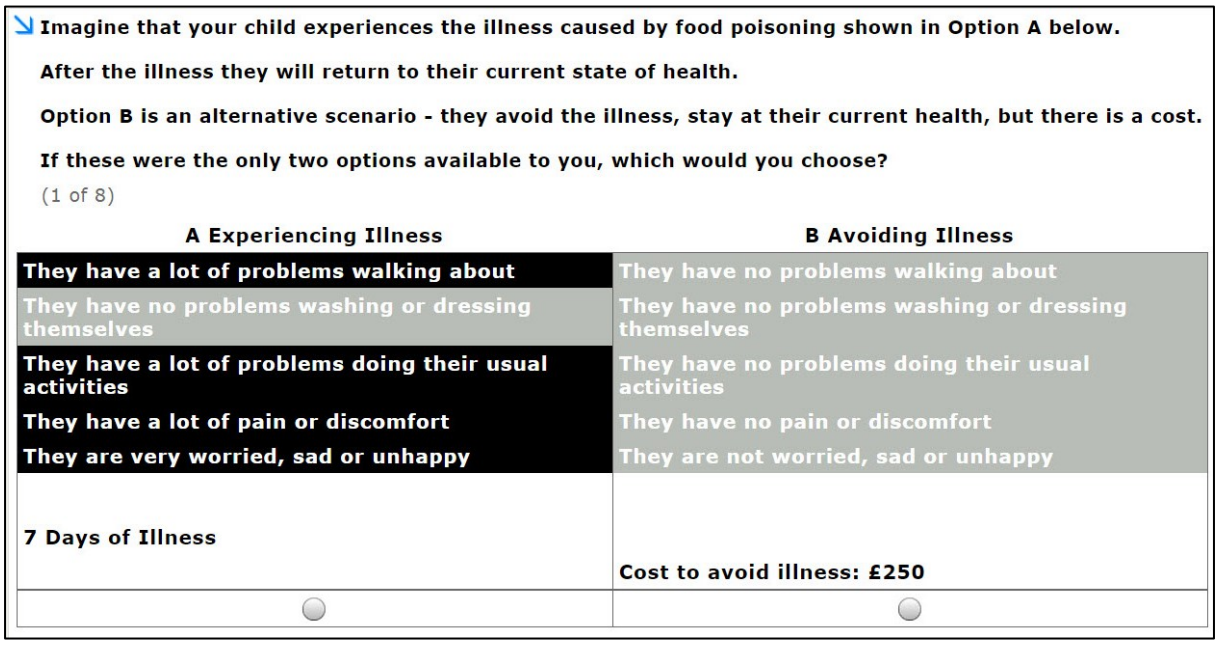
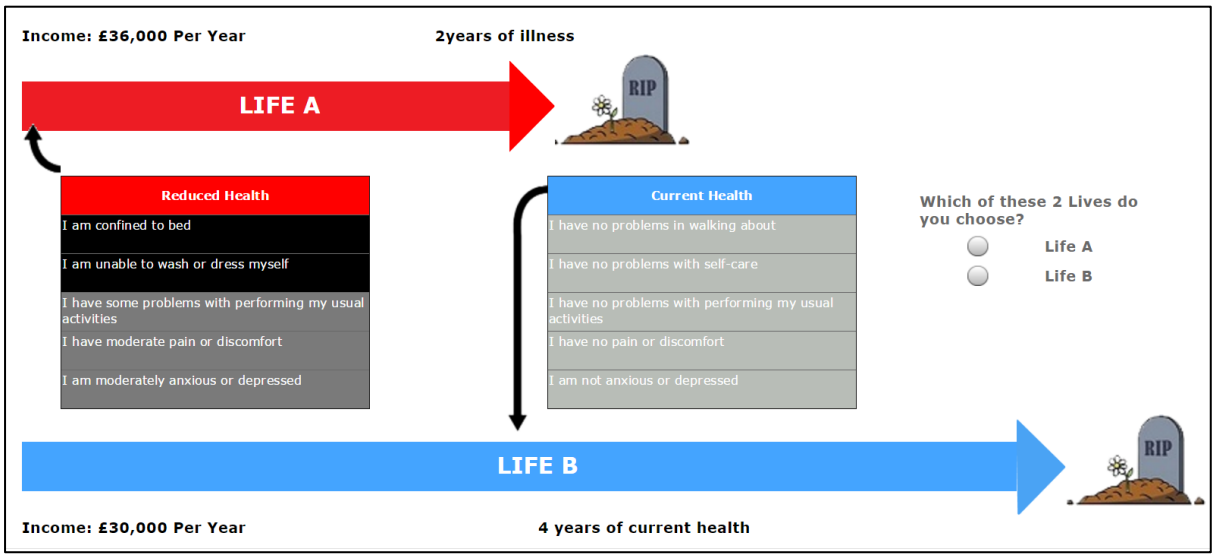


Figure F.7: Example of an EQ-5D-3L long term adult illness choice question



APPENDIX G: LONG TERM ILLNESS (INCLUDING SEQUELAE) VALUATION – DESIGN INFORMATION

G.1 Cost Levels - long term valuation questions

A respondent was assigned (at random) one of sic cost levels in each of the long term valuation questions. Below we report, alongside the illness descriptions, the minimum and maximum values for the 'standard' design - this would be seen by someone with an income level of £35,000 - £44,999.

The costs faced by respondents whose household income level fell in to another category were modified using the formula:

$$£X_{2\text{-}6} *(1 + (Z\text{-}6)*0.18)$$

where *X* is the standard value, and *Z* is a variable associated with their self-reported income level (see Table G.1) i.e. there is an 18% change in cost associated with each change in income category. The value used for the minimum level $£X_1$ was not changed.

Table G.1: Questionnaire Household Income Bands

income category	Z
Below £6,500	1
£6,500 - £11,499	2
£11,500 - £17,499	3
£17,500 - £24,999	4
£25,000 - £34,999	5
£35,000 - £44,999	6
£45,000 - £54,999	7
£55,000 - £74,999	8
£75,000 - £99,999	9
£100,000 - £124,999	10
£125,000 - £149,999	11
£150,000 - £199,999	12
more than £200,000	13

G.2 Descriptions, Durations, Costs - long term vignettes – adult illness

Below we report the text used to describe the 11 conditions used. For some conditions the duration of the illness varies within the survey (values drawn from range of predefined values). This is identified in parenthesis {..}, and the range of durations are reported below the description. The costs are based on results from Focus Groups, Cognitive Interviews and Pilot surveys - the cost ranges needed to induce sufficient variation in the Pay/No Pay responses.

1. Guillain-Barre Syndrome
2. Irritable Bowel Syndrome
3. Reactive Arthritis
4. Mesenteric Adenitis
5. Septicaemia
6. Jaundice
7. Osteomyelitis
8. Thrombotic thrombocytopenic purpura (TTP)
9. Chronic Renal Failure
10. Meningitis
11. Brain damage

Guillain-Barre Syndrome

You become ill with food poisoning and this leads to more serious symptoms.
You suffer from difficulty in moving your legs and arms, and find it hard to speak.
You have Guillain-Barre Syndrome (GBS) which means your body's immune system attacking your own nervous system.
You spend 3 weeks in hospital.
The GBS damages your nervous system so severely that you lose the use of your legs, meaning that you are restricted to a wheelchair.
There will be long term pain and tiredness for {2} years before you recover to feel like your normal self.
Length: 2,4,10 years
Cost range: £1-160k

Irritable Bowel Syndrome

You become ill with food poisoning and from which you seem to recover normally.
About a month later you develop stomach cramps and severe constipation, and sometimes you experience an urgent need to go to the toilet.
You have Irritable Bowel Syndrome (IBS).
This involves symptoms affecting you for 5-6 days, every 2 months.
It is expected to last for the rest of your life.
Cost range: £0.5-40k

Reactive arthritis

You become ill with food poisoning during which you develop symptoms which fail to clear up.
You have reactive arthritis, which means your joints (knees feet and ankles) become inflamed, red and sore.
You are prescribed painkillers and anti-inflammatory drugs to reduce the pain.
It takes {6} months before you will feel like your normal self.
Length: 0.5, 1, 10 years
Cost range: £0.5-40k

Mesenteric Adenitis

After a case of food poisoning that lasts a few days you develop MA.
This is an inflammation in the lymph glands in the gut. This causes pain in the abdomen, high temperature (fever) and feeling generally unwell; you may be nauseous and/or have diarrhoea.
The symptoms will improve within a 3 days, and will clear up completely within two weeks.
No treatment is needed other than painkillers. However, MA can be difficult to distinguish from acute appendicitis or ectopic pregnancy. You need a small operation to look inside your abdomen to make sure other important problems, like appendicitis, are not missed. You will feel some pain and discomfort where the incisions were made for a few days after the procedure. You'll be given painkillers to ease the pain. You will be able to resume your normal activities after a week.
Cost range: £0.1-5k

Septicaemia

After a case of food poisoning that lasts a few days you experience a very high temperature (fever), chills and shivering, a fast heartbeat and fast breathing. You may start to feel dizzy or faint, confused or disorientated. Your speech becomes slurred and you develop severe muscle pain and severe breathlessness.
You are told you have ***septicaemia****. This means that your immune system is fighting the infection so much that they blood supply to vital organs such as the brain, heart and kidneys is restricted.*
You are admitted to the Intensive Care Unit (ICU) where you are given antibiotics and fluids straight in to a vein (intravenously) and given oxygen.
You are in the intensive care unit for 5 days and in hospital on an ordinary ward for another 5 days.
It takes {18} months before you feel like your normal self.
Length: 1.5, 3, 10 years
Cost range: £0.5-120k

Osteomyelitis

You think that you have recovered from a bout of food poisoning when you suddenly develop a very high temperature.
You experience severe pain in your leg and you notice that it is swollen, red and warm at one spot.
It is very tender to the touch and hurts a lot when you try to move it.
You have acute osteomyelitis – a condition which affects the bones.
You are in hospital for 1 week so that antibiotics can be given intravenously (directly into a vein).
You also need to take painkillers.
You are fitted with a splint to restrict movement whilst the bone heals.
It takes {2} months before you feel like your normal self.
Length: 2 months, 4 months, 2 years
Cost range: £0.5-20k

TTP

Following a bout of diarrhoea you start to feel more unwell.
You have a bad headache and feel confused.
You have kidney damage, and are admitted as an emergency to hospital.
You spend the first few days on a ventilator to aid your breathing.
You spend a further month in hospital having blood transfusions on most days.
You are allowed home after seven weeks in hospital but are very weak.
You need regular follow-up visits to hospital.
It takes {6} months before you feel like your normal self.

Length: 0.5, 1, 3 years
Cost range: £0.5-40k

Chronic renal failure

You become ill with food poisoning which leads to your kidneys being damaged.
The damage means your kidneys cannot clean the blood.
This means having to have dialysis whilst you wait for a kidney transplant.
You will have to visit a hospital 3 times a week for dialysis, where your blood is drawn from your body, cleaned, and returned to your body.
A kidney transplant becomes available after {3} years.

It will involve 3 hours of surgery, followed by 4 days in hospital and 4 weeks of recovery at home, when mobility is reduced.
After surgery you will need to take drugs to prevent rejection of the transplanted kidney, which will lead risk of infections, and diabetes in the future.
It takes 3 months after the surgery before you start to feel like your normal self.
Length: 1, 3, 6, 10 years
Cost range: £0.5-300k

Meningitis

After a case of food poisoning that lasts a few days you experience a very high temperature (fever), chills and fast breathing. At first you think you have got 'flu.
Then you start to feel confused or disorientated and lose your balance. You have a terrible headache and a very stiff neck.
You are told you have meningitis.
You are in hospital for 2 weeks so that antibiotics can be given directly into a vein.
It takes {6} months for you to recover.
Length: 0.5, 1, 3 years
Cost range: £0.5-50k

Jaundice

You start to feel unwell - eventually feeling sick and not wanting to eat. You have pain in the upper part of your stomach and your skin and the whites of your eyes turn yellow. You visit the GP who tells you this is called Jaundice. Your skin becomes itchy, your stomach swells and you start to feel confused and very sleepy. You are admitted to hospital.

Doctors explain that you have Hepatitis E *infection. Your liver has failed and you will need a liver transplant. It takes {6} months before a donor liver is found – during which time you are unwell. You stay in hospital for two weeks after the transplant. You start to feel better after transplant, and it takes 6 months before you feel like your normal self. You need tablets every day for the rest of your life to stop your body rejecting your new liver.*
Length: 0.5, 1, 2, 4 years
Cost range: £0.5-60k

Brain Damage

You become ill with food poisoning. You start to feel dizzy, and you notice that you are confused and disorientated. The bacteria that caused the food poisoning and damaged your kidneys has also caused brain damage. This damage is permanent, and makes you very disabled. You cannot walk, talk or concentrate. You are unable to go to work. You will need specialist equipment at home to help you to cope. The consequences from the brain damage will last for the rest of your life.
Cost range: £0.5-500k

G.3 Descriptions, Durations, Costs - long term vignettes – child illness

Below we report the text used to describe the 12 conditions used for children's long term conditions. For some conditions the duration of the illness varies within the survey (values drawn from range of predefined values). This is identified in parenthesis {..}, and the range of durations are reported below the description. The costs are based on results from Focus Groups, Cognitive Interviews and Pilot surveys - the cost ranges needed to induce sufficient variation in the Pay/No Pay responses.

1. Guillain-Barre Syndrome
2. Irritable Bowel Syndrome
3. Reactive arthritis
4. Mesenteric Adenitis
5. Septicaemia
6. Osteomyelitis
7. Haemolytic Uraemic Syndrome
8. Chronic renal failure
9. Complicated jaundice
10. Meningitis
11. Brain damage
12. Febrile convulsions

Guillain-Barre Syndrome

Your child becomes ill with food poisoning and this leads to more serious symptoms. They suffer from difficulty in moving their legs and arms, and find it hard to speak. They have Guillain-Barre Syndrome (GBS) which means their body's immune system attacking their own nervous system.
They spend 3 weeks in hospital.

