

CHLAMYDIA SCREENING IN IRELAND

A pilot study of
opportunistic
screening for
genital *Chlamydia
trachomatis*
infection in Ireland
(2007–2009)

ECONOMIC EVALUATION

REPORT PREPARED BY CHLAMYDIA SCREENING STEERING GROUP



Economic Evaluation Report and Website

This economic evaluation report measures the cost effectiveness of an opportunistic Chlamydia Screening in Ireland Pilot Study conducted between 2007 and 2009. Further information including more detail on the methods and results can be found in the following accompanying reports on the Health Protection Surveillance Centre (HPSC) website.¹

Chlamydia Screening in Ireland Pilot Study. Summary Integrated Report

Chlamydia Screening in Ireland Pilot Study. Background Studies: Acceptability and Feasibility of Screening

Chlamydia Screening in Ireland Pilot Study. Screening Report

Other resources on the website include additional information on the implementation of screening, a toolkit for organising screening in non-clinical settings and links to published articles from the study.

Health Protection Surveillance Centre
25-27 Middle Gardiner Street,
Dublin 1,
Ireland.
Email: hpsc@hse.ie
Tel. +353 1 8765300
Website: www.hpsc.ie

Health Research Board
73 Lower Baggot Street
Dublin 2
Ireland
Email: hrb@hrb.ie
Tel. +353 1 234 5000
Website: www.hrb.ie

Published by the Health Protection Surveillance Centre (HPSC) Ireland and the Health Research Board (HRB) Ireland

Copyright © 2012 Health Protection Surveillance Centre and Health Research Board.
All rights reserved

¹ <http://www.hpsc.ie/hpsc/A-Z/HepatitisHIVAIDSandSTIs/SexuallyTransmittedInfections/Chlamydia/Publications/>

Acknowledgements

We thank all who contributed to the Chlamydia Screening in Ireland Pilot Study. In particular we thank all the young people who agreed to be interviewed, who took part in surveys or focus groups and who agreed to be screened for chlamydia.

We acknowledge everybody who helped with the study planning, implementation, analysis and interpretation.

The research team thanks the Health Protection Surveillance Centre and the Health Research Board for the opportunity to conduct this study, and the members of the Steering Committee and the National Advisory Committee for their input and support.

Our thanks goes to the following personnel from the general practices, student health units and family planning clinics who participated in the screening study: Dr Seamus Cryan, Dr Cairiona Waters, Dr Brendan Day, Practice Nurse Doreen Eaton, Dr John Waldron, Practice Nurse Mary Murphy, Dr Dan Murphy, Practice Nurse Antoinette Doyle, Practice Nurse Mary O'Toole, Practice Nurse Catherine Lavery, Dr Emer McHale, Practice Nurse Deirdre Cody, Dr Desmond Bluett, Dr Joan Kearney, Dr Aonghus Flavin, Dr Micheal Coughlan, Dr Eamonn O'Shea, Practice Nurse Anna Reilly, Practice Nurse Edel Quinn, Practice Manager Kevina Shaughnessy, Dr Paula Walsh, Dr Fionnuaghla Lysaght, Dr Michael Casey, Practice nurse Dee Cloherty, Dr Gerald Brennan, Dr Úna O'Connell, Dr Catherine O'Mahony, Dr David Hanney, Dr Siobhan McDonagh, Dr Angela Cowley, Dr Sinead Murphy, Dr Eilín O'Flaherty, Dr Lynda Keaveney, Dr Val Costello, Practice Nurse Dennis Costello, Dr Grace Doyle and Practice Nurse Carmel Finnerty, Dr Jim Brennan, Practice Nurse Annmarie Cunningham, Dr Mary Regan, Dr Miriam Mangan, Dr Martina Brennan, Dr Saber Elsafty, Dr Joyce Hayward, Dr Matt O'Flaherty, Dr Marie Egan and Dr Marie O'Brian.

We would like to thank the following departments and personnel for their contribution to the 'pee-in-a-pot' non-clinical screening: Student Health, the Student Union and Student Services at the National University of Ireland, Galway and Galway/Mayo Institute of Technology, Galway. Special thanks to Practice Nurses Deirdre Cody, Edel Quinn, Practice Manager Kevina Shaughnessy and Dr Paula Walsh.

We wish to acknowledge the contributions to the intranet survey made by Eric Clarke of the Royal College of Surgeons in Ireland and all staff members at the Student Unions, Student Services and IT departments and participating universities and institutes of technology. Thanks to those who contributed to the pre-screening studies: Dr Tara Conlon and all the staff at the Health Centre in Ballymun; Dr Judith Kavanagh and staff at the Mercers Medical Centre; Shirley McQuade and staff at the Well Woman Centres; Mick Quinlan, Dr Shay Keating and staff at the Gays Men's Health Service; Dr Brendan Clune and staff at the DIT health centre; and the Mayo general practitioners who facilitated with questionnaires.

Thank you to all the students and other young people who volunteered their time and participated in screening, the intranet survey, questionnaires and interviews.

We would like to thank staff at the following HSE departments for their technical support and participation throughout the study:

Colette Flaherty and other staff members at the Microbiology Department, Galway University Hospital for the processing and management of specimens during the study;

Research and administrative staff at the Public Health Department, HSE West especially Dee Goggin for the management of data and analysis throughout the project;

Genitourinary Medicine Clinic University Hospital Galway for their assistance with follow-up of the positive cases.

We would also like to acknowledge and thank the administrative staff both at NUI Galway and RSCI, especially Vivienne Batt.

Core Steering Group

Dublin

Dr Myles Balfe
Researcher
Dept. of Epidemiology & Public Health
Royal College of Surgeons in Ireland

Professor Ruairí Brugha
(Co-Principal Investigator)
Head of Department
Dept. of Epidemiology & Public Health
Division of Population Health Sciences
Royal College of Surgeons in Ireland

Galway

Dr Emer O’Connell
(Co-Principal Investigator)
Consultant in Public Health Medicine
Department of Public Health
HSE – Dublin/Mid-Leinster
Tullamore, Co. Offaly

Deirdre Vaughan
Research Health Advisor
Dept. of Health Promotion
National University of Ireland, Galway

Dr Diarmuid O’Donovan
(Co -Principal Investigator)
National University of Ireland, Galway
Director of Public Health
HSE West, Galway

Expanded Steering Group

Dr Claire Coleman
Clinical Nurse Manager
Genitourinary Medicine and Infectious
Diseases
University Hospital Galway

Professor Ronán Conroy
Statistician
Dept. of Epidemiology & Public Health
Division of Population Health Sciences
Royal College of Surgeons in Ireland

Professor Martin Cormican
Head of Department
Department of Medical Microbiology
Galway University Hospitals

Dr Margaret Fitzgerald
Consultant in Public Health Medicine
Acting Director of Public Health
HSE East

Dr Catherine Fleming
Consultant in Infectious Diseases
Genitourinary Medicine and Infectious
Diseases Department
University Hospital Galway

Professor Hannah McGee
Professor of Psychology
Dean, Faculty of Medicine and Health
Sciences
Royal College of Surgeons in Ireland

Professor Andrew Murphy
Dept. of General Practice
Clinical Science Institute
National University of Ireland, Galway

Dr Grainne Ní Fhoghlú
Dept. of General Practice (formerly)
Clinical Science Institute
National University of Ireland, Galway

Economic Steering Group

(Also included members of the Core and Expanded Steering Group)

Professor Ciaran O'Neill
School of Business and Economics
National University of Ireland, Galway

Dr Elisabeth Adams
Health Protection Agency
London, UK

Dr Paddy Gillespie
School of Business and Economics
National University of Ireland, Galway

Dr Katherine Turner
University of Bristol
Bristol, UK

National Advisory Committee

(Also included members of the Core and Expanded Steering Group)

Dr Tara Conlon
General Practitioner
Ballymun, Dublin

Dr Ailis Ní Riain
Programme Director
Irish College of General Practitioners

Dr Susan Clarke
Consultant in Infectious Diseases
St. James Hospital, Dublin

Dr Stephanie O'Keeffe
Research & Policy Manager
HSE Crisis Pregnancy Programme
(formerly the Crisis Pregnancy
Agency)

Dr Brendan Clune
Medical Director
Dublin Institute of Technology

Maeve O'Brien
Policy Officer
HSE Crisis Pregnancy Programme
(formerly the Crisis Pregnancy
Agency)

Alessandra Fantini
Higher Executive Officer
Social Inclusion Unit
Dept. of Health and Children (formerly
Women Health Council)

Mick Quinlan
Manager
Gay Men's Health Service
HSE, Dublin

Dr Shay Keating
Medical Officer
The Drug Treatment Centre Board
Dublin

Dr Shirley McQuade
Medical Director
Dublin Well Woman Centre

Contents

| | |
|------------------------------------------------------------------------|-----|
| Economic Evaluation Report and Website | ii |
| Acknowledgements | iii |
| List of Figures | ix |
| List of Tables | ix |
| Executive Summary | x |
| 1. Introduction | 1 |
| 2. Methodology | 1 |
| 2.1 Cost Analysis | 1 |
| 2.2 Modelling Analysis | 2 |
| 2.2.1 Clinical Setting Screening | 5 |
| 2.2.2 ‘Pee-in-a-pot’ Screening | 6 |
| 2.3 Incremental Cost Effectiveness Analysis | 7 |
| 2.3.1 Costs | 7 |
| 2.3.2 Effectiveness | 8 |
| 2.3.3 Decision Rules | 8 |
| 2.3.3 Sensitivity Analysis | 9 |
| 3. Results | 10 |
| 3.1 Cost Analysis Results | 10 |
| 3.2 Incremental Cost Effectiveness Results | 10 |
| 3.2.1 Clinical Setting Screening: Base-case Results | 11 |
| 3.2.2 Clinical Setting Screening: One-Way Sensitivity Analysis Results | 13 |
| 3.2.3 ‘Pee-in-a-pot’ Screening Results | 14 |
| 4. Discussion | 17 |
| 5. Summary of Key Findings | 23 |
| 6. Potential limitations of this study | 23 |
| 7. Recommendations | 24 |
| References | 25 |
| Appendix A. Dynamic Model Methodology | 29 |
| Appendix B. Costing Methodology | 32 |
| Appendix B.1. Screening Programme Costing Methodology | 32 |
| A: Clinical Setting Screening Programme | 33 |
| B: ‘Pee-in-a-pot’ Screening | 38 |
| C: Partner Notification & Treatment | 41 |

| | |
|------------------------------------------------------------------------|----|
| Appendix B.2. Cost Analysis: Screening Unit Cost Data | 43 |
| Appendix B.3. Complications of Chlamydia Infection Costing Methodology | 45 |
| Appendix C. QALY Methodology | 47 |