The GBS damages their nervous system so severely that they lose the use of their legs, meaning that they are restricted to a wheelchair.
There will be long term pain and tiredness for {2} years before they recover to feel like their normal self.
Length 2, 4, 10 years
Cost range: £1-160k

Irritable Bowel Syndrome

Your child becomes ill with food poisoning and from which they seem to recover normally.
About a month later they develop stomach cramps and severe constipation, and sometimes they experience an urgent need to go to the toilet.
They have Irritable Bowel Syndrome (IBS).
This involves symptoms affecting them for 5-6 days, every 2 months.
It is expected to last for the rest of their life.
Cost range 1-20k

Reactive arthritis

Your child becomes ill with food poisoning during which they develop symptoms which fail to clear up.
They have reactive arthritis, which means their joints (knees feet and ankles) become inflamed, red and sore.
They are prescribed painkillers and anti-inflammatory drugs to reduce the pain.
It takes {6} months before they will feel like their normal self.
Length: 6 months, 1 year 10 years
Cost range: £ 0.5-40k

Mesenteric Adenitis

After a case of food poisoning that lasts a few days your child develops MA.
This is an inflammation in the lymph glands in the gut. This causes pain in the abdomen, high temperature (fever) and feeling generally unwell; they may be nauseous and/or have diarrhoea.
The symptoms will improve within a 3 days, and will clear up completely within two weeks.
No treatment is needed other than painkillers. However, MA can be difficult to distinguish from acute appendicitis. They need a small operation to look inside their abdomen to make sure other important problems, like appendicitis, are not missed.
They will feel some pain and discomfort where the incisions were made for a few days after the procedure. They will be given painkillers to ease the pain. They will be able to resume their normal activities after a week.
Cost range: £0.1-5k

Septicaemia

After a case of food poisoning that lasts a few days your child experiences a very high temperature (fever), chills and shivering, a fast heartbeat and fast breathing.
They start to feel dizzy, confused or disorientated. Their speech becomes slurred and they develop severe muscle pain and severe breathlessness.

*You are told they have **septicaemia**. This means that their immune system is fighting the infection so much that their blood supply to vital organs such as the brain, heart and kidneys is restricted.*
They are admitted to the Intensive Care Unit (ICU) where they are given antibiotics and fluids straight in to a vein (intravenously) and given oxygen.
They are in the intensive care unit for 5 days and in hospital on an ordinary ward for another 5 days.
It takes {18} months before they feel like their normal self.
Length: 18 months, 3 years 10 years
Cost range: £0.5-120k

Osteomyelitis

You think that your child has recovered from a bout of food poisoning when they suddenly develop a very high temperature.
They experience severe pain in their leg and you notice that it is swollen, red and warm at one spot.
It is very tender to the touch and hurts a lot when they try to move it.
They have acute osteomyelitis – a condition which affects the bones.
They are in hospital for 1 week so that antibiotics can be given intravenously (directly into a vein).
They also need to take painkillers.
They are fitted with a splint to restrict movement whilst the bone heals.
It takes {2} months before they feel like their normal self.
Length: 2 months, 10 years
Cost range: £1-20k

Haemolytic Uraemic Syndrome

Your child becomes ill with food poisoning which leads to their kidneys being damaged.
The damage means their kidneys cannot clean the blood.
They go to hospital where you are told they have Haemolytic Uraemic Syndrome.
They spend a month in intensive care, and you are taught how to conduct dialysis, where their blood is drawn from their body, cleaned, and returned to their body each night.
Your child returns home, and you have to continue dialysis for 4 months.
A kidney transplant becomes available after {3} years.
It will involve 3 hours of surgery, followed by 4 days in hospital and 4 weeks of recovery at home, when mobility is reduced.
After surgery they will need to take drugs to prevent rejection of the transplanted kidney, which will lead risk of infections, and diabetes in the future.
It takes 3 months after the surgery before they start to feel like their normal self, but they do not achieve normal growth milestones.
Length: 1, 3, 6,10 years
Cost range: £1-300k

Chronic renal failure

Your child becomes ill with food poisoning which leads to their kidneys being damaged.
The damage means their kidneys cannot clean the blood.
This means having to have dialysis whilst they wait for a kidney transplant.
They will have to visit a hospital 3 times a week for dialysis, where their blood is drawn from their body, cleaned, and returned to their body.
A kidney transplant becomes available after {3} years.
It will involve 3 hours of surgery, followed by 4 days in hospital and 4 weeks of recovery at home, when mobility is reduced.
After surgery they will need to take drugs to prevent rejection of the transplanted kidney, which will lead risk of infections, and diabetes in the future.
It takes 3 months after the surgery before they feel like their normal self.
Length: 1, 3, 6, 10 years
Cost range: £1-300k

Complicated jaundice

Your child starts to feel unwell - eventually feeling sick and not wanting to eat.
They notice pain in the upper part of their tummy and their skin and the whites of their eyes turn yellow. You visit the GP who tells you this is called Jaundice.
Their skin becomes itchy, their tummy swells and they start to feel confused and very sleepy.
They are admitted to hospital.
Doctors explain that they have a rare complication of Hepatitis E *infection.*
Their liver has failed and they will need a liver transplant.
It takes 6 months before a donor liver is found – during which time they are unwell.
They stay in hospital for two weeks after the transplant.
They start to feel better after transplant, and it takes {6} months before they feel like their normal self.
They take tablets every day for the rest of their life to stop their body rejecting their new liver.
Length: 6 months 2 years
Cost range: £1-200k

Meningitis

After a case of food poisoning that lasts a few days your child experience a very high temperature (fever), chills and fast breathing. At first you think they have got 'flu.
Then they start to feel confused or disorientated and lose their balance. They have a dreadful headache and a very stiff neck.
You are told they have ***meningitis****.*
They are in hospital for 2 weeks so that antibiotics can be given directly into a vein.
It takes 6 months before you feel like their normal self.
Length: 6 months, 1, 3 years
Cost range: 0.5-300k

Brain damage

Your child starts to feel dizzy, and you notice that they are confused and disorientated. They cry a lot and you cannot console them.
The bacteria that caused their food poisoning and damaged their kidneys has also caused brain damage. This damage is permanent, and makes your child very disabled. They cannot walk, talk or concentrate. They are unable to go to nursery or school. They will never be able to work or to look after themselves. You will need specialist equipment at home to help you to cope.
The consequences from the brain damage will last for the rest of their life.
Cost range: £1-500k

Febrile convulsions

Your child becomes ill with diarrhoea and vomiting. They develop an infection and a very high temperature. Your notice that suddenly your child's body becomes stiff, and their arms and legs begin to twitch. They lose consciousness and they wet themselves. They vomit and foam at the mouth. Their eyes roll back in their head. Although the seizure lasts for less than five minutes it feels like a lifetime to you. You rush your child to A&E. Your child is still very sleepy.
They tell you that your child has had a febrile convulsion. They show you how to put your child in the recovery position if they have another seizure and they tell you how to bring your child's temperature down. They make sure that you child is not dehydrated.
They allow you to go home once your child has recovered.
Cost range: £0.5-20k

APPENDIX H: VIGNETTE SURVEY (ADULTS)

This Appendix presents a pdf version of the survey for adults. It is provided as a separate file accompanying this report.

APPENDIX I: VIGNETTE SURVEY (PARENTS)

This Appendix presents a pdf version of the survey for parents. It is provided as a separate file accompanying this report.

APPENDIX J: EQ-5D-3L SURVEY (ADULTS)

This Appendix presents a pdf version of the survey for parents. It is provided as a separate file accompanying this report.

APPENDIX K: EQ-5D-3L SURVEY (PARENTS)

This Appendix presents a pdf version of the survey for parents. It is provided as a separate file accompanying this report.

APPENDIX L: DATA ANALYSIS (VIGNETTE SAMPLE)

L.1 Econometric Models and Results

Short term - Adults

The valuation tasks for short term conditions (Adult, Parent) comprise a discrete choice experiment. They are analysed via estimation of random utility models, specifically conditional logit models with an error component specification to allow for differing error variance between the illness and no illness options which comprise each set.

Estimation of these models gives estimates of the marginal utilities or preference weights (βs) implicitly assigned by respondents to each of the constituent attributes (e.g. symptoms, duration, cost). The WTP for a marginal change in attribute *j* is given by ($-\beta_j/\beta_{cost}$) where βj is the estimated marginal utility of the attribute j, and β_{cost} is the estimated preference weight on the cost term.

We assume that the impact of symptoms is moderated by their duration, i.e. vomiting for 3 days will be treated differently to vomiting for 1 day. Some attributes are treated as independent of duration: uncontrolled vomiting (which had a fixed duration of two days) and the number of doctor visits.

Results from estimating the model are reported in Table L.1. The model includes duration, doctor visits, uncontrolled vomiting, vomiting*days and blood in stools*days. Stomach cramps were consistently insignificant and excluded from the models. Doctor visits were found to increase the disutility of the illness but were collapsed into a yes/no variable as there was no differentiation between 1 or 2 visits. The model includes interaction terms between (i) cost and household income[6] (to accommodate wealthier people being willing to pay more) and (ii) duration and the costs[7] the respondent indicated would be incurred if they missed work (to test if this has any unintended influence on their WTP for pain and suffering).

Short Term - Parents

Parents' income influenced the marginal value of the cost attribute (Cost*Incxmd, income defined as deviation from £31 655), but no other interaction effects were found to be significant (i.e. child age, child gender, lost earnings). Also, a smaller number of the attributes used to describe the illness were significant. The presence of vomiting, cramps or visits to a doctor did not influence WTP to avoid the illness. The duration of the illness, whether there was blood in the stools and the extreme vomiting all increased the disutility of the child's illness (see Table L.2).

[6] *incxmd* is the deviation of respondent's household income from £31 655.

[7] *lostearn* is the respondent's daily cost (lost wages, childcare, etc) of being too ill to work.

Table L.1: Conditional logit estimates for short term adult illness

	Coef.	Std. Err.	z	P>z	[95% Conf.	Interval]
Cost	-0.019241	0.000749	-25.68	0	-0.020709	-0.017772
Cost * incxmd	0.000033	0.000014	2.28	0.023	0.000005	0.000061
Days	-0.076599	0.009002	-8.51	0	-0.094242	-0.058956
Days * vomiting	-0.032329	0.011720	-2.76	0.006	-0.055301	-0.009358
2 days uncontrolled vomiting	-0.514935	0.114023	-4.52	0	-0.738415	-0.291455
Days *blood	-0.057032	0.016776	-3.4	0.001	-0.089913	-0.024152
Dr visit	-0.333834	0.073010	-4.57	0	-0.476931	-0.190738
Days*lostearn	-0.000133	0.000042	-3.2	0.001	-0.000214	-0.000052
ASC * incxmd	0.000015	0.000003	5.18	0	0.000010	0.000021
ASC	0.831096	0.114844	7.24	0	0.606006	1.056186
Error variance effect						
σ	2.401816	0.092016	26.1	0	2.221469	2.582163
ASC is an alternative specific constant for the no illness option Number of choices = 7816 Number of respondents = 977 Log likelihood = -3756.8444						

Table L.2: Conditional logit estimates for short term child illness - Parents

	Coef.	Std. Err.	z	P>z	[95% Conf. Interval]	
Cost	-0.02033	0.00091	-22.44	0	-0.02211	-0.01856
Cost*Incxmd	0.00003	0.00001	2.16	0.031	2.87E-06	6.04E-05
Days	-0.09895	0.01101	-8.98	0	-1.21E-01	-7.74E-02
Days *blood	-0.10251	0.02158	-4.75	0	-0.1448	-0.06021
2 days extreme vomiting	-0.35420	0.12367	-2.86	0.004	-0.5966	-0.11181
ASC	2.55710	0.17436	14.67	0	2.215368	2.898838
Error variance effect						
σ	2.68084	0.14425	18.58	0	2.398114	2.963561
ASC is an alternative specific constant for the no illness option Number of choices = 4488 Number of respondents = 561 Log likelihood = -1942.3589						

Long Term – Adults

The long term vignettes are single items to be valued, rather than being composed of constituent attributes. The elements which varied in the long term sets were the duration[8] and cost to avoid. The respondents' decisions to pay /not pay (1,0) were analysed via estimation of a logit model for each condition. Explanatory variables included the cost to the respondent, and (where appropriate) the duration of the illness.

[8] Durations did not vary for IBS, MA, or brain damage.

As with the short term condition model the cost was interacted with the income level of the household (defined as deviation from the household income of £31,655). The age of respondent was included as an interaction term with duration (ageoemd) as age was thought likely to influence willingness to pay to avoid long duration illnesses. Results are reported in Table L.3.

Table L.3: Logit estimates for 11 conditions: adults

	cost	Cost *incxmd	Duration	ageoemd	constant	N
GBS	-9.29e-6 (7.46)	1.10e-7 (5.31)	0.070 (4.20)	-0.0.01 (2.29)	ns	936
IBS	-0.317e-5 (3.95)	3.45e-7 (3.40)	na	-0.012 (2.45)	0.432 (3.40)	710
RA	-0.615e-4 (12.04)	5.05e-7 (6.99)	0.097 (5.80)	ns	ns	933
MA	-0.49e-3 (5.92)	6.19e-6 (4.98)	na	ns	-0.186 (1.17)	473
Septicaemia	-0.16e-4 (7.70)	1.72e-7 (6.18)	ns	ns	0.318 (3.03)	935
Osteomyelitis	-0.67e-4 (5.63)	6.97e-7 (4.85)	0.538 (5.94)	ns	-0.267 (2.10)	935
TTP	-0.376e-4 (7.07)	4.31e-7 (6.26)	0.198 (3.08)	ns	0.227 (1.87)	1162
CRF	-6.73e-6 (8.04)	5.93e-8 (5.69)	ns	ns	0.308 (2.81)	935
Meningitis	-3.60e-5 (7.86)	3.51e-7 (5.50)	0.184 (3.30)	ns	ns	711
Jaundice	-2.03e-5 (5.25)	1.76e-7 (3.85)	0.104 (2.03)	ns	0.542 (3.74)	936
Brain damage	-3.29e-6 (4.77)	3.65e-8 (3.66)	na	-0.015 (2.48)	0.737 (4.58)	463

Note:
values in parentheses are z-statistics
'na' indicates not available in the model,
'ns' indicates not significant and dropped from the model.

Long Term – Parents

Table L.4 reports the results of the logit model estimation for the child illness sample. The cost term is significant in all models, and the income effect on cost is significant for all but one of the conditions (mesenteric adenitis). The age of the "nominated child" the respondent was asked to think about when answering all of the valuation questions was not significant. In contrast to the Adult results, many duration effects were not significant although there were duration effects for GBS, Reactive Arthritis and Osteomyelitis.

Table L.4: Logit estimates for 11 conditions: child illness sample

	cost	Cost *incxmd	duration	constant	N
GBS	-9.25e-6 (4.73)	8.81e-11 (3.92)	0.065 (1.98)	0.591 (2.84)	489
IBS	-5.31e-5 (3.42)	3.95e-10 (2.49)	na	1.207 (6.71)	489
RA	4.12e-5 (5.34)	2.69e-10 (3.79)	0.091 (3.16)	0.609 (3.56)	489
MA	-3.21e-4 (3.79)	8.54e-10 (1.10)	na	0.562 (2.60)	263
Septicaemia	-9.80e-6 (3.62)	7.34e-11 (2.86)	ns	0.961 (5.97)	489
Osteomyelitis	-5.79e-5 (3.73)	5.31e-10 (3.16)	0.334 (2.26)	0.513 (2.74)	460
HUS	-4.33e-6 (4.24)	2.88e-11 (2.80)	ns	0.751 (4.75)	489
CRF	-5.77e-6 (5.53)	4.49e-11 (3.85)	ns	0.844 (5.44)	489
Meningitis	-1.74e-5 (4.34)	1.18e-10 (3.10)	ns	1.00 (6.01)	489
Jaundice involving a liver transplant	-1.11e-5 (4.54)	9.98e-11 (3.35)	na	1.283 (5.29)	234
Brain damage	-4.04e-6 (4.31)	5.48e-11 (3.65)	na	1.425 (5.58)	255
Febrile convulsions	-5.81e-5 (2.78)	4.78e-10 (2.21)	na	0.464 (2.07)	255

Notes:
values in parentheses are z-statistics
na: length of illness not included for the condition
ns: length of illness was included but not significant & dropped from the model

L.2 Adult Sample – demographics and health

The total sample collected for adults was 1189. Some were removed because their speed of completion was so great that the data quality was considered unreliable. The active sample was then 1040. The sample was 53-47 split between females and males.

Table L.5: Gender

male	Freq.	Percent	Cum.
male	492	47.31	47.31
female	546	52.5	99.81
other	2	0.19	100
Total	1,040	100	

Table L.6: Occupation

We would like to know about the Chief Income Earner in your household *This is the person with the largest income.*

If this person is • *retired with an occupational pension then answer about their most recent occupation.* • *not in a paid job but has been out of work for less than 6 months, then answer about their most recent job.*			
The Chief Income Earner is (or was):			
	Freq.	**Percent**	**Cum.**
Semi or unskilled manual work	108	10.38	10.38
Skilled manual worker	170	16.35	26.73
Supervisory or clerical/ junior managerial/ professional/ administrative	269	25.87	52.6
Intermediate managerial/ professional/ administrative	267	25.67	78.27
Higher managerial/ professional/ administrative	99	9.52	87.79
Student	13	1.25	89.04
Casual worker – not in permanent employment	5	0.48	89.52
Housewife/ Homemaker	15	1.44	90.96
Retired and living on state pension	37	3.56	94.52
Unemployed or not working due to long-term sickness	50	4.81	99.33
Full-time carer of other household member	7	0.67	100
Total	1,040	100	

The geographical split of the sample is shown in Table L.7. The division between UK nations is close to the true population proportions with 8.2% from Scotland (nationally 8.4%), 5% from Wales (nationally 4.8%) and 3.1% from Northern Ireland (nationally 2.9%). Ethnicity and Education are summarised in Tables L.8 and L.9.

Table L.7: Region

region	**Freq.**	**Percent**	**Cum.**
East Midlands	67	6.44	6.44
East of England	86	8.27	14.71
London	140	13.46	28.17
North East	46	4.42	32.6
North West	112	10.77	43.37
South East	163	15.67	59.04
South West	98	9.42	68.46
West Midlands	85	8.17	76.63
Yorkshire & Humber	74	7.12	83.75
Northern Ireland	32	3.08	86.83
Scotland	85	8.17	95
Wales	52	5	100
Total	1,040	100	

Table L.8: Ethnicity

ethnicity	Freq.	Percent	Cum.
White British	878	84.42	84.42
White Irish	14	1.35	85.77
Other White	50	4.81	90.58
Black or Black British - Caribbean	10	0.96	91.54
Black or Black British – African	7	0.67	92.21
Other Black	3	0.29	92.5
Asian British – Indian	21	2.02	94.52
Asian British - Bangladeshi	5	0.48	95
Chinese	7	0.67	95.67
Other Asian	20	1.92	97.6
Mixed ethnicity - white & black Caribbean	5	0.48	98.08
Mixed ethnicity - white & black African	1	0.1	98.17
prefer not to say	19	1.83	100
Total	1,040	100	

Table L.9: Education

Which of these best describes the highest educational qualification you have obtained so far?			
education	Freq.	Percent	Cum.
No formal qualifications	37	3.56	3.56
GCSE Level education (e.g. GCSE, O-Levels or Standards)	218	20.96	24.52
A-Level education (e.g. A, AS, S-Levels, Highers)	223	21.44	45.96
Degree or Graduate education (e.g. BSc, BA)	307	29.52	75.48
Post-graduate education (e.g. PhD, MSc, MA)	139	13.37	88.85
Vocational education (e.g. NVQ, HNC, HND)	105	10.1	98.94
Prefer not to say	11	1.06	100
Total	1,040	100	

Median household pre-tax income was in the range £25,000 - £34,999. The 2013/14 Households below average income (HBAI) statistics report from the DWP gives a median household income (2 adults) as £23,556. The age distribution is shown in Table L.11.

Table L.10: Household Income

Please tell us your Household income group *This is the amount you earn before tax, and includes the people you live with (partner, family) – but do not include people you house/flat share with.*			
income	Freq.	Percent	Cum.
Below £6,500	42	4.04	4.04
£6,500 - £11,499	85	8.18	12.22
£11,500 - £17,499	99	9.53	21.75
£17,500 - £24,999	159	15.3	37.05
£25,000 - £34,999	184	17.71	54.76
£35,000 - £44,999	157	15.11	69.87
£45,000 - £54,999	99	9.53	79.4
£55,000 - £74,999	91	8.76	88.16
£75,000 - £99,999	63	6.06	94.23
£100,000 - £124,999	25	2.41	96.63
£125,000 - £149,999	20	1.92	98.56
£150,000 - £199,999	9	0.87	99.42
more than £200,000	6	0.58	100
Total	1,039	100	

Table L.11: Age Groups

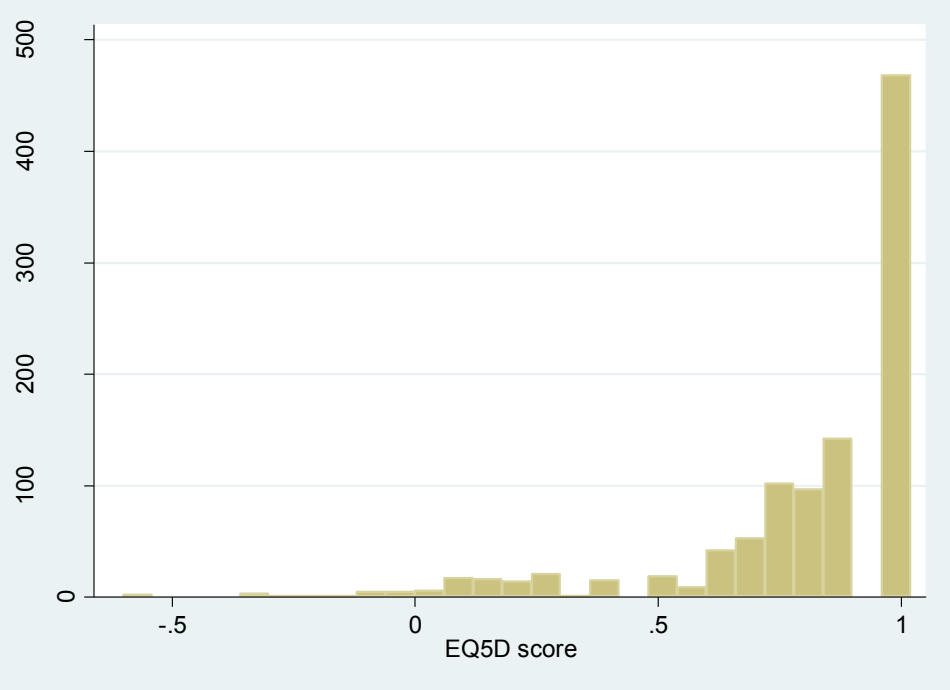
agecat	**Freq.**	**Percent**	**Cum.**
18-19	16	1.54	1.54
20-29	168	16.15	17.7
30-39	194	18.65	36.4
40-49	209	20.1	56.4
50-59	176	16.92	73.4
60-69	184	17.69	91.1
70-79	80	7.69	98.8
80-89	13	1.25	100
Total	1,040	100	

468 (45%) of the sample reported full being at the best level of health using the EQ5D -3L form. The mean EQ5D utility score value (maximum value of 1) was 0.802

eq5d utility score	**Obs**	**Mean**	**Std. Dev.**	**Min**	**Max**
eq5dutility	1,040	0.802	0.267	-0.594	1

The distribution of EQ5D utility scores is shown in Figure L.1. A total of 18 people in the sample reported a health state less than 0 (worse than death).

Figure L.1: Histogram EQ5D utility scores – Adult sample



The history of the sample and their family members with diarrhoea and/or vomiting in the past year are shown in Table L.12 which shows proportions – e.g. 48% of the sample have had mild diarrhoea and/or vomiting lasting less than a day in the last year.

Table L.12: History of diarrhoea and/or vomiting in past year

In the past year please tell us if you or family members have had illnesses like this?				
	You	Other adults in the family	Children in the family	None of them
Mild diarrhoea and/or vomiting <1 day	0.488	0.263	0.0915	0.395
Mild diarrhoea and/or vomiting , 1-3 days, time off work/school, no Dr contact	0.217	0.164	0.080	0.656
Mild diarrhoea and/or vomiting , 1-3 days, time off work/school, Dr contact	0.090	0.072	0.040	0.832
Severe diarrhoea and/or vomiting, time off work/school, > 1 Dr contact	0.057	0.049	0.021	0.891
Severe food poisoning, 1+ nights in hospital	0.037	0.038	0.014	0.921

Table L.13: History of long run FBD conditions

Please indicate if either you, or someone in your close family, has any experience of the following illnesses.		
	you	member of close family
Guillain-Barre Syndrome	0.018	0.025
Irritable Bowel Syndrome	0.164	0.181
Arthritis	0.160	0.265
Febrile Convulsions	0.013	0.025
Mesenteric adenitis	0.010	0.021
Septicaemia	0.017	0.053
Complicated Jaundice	0.013	0.023
Osteomyelitis	0.017	0.019
Hemolytic uremic syndrome (HUS)	0.009	0.009
Thrombotic thrombocytopenic purpura (TTP)	0.013	0.013
Renal Failure/ Dialysis	0.013	0.042
Meningitis	0.029	0.041

L.3. Choices, Task Difficulty & Protests – Adult sample

Possible protest behaviour were investigated for people who selected a pay, or a no pay, option in all of the sets they faced.

People with this pattern of choices in the short term sets were prompted as to why that was the case using the responses shown in Tables L.14 and L.15.

Table L.14: Why never chose to pay – short term

Please select the option that best explains why you never chose to pay to avoid the illness.			
	Freq.	Percent	Cum.
1. The illness wouldn't be too bad - I could live with it.	36	3.46	3.46
2. I would get better anyway, so it is not worth paying for the treatment.	46	4.42	7.88
3. I would like to avoid the illness but I could not afford to pay what was asked	20	1.92	9.81
4. I shouldn't have to pay because the government should provide health care.	20	1.92	11.73
5. I have an ethical/religious objection to taking medicines	2	0.19	11.92
6. Other [please specify]	10	0.96	12.88
n/a	906	87.12	100
Total	1,040	100	

Table L.15: Why always chose to pay – short term

Please select the option that best explains why you always chose to pay to avoid the illness.	Freq.	Percent	Cum.
1. I did not think the request for payment was realistic so I ignored it	10	0.96	0.96
2. The cost was small compared to the pain and suffering	108	10.38	11.35
3. The cost was small compared to what I would lose missing work	46	4.42	15.77
4. Other (please specify)	21	2.02	17.79
n/a	855	82.21	100
Total	1,040	100	

People choosing options 4-6 in Table L.14, and options 1 or 4 in Table L.15 were excluded from the estimation sample. The rates of such 'protests' were very low considering this was a health-payment study in the UK.

Possible protest behaviour were investigated for people who selected a pay, or a no pay, option in all of the sets they faced.

People who selected a pay, or a no pay, option in all of the long term sets were prompted as to why that was the case using the responses shown in Tables L.16 and L.17.

Table L.16: Why never chose to pay – long term

Please select the option that best explains why you never chose to pay to avoid the illness.	Freq.	Percent	Cum.
1. The illness wouldn't be too bad - I could live with it.	22	2.12	2.12
2. I would get better anyway, so it is not worth paying for the treatment.	18	1.73	3.85
3. I would like to avoid the illness but I could not afford to pay what was asked.	91	8.75	12.6
4. I shouldn't have to pay because the government should provide health care.	44	4.23	16.83
5. I may not live for all those years, so not worth paying to avoid the illness.	10	0.96	17.79
6. I would rather leave money to family/partner than spend to avoid the illness.	12	1.15	18.94
7. Other [please specify]	23	2.21	21.15
n/a	820	78.85	100
Total	1,040	100	

Table L.17: Why always chose to pay – long term

Please select the option that best explains why you always chose to pay to avoid the illness.	Freq.	Percent	Cum.
1. I did not think the request for payment was realistic so I ignored it	15	1.44	1.44
2. The cost was small compared to the pain and suffering	83	7.98	9.42
3. The cost was small compared to what I would lose missing work	9	0.87	10.29
4. Other (please specify)	21	2.02	12.31
n/a	912	87.69	100
Total	1,040	100	

People choosing options 4-7 in Table L.16, and options 1 or 4 in Table L.17 were excluded from the estimation sample. As with the short term sets the rates of such 'protests' were very low.

Respondents were debriefed on how hard to was to understand the sets, and how hard it was to make the choices within them

Table L.18: How hard was it to <u>understand</u> the choice questions involving illness and money? – short term

	Freq.	Percent	Cum.
very difficult	18	1.73	1.73
difficult	85	8.17	9.9
neutral	211	20.29	30.19
easy	372	35.77	65.96
very easy	354	34.04	100
Total	1,040	100	

Table L.19: How hard was it to <u>make</u> the choice questions involving illness and money? – short term

	Freq.	Percent	Cum.
very difficult	29	2.79	2.79
difficult	155	14.9	17.69
neutral	261	25.1	42.79
easy	357	34.33	77.12
very easy	238	22.88	100
Total	1,040	100	

The choice tasks were complex, which was why so much effort had been assigned to preparation of the materials and testing and refining them in focus groups, interviews and pilot surveys.

Rates of 2% and 8% respectively describing the short term sets as very difficult and difficult to understand were regarded as validating those efforts. Making the choices was more often reported as more difficult than understanding the choices.

Table L.20: How hard was it to understand the choice questions involving illness and money? – long term

	Freq.	Percent	Cum.
very difficult	46	4.42	4.42
difficult	94	9.04	13.46
neutral	199	19.13	32.6
easy	386	37.12	69.71
very easy	315	30.29	100
Total	1,040	100	

Table L.21: How hard was it to make the choice questions involving illness and money? – long term

	Freq.	Percent	Cum.
very difficult	120	11.54	11.54
difficult	243	23.37	34.9
neutral	198	19.04	53.94
easy	290	27.88	81.83
very easy	189	18.17	100
Total	1,040	100	

The long term conditions included much more information and were more demanding. Rates of 4% and 9% respectively describing the sets as very difficult and difficult to understand were regarded as not signifying fundamental problems with the long term valuation process. Making the choices was more often reported as more difficult than understanding the choices, and more often so in the long term sets than the short term ones.