List of Figures

| | |
|-------------------------------------------------------------------------------------------------------------------------------|----|
| Figure 1. The flow of complications in women with PID and neonates exposed to infected others | 4 |
| Figure 2. Pre-screening age-specific prevalence: the equilibrium (steady-state) prevalence by males and females by age groups | 11 |
| Figure 3. Prevalence Pre and Post Screening Implementation – Clinical Setting Screening | 12 |
| Figure 4. Cost Effectiveness Acceptability Curve – Clinical Setting Screening | 13 |
| Figure 5. Prevalence Pre and Post Screening Implementation – ‘Pee-in-a-pot’ Screening | 15 |
| Figure 6. Cost Effectiveness Acceptability Curve - ‘Pee-in-a-pot’ Screening | 16 |

List of Tables

| | |
|-------------------------------------------------------------------------------------------|----|
| Table 1. Probabilities for developing complications following acute chlamydial infection | 4 |
| Table 2 Clinical Setting Analysis Input Parameters for Base-case and Sensitivity Analyses | 6 |
| Table 3. Chlamydial Complications: Cost and QALY Loss Impacts | 8 |
| Table 4. Cost Analysis Results | 10 |
| Table 5. Incremental Cost Effectiveness Results (Screening Versus No Screening) | 21 |

Executive Summary

Economic Evaluation

The aim of the economic evaluation was to examine the cost effectiveness of the two screening models tested in the Chlamydia Screening in Ireland Pilot (CSIP) study: (a) Clinical Setting screening, and (b) 'Pee-in-a-pot' periodic screening in third level institution/college settings. The methodological approach comprised of a dynamic transmission model paired with an economic model. In both analyses, screening was compared to a control strategy of no organised screening, that is existing care in Ireland.

A public health system or provider perspective was adopted with respect to costs. The analysis considered the cost of screening to the health service, and the costs of infection and complications, not any additional costs reported by young people in accepting a chlamydia screening test. Health outcomes were assessed in terms of major outcomes (MOs) averted and quality adjusted life years (QALYs) gained.

The costs of Clinical Setting screening were presented in terms of the *cost per offer* (€26), the *cost per negative case* (€66), the *cost per positive case* (€152), and the *cost per partner notified and treated* (€74). The costs of 'Pee-in-a-pot' screening were presented in terms of the *cost per negative case* (€39), the *cost per positive case* (€125), and the *cost per partner notified and treated* (€74).

In both analyses, screening was estimated to result in fewer major outcomes, fewer QALYs lost, and higher healthcare costs compared to the control strategy. The incremental cost effectiveness analyses indicated that screening in the Clinical Setting would result in an incremental cost per MO averted of €6,093 and an incremental cost per QALY gained of €94,717. 'Pee-in-a-pot' screening was estimated to result in incremental cost effectiveness ratios of €2,294 per MO averted and €34,486 per QALY gained respectively.

In Ireland, there is no fixed and generally agreed cost effectiveness threshold below which health care technologies would be considered by policy makers to be cost-effective. Nonetheless, on the basis of other technologies that are currently funded, it is not likely that screening delivered in the Clinical Setting, given an incremental cost per QALY in the region of the €94,717 found in this study, would be considered cost effective.

'Pee-in-a-pot' screening in third level institution/college settings may be considered cost effective if a cost effectiveness threshold in the region of €45,000 per QALY gained is used. This is open to question, however, given the current economic climate and its resulting impact in terms of imposing further constraints on future healthcare budgets. It is also important to note that this strategy would have minimal impact in reducing overall chlamydia prevalence in the population, if not supported by general population screening and prevention strategy.

1. Introduction

The purpose of economic evaluation is to evaluate the cost effectiveness of health care technologies and to provide advice to decision makers charged with the allocation of health care resources. It involves a set of techniques for the systematic appraisal of alternative health care interventions in order to identify those strategies which provide the most efficient use of resources. In this study, we undertake an economic evaluation to explore the cost effectiveness of two models of opportunistic screening piloted in the Chlamydia Screening in Ireland Pilot (CSIP) study: (a) Clinical Setting screening, and (b) 'Pee-in-a-pot' screening.

2. Methodology

The process of economic evaluation involves the comparative analysis of alternative courses of action in terms of their costs and consequences [1]. The methodological approach adopted in this analysis comprised of a dynamic transmission model paired with an economic model. In the base-case analyses, screening was modelled to represent the opportunistic screening approaches tested in the pilot study. In both cases, screening was compared to a control strategy of no organised screening, or in other words existing care in Ireland. The methodological process consisted of three phases of analysis: (1) cost analysis; (2) modelling analysis, and (3) incremental cost effectiveness analysis. Each stage of analysis is described in the following paragraphs.

2.1 Cost Analysis

The purpose of the cost analysis was to estimate the healthcare resource implications associated with implementing the opportunistic screening programmes in the pilot study. Consistent with HIQA guidelines [2] a publicly funded health system perspective was adopted in that costs falling outside the publicly funded healthcare system, including costs to patients such as direct payment to general practitioners (GPs) when attending due to an unrelated medical complaint, travel and time off work, were excluded from the analysis.

Resource items were identified and measured using resource-use record forms, healthcare provider questionnaires, interviews with research staff, and directly from the study financial accounts. A resource-use form completed by healthcare providers was used to prospectively record the time input requirements for each patient episode at various stages of the screening process. A healthcare provider questionnaire was conducted to identify setting specific resource use for the participating providers. Interviews with research staff and a detailed review of the study accounts provided further information on the resources required to implement the screening programmes and the overhead costs involved.

Specific resource items included in the cost analysis were overheads, provider, support staff and volunteer time input, information leaflets, screening materials and consumables, laboratory materials and testing, antibiotic medications, referrals, and telephone, fax, and postage charges. Overheads included the costs of project management and coordination by the Research Health Adviser, stationary, computer equipment, advertising, printing, photocopying and packaging, charges, and travel expenses.

Resource use data collected alongside the pilot study were combined with Irish unit cost data to complete the cost analysis. Unit costs were obtained from national data sources and were transformed to Euros (€) in 2008 prices using an appropriate inflation rate index [3]. For further details on specific screening resource items and unit costs see Appendix B.1.

The results from the cost analysis were calculated for each screening programme and for each stage of the screening process. The results for Clinical Setting screening were presented in terms of the *average cost per offer*, the *average cost per negative case*, the *average cost per positive case*, and the *average cost per partner notified and treated*. The results for 'Pee-in-a-pot' screening were presented in terms of the *average cost per negative case*, the *average cost per positive case*, and the *average cost per partner notified and treated*.

The divergence in the costing process for Clinical Setting screening and 'Pee-in-a-pot' screening derives from how screening was offered in each case. Whereas screening was offered by a clinician in the former, this was not the case in the latter. The cost estimates for each programme were incorporated as input parameters in the modelling analysis, described in the following section, to undertake the economic evaluation.

2.2 Modelling Analysis

The modelling analysis was undertaken to facilitate the estimation of the cost effectiveness of screening and comprised of a dynamic transmission model paired with an economic model. The modelling component was required due to two broad factors which make predicting the impact and cost of chlamydia screening programmes difficult: 1) as chlamydia is an infectious disease there are benefits to reducing population prevalence beyond that of the individual, and 2) as chlamydia is highly transmissible via sexual contact treatment does not produce lasting immunity as it does not eradicate the risk of future infection. As a result, modelling frameworks which explicitly allow for the possibility of infection, transmission to partners, and re-infection are required for the evaluation of chlamydia screening programmes [4].

A dynamic model of sexual partner change and chlamydia transmission that not only incorporates the identification and treatment of the individual but also partner notification and treatment was used for the analysis. The dynamic model by Turner et al [5] and the economic model by Adams et al [6], which were applied in an economic evaluation of opportunistic chlamydia screening in England, were adopted for the analysis. For the current study, the approach of Turner et al [5] and Adams et al [6] was adapted to reflect the Irish healthcare setting.

A number of alternative models of chlamydia transmission have been published, each of which differ with respect to the underlying dynamics and assumptions regarding sexual behaviour and transmission parameters. Kretzschmar et al [4], in a study comparing three alternative modelling approaches, found that predictions from the alternative models may result in inconsistent policy recommendations about the likely effectiveness of a screening programme. Kretzschmar et al [4] were unable to identify a superior model because of uncertainty about a large number of key parameters and the lack of data for external comparison.

Of the three approaches considered, the model by Turner et al [5] was the most optimistic in terms of its predicted reduction in prevalence resulting from the implementation of screening. This is attributed in part to the relatively low level of

pre-screening treatment of chlamydia assumed in this model compared to the alternatives. Given the uncertainty surrounding the superiority of the alternative modelling approaches, the current approach was adopted with the caveat that adopting the alternative approaches would result in more pessimistic predictions of the effectiveness of screening in reducing chlamydia prevalence levels.

To summarise, the dynamic model simulates several processes. The sexual contact network provides the framework within which chlamydia transmission occurs. Sexual partnerships form and break according to behavioural algorithms, which adjust according to an individual's age. Chlamydia is introduced into the population and is transmitted through current sexual contacts. Individuals can recover spontaneously or through seeking treatment, partner notification or screening. Since individuals and their partnerships are explicitly represented, partner notification and treatment (including of previous partners) can be modelled and infection status and screening histories recorded.

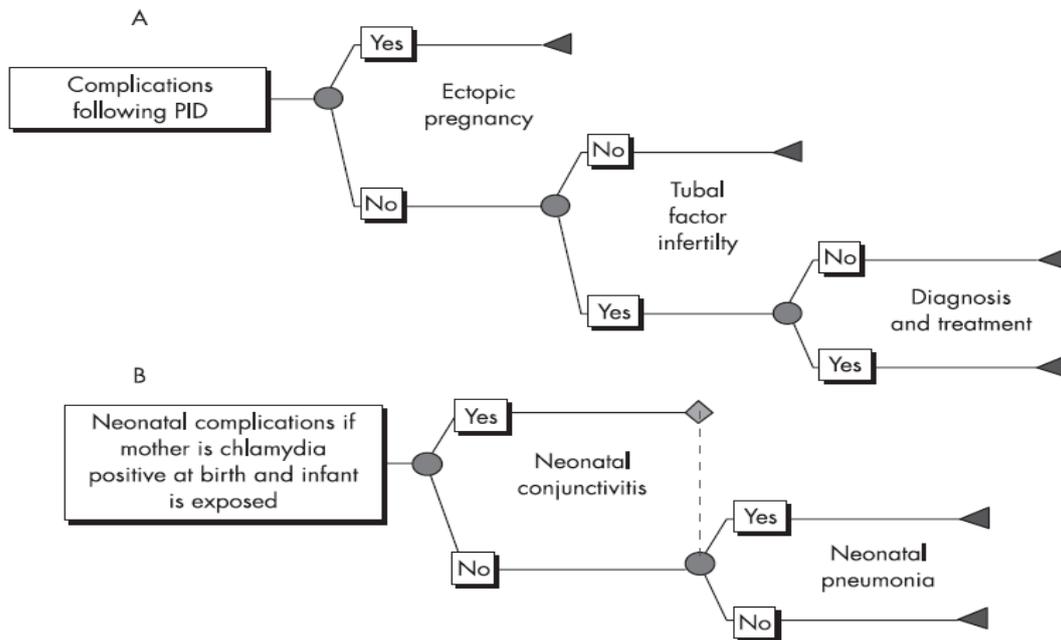
The dynamic model was parameterised such that the sexual behaviour and chlamydia prevalence was representative of that in England [7, 8, 9, 10]. For the current analysis, the original model settings for sexual behaviour and prevalence were used and assumed to be transferable to Ireland. For further details on specific input parameters see Appendix A. While sexual attitudes and culture in Ireland may once have been different to other western European countries, more recently they have converged towards those of the United Kingdom and continental Europe [11] and clinical case management is similar to that of the UK. Therefore it was considered appropriate to use the English model for the Irish setting.

The dynamic model simulates a hypothetical, heterosexual population of 20,000 men and 20,000 women aged 16 to 45 years and estimates the annual number of acute cases of chlamydia infection (asymptomatic and symptomatic) and the number of complications resulting from untreated infection for the simulated population.

The complications modelled include pelvic inflammatory disease (PID), ectopic pregnancy, and tubal factor infertility in women, neonatal conjunctivitis and pneumonia, and epididymitis in men (see Figure 1 and Table 1). This represents a simplification of the true natural history which is not well understood. Only symptomatic PID is modelled as the probability of further complications is directly related to symptom severity. Furthermore, there is conflicting evidence about the proportion of chlamydia cases that result in PID [12, 13, 14] and about the proportion of PID cases that can be prevented by the detection and treatment of chlamydia [15].

Therefore, a probability of 10% was adopted in the base-case analysis and probabilities of 1% and 30% were tested in sensitivity analyses to reflect the range of data presented in the literature. It is assumed that PID can lead to ectopic pregnancy and tubal factor infertility, and if a woman gives birth she can transmit infection to her infant causing neonatal conjunctivitis and pneumonia.

Figure 1. The flow of complications in women with PID and neonates exposed to infected others



(Source: Adams et al [6])

Table 1. Probabilities for developing complications following acute chlamydial infection

| Complication | Probability Value | Probability applied to: |
|----------------------------------|-------------------|-------------------------------------------|
| Symptomatic PID (women) | 1%, 10%, 30% | Asymptomatic chlamydia infection |
| Ectopic pregnancy (women) | 7.6% | Symptomatic PID |
| Tubal factor infertility (women) | 10.8% | Symptomatic PID (excluding those with EP) |
| Neonatal conjunctivitis | 14.8% | Infected women giving birth vaginally |
| Neonatal pneumonia | 7.0% | Infected women giving birth vaginally |
| Epididymitis (men) | 2% | Asymptomatic chlamydial infection |

(Source: Adams et al [6])

The output from the dynamic model is used in the economic model to estimate the health service costs and health outcomes associated with the predicted infections and complications. As the dynamic model is stochastic and each realisation of the model yields distinct estimates, an average of 40 realisations was inputted into the economic model. The existing economic model was adapted by incorporating Irish unit cost data so to make it appropriate for the analysis of screening programmes delivered in the Irish healthcare system.

The modelling framework allows for the incremental analysis to be undertaken whereby alternative screening strategies are evaluated in terms of their relative impact

on the estimated number of infections and complications, the number of people screened and treated, and health outcomes and costs which result. The model is run for a time horizon of 10 years to observe the impact of screening on longer term complications, with all future costs and health outcomes discounted at an annual rate of 3.5%, an appropriate rate for health technology assessment in Ireland.

Two screening scenarios were modelled to represent both screening approaches tested in the pilot study: (a) Clinical Setting screening; (b) ‘Pee-in-a-pot’ screening. In both cases, the screening scenario was compared to a control strategy of no organised screening, or in other words existing care in Ireland.

2.2.1 Clinical Setting Screening

In the pilot, individuals aged 18 to 29 years old who accessed one of three clinical settings – general practices, family planning and student health clinics - were invited to participate in the study. Those who agreed were offered a screen.

Men who agreed to participate were asked to provide a urine sample and women either urine or cervical swab. In general practice, both general practitioners and practice nurses offered screening while in family planning and student health clinics offers were made by nurses.

Urine or endocervical swab samples were tested for each participant by the virology laboratory at a local hospital. Specimens were batch tested with Polymerase Chain Reaction testing technology. The test used was the *COBAS[®] TaqMan[®] CT Test v2.0* manufactured by Roche Diagnostics, Switzerland.

All individuals were notified of their test results by the healthcare provider and those with positive results were invited to attend a consultation where they received treatment (with Azithromycin or Doxycycline), information and counselling from a GP. Individuals with positive results were recalled for retesting at three to six months after treatment when the testing process was repeated.

Notification of partners was undertaken by the patient, the healthcare provider or the Research Health Advisor who worked exclusively on the pilot study. Partner treatment and testing took place in general practice, family planning, student health and genitourinary medicine clinics.

In the economic evaluation, screening in the clinical setting was modelled as a continuous process to reflect the programme delivered in the pilot study, incorporating a range of data on clinical setting attendance, provision of screen offer, participation, treatment, resource-use and cost (see Table 2).

In the base-case analysis it was assumed that 80% of women and 50% of men attended a health care setting in a given year. This is based on data from a national population survey for representative sample of 18-29 year olds in Ireland [16]. Of those who attended, it was assumed for the model that 70% were offered a screen by the resident healthcare provider. This estimate is based on the findings from a systematic review of opportunistic screening strategies internationally [17]. This figure is higher than that which was observed in the pilot study but alternative offer rates, including those observed in the study, were examined in sensitivity analysis.

It was assumed for the model that 85% of females and 64% of males accepted the screen offer, based on rates observed in a sample of pilot study practices. An effective

partner notification and treatment rate of 20% was assumed based on rates used elsewhere [6].

Finally, we assume for the model that once an individual is screened they will not be offered screening for 1 year. While an individual may request a test within the same year that a screen has been offered, it is unlikely that a provider would be reimbursed or choose to offer repeated screens within the same calendar year to those who had declined a screen or been screened negative.

The base-case assumptions result in a screening coverage rate, that is the overall fraction of the target population who are screened, of 48% for females and 22% for males. A series of one-way sensitivity analysis was undertaken to explore the impact of varying the assumptions of the base-case analysis (See Table 2).

Table 2 Clinical Setting Analysis Input Parameters for Base-case and Sensitivity Analyses

| Input Parameter | Base-Case Analysis | Sensitivity Analysis |
|----------------------------------------------|-----------------------------------------------|---------------------------------|
| Male Attendance Rate | 50% | n/a |
| Female Attendance Rate | 80% | n/a |
| Healthcare Provider Offer Rate | 70% | 5%, 20%, 40%, 100% |
| Male Acceptance Rate | 64% | 50%, 85% |
| Female Acceptance Rate | 85% | 50%, 64% |
| Effective Partner Notification and Treatment | 20% | 40% |
| Screen frequency | 1 per year (365 days minimum between screens) | No minimum time between screens |

2.2.2 'Pee-in-a-pot' Screening

In the pilot 'Pee-in-a-pot' programme, males and females aged 18 to 29 years old attending two third level institution/college settings in Galway city were opportunistically targeted for screening over a period of one week.

A marketing and promotional campaign was conducted in each setting by the Research Health Advisor, supported by a team of student volunteers who were paid a daily reimbursement rate, to inform the target population about the screening programme.

Informational materials and specimen sample packs, which included a test sample container and an anonymised contact form to record a mobile telephone number for the purposes of communicating the test result, were made freely available at various locations on campus in both settings.

Participants returned completed specimens and contact forms to unmanned, sealed collection points. Urine samples were collected and sent for testing at the virology laboratory at a local hospital. Specimens were batch tested with Polymerase Chain Reaction testing technology. The test used was the *COBAS[®] TaqMan[®] CT Test v2.0* manufactured by Roche Diagnostics, Switzerland.

All individuals were notified of their test results by text message and those with positive results were invited to attend a consultation where they received treatment (with Azithromycin or Doxycycline), information and counselling from a GP. Individuals with positive results were recalled for retesting at three to six months after treatment when the testing process was repeated.

Notification of partners of positive cases was undertaken by the patient, the healthcare provider or the Research Health Advisor, depending on the patient's preference. Partner treatment and testing took place in general practice, family planning, student health and genitourinary medicine clinics.

In the economic evaluation, screening was modelled as a pulse process to reflect a once-off, annual, week-long programme as delivered in the pilot study.

The combined student population in the two participating third level institutions consisted of 6,977 males and 11,076 females. Assuming all these individuals fall within the target population (aged 18-29 years), the student population comprised 25% of the total male target population (29,737 males) and 38% of the total target female population (29,060 females) in the Galway city and county region.

These data were incorporated as the eligible screening population in the modelling analysis. In addition, data from the Irish College Lifestyle and Attitudinal National Survey [18] were used to further classify the eligible population into the respective age profile categories attending third level institutions.