L.4 Parents Sample – demographics and health

The total sample collected within the Vignette design for parents was 653. A similar sized sample was collected for parents who were presented with Valuation questions using EQ5D information rather than vignettes (not reported here). Some were removed because their speed of completion was so great that the data quality was considered unreliable. The active sample was then 592. The sample was 60-40 split between females and males.

Table L.22: Gender

male	Freq.	Percent	Cum.
male	240	40.61	40.61
female	350	59.22	99.83
other	1	0.17	100
Total	591	100	

The distribution of occupations and class are shown in Table L.23.

Table L.23: Occupation

We would like to know about the Chief Income Earner in your household *This is the person with the largest income.* *If this person is* • *retired with an occupational pension then answer about their most recent occupation.* • *not in a paid job but has been out of work for less than 6 months, then answer about their most recent job.*			
The Chief Income Earner is (or was):			
	Freq.	Percent	Cum.
Semi or unskilled manual work	65	11	11
Skilled manual worker	116	19.63	30.63
Supervisory or clerical/ junior managerial/ professional/ administrative	152	25.72	56.35
Intermediate managerial/ professional/ administrative	137	23.18	79.53
Higher managerial/ professional/ administrative	59	9.98	89.51
Student	6	1.02	90.52
Casual worker – not in permanent employment	7	1.18	91.71
Housewife/ Homemaker	18	3.05	94.75
Retired and living on state pension	7	1.18	95.94
Unemployed or not working due to long-term sickness	13	2.2	98.14
Full-time carer of other household member	11	1.86	100
Total	591	100	

The geographical split of the sample is shown in Table L.24. The division between UK nations is close to the aggregate national population proportions with 7.8% from Scotland (nationally 8.4%), 3.7% from Wales (nationally 4.8%) and 3.6% from Northern Ireland (nationally 2.9%). Ethnicity and Education are summarised in Tables L.25 and L.26.

Table L.24: Region

region	Freq.	Percent	Cum.
East Midlands	41	6.93	6.93
East of England	47	7.94	14.86
London	72	12.16	27.03
North East	29	4.9	31.93
North West	75	12.67	44.59
South East	94	15.88	60.47
South West	47	7.94	68.41
West Midlands	58	9.8	78.21
Yorkshire & Humber	40	6.76	84.97
Northern Ireland	21	3.55	88.51
Scotland	46	7.77	96.28
Wales	22	3.72	100
Total	592	100	

Table L.25: Ethnicity

ethnicity	Freq.	Percent	Cum.
White British	481	81.25	81.25
White Irish	8	1.35	82.6
Other White	31	5.24	87.84
Black or Black British - Caribbean	9	1.52	89.36
Black or Black British – African	7	1.18	90.54
Other Black	17	2.87	93.41
Asian British – Indian	6	1.01	94.43
Asian British - Bangladeshi	7	1.18	95.61
Chinese	10	1.69	97.3
Other Asian	4	0.68	97.97
Mixed ethnicity - white & black Caribbean	4	0.68	98.65
Mixed ethnicity - white & black African	8	1.35	100
prefer not to say	481	81.25	81.25
Total	592	100	

Table L.26: Education

Which of these best describes the highest educational qualification you have obtained so far?			
education	Freq.	Percent	Cum.
No formal qualifications	17	2.87	2.87
GCSE Level education (e.g. GCSE, O-Levels or Standards)	128	21.62	24.49
A-Level education (e.g. A, AS, S-Levels, Highers)	128	21.62	46.11
Degree or Graduate education (e.g. BSc, BA)	163	27.53	73.65
Post-graduate education (e.g. PhD, MSc, MA)	85	14.36	88.01
Vocational education (e.g. NVQ, HNC, HND)	63	10.64	98.65
Prefer not to say	8	1.35	100
Total	592	100	

Median household pre-tax income was in the range £25,000 - £34,999. The 2013/14 Households below average income (HBAI) statistics report from the DWP gives a median household income (2 adults) as £23,556.

The age distribution is shown in Table L.28.

Table L.27: Household Income

Please tell us your Household income group *This is the amount you earn before tax, and includes the people you live with (partner, family) – but do not include people you house/flat share with.*			
income	Freq.	Percent	Cum.
Below £6,500	12	2.03	2.03
£6,500 - £11,499	43	7.26	9.29
£11,500 - £17,499	38	6.42	15.71
£17,500 - £24,999	79	13.34	29.05
£25,000 - £34,999	110	18.58	47.64
£35,000 - £44,999	90	15.2	62.84
£45,000 - £54,999	66	11.15	73.99
£55,000 - £74,999	56	9.46	83.45
£75,000 - £99,999	44	7.43	90.88
£100,000 - £124,999	23	3.89	94.76
£125,000 - £149,999	14	2.36	97.13
£150,000 - £199,999	8	1.35	98.48
more than £200,000	9	1.52	100
Total	592	100	

Table L.28: Age Groups

agecat	Freq.	Percent	Cum.
18-19	18	3.04	3.21
20-29	98	16.55	19.76
30-39	157	26.52	46.28
40-49	158	26.69	72.97
50-59	102	17.23	90.2
60-69	49	8.28	98.48
70-79	7	1.18	99.66
80-89	2	0.34	100
Total	591	100	

Health

The mean EQ5D utility score value (maximum value of 1) was 0.88

eq5d utility score	Obs	Mean	Std. Dev.	Min	Max
eq5dutility	446	0.882762	0.226135	-0.429	1

The distribution of EQ5D utility scores is shown in Figure L.2. A total of 9 people in the sample reported a health state less than 0 (worse than death).

The history of the sample and their family members with diarrhoea and/or vomiting in the past year are shown in Table L.29 which shows proportions – e.g. 48% of the sample have had mild diarrhoea and/or vomiting lasting less than a day in the last year.

Figure L.2: Histogram EQ5D utility scores – Adult sample

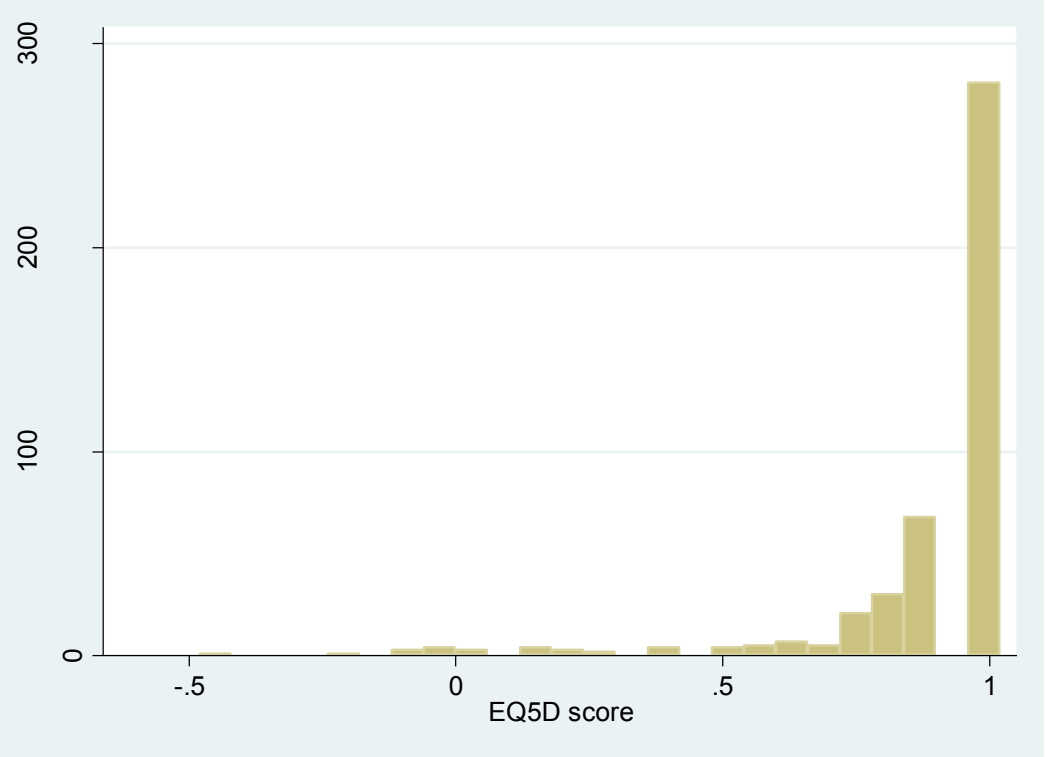


Table L.29: History of diarrhoea and/or vomiting in past year

In the past year please tell us if you or family members have had illnesses like this?				
	You	Other adults in the family	Children in the family	None of them
Mild diarrhoea and/or vomiting <1 day	0.476	0.282	0.390	0.316
Mild diarrhoea and/or vomiting , 1-3 days, time off work/school, no Dr contact	0.248	0.228	0.311	0.468
Mild diarrhoea and/or vomiting , 1-3 days, time off work/school, Dr contact	0.120	0.096	0.140	0.720
Severe diarrhoea and/or vomiting, time off work/school, > 1 Dr contact	0.074	0.063	0.073	0.828
Severe food poisoning, 1+ nights in hospital	0.049	0.024	0.035	0.905

The long run vignettes included in the valuation study featured a series of conditions as shown in Table L.30.

Table L.30: History of long run FBD conditions

Please indicate if either you, or someone in your close family, has any experience of the following illnesses.		
	you	member close family
Guillain-Barre Syndrome	0.037	0.042
Irritable Bowel Syndrome	0.159	0.233
Arthritis	0.110	0.289
Febrile Convulsions	0.020	0.108
Mesenteric adenitis	0.012	0.049
Septicaemia	0.019	0.088
Complicated Jaundice	0.010	0.069
Osteomyelitis	0.012	0.042
Hemolytic uremic syndrome (HUS)	0.010	0.044
Thrombotic thrombocytopenic purpura (TTP)	0.012	0.037
Renal Failure/ Dialysis	0.005	0.066
Meningitis	0.035	0.076

L.5. Choices, Task Difficulty & Protests – Parent sample

Possible protest behaviour were investigated for people who selected a pay, or a no pay, option in all of the sets they faced.

People with this pattern of choices in the short term sets were prompted as to why that was the case using the responses shown in Tables L.31 and L.32.

Table L.31: Why never chose to pay – short term

Please select the option that best explains why you never chose to pay to avoid the illness.			
	Freq.	Percent	Cum.
1. The illness wouldn't be too bad.	6	1.01	1.01
2. My child would get better anyway, so it is not worth paying for the treatment.	11	1.86	2.87
3. I would like my child to avoid the illness but I could not afford to pay what was asked	7	1.18	4.05
4. I shouldn't have to pay because the government should provide health care.	7	1.18	5.24
5. I have an ethical/religious objection to my child taking medicines	1	0.17	5.41
6. Other (please specify)	5	0.84	6.25
n/a	555	93.75	100
Total	592	100	

Table L.32: Why always chose to pay – short term

Please select the option that best explains why you always chose to pay to avoid the illness.	Freq.	Percent	Cum.
1. I did not think the request for payment was realistic so I ignored it	11	1.86	1.86
2. The cost was small compared to my child's pain and suffering	107	18.07	19.93
3. The cost was small compared to the costs involved in caring for my ill child.	18	3.04	22.97
4. Other (please specify)	7	1.18	24.16
n/a	449	75.84	100
Total	592	100	

People choosing options 4-6 in Table L.31, and options 1 or 4 in Table L.32 were excluded from the estimation sample. The rates of such 'protests' were very low considering this was a health-payment study in the UK.

Possible protest behaviour were investigated for people who selected a pay, or a no pay, option in all of the sets they faced.

People who selected a pay, or a no pay, option in all of the long term sets were prompted as to why that was the case using the responses shown in Tables L.33 and L.34.

Table L.33: Why never chose to pay – long term

Please select the option that best explains why you never chose to pay to avoid the illness.	Freq.	Percent	Cum.
1. The illness wouldn't be too bad - I could live with it.	6	1.01	1.01
2. I would get better anyway, so it is not worth paying for the treatment.	12	2.03	3.04
3. I would like to avoid the illness but I could not afford to pay what was asked.	34	5.74	8.78
4. I shouldn't have to pay because the government should provide health care.	13	2.2	10.98
5. I have an ethical/religious objection to my child taking medicines			
6. Other (please specify)	2	0.34	11.32
n/a	525	88.68	100
Total	592	100	

Table L.34: Why always chose to pay – long term

Please select the option that best explains why you always chose to pay to avoid the illness.	Freq.	Percent	Cum.
1. I did not think the request for payment was realistic so I ignored it	16	2.7	2.7
2. The cost was small compared to my child's pain and suffering	109	18.41	21.11
3. The cost was small compared to the costs involved in caring for my ill child.	20	3.38	24.49
4. Other (please specify)	20	3.38	27.87
n/a	427	72.13	100
Total	592	100	

People choosing options 4-6 in Table L.33, and options 1 or 4 in Table L.34 were excluded from the estimation sample. As with the short term sets the rates of such 'protests' were very low. Respondents were debriefed on how hard to was to understand the sets, and how hard it was to make the choices within them

Table L.35: How hard was it to <u>understand</u> the choice questions involving illness and money? – short term

	Freq.	Percent	Cum.
very difficult	21	3.55	3.55
difficult	49	8.28	11.82
neutral	108	18.24	30.07
easy	195	32.94	63.01
very easy	219	36.99	100
Total	592	100	

Table L.36: How hard was it to <u>make</u> the choice questions involving illness and money? – short term

	Freq.	Percent	Cum.
very difficult	36	6.08	6.08
difficult	114	19.26	25.34
neutral	127	21.45	46.79
easy	188	31.76	78.55
very easy	127	21.45	100
Total	592	100	

The choice tasks were complex, which was why so much effort had been assigned to preparation of the materials and testing and refining them in focus groups, interviews and pilot surveys.

Rates of 4% and 8% respectively describing the short term sets as very difficult and difficult to understand were regarded as validating those efforts. Making the choices was more often reported as more difficult than understanding the choices.

Table L.37: How hard was it to understand the choice questions involving illness and money? – long term

	Freq.	Percent	Cum.
very difficult	36	6.08	6.08
difficult	63	10.64	16.72
neutral	101	17.06	33.78
easy	221	37.33	71.11
very easy	171	28.89	100
Total	592	100	

Table L.38: How hard was it to make the choice questions involving illness and money? – long term

	Freq.	Percent	Cum.
very difficult	134	22.64	22.64
difficult	137	23.14	45.78
neutral	91	15.37	61.15
easy	130	21.96	83.11
very easy	100	16.89	100
Total	592	100	

The long term conditions included much more information and were more demanding. Rates of 6% and 11% respectively describing the sets as very difficult and difficult to understand were regarded as not signifying fundamental problems with the long term valuation process.

Making the choices was more often reported as more difficult than understanding the choices, and more often so in the long term sets than the short term ones.

APPENDIX M: DATA ANALYSIS (EQ-5D-3L SAMPLE)

M.1 Econometric Models and Results

In the EQ-5D DCE for short term conditions respondents chose between remaining in current health at a cost, or experiencing reduced health (defined in terms of EQ-5D-3L levels) for a defined duration (between 1 and 14 days). The utility functions for the two Alternatives are given in (1a) and (1b).

$$U_i^{Ill} = T\left(\sum_{n=1}^{5}\sum_{l=2}^{3}\beta_{nl}EQ5D_{nli}^{ILL}\right) + \alpha_t T + \alpha_e T \times LE_i + \alpha_{0i} \quad (1a)$$

$$U_i^{C} = T\left(\sum_{n=1}^{5}\sum_{l=2}^{3}\beta_{nl}EQ5D_{nli}^{C}\right) + \delta_c Cost + \delta_m Cost \times IncomeMD \quad (1b)$$

Utility is determined by the health level given by the EQ-5D-3L levels. This is multiplied by the duration of the health state (T). $EQ5D^{ILL}_{nli}$ are dummy variables indicating the health state in the reduced health option, (n=5 dimensions, l= 3 levels)

$EQ5D^{C}_{nli}$ are dummy variables indicating the health state in the current health option, (n=5 dimensions, l= 3 levels). The introduction of the current health state is required, as otherwise the model would over-state the benefits of avoiding the illness.

Utility in the ill state (1a) is augmented by terms capturing

(i) the length of the illness, irrespective of health state,
(ii) the length of illness interacted with the self-reported lost earnings per day (LE), and
(iii) an individual specific Alternative Specific Constant (ASC) to capture any baseline aversion to suffering reduced health, irrespective of length and severity of the reduced health.

Utility in the current health state (1b) is augmented by terms capturing

(i) the cost of avoiding the illness state, and
(ii) an interaction of cost with income (defined as mean deviations) to account for a differing marginal utility of money over income levels.

The model is estimated as a Mixed Logit model, with the individual specific constant α_{0i} modelled as a normally distributed random parameter that is constant over all choices by that individual. Estimation results are reported in Table M.1.

Table M.1: Mixed Logit Results - Adult EQ-5D (short term)

	Coeff	SE	Z
T x mobility_D2	-0.02953	0.007997	-3.69
T x mobility_D3	-0.07657	0.010904	-7.02
T x selfcare_D2	-0.04879	0.008099	-6.02
T x selfcare_D3	-0.14504	0.013146	-11.03
T x usualactivities_D2	-0.03142	0.007535	-4.17
T x usualactivities_D3	-0.07179	0.010815	-6.64
T x pain_D2	-0.03988	0.007825	-5.1
T x pain_D3	-0.17392	0.011282	-15.42
T x anxiety_D2	-0.00872	0.00815	-1.07
T x anxiety_D3	-0.11936	0.012935	-9.23
T	-0.10538	0.008967	-11.75
T x LE	-3.5E-05	1.71E-05	-2.04
Ill	-0.47611	0.06874	-6.93
Cost	-0.02006	0.000629	-31.90
Cost x IncomeMD	7.70E-08	7.64E-09	10.08
St Dev of random parameter			
ill	2.148459	0.057391	37.44
Choices=15888; Individuals =1986; LL=-8160.8101			

Cost is significant and negative – respondents took account of the costs in their choices. All EQ-5D health parameters are significant and with the anticipated ordering, with the exception of T x anxiety_D2.

Poorer health states reduce utility (apart from anxiety_D2 where there appears to be no differentiation between full health and level 2), and there is a significant differentiation between state 2 and state 3 for all 5 measures.

The negative coefficient for T implies that there is an effect of the length of illness in addition to that associated with any specific health state, and the negative coefficient on ill (the ASC associated with the illness state) implies that there is a negative utility associated with illness irrespective of illness state *or* duration. The interaction between T and lost earnings (LE) is negative which suggests that the 'duration' effect is larger for those who expect to lose more income per day because of it.

The structure of the short term EQ-5D- 3L DCE sets for parents answering regarding their child's health states were identical to that for the adults. Parents were asked to choose between (i) a specified period of ill health for their child, followed by a return to current health and (ii) remaining at current health but at a cost.

Table M.2 reports results from the estimation of a mixed logit model upon the parents' choice data regarding their children's health states.

Table M.2: Parent EQ-5D DCE mixed logit results, short term illness

	Coeff	SE	Z
T x mobility_D2	-0.03437	0.014926	-2.30
T x mobility_D3	-0.0514	0.019519	-2.64
T x selfcare_D2	0.012722	0.014598	0.87
T x selfcare_D3	-0.05669	0.02281	-2.49
T x usualactivities_D2	-0.02996	0.013879	-2.16
T x usualactivities_D3	-0.08726	0.019538	-4.47
T x pain_D2	-0.07250	0.014549	-4.98
T x pain_D3	-0.17891	0.01975	-9.06
T x anxiety_D2	0.012692	0.014840	0.86
T x anxiety_D3	-0.09042	0.023060	-3.92
Cost	-0.01848	0.001136	-16.27
T	0.076965	0.017190	4.48
Cost x IncomeMD	4.83E-08	1.15E-08	4.18
ill	-1.47333	0.132799	-11.09
St Dev of random parameter			
ill	2.2555	0.1077992	20.92
Choices=5080; Individuals =635; LL = -2521.5993			

Cost is significant and negative – parents took account of the costs to them of their child avoiding ill health when making their choices. The marginal utility of cost is affected by income as economic theory would suggest.

All EQ-5D health parameters are significant and with the exception of *T x SelfCareD2* and *T x anxietyD2* which are not significantly different from the baseline EQ-5D level.

The negative coefficient for T implies that there is an effect of the length of illness in addition to that associated with any specific health state, and the negative coefficient on ill (the ASC associated with the illness state) implies that there is a negative utility associated with a child's illness irrespective of illness state *or* duration. This term is specified as random with the St.Dev estimate indicating large heterogeneity in this illness aversion.

The utility function associated with the long run EQ5D model differs since respondents are asked to consider two alternative life paths with different health states, lasting for different periods. The monetary attribute is not a marginal change in income, but the average annual income.

Our starting point for the model is a specific implementation of the general model presented by Bleichrodt and Quiggin (1999):

$$U = \sum_{t=1}^{T} v(c)q(h_t) \qquad (2)$$

Where T is the life span expected, v(c) is the utility over consumption and is strictly increasing in c, and q(h) is the utility over the health state h.

Our formal representation of utility takes the form

$$U_i = T \times Income^{\alpha} \times \exp\left(\sum_{n=1}^{5}\sum_{l=2}^{3}\beta_{nl} EQ5D_{nli}^{Ill}\right) \quad (3)$$

taking logs gives:

$$\overline{U_i} = \ln(T) + \alpha \ln(Income) + \sum_{n=1}^{5}\sum_{l=2}^{3}\beta_{nl} EQ5D_{nli}^{Ill} \quad (4)$$

We impose the restriction that the coefficient on ln(*T*) = 1 by using a 'WTP space representation of the model, allowing the error variance to be freely estimated.

We include an alternative specific constant for the illness alternative, specified as a random parameter. We introduce an anchoring effect on the income level since analysis indicated that respondents do not place the same value on increases in income above their current income, as they do on reductions in income below it. This effect appears to be absolute: respondents place no additional utility on income levels above their current level, although they do place utility on changes in income below it. The behavioural interpretation of this effect is that respondents would not be prepared to accept any reductions in length of life, or reductions in health status, if the only compensation for that change was an increase in income. They would be prepared to accept a reduction in income to achieve an improvement in health status or years of life i.e. they are willing to pay to achieve those improvements, but they are not willing to accept increases in income above their current income to compensate for health/longevity decrements.

The estimated model is therefore based on the utility function:

$$\overline{U_i} = \ln(T) + \alpha \ln(Income') + \sum_{n=1}^{5}\sum_{l=2}^{3}\beta_{nl} EQ5D_{nli}^{Ill} + \alpha_{0i} \quad (5)$$

Where Income' is the transformed income level, where income levels above the respondent's current level are recoded as that current level. This transformation hugely improves model fit and has the behavioural interpretation explained above. The results from estimation of this model are reported in Table M.3.

Table M.3: Mixed Logit Model, Long Term Adult EQ-5D Sample

variable	coefficient	SE	Z
Ln(T)	1	..	..
Ln(Income')	0.420932	0.093394	4.51
mobility_D2	-0.28457	0.040111	-7.09
mobility_D3	-1.18728	0.064498	-18.41
selfcare_D2	-0.15041	0.041118	-3.66
selfcare_D3	-0.81302	0.056987	-14.27
usualactivities_D2	-0.16082	0.039628	-4.06
usualactivities_D3	-0.41987	0.06288	-6.68
pain_D2	-0.24883	0.04627	-5.38
pain_D3	-0.81532	0.0652	-12.5
anxiety_D2	-0.27736	0.042369	-6.55
anxiety_D3	-0.75846	0.067625	-11.22
ill	0.420932	0.093394	4.51
St Dev of random parameter			
ill	1.05665	0.035822	29.5
Error variance			
	0.363617	0.027707	13.12
number of choices =12504; number of individuals =1563; LL = -6095.8563			

These results suggest respondents are attending to health, income and duration terms. Increased annual income (up to current income) increases utility, and all the EQ5D deviations from full health reduce utility. In all cases respondents are sensitive to the degree of health reduction (in all cases the Marginal Utility for an EQ-5D level 3 attribute is significantly different from its level 2 equivalent).

The marginal WTP to avoid a year in each of the 10 health states below full health is given by:

$$WTP_{nl} = 1 - \exp(\beta_{nl} / \alpha) \quad (6)$$

In the Parent EQ-5D DCE study for long-term child ill health the structure of the DCE was the same as the short term, except the durations increased greatly, as did the cost. The child returned to current health after any illness: the parent was never asked to choose between lives of differing length for their child. Estimates from a mixed logit model estimated on these data are reported in Table M.4.

Table M.4: Parent EQ-5D DCE mixed logit results, long term illness

	Coeff	SE	Z
T x mobility_D2	-0.02142	0.015942	-1.34
T x mobility_D3	-0.04355	0.022073	-1.97
T x selfcare_D2	0.033997	0.015852	2.14
T x selfcare_D3	0.000705	0.024817	0.03
T x usualactivities_D2	0.002245	0.015353	0.15
T x usualactivities_D3	0.007959	0.022451	0.35
T x pain_D2	0.002724	0.015543	0.18
T x pain_D3	-0.08445	0.02115	-3.99
T x anxiety_D2	0.001874	0.016328	0.11
T x anxiety_D3	-0.02804	0.025172	-1.11
Cost	-0.01202	0.0012146	-9.90
Cost x IncomeMD	5.86E-08	1.17E-08	5.01
Ill x IncomeMD	-1.72E-05	4.25E-06	4.12
T x Ill	-0.078154	0.018492	4.27
Ill	0.2654986	0.176412	1.50
St Dev of random parameter			
Ill	3.072886	0.1561762	19.68
Choices=4696; Individuals =587; LL = -2183.9668			

The pattern observed thus far in all the WTP studies (Vignette, EQ-5D; Adult, Parent) of significance of (nearly) all parameters breaks down in this case.
The choice data indicate very little attention paid to the health attributes. The respondents do attend to the duration of the illness, the cost to avoid illness, and those with higher incomes are willing to pay more to avoid the illness. Although these results indicate that parents are willing to avoid long run illness for their children, they are of little use as the choices and hence the WTPS are not differentiated by the severity of the illness experienced by the child.

Monetary Value of a QALY

The model estimated for the responses to the EQ5D version of the questionnaire (Appendix M) can be used to estimate the value of obtaining an additional year of full health i.e. the WTP to acquire a QALY. Conceptually this identifies the reduction in income that would exactly offset the increase in utility associated with the length of life being extended by one year at full health.

As Bleichrodt and Quiggin (1999) note, this value will depend on: the relative substitutability of income and time in the utility function (as defined by the relative sizes of the coefficients on ln(T) and ln(Income')), the income of the respondent, and the number of years before the additional year of life is gained.

Analysis of the choice data indicated that respondents were not discounting. Hence in the analysis that follows we ignore all discounting of time i.e. respondents are indifferent to when consumption or extra years occur. This simplifying assumption is justified by the data.

An assumption has to be made as to whether additional income is earned when the additional year of life is gained. We start by assuming that that does not occur, and hence that the respondent has a fixed wealth which does not change as a result of the additional year of health being gained. We relax this below. We also assume that the respondent is at full health for all years considered.

Assume that an individual has an initial wealth of W, and an expected life span of T. Given the utility function

$$U_1 = \sum_{t=1}^{T} Income_t^{\alpha} \tag{7}$$

The optimal allocation of wealth over time is to equalise it, so that $Income_t = W/T = Y$

$$U_1 = \sum_{t=1}^{T} \left(\frac{W}{T}\right)^{\alpha} \tag{8}$$

If an additional year of life is given, and wealth is unchanged, then the utility over the life time is now:

$$U_2 = \sum_{t=1}^{T+1} \left(\frac{W}{T+1}\right)^{\alpha} \tag{9}$$

To identify the maximum WTP for the extra year of health one has to identify the reduction in wealth that would leave the 2 utilities equal:

$$\sum_{t=1}^{T} \left(\frac{W}{T}\right)^{\alpha} = \sum_{t=1}^{T+1} \left(\frac{W-\delta}{T+1}\right)^{\alpha} \tag{10}$$

Solving for δ (the WTP to acquire the extra year) gives:

$$\delta = W\left[\left(\frac{T}{T+1}\right)^{\frac{1-\alpha}{\alpha}} - 1\right] \tag{11}$$

Or if defined in terms of the initial annual income:

$$\delta = (Y \times T)\left[\left(\frac{T}{T+1}\right)^{\frac{1-\alpha}{\alpha}} - 1\right] \tag{12}$$

The WTP for a QALY depends on the rate of substitution between time and income. As α tends towards 1 the WTP tends towards zero. At the limit, where α=1 the individual maximises utility over total wealth, and is not concerned about when it occurs (there is no decreasing marginal utility of income) and hence is not prepared

to sacrifice any wealth to obtain an extra year of life. However, if α<1 i.e. there is decreasing marginal utility in consumption, spreading the same wealth over more years increases welfare, as, at the margin, the marginal utility of consumption is increased in all years. Thus, as α gets smaller, WTP for a QALY will increase. WTP also increases in T, the original life expectancy.

If the original T is equal to 1, then the addition of an additional year represents a 100% increase in the amount of time over which the original fixed wealth has to be allocated: income per year will be halved. Forcing consumption back by this amount will cause significant reductions in utility and substantial increases in the marginal utility of income.

If the original T =10, and the initial allocation of wealth is increased commensurately, so initially the average income is the same, then an addition of 1 year of life represents only a 10% increase in life expectancy: if initial wealth is allocated over all 11 years, then average income per year does not fall greatly. Thus marginal utility of income does not increase as much. Hence, in the case of T=10, there is greater scope to reduce wealth in the quest for equalizing utility before and after the addition of a year of life.