Over the course of the week-long pilot study, 1249 screening kits/packs were made available to the student population. As a result, 7% of the student population were eligible to participate in the screening programme (*Denominator*: combined (6,977+11,076) student population; *Numerator*: 1249 kits/packs distributed). A screening uptake rate of 47%, estimated based on the uptake rate of the screening kits/packs in the pilot study, was assumed for both males and females (*Denominator*: 1249 kits/packs distributed; *Numerator*: 592 kits/packs returned/used).

In addition, a range of data on process, resource use and cost were collected for the participating student health clinics and incorporated in the analysis.

2.3 Incremental Cost Effectiveness Analysis

An incremental analysis was undertaken to explore the cost effectiveness of both opportunistic screening strategies relative to no organised screening, that is, current practice. This involved comparing the alternative strategies in terms of both their costs and effectiveness and applying a set of decision rules which define one treatment option as cost effective relative to a comparator. In addition, uncertainty in the analysis was explored using sensitivity analysis. Each stage in this process is detailed in the following paragraphs.

2.3.1 Costs

A public health system perspective was adopted with respect to costs, with two broad components of healthcare cost included in the analysis: the costs of screening, and the costs of infections and complications. As described above, the costs of screening were estimated prospectively alongside the pilot study (for further details on specific resource items and unit costs see Appendix B.1).

The average cost per complication arising from undiagnosed infection was estimated using a range of resource utilisation and unit cost data. As data on the resource utilisation associated with the treatment of symptomatic infection and chlamydial complications were not collected alongside the pilot study, this information was obtained retrospectively from a variety of national data sources and, where necessary, published UK data sources.

In particular, the treatment process for chlamydial complications was informed by the treatment protocols adopted in the study by Adams et al [6] when evidence for Ireland was unavailable. The adopted treatment protocols were reviewed by the study clinicians to ensure that they were applicable to the Irish healthcare setting. In all cases, resource utilisation for diagnosis, testing, treatment, and healthcare setting attendance (primary care and secondary care) were combined with Irish unit cost data to estimate the average costs of care (for further details on specific resource items and unit costs see Appendix B.3).

Unit costs were obtained from national data sources and were transformed to Euros (€) in 2008 prices using an appropriate inflation index [3]. The average costs per complication are presented in Table 3.

2.3.2 Effectiveness

Two measures of health outcome were considered in the effectiveness analysis: the number of major outcomes (MOs) averted and quality adjusted life years (QALYs) gained. MOs comprised of the complications which were predicted to arise from untreated infection and included cases of PID, ectopic pregnancy, tubal factor infertility, neonatal conjunctivitis, neonatal pneumonia and epididymitis.

The QALY losses associated with chlamydial complications were estimated by multiplying a utility valuation for each condition by the duration spent in that particular health state. Estimates of utility weights were taken from studies by the Institute of Medicine [19] and Smith et al [20], and the duration periods were assumed to be the same as in Adams et al [6]. The average QALY loss per acute complication is presented in Table 3 (for further details see Appendix C).

Table 3. Chlamydial Complications: Cost and QALY Loss Impacts

| Infections and Complications | Cost (€) | QALY Loss |
|-----------------------------------|----------|-----------|
| Pelvic inflammatory disease (PID) | 328.88 | 0.008 |
| Ectopic pregnancy | 3,935.07 | 0.010 |
| Tubal factor infertility | 1,182.00 | 0.871 |
| Epididymitis | 450.32 | 0.011 |
| Neonatal conjunctivitis | 88.04 | 0.001 |
| Neonatal pneumonia | 876.29 | 0.037 |

Note: See Appendix C for further details

2.3.3 Decision Rules

The economic evaluation framework requires a set of decision rules which define a health care technology as cost effective relative to a comparator [1]. These include if:

- (a) It is less costly and more effective;

- (b) It is more costly and more effective, but its additional cost per additional unit of effect is considered worth paying by decision makers; and
- (c) It is less costly and less effective, but the additional cost per additional unit of effect generated by the comparator is not considered worth paying by decision makers.

In scenario (a), the outcome is straightforward, that is, the less costly and more effective comparator is dominant. In scenarios (b) and (c), a key factor in the determination of cost effectiveness is the threshold value or ceiling ratio, which is interpreted as the decision maker's maximum willingness to pay for an additional unit of health gain. In such cases, the results from economic evaluation are presented in terms of an incremental cost effectiveness ratio or ICER (*Difference in Mean Cost/Difference in Mean Effect*) which is compared directly to the appropriate threshold value. The results from economic evaluation should enable the identification of the decision rule scenario which applies for a given comparative analysis.

In Ireland, there is no fixed and generally agreed cost effectiveness threshold below which health care technologies would be considered by policy makers to be cost effective [2]. However, in the current economic climate it is likely to be somewhat less than the €45,000 per QALY gained that has previously been mooted in the literature. Indeed, it is now likely that only those interventions with an incremental cost effectiveness ratio of €20,000 per QALY gained or less will have any likelihood of being considered cost effective.

Given the uncertainty relating to the appropriate cost effectiveness threshold value and the underlying assumptions of the modelling approaches adopted, a series of sensitivity analyses was undertaken to explore the robustness of the cost effectiveness results across alternative threshold values and to variations in the modelling assumptions adopted for the base-case analyses.

2.3.3 Sensitivity Analysis

To explore the uncertainty in the analysis a range of sensitivity analyses were undertaken.

First, a probabilistic sensitivity analysis was used to translate the uncertainty in individual input parameters into a measure of uncertainty in the overall cost effectiveness results [21]. Clinical, resource and cost input parameters in the model were assigned probability distributions (see Appendix A for further details), and for each of the 40 stochastic realisations of the dynamic model, the model results were re-estimated 500 times drawing randomly from that distribution. The probabilistic results were used to construct cost effectiveness acceptability curves, which estimate the probability of the screening programme being cost effective for a range of potential cost effectiveness threshold values per additional QALY gained [22].

Second, a series of one-way sensitivity analyses were undertaken to examine the impact of varying the assumptions of the base-case analyses on the cost effectiveness results (as detailed in Tables 1 and 2).

3. Results

The results from each stage of the economic evaluation are presented in the following sections.

3.1 Cost Analysis Results

The costs of screening were estimated prospectively alongside the pilot study and are presented in Table 4. The results from the cost analysis were calculated individually for each screening programme and for each stage of the screening process.

The results for the Clinical Setting screening programme are presented in terms of the average *cost per offer* (**€26**), the average *cost per negative case* (**€66**), the average *cost per positive case* (**€152**), and the average *cost per partner notified and treated* (**€74**).

In the base-case analysis, it was assumed that GPs and practice nurses equally shared the work of offering screens in general practice. Given the cost differential between GP and nurse led care, cost results for scenarios in which GPs and nurses offered the screen alone were estimated as part of the sensitivity analysis.

The results for the ‘Pee-in-a-pot’ screening programme are presented in terms of the average *cost per negative case* (**€39**), the average *cost per positive case* (**€125**), and the average *cost per partner notified and treated* (**€74**).

Table 4. Cost Analysis Results

| Screening Programme | Clinical Setting Base-Case € | Clinical Setting GP Only € | Clinical Setting PN Only € | Non-Clinical Setting ‘Pee-in-a-pot’ € |
|-----------------------------------------|------------------------------------|----------------------------------|----------------------------------|---------------------------------------------|
| Cost per Offer (no screening uptake) | 26 | 38 | 15 | n/a |
| Cost per Negative Case | 66 | 91 | 42 | 39 |
| Cost per Positive Case | 152 | 177 | 128 | 125 |
| Cost per Partner Notified and Treated | 74 | 74 | 74 | 74 |

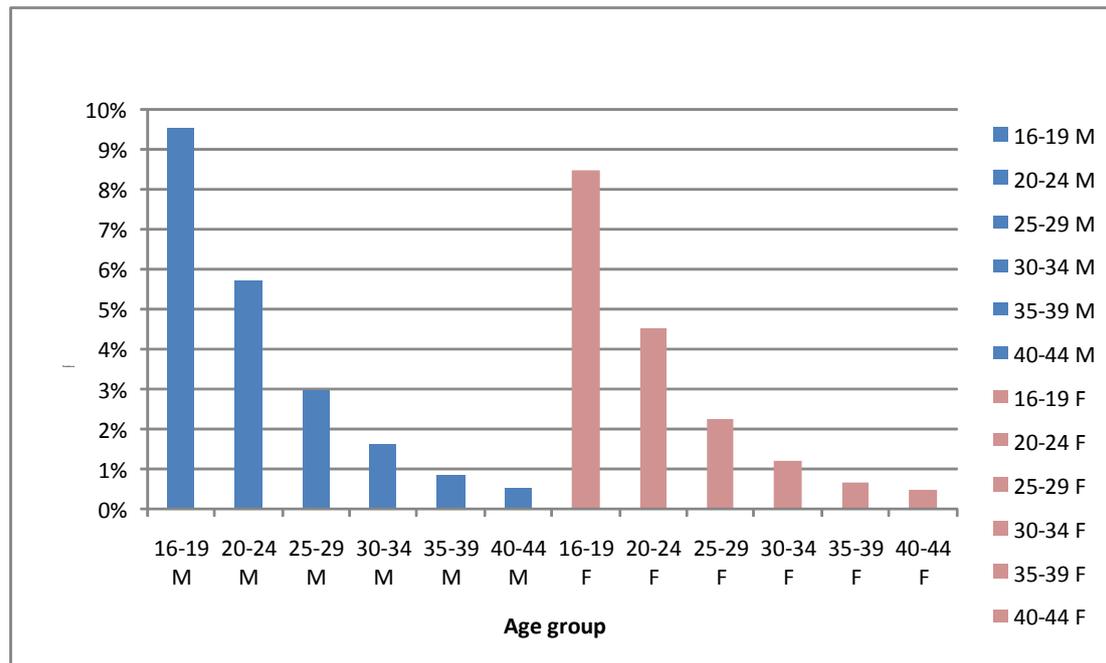
(Euros (€) in 2008 prices) GP – general practitioner; PN – practice nurse

3.2 Incremental Cost Effectiveness Results

The results from the cost analysis were combined with a range of additional clinical, utility, resource use and cost data within the modelling framework to complete the economic evaluation of the proposed screening strategies.