To illustrate these effects, Table M.5 reports the values for a QALY for three different income levels, and for an initial T of 1 and 10.

Table M.5: WTP for a QALY, by income level, and number of years of life remaining (£)

	Gross Household Income		
	£10,000	£31,655	£100,000
T=1	6,100 (3,400-8,90)	19,456 (10,700-28,200)	61,500 (33,900-89,100)
T=10	12,300 (3,600-20,900)	38,900 (11,600-66,200)	122,900 (36,500-209,200)

As expected, the WTP increases in proportion to income. If one takes the median income of £31,655 then the WTP for a QALY would be £19,456 for a year gained immediately.

These results assume that there is no rate of time preference. As the additional year of life occurs at the end of the period, then discounting with a positive discount rate will reduce the WTP.

These results are based on the assumption above that the additional year of life does not affect wealth, i.e. that consumption in that year has to be met by reallocating consumption from other years. An alternative assumption is that the earning capacity of the individual was the same in that additional year. This changes the fundamental object being valued: it is now an additional year of life, plus an addition to wealth of Y.

Again assuming no discounting over time, the implications for WTP is simple to derive:

$$\delta = (Y \times T)\left[\left(\frac{T}{T+1}\right)^{\frac{1-\alpha}{\alpha}} - 1\right] + Y \quad (13)$$

WTP for a QALY increases simply by the amount of annual income. The logic of this is straightforward. When considering what reduction in wealth is required to make a person indifferent to gaining an additional year of life, with income, one knows that one can reduce wealth by the amount of that additional income as an initial estimate (that would leave them in their initial wealth position, with an additional year of life but with no income, so their utility cannot be reduced). That then leaves the individual at the point of the previous analysis (an additional year of life without income) and one can then proceed with the previous analysis to identify the additional reduction in wealth that can occur.

Thus, WTP for a QALY for an individual at median income, under these assumptions, would be £31,655 + £19,456 = £51,111 per year. Similarly, all other estimates simply need to be updated by the value of annual income.

M.2 Adult Sample – demographics and health

A sample of 2211 adults was collected within the EQ5D sample. Some were removed because their speed of completion was so great that the data quality was considered unreliable. The active Adult EQ5D sample was then 2097.

Demographics

The sample was 52-48 split between females and males.

Table M.6: Gender

male	Freq.	Percent	Cum.
male	1,015	48.4	48.4
female	1,081	51.55	99.95
other	1	0.05	100
Total	2097	100	

The distribution of occupations and class are shown in Table M.7.

Table M.7: Occupation

We would like to know about the Chief Income Earner in your household
This is the person with the largest income.
If this person is

- *retired with an occupational pension then answer about their most recent occupation.*
- *not in a paid job but has been out of work for less than 6 months, then answer about their most recent job.*

The Chief Income Earner is (or was):			
	Freq.	**Percent**	**Cum.**
Semi or unskilled manual work	231	11.02	11.02
Skilled manual worker	398	18.98	30
Supervisory or clerical/ junior managerial/ professional/ administrative	510	24.32	54.32
Intermediate managerial/ professional/ administrative	526	25.08	79.4
Higher managerial/ professional/ administrative	177	8.44	87.84
Student	24	1.14	88.98
Casual worker – not in permanent employment	22	1.05	90.03
Housewife/ Homemaker	21	1	91.03
Retired and living on state pension	74	3.53	94.56
Unemployed or not working due to long-term sickness	100	4.77	99.33
Full-time carer of other household member	14	0.67	100
Total	2097	100	

The geographical split of the sample is shown in Table M.8. The division between UK nations is close to the aggregate national population proportions with 9.3% from Scotland (nationally 8.4%), 5.3% from Wales (nationally 4.8%) and 2.1% from Northern Ireland (nationally 2.9%). Ethnicity and Education are summarised in Tables M.9 and M.10.

Table M.8: Region

region	**Freq.**	**Percent**	**Cum.**
East Midlands	177	8.44	8.44
East of England	206	9.82	18.26
London	214	10.21	28.47
North East	102	4.86	33.33
North West	172	8.2	41.54
South East	337	16.07	57.61
South West	195	9.3	66.91
West Midlands	195	9.3	76.2
Yorkshire & Humber	149	7.11	83.31
Northern Ireland	45	2.15	85.46
Scotland	194	9.25	94.71
Wales	110	5.25	99.95
Total	2097	100	

Table M.9: Ethnicity

ethnicity	Freq.	Percent	Cum.
White British	1,818	86.7	86.7
White Irish	31	1.48	88.17
Other White	104	4.96	93.13
Black or Black British - Caribbean	17	0.81	93.94
Black or Black British – African	12	0.57	94.52
Other Black	0	0	94.52
Asian British – Indian	33	1.57	96.09
Asian British - Bangladeshi	3	0.14	96.23
Chinese	12	0.57	96.8
Other Asian	24	1.14	97.95
Mixed ethnicity - white & black Caribbean	14	0.67	98.62
Mixed ethnicity - white & black African	2	0.1	98.71
prefer not to say	27	1.29	100
Total	2097	100	

Table M.10: Education

Which of these best describes the highest educational qualification you have obtained so far?			
education	**Freq.**	**Percent**	**Cum.**
No formal qualifications	111	5.29	5.29
GCSE Level education (e.g. GCSE, O-Levels or Standards)	442	21.08	26.37
A-Level education (e.g. A, AS, S-Levels, Highers)	447	21.32	47.69
Degree or Graduate education (e.g. BSc, BA)	574	27.37	75.06
Post-graduate education (e.g. PhD, MSc, MA)	272	12.97	88.03
Vocational education (e.g. NVQ, HNC, HND)	240	11.44	99.48
Prefer not to say	11	0.52	100
Total	2097	100	

Median household pre-tax income was in the range £25,000 - £34,999. The 2013/14 Households below average income (HBAI) statistics report from the DWP gives a median household income (2 adults) as £23,556.

The age distribution is shown in Table M.12.

Table M.11: Household Income

Please tell us your Household income group *This is the amount you earn before tax, and includes the people you live with (partner, family) – but do not include people you house/flat share with.*			
income	**Freq.**	**Percent**	**Cum.**
Below £6,500	87	4.15	4.15
£6,500 - £11,499	165	7.87	12.02
£11,500 - £17,499	186	8.87	20.89
£17,500 - £24,999	314	14.97	35.86
£25,000 - £34,999	397	18.93	54.79
£35,000 - £44,999	311	14.83	69.62
£45,000 - £54,999	206	9.82	79.45
£55,000 - £74,999	207	9.87	89.32
£75,000 - £99,999	132	6.29	95.61
£100,000 - £124,999	42	2	97.62
£125,000 - £149,999	20	0.95	98.57
£150,000 - £199,999	16	0.76	99.33
more than £200,000	14	0.67	100
Total	2097	100	

Table M.12: Age Groups

agecat	**Freq.**	**Percent**	**Cum.**
18-19	25	1.19	1.19
20-29	272	12.97	14.16
30-39	414	19.74	33.91
40-49	418	19.93	53.84
50-59	439	20.93	74.77
60-69	352	16.79	91.56
70-79	163	7.77	99.33
80+	14	0.67	100
Total	2097	100	

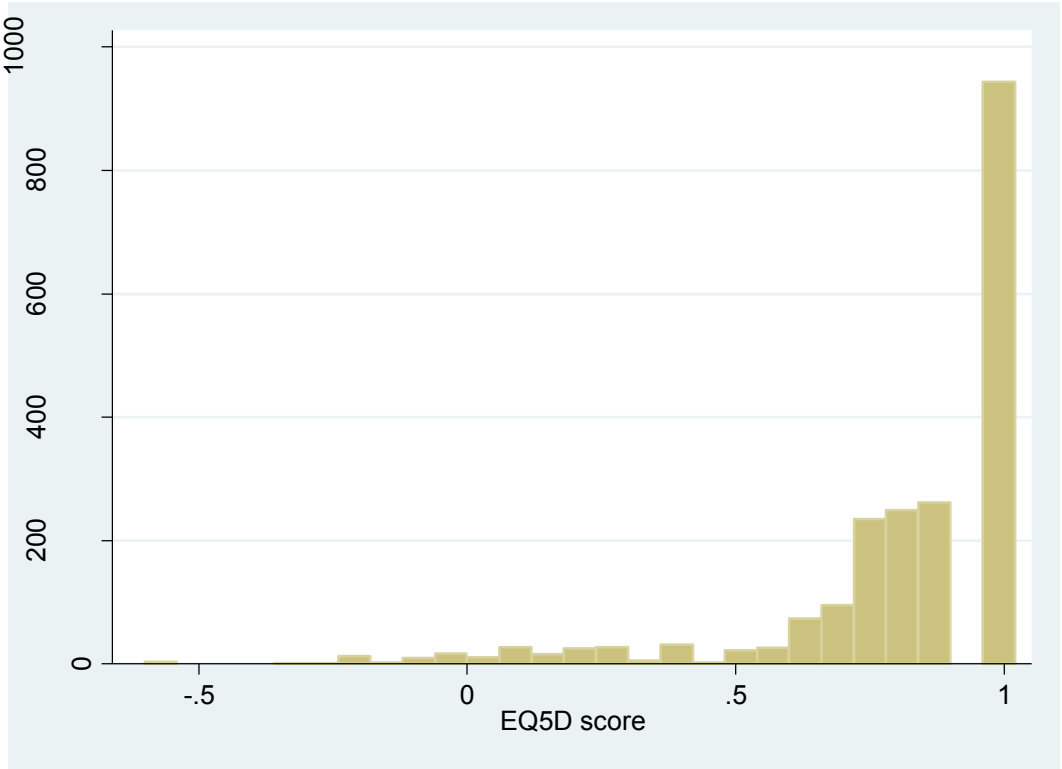
Health

The mean EQ5D utility score value (maximum value of 1) was 0.81

eq5d utility score	**Obs**	**Mean**	**Std. Dev.**	**Min**	**Max**
eq5dutility	2,097	0.812	0.255	-0.594	1

The distribution of EQ5D utility scores is shown in Figure M.1. A total of 47 people in the sample reported a health state less than 0 (worse than death).

Figure M.1: Histogram EQ5D utility scores – Adult sample



The history of the sample and their family members with diarrhoea and/or vomiting in the past year are shown in Table M.13 which shows proportions – e.g. 51% of the sample have had mild diarrhoea and/or vomiting lasting less than a day in the last year, 2% report having been hospitalised by diarrhoea and/or vomiting in the past year.

Table M.13: History of diarrhoea and/or vomiting in past year

In the past year please tell us if you or family members have had illnesses like this?				
	You	Other adults in the family	Children in the family	None of them
Mild diarrhoea and/or vomiting <1 day	0.512	0.282	0.114	0.375
Mild diarrhoea and/or vomiting , 1-3 days, time off work/school, no Dr contact	0.214	0.153	0.095	0.663
Mild diarrhoea and/or vomiting , 1-3 days, time off work/school, Dr contact	0.069	0.050	0.036	0.870
Severe diarrhoea and/or vomiting, time off work/school, > 1 Dr contact	0.052	0.033	0.021	0.906
Severe food poisoning, 1+ nights in hospital	0.022	0.016	0.010	0.954

The long term impacts of FBD can include a number of conditions. These conditions featured explicitly in the valuation scenarios in the Vignette sample.
To aid comparison between the two adult samples (vignette, EQ5D), we report in Table M.14 the experience of the Adult EQ5D sample of those conditions.
This reveals that 16% of the sample reported having experienced IBS, 16% arthritis and 1.8% Meningitis.

Table M.14: History of long run FBD conditions

Please indicate if either you, or someone in your close family, has any experience of the following illnesses.		
	you	**member close family**
Guillain-Barre Syndrome	0.018	0.018
Irritable Bowel Syndrome	0.156	0.181
Arthritis	0.161	0.296
Febrile Convulsions	0.008	0.024
Mesenteric adenitis	0.009	0.014
Septicaemia	0.021	0.050
Complicated Jaundice	0.011	0.022
Osteomyelitis	0.010	0.019
Hemolytic uremic syndrome (HUS)	0.008	0.014
Thrombotic thrombocytopenic purpura (TTP)	0.005	0.020
Renal Failure/ Dialysis	0.011	0.042
Meningitis	0.018	0.049

M.3. Choices, Task Difficulty & Protests – Adult sample

Possible protest behaviour were investigated for people who selected a pay, or a no pay, option in all of the DCE sets they faced.

People with this pattern of choices in the short term sets were prompted as to why that was the case using the responses shown in Tables M.15 and M.16.

Table M.15: Why never chose to pay – short term

Please select the option that best explains why you never chose to pay to avoid the illness.			
	Freq.	**Percent**	**Cum.**
1. The illness wouldn't be too bad - I could live with it.	54	2.58	2.58
2. I would get better anyway, so it is not worth paying for the treatment.	61	2.91	5.48
3. I would like to avoid the illness but I could not afford to pay what was asked	54	2.58	8.06
4. I shouldn't have to pay because the government should provide health care.	36	1.72	9.78
5. I have an ethical/religious objection to taking medicines.	1	0.05	9.82
6. Other (please specify)	18	0.86	10.68
n/a	1,873	89.32	100
Total	2097	100	

Table M.16: Why always chose to pay – short term

Please select the option that best explains why you always chose to pay to avoid the illness.			
	Freq.	**Percent**	**Cum.**
1. I did not think the request for payment was realistic so I ignored it	27	1.29	1.29
2. The cost was small compared to the pain and suffering	270	12.88	14.16
3. The cost was small compared to what I would lose missing work	75	3.58	17.74
4. Other (please specify)	29	1.38	19.12
n/a	1,696	80.88	100
Total	2097	100	

People choosing options 4-6 in Table M.15, and options 1 or 4 in Table M.16 were excluded from the estimation sample. The rates of such 'protests' were very low considering this was a health-payment study in the UK.

The LR sets did not feature "pay" and "no pay" options, they comprised sets with differing lifespans and annual incomes – so the debrief questions were different.

Life A always involved ill health, and respondents who always chose this option in the eight sets were prompted as to why that was the case.
Life B always involved current health, and respondents who always chose this option in the eight sets were prompted as to why that was the case.

The responses are shown in Tables M.17 and M.18.

Table M.17: Why always chose a poorer health option

Please select the option that best explains why you always chose Life A - the option in which there was a period of (red) ill health.			
	Freq.	**Percent**	**Cum.**
1. I considered income, time spent in both good and ill health, and the severity of illness - and I always preferred Life A	27	1.41	1.41
2. I always picked the option with the longest total life, regardless of the income or severity of illness.	20	1.04	2.45
3. Other	2	0.1	2.56
4. n/a	1,866	97.44	100
Total	1915	100	

Table M.18: Why never chose a poorer health option

Please select the option that best explains why you never chose Life A - the option in which there was a period of (red) ill health.			
	Freq.	**Percent**	**Cum.**
1. I considered income, time spent in both good and ill health, and the severity of illness - and I always preferred Life B.	204	10.65	10.65
2. I always avoided the option with (red) ill health, regardless of the income or overall length of life	188	9.82	20.47
3. Other	26	1.36	21.83
4. n/a	1,497	78.17	100
Total	1915	100	

Respondents were debriefed on how hard it was to understand the sets, and how hard it was to make the choices within them.