Prior to screening implementation, the steady state prevalence levels projected by the dynamic model ranged from 2.5% to 3.5%. Highest levels were observed in the youngest age groups reflecting their higher turnover of partners compared with older ages (see Figure 2).

Figure 2. Pre-screening age-specific prevalence: the equilibrium (steady-state) prevalence by males and females by age groups



Prevalence data from the UK [7, 8, 9, 10] were used to parameterize the model. The decision to adopt UK data was pragmatic in nature and was informed by the limited availability of prevalence data for an Irish population, and in particular for those aged 18 years old and younger.

The modelled screening scenarios were then entered into the model and evaluated in terms of their impact on projected prevalence, the resulting numbers of infections and complications, and the health outcomes and costs associated. The findings from the incremental analyses which compared each modelled scenario to the control of no organised screening are detailed in Table 5 and in the following sections.

3.2.1 Clinical Setting Screening: Base-case Results

The results for the analysis of opportunistic screening delivered in the Clinical Setting indicate that screening led to improved health outcomes but required additional health care resources even when programme outlays were set against projected savings from avoided infections and complications.

Within the modelled population of 20,000 males and 20,000 females males aged 16 to 45 years, the annual number of screens in the target population of 18 to 29 year olds was 1,960 in men and 4,128 in women. The impact of screening was a fall in the projected prevalence level, as depicted in Figure 3, and an improvement in population health through reductions in the number of MOs experienced and the number of QALYs lost.

The incremental results indicate that screening, when compared to control, was associated with 699 MOs averted and 45 QALYs gained at an additional cost of €4,258,868 over a 10 year period. Discounting future costs and effects to the base year, this translated into an incremental cost per MOA of €6,093 and an incremental cost per QALY gained of €94,717.

While no single cost effectiveness threshold for health technology assessment is in operation in Ireland, the cost effectiveness acceptability curve in Figure 4 indicates that the probability of screening being cost effective is less than 1% for a range of potential threshold values of up to and including €45,000 per QALY gained. This would suggest that Clinical Setting screening, as modelled in the analysis, is unlikely to be considered cost effective.

Figure 3. Prevalence Pre and Post Screening Implementation – Clinical Setting Screening

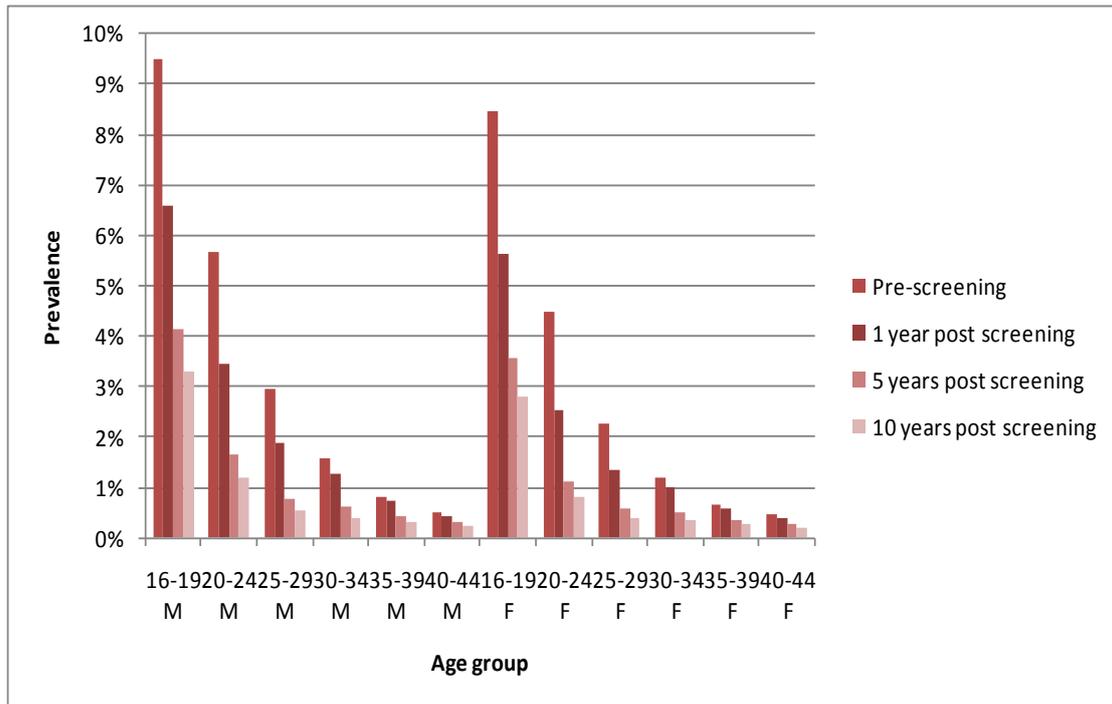
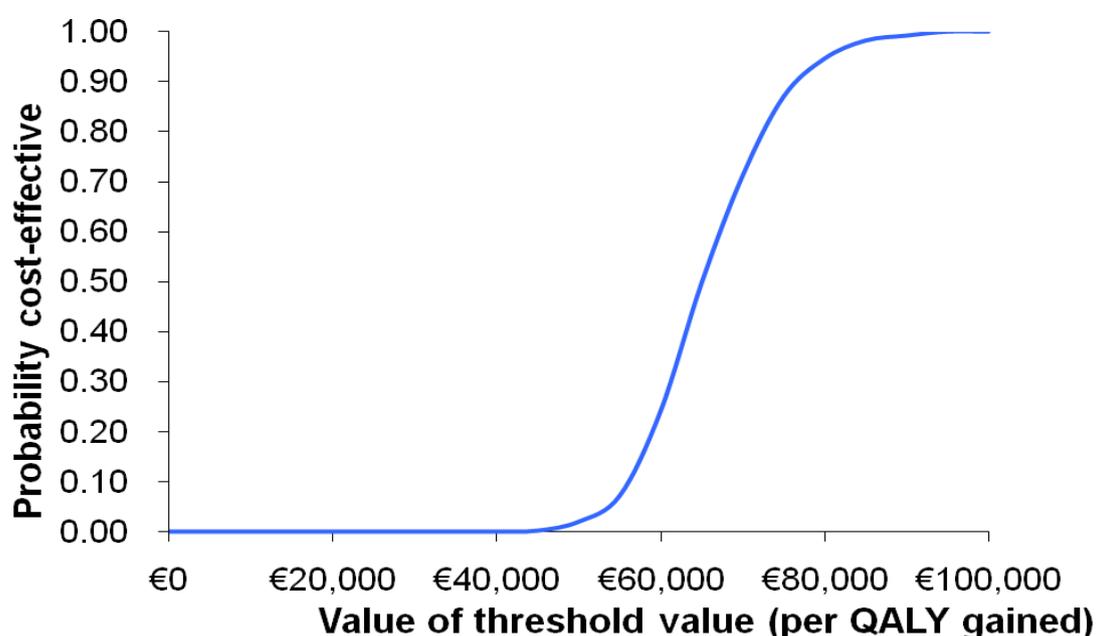


Figure 4. Cost Effectiveness Acceptability Curve – Clinical Setting Screening



3.2.2 Clinical Setting Screening: One-Way Sensitivity Analysis Results

A series of one-way sensitivity analyses were undertaken to explore the impact of varying the assumptions of the base-case analysis. The results are presented in Table 5 and were broadly similar to those observed in the base-case analysis, in that screening was predicted to result in fewer major outcomes, fewer QALYs lost, and higher healthcare costs than the control strategy. The sensitivity analysis undertaken included the following:

- PID Progression Rate: 10%, 30%
- Nurse Led Screening Programme
- GP Led Screening Programme
- Student Health Clinic Screening Programme
- Family Planning Screening Programme
- No minimum Gap Between Screens
- Provider Offer Rate: 5%, 20%, 40%, 100%
- Patient Acceptance Rate: 50%, 64%, 80%
- Partner Notification Rate: 40%
- Discount Rate: 0%, 6%

The PID progression rate was shown to be a significant parameter in the cost effectiveness analysis. Increasing the rate from 10% to 30% had the effect of reducing the incremental cost per QALY gained to €39,126. However, recent evidence calls into question the likelihood of chlamydia progression to PID being as high as 30%

[15]. Conversely, reducing the PID progression rate to 1% increased the ICER to €700,144 per QALY gained.

Nurse led screening (one in which only the nurse offered testing to eligible individuals) was shown to be a less costly strategy than GP led screening. However neither strategy is likely to be considered cost effective, yielding incremental cost per QALY ratios of €62,603 and €113,523 respectively.

Screening offered individually in student health and family planning clinics yielded ICERs of €46,618 and €39,185 per QALY gained respectively. While these results are more cost effective than those reported for the clinical settings combined, they are subject to a number of caveats. Firstly, data on screening coverage for both family planning and student health settings were only obtained for the limited number of these clinics which participated in the pilot study. Evidence from a larger range and number of settings would be required to substantiate the robustness of these results.

Secondly, screening in these settings has lower coverage in the target population than the base-case strategy and are less effective in identifying infection and reducing overall prevalence levels. This has direct implications for the cost effectiveness analysis as the total cost of implementing screening is less for programmes with low coverage than programmes with high coverage.

In addition, the cost of identifying a positive case in the years after screening implementation is less in a low coverage programme. This is because the impact of screening in reducing chlamydia prevalence is less in a low coverage programme, which means that there are more residual cases in the target population, which can be detected at a lower cost per case than would be the case if the programme had high coverage. Consideration must be also given to equity concerns arising from offering screening in a manner that potentially excludes members of the target population who do not attend third level institutions or family planning clinics.

In the base-case analysis, we assume that once an individual is screened they are ineligible for an opportunistic screening offer for 1 year. An alternative approach is to assume that individuals are eligible for a screening offer each time they attend the clinical setting. Eliminating the assumption of a minimum gap between screens has the result of increasing the ICER to €129,303.

Altering the healthcare provider offer rate to 5%, 20% and 40% to reflect the rates observed in the pilot study did have the impact of reducing the ICER to €69,991, €74,045, and €87,132 respectively. Alternatively, increasing the offer rate to 100% had the impact of increasing the ICER to €97,733. This can be attributed to the positive relationship between the offer rate and the coverage rate of the screening programme, and the resulting impacts on the total cost of screening implementation.