Table M.19: How hard was it to <u>understand</u> the choice questions involving illness and money? – short term

	Freq.	**Percent**	**Cum.**
very difficult	36	1.72	1.72
difficult	232	11.06	12.78
neutral	476	22.7	35.48
easy	845	40.3	75.77
very easy	508	24.23	100
Total	2097	100	

Table M.20: How hard was it to <u>make</u> the choice questions involving illness and money? – short term

	Freq.	**Percent**	**Cum.**
very difficult	79	3.77	3.77
difficult	465	22.17	25.94
neutral	482	22.99	48.93
easy	704	33.57	82.5
very easy	367	17.5	100
Total	2097	100	

The choice tasks were complex, which was why so much effort had been assigned to preparation of the materials and testing and refining them in focus groups, interviews and pilot surveys.

Rates of 2% and 11% respectively describing the short term sets as very difficult and difficult to understand were regarded as validating those efforts. The proportion finding the short run EQ5D DCE (very) difficult was 12%, slightly higher than the 10% reporting this for the equivalent Vignette sets.

Making the choices was more often reported as more difficult than understanding the choices, but this concerns difficulty making the decision rather than necessarily being confused by the information comprising the options. 26% of the Adult EQ5D

sample found making the choices (very) difficult, compared to 18% in the equivalent Vignette sets.

Table M.21: How hard was it to understand the choice questions involving illness and money? – long term

	Freq.	Percent	Cum.
very difficult	74	3.53	3.53
difficult	252	12.02	15.55
neutral	411	19.6	35.15
easy	863	41.15	76.3
very easy	497	23.7	100
Total	2097	100	

Table M.22: How hard was it to make the choice questions involving illness and money? – long term

	Freq.	Percent	Cum.
very difficult	135	6.44	6.44
difficult	456	21.75	28.18
neutral	466	22.22	50.41
easy	691	32.95	83.36
very easy	349	16.64	100
Total	2097	100	

The long term DCEs were different and we expected them to be more of a challenge. Only 3.5% reported understanding them was very difficult, with another 12% reporting them as difficult. The equivalent vignette values were 4% and 9%. 28% found making the choices between the two lifepaths DCE (very) difficult; this was less than the 35% reporting this to be the case for the vignette long term choice sets.

M.4 Parents Sample – demographics and health

A sample of 720 parents was collected within the EQ5D (a sample size of 653 was achieved for the Vignette sample).

Some were removed because their speed of completion was so great that the data quality was considered unreliable. The active Parent EQ5D sample was then 668 (592 in vignette sample).

Demographics

The sample was 50-50 split between females and males (Table M.23). The distribution of occupations and class are shown in Table M.24.

Table M.23: Gender

male	Freq.	Percent	Cum.
male	331	49.55	49.55
female	337	50.45	100
Total	668	100	

Table M.24: Occupation

We would like to know about the Chief Income Earner in your household *This is the person with the largest income.* *If this person is* • *retired with an occupational pension then answer about their most recent occupation.* • *not in a paid job but has been out of work for less than 6 months, then answer about their most recent job.*			
The Chief Income Earner is (or was):			
	Freq.	Percent	Cum.
Semi or unskilled manual work	67	10.03	10.03
Skilled manual worker	125	18.71	28.74
Supervisory or clerical/ junior managerial/ professional/ administrative	177	26.5	55.24
Intermediate managerial/ professional/ administrative	150	22.46	77.69
Higher managerial/ professional/ administrative	84	12.57	90.27
Student	8	1.2	91.47
Casual worker – not in permanent employment	6	0.9	92.37
Housewife/ Homemaker	14	2.1	94.46
Retired and living on state pension	8	1.2	95.66
Unemployed or not working due to long-term sickness	18	2.69	98.35
Full-time carer of other household member	11	1.65	100
Total	668	100	

The geographical split of the sample is shown in Table M.25. The division between UK nations is close to the aggregate national population proportions with 7.6% from Scotland (nationally 8.4%), 5.5% from Wales (nationally 4.8%) and 2% from Northern Ireland (nationally 2.9%).

Table M.25: Region

region	Freq.	Percent	Cum.
East Midlands	41	6.14	6.14
East of England	59	8.83	14.97
London	92	13.77	28.74
North East	29	4.34	33.08
North West	77	11.53	44.61
South East	96	14.37	58.98
South West	62	9.28	68.26
West Midlands	53	7.93	76.2
Yorkshire & Humber	58	8.68	84.88
Northern Ireland	13	1.95	86.83
Scotland	51	7.63	94.46
Wales	37	5.54	100
Total	668	100	

Ethnicity and Education are summarised in Tables M.26 and M.27.

Table M.26: Ethnicity

ethnicity	Freq.	Percent	Cum.
White British	555	83.08	83.08
White Irish	11	1.65	84.73
Other White	30	4.49	89.22
Black or Black British - Caribbean	4	0.6	89.82
Black or Black British – African	10	1.5	91.32
Other Black	1	0.15	91.47
Asian British – Indian	18	2.69	94.16
Asian British - Bangladeshi	5	0.75	94.91
Chinese	6	0.9	95.81
Other Asian	12	1.8	97.6
Mixed ethnicity - white & black Caribbean	5	0.75	98.35
Mixed ethnicity - white & black African	1	0.15	98.5
prefer not to say	10	1.5	100
Total	668	100	

Table M.27: Education

Which of these best describes the highest educational qualification you have obtained so far?			
education	Freq.	Percent	Cum.
No formal qualifications	17	2.54	2.54
GCSE Level education (e.g. GCSE, O-Levels or Standards)	158	23.65	26.2
A-Level education (e.g. A, AS, S-Levels, Highers)	151	22.6	48.8
Degree or Graduate education (e.g. BSc, BA)	193	28.89	77.69
Post-graduate education (e.g. PhD, MSc, MA)	84	12.57	90.27
Vocational education (e.g. NVQ, HNC, HND)	60	8.98	99.25
Prefer not to say	5	0.75	100
Total	668	100	

Median household pre-tax income was in the range £25,000 - £34,999. The 2013/14 Households below average income (HBAI) statistics report from the DWP gives a median household income (2 adults) as £23,556.

The age distribution is shown in Table M.29.

Table M.28: Household Income

Please tell us your Household income group *This is the amount you earn before tax, and includes the people you live with (partner, family) – but do not include people you house/flat share with.*			
income	Freq.	Percent	Cum.
Below £6,500	12	1.8	1.8
£6,500 - £11,499	33	4.94	6.74
£11,500 - £17,499	51	7.63	14.37
£17,500 - £24,999	99	14.82	29.19
£25,000 - £34,999	113	16.92	46.11
£35,000 - £44,999	100	14.97	61.08
£45,000 - £54,999	73	10.93	72.01
£55,000 - £74,999	76	11.38	83.38
£75,000 - £99,999	57	8.53	91.92
£100,000 - £124,999	26	3.89	95.81
£125,000 - £149,999	10	1.5	97.31
£150,000 - £199,999	9	1.35	98.65
more than £200,000	9	1.35	100
Total	668	100	

Table M.29: Age Groups (Parent)

agecat	**Freq.**	**Percent**	**Cum.**
18-19	26	3.89	3.89
20-29	70	10.48	14.37
30-39	149	22.31	36.68
40-49	206	30.84	67.51
50-59	146	21.86	89.37
60-69	53	7.93	97.31
70-79	18	2.69	100
Total	668	100	

Parents were asked to think about a specific child when making their choices within the survey. This was to help make the valuation choices as realistic as possible. The ages of the children chosen as their “Nominated Child” are shown in Table M.30. If their nominated child was less than 4 they were directed into the Vignette version of the survey as this age is too young for the EQ-5D-3L Y form for recording children’s health status.

Table M.30: Age Groups (Child)

Nominated Child Age	Freq.	Percent	Cum.
4	48	7.19	7.19
5	52	7.78	14.97
6	38	5.69	20.66
7	54	8.08	28.74
8	40	5.99	34.73
9	35	5.24	39.97
10	55	8.23	48.2
11	38	5.69	53.89
12	56	8.38	62.28
13	51	7.63	69.91
14	42	6.29	76.2
15	55	8.23	84.43
16	40	5.99	90.42
17	64	9.58	100
Total	668	100	

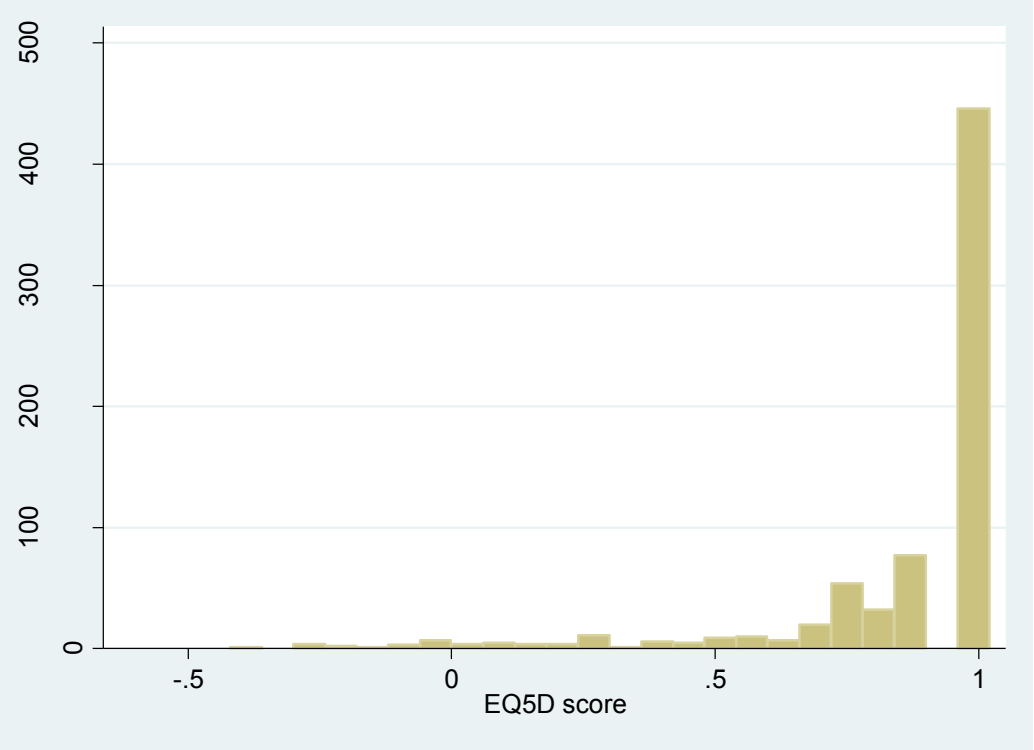
Health

The mean EQ5D utility score value (maximum value of 1) was 0.87

eq5d utility score	Obs	Mean	Std. Dev.	Min	Max
eq5dutility	661	0.872	0.244	-0.371	1

The distribution of EQ5D utility scores is shown in Figure M.2. A total of 18 people in the sample reported a health state less than 0 (worse than death).

Figure M.2: Histogram EQ5D utility scores – Parent sample



The history of the sample and their family members with diarrhoea and/or vomiting in the past year are shown in Table M.31 which shows proportions – e.g. 49% of the sample have had mild diarrhoea and/or vomiting lasting less than a day in the last year, 3% report having been hospitalised by diarrhoea and/or vomiting in the past year.

Table M.31: History of diarrhoea and/or vomiting in past year

In the past year please tell us if you or family members have had illnesses like this?				
	You	Other adults in the family	Children in the family	None of them
Mild diarrhoea and/or vomiting <1 day	0.493	0.334	0.382	0.292
Mild diarrhoea and/or vomiting , 1-3 days, time off work/school, no Dr contact	0.217	0.187	0.314	0.485
Mild diarrhoea and/or vomiting , 1-3 days, time off work/school, Dr contact	0.084	0.100	0.151	0.734
Severe diarrhoea and/or vomiting, time off work/school, > 1 Dr contact	0.058	0.061	0.046	0.859
Severe food poisoning, 1+ nights in hospital	0.031	0.045	0.033	0.900

The long term impacts of f FBD can include a number of conditions. These conditions featured explicitly in the valuation scenarios in the Vignette sample.
To aid comparison between the two parental samples (vignette, EQ5D), we report in Table 9 the experience of the Parent EQ5D sample of those conditions.
This reveals that 17% of the sample reported having experienced IBS, 13% arthritis and 1.5% Meningitis.

Table M.32: History of long run FBD conditions

Please indicate if either you, or someone in your close family, has any experience of the following illnesses.		
	you	**member close family**
Guillain-Barre Syndrome	0.031	0.028
Irritable Bowel Syndrome	0.174	0.180
Arthritis	0.127	0.256
Febrile Convulsions	0.018	0.052
Mesenteric adenitis	0.018	0.025
Septicaemia	0.021	0.057
Complicated Jaundice	0.012	0.031
Osteomyelitis	0.006	0.037
Hemolytic uremic syndrome (HUS)	0.007	0.022
Thrombotic thrombocytopenic purpura (TTP)	0.010	0.019
Renal Failure/ Dialysis	0.012	0.031
Meningitis	0.015	0.063

M.5. Choices, Task Difficulty & Protests – Parent sample

Possible protest behaviour were investigated for people who selected a pay, or a no pay, option in all of the DCE sets they faced.

People with this pattern of choices in the short term sets were prompted as to why that was the case using the responses shown in Tables M.33 and M.34.

Table M.33: Why never chose to pay – short term

Please select the option that best explains why you never chose to pay to avoid the illness.			
	Freq.	**Percent**	**Cum.**
1. The illness wouldn't be too bad.	4	0.6	0.6
2. My child would get better anyway, so it is not worth paying for the treatment.	10	1.5	2.1
3. I would like my child to avoid the illness but I could not afford to pay what was asked	15	2.25	4.34
4. I shouldn't have to pay because the government should provide health care.	11	1.65	5.99
5. I have an ethical/religious objection to my child taking medicines	0	0	5.99
6. Other (please specify)	5	0.75	6.74
n/a	623	93.26	100
Total	668	100	

Table M.34: Why always chose to pay – short term

Please select the option that best explains why you always chose to pay to avoid the illness.			
	Freq.	**Percent**	**Cum.**
1. I did not think the request for payment was realistic so I ignored it	11	1.65	1.65
2. The cost was small compared to my child's pain and suffering	140	20.96	22.6
3. The cost was small compared to the costs involved in caring for my ill child.	25	3.74	26.35
4. Other (please specify)	6	0.9	27.25
n/a	486	72.75	100
Total	668	100	

People choosing options 4-6 in Table M.33, and options 1 or 4 in Table M.34 were excluded from the estimation sample. The rates of such 'protests' were very low considering this was a health-payment study in the UK.