The remaining one-way sensitivity analyses, which varied the acceptance, effective partner notification and discount rates, did not show significant impacts in terms of improving the likely cost effectiveness of screening (see Table 5).

3.2.3 'Pee-in-a-pot' Screening Results

The results for the analysis of opportunistic 'Pee-in-a-pot' screening offered in non-clinical third level institution/college settings also indicate that screening led to improved health outcomes but required additional health care expenditures relative to control.

Within the modelled population of 20,000 males and 20,000 females aged 16 to 45 years, screening led to a fall in the projected prevalence level, as depicted in Figure 5, leading to an improvement in population health through reductions in the number of MOs experienced and the number of QALYs lost.

The incremental results indicate that screening, when compared to control, was associated with 44 MOs averted and 3 QALYs gained at an additional cost of €100,513 over 10 years. Discounting future costs and effects to the base year, this translated into an incremental cost per MOA of €2,294 and an incremental cost per QALY gained of €34,486.

The cost effectiveness acceptability curve in Figure 6 indicates that for the potential cost effectiveness threshold values of €15,000, €30,000 and €45,000, the probability of the screening being cost effective is 14%, 41% and 94% respectively.

This would suggest that the ‘Pee-in-a-pot’ screening programme may be considered cost effective if a cost effectiveness threshold in the region of €45,000 per QALY gained is in operation. This is open to debate as the likely threshold value of a public health system will be a function of its budget constraint, which in turn is influenced by the broader economic environment. The implication being that decision makers in Ireland may not be willing or able to pay as much in the future as was the case in years gone by.

Figure 5. Prevalence Pre and Post Screening Implementation – ‘Pee-in-a-pot’ Screening

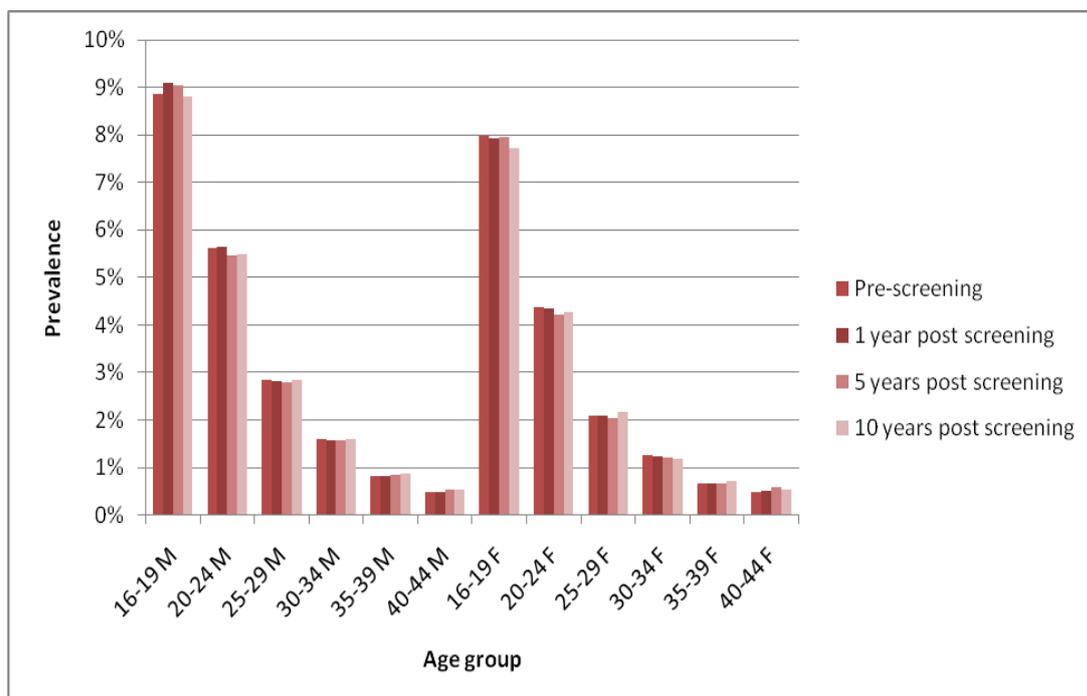
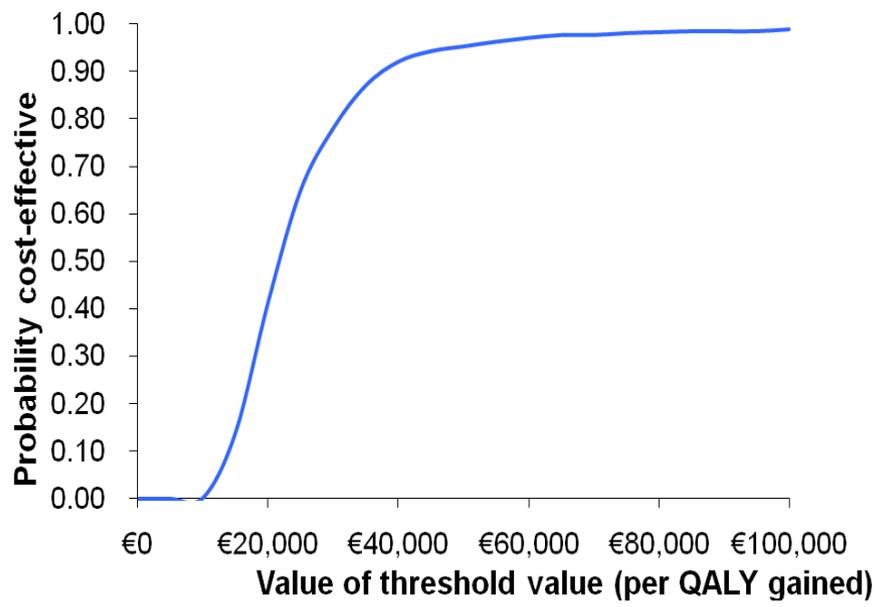


Figure 6. Cost Effectiveness Acceptability Curve - ‘Pee-in-a-pot’ Screening



4. Discussion

In conclusion, we examined the costs and cost effectiveness of opportunistic chlamydia screening delivered in clinical and non-clinical settings in Ireland, as proposed in the Chlamydia Screening in Ireland Pilot (CSIP) study. The consideration of alternative screening models was beyond the remit of the study.

The results indicate that the Clinical Screening strategy, as modelled, could reduce prevalence and improve population health, if sufficient coverage was achieved in the likely target population, which would be dependent on provider offer rates and patient / client acceptance rates (see 2.2). However, this would be expensive, and is unlikely to be considered cost effective given current budget constraints in Ireland.

The results from the 'Pee-in-a-pot' strategy, as modelled, may be considered cost effective if decision makers are willing to pay a threshold in the region of €45,000 per QALY gained. However, whereas this might have merited serious consideration when the pilot study was first commissioned in late 2006, this option would be subject to much more stringent consideration given current economic conditions in Ireland. Indeed, it is now likely that only those interventions with an incremental cost effectiveness ratio of €20,000 per QALY gained or less will have any likelihood of being considered cost effective. Furthermore, it is evident that 'Pee-in-a-pot' screening would have a low level of coverage in the target population and, as a result, a minimal effect in terms of reducing overall prevalence levels and improving population health.

The process of offering screening solely in third level institution/college settings also gives rise to important equity concerns as members of the target population who do not attend such institutions would be excluded from screening. Therefore, the potential for adopting the 'Pee-in-a-pot' strategy to settings frequented by more disadvantaged young people would need to be explored.

The results from the sensitivity analyses generally confirm those from the base-case Clinical Setting analysis. Most notably, an increased probability of 30% for chlamydia infection progressing to PID had the effect of reducing the incremental cost per QALY gained to €39,126. However, recent evidence from a study by Oakeshott et al [15] suggests that this may significantly overestimate the true probability value and estimated rates of progression to PID between 10% and 1% (with ICERs €94,717 and €700,144 respectively) may be more appropriate.

Eliminating the minimum gap of one year between screenings had the result of increasing the ICER, indicating that increasing the annual rate of screening does not improve cost effectiveness. Lowering the healthcare provider offer rate had the impact of reducing the ICER while increasing the offer rate increased the ICER. This reflects the positive relationship between the offer rate, the coverage rate, and the total costs of screening implementation, and conversely the negative relationship between total costs and cost effectiveness.

Practice nurse led screening was shown to be a less costly strategy than GP led screening; however neither strategy is likely to be considered cost effective. As was the case in the other sensitivity analyses, which varied offer, acceptance, effective partner notification, and discount rates, there was little evidence to suggest that the proposed Clinical Setting strategy is likely to be considered cost effective by policy makers in Ireland.

The findings from our analysis of Clinical Setting screening can be directly compared to those from the study by Adams et al [6] which applied the same modelling approach to examine the cost effectiveness of opportunistic screening in clinical settings in England. That study reported that offering an annual screening test to men and women aged less than 20 years may be cost effective. Moreover, the ICER for an equivalent screening scenario to that modelled in our study was €54,000 per QALY gained, suggesting that it is also unlikely to be deemed cost effective.

Notably, the results from our cost analysis indicated that cost estimates for screening and for the treatment of complications were appreciably higher in Ireland than in the earlier English study. In addition, the cost estimates reported here are higher than those reported in more recent English study examining the costs of different strategies for chlamydia screening and partner notification by Turner et al [23]. The divergence in costs across the two countries may be attributed to a range of factors including actual differences in the unit costs of healthcare as well as differences in how healthcare services are financed.

These results can also be compared to those from other studies which, using alternative dynamic modeling frameworks, reported conflicting results for the cost effectiveness of chlamydia screening strategies in various countries. Anderson et al [24], Gift et al [25], Welte et al [26] and deVries et al [27] individually found that various forms of opportunistic and proactive screening were cost effective in Denmark, the United States and the Netherlands respectively. Conversely, Roberts et al [28] found that proactive register based screening in the United Kingdom was not cost effective.

Notwithstanding the differences in the screening strategies evaluated, the healthcare systems involved, and the costing methods adopted, the divergence in results across the reported studies is likely in part to reflect key differences in the underlying dynamics and assumptions in the models adopted [4]. For example, as in the study by Roberts et al [28], we adopted a conservative estimate of 10% with respect to PID progression. This is in contrast to the studies by Anderson et al [24], Gift et al [25], Welte et al [26] and deVries et al [27], which adopted equivalent probabilities of 25%, 20%, 20% and 15% respectively. As noted, this parameter has a major influence on cost effectiveness and, importantly, recent evidence would appear to support a more conservative approach in the modelling of the link between chlamydia and PID [15].

There are a number of limitations in our study. Firstly, the adopted modeling approach is open to criticism. In a study comparing three alternative models, Kretzschmar et al [4] provide an overview of the general weaknesses in such models including the approach adopted in this analysis. These relate broadly to the technical difficulties associated with the modelling of dynamic sexual networks as well as the lack of good quality empirical data to parameterise and fit the models.

More specifically, the model we adopt is the most optimistic of three considered by Kretzschmar et al [4] in terms of its impact on prevalence rates. This is attributed in part to the relatively low level of pre-screening treatment of chlamydia infection assumed in this model compared to the alternatives. Were prevalence rates to remain higher screening would appear more cost effective than suggested here. This further highlights the importance of the underlying assumptions of the models used to evaluate chlamydia screening programmes in determining their cost effectiveness and raises the question as to whether adopting an alternative approach would materially

alter the results presented. It also points to the need for accurate chlamydia prevalence estimates, both in the generally population and in population sub-groups.

While we would expect the cost of identifying a positive case in the years post screening implementation to be reduced if a more pessimistic model was adopted (given that there would be more residual cases in the target population), we would not expect the resulting impact in terms of overall cost effectiveness to be considerable. This conclusion is based on the results from the ‘Pee-in-a-pot’ analysis and the Clinical Setting sensitivity analyses which explored screening scenarios with lower coverage in the target population (based on lower offer and acceptance rates) than the base-case strategy.

As would be the case with a more pessimistic model, the impact of screening in reducing prevalence is less for the lower coverage scenarios than for the base-case strategy, resulting in more residual cases in the target population which can be detected at a lower cost per case. However, the results for these ‘low coverage’ analyses did not fundamentally differ from those of the base-case analysis in that there remained substantial uncertainty as regards the likely cost effectiveness of the screening strategies. Consequently, we believe our results to be robust to the choice of a more pessimistic model than that which was employed.

Finally, the modeling analysis does not allow for the consideration of additional ‘spillover’ effects which may arise, specifically in terms of the other sexually transmitted infections which would be identified and treated as a result of chlamydia screening. Given the complexities of including such effects in the modeling framework, these were not examined.

Secondly, we assume that England and Ireland share similar age-related patterns of sexual behaviour so that the dynamic network model deployed was applicable to the Irish setting. While there may be real differences that were not accounted for, the differences in behaviours are considered to be small and unlikely to have a major impact on results. Furthermore, an important difference between the settings is that screening in the pilot study was not offered to young persons less than 18 years of age due to legal advice received by the study research team.

The risk of complications may be greater in adolescent females in this age group and a pool of infection could be maintained in this cohort, if their sexual networks include older men who do not accept screening, which could mean that prevalence reductions would be more modest than those modelled. Nonetheless, given the results from the English analysis by Adams et al [6] which explicitly include this cohort, it is unlikely that their inclusion of in this analysis would fundamentally change the results from a cost effectiveness perspective.

Thirdly, approximately two thirds of the population in Ireland, who do not meet the financial eligibility criteria, must pay (per-visit) to access primary care services. Eligibility for free services has been shown to have a significant impact on primary care attendance rates in Ireland [29]. In the base-case Clinical Setting analysis, we adopted combined attendance rate data for eligible and ineligible patient groups from a nationally representative study [16]. In doing so, we do not explicitly distinguish the results for those individuals who are eligible and those who must pay to access such care. Nonetheless, it is important to note that given the nature of the programme those in higher socioeconomic groups who are ineligible for free primary care services are less likely to be offered screening than those who are eligible, if the latter are more

frequent attenders. If this was the case, it could contribute to a negative effect on equity, in the sense that, assuming there is equal need, it would not provide equal access to chlamydia screening especially for those just above the income threshold for a medical card.

Finally, economic evaluation in Ireland is complicated by a paucity of resource utilisation, unit costs and utility data. In some cases, we adopted UK resource data to detail the treatment process of chlamydia complications, as national data were not readily available. The assumption that the management of infection matches that in the UK was deemed acceptable by expert opinion from within our study group that included public health consultants as well as those involved in the treatment of chlamydia. Similarly, utility data were estimated based from external data sources. Indeed, utility data associated with chlamydia infection and complications is not widely available and further research is required to improve the QALY estimates adopted in studies such as ours.

In conclusion, we examined the costs and cost effectiveness of opportunistic screening delivered in clinical and non-clinical settings in Ireland. Clinical Setting screening is unlikely to be considered cost effective while the cost effectiveness of 'Pee-in-a-pot' screening is dependent on decision makers being willing to pay a threshold in the region of €45,000 per QALY gained. This is open to question given current economic conditions in Ireland. Finally, all evidence presented is qualified by the underlying assumptions of the adopted models, which play an important role in evaluating chlamydia screening programmes and in determining their cost effectiveness.

Table 5. Incremental Cost Effectiveness Results (Screening Versus No Screening)

| Screening Scenario | Total Cost (€) | MOs | QALYs Lost | | |
|----------------------------------------------------------------|---------------------------------|----------------------------|------------------------------|-----------------------------------------|-------------------------------------------------|
| No Screening | 702,074 | 1,317 | 84 | | |
| Clinical Screening Programme | 4,960,942 | 618 | 39 | | |
| 'Pee-in-a-pot' Screening Programme | 802,587 | 1,273 | 81 | | |
| Incremental Analysis (Screening minus No Screening) | Incremental Cost (€) | Incremental MOs | Incremental QALYs | Incremental Cost per MOA (€) | Incremental Cost per QALY Gained (€) |
| Clinical Screening : <i>Base-Case Analysis</i> | 4,258,868 | 699 | 45 | 6,093 | 94,717 |
| Pee in the Pot Screening Programme | 100,513 | 44 | 3 | 2,294 | 34,486 |
| Sensitivity Analysis | | | | | |
| PID Progression Rate = 1% (down from 10%) | 4,406,776 | 191 | 6 | 23,107 | 700,144 |
| PID Progression Rate = 30% (up from 10%) | 3,874,293 | 1,731 | 99 | 2,238 | 39,126 |
| Male Acceptance 50% (down from 64%) | 4,155,594 | 688 | 44 | 6,037 | 93,890 |
| Female Acceptance 64% (down from 85%) | 4,177,059 | 661 | 42 | 6,321 | 98,802 |
| Male and Female Acceptance 50% | 4,029,756 | 583 | 37 | 6,907 | 108,254 |
| Male and Female Acceptance 80% | 4,318,392 | 722 | 46 | 5,984 | 92,949 |
| Partner Notification 40% (up from 20%) | 4,560,910 | 838 | 54 | 5,446 | 84,541 |
| Offer 5% (down from 70%) | 548,702 | 124 | 8 | 4,427 | 69,991 |
| Offer 20% (down from 70%) | 1,800,512 | 384 | 24 | 4,686 | 74,045 |
| Offer 40% (down from 70%) | 3,025,369 | 543 | 35 | 5,573 | 87,132 |
| Offer 100% (up from 70%) | 5,094,959 | 810 | 52 | 6,291 | 97,733 |
| No minimum gap between screens | 6,760,135 | 805 | 52 | 8,403 | 129,303 |

| | | | | | |
|-----------------------------------|-----------|-----|----|-------|---------|
| GP Only Led Programme | 4,836,584 | 673 | 43 | 7,189 | 113,523 |
| Practice Nurse Only Led Programme | 2,814,887 | 699 | 45 | 4,027 | 62,603 |
| Discount Rate 0% (down from 3.5%) | 4,835,806 | 906 | 86 | 5,336 | 56,020 |
| Discount Rate 6% (up from 3.5%) | 3,690,117 | 592 | 30 | 6,233 | 124,576 |

5. Summary of Key Findings

1. While the modelled scenario for chlamydia screening in combined clinical settings (general practice, student health and family planning clinics) would likely to be an effective strategy for reducing overall prevalence, if adequate rates of test offers and uptakes were achieved, it would be expensive in that it would require extensive additional healthcare resources. Decision makers must determine whether the benefits generated are sufficient to justify the additional resources required to implement the intervention in practice. This notwithstanding, it appears unlikely that Clinical Setting screening would be considered cost effective given current economic circumstances in Ireland.
2. The modelled scenario for screening offered in the form of a short duration mass testing ‘Pee-in-a-pot’ campaign in third level educational/college settings may be cost effective if decision makers in Ireland are willing to pay a cost effectiveness threshold in the region of €45,000 per additional QALY gained. This is open to question given the current economic climate and its resulting impact in terms of imposing further constraints on healthcare budgets. It is also important to note that this strategy would have minimal impact in reducing overall chlamydia prevalence in the population, if not supported by general population screening and prevention strategy. Furthermore, consideration must be given to equity concerns arising from offering screening in a manner that excludes members of the target population who do not attend third level institutions.

6. Potential limitations of this study

1. Economic modelling of infectious disease is a highly complex and imperfect science. We used a model which represents current best practice with respect to the state of the art for the modelling of chlamydia. The technical limitations associated with individual based stochastic simulation models, which are discussed in detail by Kretzschmar et al [4], are applicable to the current analysis. Furthermore the adopted approach is considered optimistic when compared to the alternative modelling approaches available. Nonetheless, it is unlikely that applying the more conservative models would have generated fundamentally different results from those presented.
2. The economic modelling process was limited in some cases by a lack of nationally available data. In such instances, we adopted data from the international clinical and economic literature. This approach, whilst unavoidable, assumes that epidemiological data, healthcare utilisation data and utility/QALY data from external sources are directly transferable to the Irish setting.
3. The process of conducting economic evaluation in Ireland is complicated by the lack of a national database of unit cost data for the Irish health care system.

7. Recommendations

A. If a Chlamydia screening programme is recommended:

- The results from the economic evaluation do not support the widespread adoption of opportunistic chlamydia screening in combined clinical settings as delivered in the pilot study. Alternative models, in which screening is offered to a subsection of the target population or to those who are most likely to benefit, would need to be identified and evaluated if policy makers wish to have a better knowledge-base for decision-making.