People who selected a pay, or a no pay, option in all of the long term DCE sets were prompted as to why that was the case using the responses shown in Tables M.35 and M.36.

Table M.35: Why never chose to pay – long term

Please select the option that best explains why you never chose to pay to avoid the illness.			
	Freq.	**Percent**	**Cum.**
1. The illness wouldn't be too bad.	10	1.5	1.5
2. My child would get better anyway, so it is not worth paying for the treatment.	10	1.5	2.99
3. I would like my child to avoid the illness but I could not afford to pay what was asked	110	16.47	19.46
4. I shouldn't have to pay because the government should provide health care.	28	4.19	23.65
5. I have an ethical/religious objection to my child taking medicines	1	0.15	23.8
6. Other (please specify)	19	2.84	26.65
n/a	490	73.35	100
Total	668	100	

Table M.36: Why always chose to pay – long term

Please select the option that best explains why you always chose to pay to avoid the illness.			
	Freq.	**Percent**	**Cum.**
1. I did not think the request for payment was realistic so I ignored it	15	2.25	2.25
2. The cost was small compared to my child's pain and suffering	92	13.77	16.02
3. The cost was small compared to the costs involved in caring for my ill child.	14	2.1	18.11
4. Other (please specify)	18	2.69	20.81
n/a	529	79.19	100
Total	668	100	

People choosing options 4-6 in Table M.35, and options 1 or 4 in Table M.36 were excluded from the estimation sample. As with the short term sets the rates of such 'protests' were very low.

Respondents were debriefed on how hard to was to understand the sets, and how hard it was to make the choices within them

Table M.37: How hard was it to <u>understand</u> the choice questions involving illness and money? – short term

	Freq.	**Percent**	**Cum.**
Very difficult	30	4.49	4.49
Difficult	81	12.13	16.62
Neutral	144	21.56	38.17
Easy	225	33.68	71.86
very easy	188	28.14	100
Total	668	100	

Table M.38: How hard was it to <u>make</u> the choice questions involving illness and money? – short term

	Freq.	**Percent**	**Cum.**
Very difficult	55	8.23	8.23
Difficult	143	21.41	29.64
Neutral	154	23.05	52.69
Easy	190	28.44	81.14
very easy	126	18.86	100
Total	668	100	

The choice tasks were complex, which was why so much effort had been assigned to preparation of the materials and testing and refining them in focus groups, interviews and pilot surveys.

Rates of 5% and 12% respectively describing the short term sets as very difficult and difficult to understand were regarded as validating those efforts. But we note that the proportion finding the short run EQ5D DCE (very) difficult was 17% as compared to 12% for the equivalent Vignette sets.

Making the choices was more often reported as more difficult than understanding the choices, but this concerns difficulty making the decision rather than necessarily being confused by the information comprising the options.

Table M.39: How hard was it to <u>understand</u> the choice questions involving illness and money? – long term

	Freq.	Percent	Cum.
very difficult	55	8.23	8.23
Difficult	83	12.43	20.66
Neutral	142	21.26	41.92
Easy	225	33.68	75.6
very easy	163	24.4	100
Total	668	100	

Table M.40: How hard was it to <u>make</u> the choice questions involving illness and money? – long term

	Freq.	Percent	Cum.
very difficult	147	22.01	22.01
difficult	145	21.71	43.71
neutral	135	20.21	63.92
easy	134	20.06	83.98
very easy	107	16.02	100
Total	668	100	

The long term conditions included much more information and were more demanding. Rates of 8% and 12% respectively described the sets as very difficult and difficult to understand, these were only marginally higher than the equivalent figures for the vignettes sets.

Making the choices was more often reported as more difficult than understanding the choices and more often so in the long term sets than the short term ones.
We note that the proportion finding making choices in the long run EQ5D DCE (very) difficult was 44% compared to 46% for the equivalent Vignette sets.

APPENDIX N: AGGREGATION OF WTP TO AVOID FOODBORNE ILLNESS – *CAMPYLOBACTER* SPP.

The study reports estimates of average WTP to avoid foodborne illness experienced by adults or children, for both short and long term conditions from the stated preference study.

Those estimates are at the level of the individual. This appendix sets out the process of aggregation from the individual WTP to the aggregate, national, value. This is described here in detail for *Campylobacter* spp. The process is the same for the other pathogens studied in the project.

The Markov Transition Models (MTMs) developed within the project provide the foundation for the monetary aggregation. They provide estimates of the burden of disease in terms of QALY losses.

The starting point of the MTM is the healthy state, whereby upon suffering from the FBD, the patient can move between states or stay in their initial state (with a step period of one week).

In the case of *Campylobacter* spp. (see Figures N.1 - N.3) a patient can for example stay within their health state, or go from a healthy state to either uncomplicated diarrhoea or death. From uncomplicated diarrhoea, a patient could continue to have uncomplicated diarrhoea for more than one week, return to a healthy state or to develop a range of complications or sequelae. With the exception of death, it would be anticipated that a patient would eventually return to a healthy state, although with sequelae, the length of time before that occurs could be substantial. The likelihood of moving between states is captured by the transition probabilities associated with each arrow connecting the states in Figures N.1-N.3.

Figures N.1 – N.3 illustrate the structure of the model. Figure N.2 shows the four types of complications possible with *Campylobacter* spp. such as hospitalising diarrhoea or septicaemia. As illustrated it is possible for a patient to remain with this complication for more than one week, eventually return to a healthy state, develop sequelae (Figure N.3) or die. At the end of 12 months, the model assumes that there are no further new cases of *Campylobacter* spp., but the impacts after that year of cases that developed within it are incorporated, using a 1 year time step, for a further 100 years, with patients returning to a health state, or dying, with probability of the latter being based on a combination of the “all causes” death rate and any increases due to sequelae.

Figure 1: Campylobacter spp.

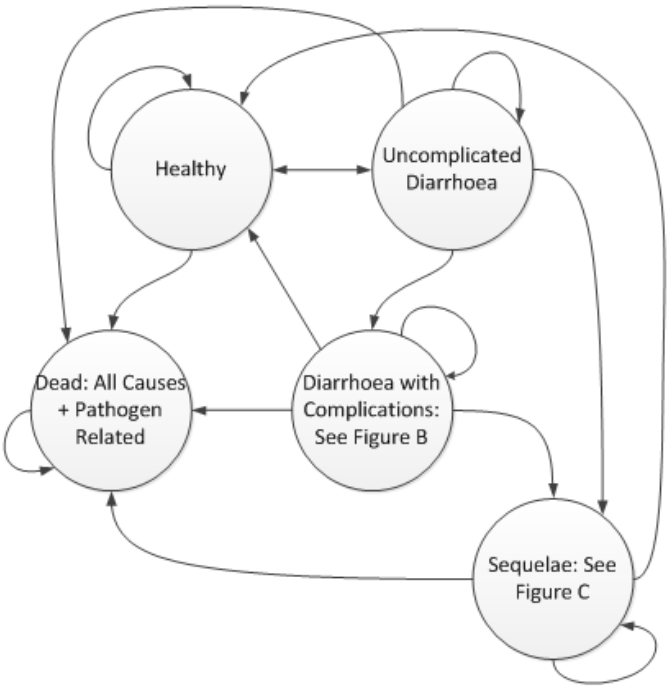


Figure 2: Campylobacter spp. Complications

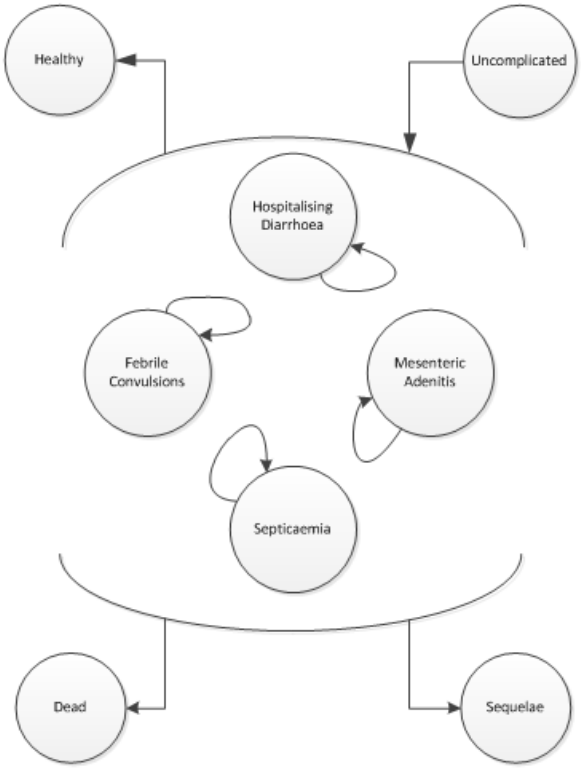
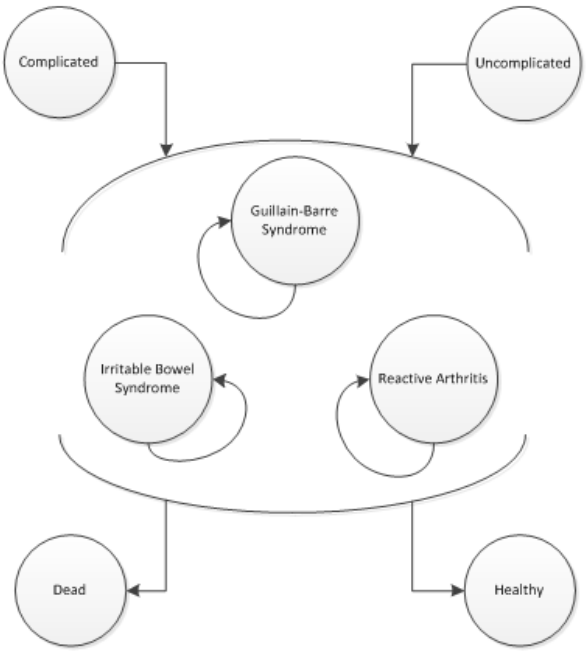


Figure 3: Campylobacter spp. sequelae



The MTMs determine the burden associated with the illness by comparing the aggregate QALY achieved if there was no illness to what is achieved when there is illness. The latter is identified using the utility burden associated with each state, and the number of person weeks/years that the population is modelled to spend in those states (including premature deaths). Given the long time horizon involved (since people may live with sequelae for many years after initially becoming ill), the QALY impacts are discounted at a value of 3.5% per annum.

Generating aggregate WTP estimates of burden requires replacement of the QALY disutility of the states with the estimated WTP to avoid those states. There are two complications to that process.

The first is that for many of the sequelae the WTP studies identified 'fixed effects' for illnesses with stated durations. For example, the vignette used to convey septicaemia in the valuation study included both short term impacts (being in an ICU) and also the duration until one recovered. Respondents were not sensitive to the longer duration, meaning we have only a WTP for a "fixed effect" of the illness itself. Essentially in the WTP estimates respondents are valuing a 'case' of septicaemia, not the duration of any recuperation from it to. Such duration-invariant WTPs are accommodated within the WTP aggregation by multiplying the estimate of the fixed effect by the number of cases simulated by the model nationally.

For some conditions there is both a fixed and marginal effect: respondents reveal that their WTP is influenced by the duration, but there is also an additional fixed effect associated with each case. In that case we include both a WTP value associated with the number of cases, and a value associated with the duration of those cases.

The second issue is that the vignette-based WTP estimates do not include a direct measure of the disutility associated with death. To address this gap we use the value of a QALY derived in the study: £19,456 as a conservative estimate of the value of years of life lost due to death arising from FBI. In terms of benchmarking, we note that a recent review the literature on WTP estimates for a QALY suggest a median value of €24,226, which is equivalent to £23,174 per QALY in 2015 prices (Ryen and Svensson, 2015).

We use the *Campylobacter* spp. MTM as an exemplar of how the WTP aggregation process works. As explained above the health states and the numbers moving through each year are defined. Monetisation requires assignment of a WTP value to each episode spent in each state.

From the *Campylobacter* spp. MTM model, disutility values are required for 9 elements. Table N.1 reports the disutility scores derived from the literature that are used in the QALY estimates. For the initial year, where the condition is reported in 1 week steps, the MTM takes the annual value of the disutility associated with a condition, and divides it by 52 to identify the loss associated with a week in the condition. The transition probabilities within the MTM are calibrated to account for conditions (such as uncomplicated diarrhoea) where the median duration may be less than 1 week.

Table N.1: Disutility scores from the *Campylobacter* spp. MTM, derived from the literature

	Disutility
Healthy	0
Uncomplicated Diarrhoea	0.0912
Hospitalizing Diarrhoea	0.167
Febrile Convulsions	0.307
Mesenteric Adenitis	0.552
Septicaemia	0.606
GBS	0.496
IBS	0.181
RA	0.388
Dead	0.856

Table N.2 reports WTP values estimated by this study: both the marginal value for a year in each state, and any fixed effects. These estimates are weighted averages of the adult and child estimates, as the cases in the population reflect both of these sources. It also reports the implied values that would be derived if one used £19,456 per QALY for the disutility decrements reported in Table N.1.

Table N.2: Values used in estimating aggregate WTP to avoid disease – *Campylobacter* spp.

Conditions relevant to *Campylobacter* spp. only. Estimated as weighted average of Adult and Parent values.	**Stated preference estimates**		**QALY estimates**
	Fixed effect £'000 per year	Marginal effect £'000 per case	Marginal effect
Uncomplicated Diarrhoea /vomiting	0.060	2.006	1.77
Hospitalizing Diarrhoea /vomiting	0.084	3.313	3.25
Febrile Convulsions	7.978	0	5.97
Mesenteric Adenitis	1.747	0	10.74
Septicaemia	35.98	0	11.79
GBS	6.83	7.581	9.65
IBS	14.05	0	3.52
RA	6.51	1.584	7.55
Dead	--	19.5	16.65

The values in Table N.3 are multiplied by the number of person episodes spent in each state. Table N.3 reports these values for the WTP approach, and the contribution due to each condition. Deaths from all sources are aggregated.

Table N.3: Estimates of monetary burden from pain and suffering arising from an annual caseload of *Campylobacter* spp.

	WTP (£'000)	
Total	**424,244**	**(308,244 - 540,264)**
Uncomplicated Diarrhoea	34,939	(30,900 - 38,900)
Hospitalizing Diarrhoea	472	(427 - 518)
Febrile Convulsions	339	(138 - 540)
Mesenteric Adenitis	426	(218 - 635)
Septicaemia	22,515	(15,700 – 29,300)
GBS	6,855	(4,800 - 8,900)
IBS	302,071	(187,160 - 417,00)
RA	41,972	(29,800 – 54,100)
Dead	**14,654**	**(7,900 - 21,400)**

A caveat to note when considering the values in Table N.3 is that the value of deaths from each condition is aggregated into the 'deaths' total. A death caused by Septicaemia is captured in the Death category and not assigned to Septicaemia.