B: Further studies needed

- Further research is required to identify and evaluate alternative models of opportunistic screening which target subsections of the population of interest and those who are most likely to benefit.
- Further evidence is required to address the uncertainties that pervade the existing models of chlamydia infection and transmission
- Further evidence is required on the chlamydia prevalence, QALY impacts and healthcare utilisation related to the complications associated with chlamydia both in Ireland and internationally
- A national healthcare unit cost database, along the lines of the reference cost databases that are in existence in the UK, is required to facilitate the process of economic evaluation and health technology assessment in Ireland.

References

1. Drummond, M.F., Sculpher, M.J., Torrance, G.W., O'Brien, J., Stoddart, G.L.: *Methods for the Economic Evaluation of Health Care Programmes*. Oxford University Press. 2005.
2. Health Information of Quality Authority: Guidelines for the Economic Evaluation of Health Technologies in Ireland. 2010. Available from: www.hiqa.ie
3. Central Statistics Office. Dublin (www.cso.ie)
4. Kretzschmar M, Turner KM, Barton PM, Edmunds WJ, Low N. Predicting the population impact of chlamydia screening programmes: comparative mathematical modelling study. *Sex Transm Infect* 2009; 85(5):359-366.
5. Turner KME, Adams EJ, Gay NJ, Ghani AC, Mercer CH, Edmunds WJ. Developing a realistic sexual network model of chlamydia transmission in Britain. *Theor Biol Med Model* 2006;3:3.
6. Adams EJ, Turner KM, Edmunds WJ. The cost-effectiveness of opportunistic chlamydia screening in England. *Sex Transm Infect*. 2007;83:267-275
7. Fenton KA, Korovessis C, Johnson AM, McCadden A, McManus S, Wellings K et al. Sexual behaviour in Britain: reported sexually transmitted infections and prevalent genital Chlamydia trachomatis infection. *Lancet* 2001; 358(9296):1851-1854.
8. Johnson AM, Mercer CH, Erens B, Copas AJ, McManus S, Wellings K et al. Sexual behaviour in Britain: partnerships, practices, and HIV risk behaviours. *Lancet* 2001; 358(9296):1835-1842.
9. Adams EJ, Charlett A, Edmunds WJ, Hughes G. Chlamydia trachomatis in the United Kingdom: a systematic review and analysis of prevalence studies. *Sex Transm Infect* 2004; 80(5):354-362
10. LaMontagne D S, Fenton K A, Randall S. et al Establishing the National Chlamydia Screening Programme in England: results from the first full year of screening. *Sex Transm Infect* 2004. 80:335–341.

11. The Irish Study of Sexual Health and Relationships. Crisis Pregnancy Agency and Department of Health and Children. 2006. Available from: http://www.dohc.ie/publications/pdf/ISSHR_Main_Report.pdf?direct=1
12. Stamm W, Guinan M, Johnson C, et al. Effect of treatment regimens for *Neisseria gonorrhoeae* on simultaneous infection with *Chlamydia trachomatis*. *N Engl J Med* 1984;310:545–9.
13. Morre S, van den Brule A, Rozendaal L, et al. The natural course of asymptomatic *Chlamydia trachomatis* infections: 45% clearance and no development of clinical PID after one-year follow-up. *Int J STD AIDS*. 2002;13 (2):12–8.
14. Van Valkengoed IG, Morre SA, van Den Brule AJ, et al. Overestimation of complication rates in evaluations of *Chlamydia trachomatis* screening programmes--implications for cost-effectiveness analyses. *Int J Epidemiol*. 2004;33:416–25.
15. Oakeshott P, Kerry S, Aghaizu A, Atherton H, Hay S, Taylor-Robinson D, et al. Randomised controlled trial of screening for *Chlamydia trachomatis* to prevent pelvic inflammatory disease: the POPI (prevention of pelvic infection) trial. *BMJ*. 2010; 340: c1642
16. SLAN 2007: Survey of Lifestyle, Attitudes and Nutrition in Ireland. Department of Health and Children. 2008. Available from: http://www.dohc.ie/publications/pdf/slan07_report.pdf?direct=1
17. Low N, Bender N, Nartey L, Redmond S, Shang A, Stephenson JM. Review 2 - Review of evidence for the effectiveness of screening for genital chlamydial infection in sexually active young women and men. 2006. Available from: http://www.nice.org.uk/nicemedia/pdf/Chlamydia_Screening_Revised_Review_of_Effectiveness.pdf
18. Hope A, Dring C and Dring J. College Lifestyle and Attitudinal National (CLAN) Survey. In: Health Promotion Unit. The Health of Irish Students. Dublin: Health Promotion Unit, Department of Health and Children. 2005
19. Institute of Medicine. Vaccines for the 21st Century: A tool for decision making. Washington DC: National Academy Press. 2000.

20. Smith KJ, Tsevat J, Ness RB, Wiesenfeld HC, Roberts MS. Quality of life utilities for pelvic inflammatory disease health states. *Sex Transm Dis.* 2008; 35(3):307-311.
21. Briggs, A. Handling uncertainty in economic evaluation and presenting the results. *Economic Evaluation in Health Care. Merging Theory and Practice.* Drummond, M., McGuire, A. Oxford University Press. 2001
22. Fenwick, E., Claxton, K., Sculpher, M. Representing uncertainty: the role of cost-effectiveness acceptability curves. *Health Econ.* 2001; 10(8): 779-87.
23. Turner K, Adams E, Grant A, Macleod J, Bell G, Clarke J, Horner P. Costs and cost effectiveness of different strategies for chlamydia screening and partner notification: an economic and mathematical modelling study. *BMJ.* 2011; 342:c7250
24. Andersen B, Gundgaard J, Kretzschmar M, et al. Prediction of costs, effectiveness, and disease control of a population-based program using home sampling for diagnosis of urogenital *Chlamydia trachomatis* infections. *Sex Transm Dis.* 2006; 33:407-415.
25. Gift T, Gaydos C, Kent C, Marrazzo J, Rietmeijer C, Schillinger J, Dunne E. The Program Cost and Cost-Effectiveness of Screening Men for Chlamydia to Prevent Pelvic Inflammatory Disease in Women. *Sexually Transmitted Diseases*, 2008;35(11):S66-S75
26. Welte R, Kretzschmar M, Leidl R, van den Hoek A, Jager JC, Postma MJ. Cost-effectiveness of screening programs for *Chlamydia trachomatis*: a population-based approach. *Sex Transm Dis*, 2000; 27(9):518-529
27. de Vries R, van Bergen JE, de Jong-van den Berg LT, et al. Systematic screening for *Chlamydia trachomatis*: Estimating cost-effectiveness using dynamic modeling and Dutch data. *Value in Health.* 2006; 9:1–11.
28. Roberts TE, Robinson S, Barton PM, et al. Cost effectiveness of home based population screening for *Chlamydia trachomatis* in the UK: Economic evaluation of chlamydia screening studies (ClASS) project. *BMJ.* 2007; 335:291A-294A.

29. Nolan A. Evaluating the impact of eligibility for free care on the use of general practitioner services: a difference-in-difference matching approach. *Soc Sci Med.* 2008;67(7):1164-72.

Appendix A. Dynamic Model Methodology

The dynamic model was parameterised using empirical data from national and international data sources. Where possible, data from the pilot study and other Irish data sources were adopted. In other cases, such as with respect to behavioural settings, adopted input parameters were based on earlier published work by Adams et al [6] and Turner et al [5].

Appendix Table 1. Base case input parameter values used in dynamic model

| PARAMETER LIST | | |
|------------------------------|-------|---------------------------------------------------------------------------------------------------------------|
| SETUP PARAMETERS | | |
| 40 | | Number of realisations |
| 20000 | | Number of men + women (total population = 2N) |
| 16 | 45 | Start age, end age |
| SCREENING PARAMETERS | | |
| 0.5 | 0.8 | Proportion attending health care setting in a year (Male, Female), used to calculate number attending per day |
| 1 | 1 | Individual chance attending (M/F) e.g. 1 – everyone may attend, 0.5 half attend, the rest never attend |
| 0 | 365 | Screen type (0 - continuous, 1 - pulse), screen frequency (if pulse) |
| 16 | 29 | Start screen age (Male & Female), end screen age (Male & Female) |
| 0.64 | 0.85 | Screen accept (Male, Female) |
| 0.7 | 0.7 | Screen offer (Male, Female) |
| 1 | 1 | Individual accept (Male, Female) |
| 0.95 | 0.95 | Treatment effectiveness (Male, female) |
| 1 | 1 | Test sensitivity, specificity |
| 7 | 10 | Mean refractory period following infection in days, (distribution) |
| 365 | | Screen interval |
| 0.2 | 0.2 | Proportion of partners of men notified, proportion of partners of women notified |
| 90 | | Time frame for notifying partners (notify partners from last 3 months) |
| 7 | 2 | Delay in partner notification following index treatment mean (distribution) |
| 180 | | Definition of recent partner (duration of partnership < x days) |
| 0.25 | 1 | Frequency of sex acts in long partnerships (per day), frequency of sex acts in short partnerships |
| BIOLOGICAL PARAMETERS | | |
| 0.0375 | | Transmission probability (Male to Female and Female to Male) |
| 30 | | Average duration of symptomatic infection (Male & Female) |
| 180 | | Average duration of asymptomatic infection (Male & Female) |
| 1825 | | Maximum duration of infection before spontaneous resolution (5 years) |
| 0.05 | | Proportion population initially infected |
| 0 | 0.045 | Proportion symptomatic infections (Male, female) |
| 0.1 | | Proportion progressing to PID from untreated chlamydia infection (F) |
| 0.02 | | Proportion progressing to epididymitis from untreated chlamydia infection (M) |

| SEXUAL BEHAVIOUR PARAMETERS | | |
|------------------------------------|------|---------------------------------------------------------------------------------------------------------------|
| 14 | | Average duration of short partnerships (days) |
| 900 | 900 | Average duration of long partnerships (Male, female) |
| 0.6 | 0.5 | Initial proportion preferring short partnerships (Male, female) |
| 0.04 | 0.08 | Proportion that switch from short to long per year (Male, female) |
| 200 | 200 | Duration increase in long partnerships per year, Male Female (i.e. partnerships become more stable over time) |
| 14 (2) | | Average gap between partnerships (distribution) |
| 0.05 | | Proportion with concurrent partnerships, if under 35 years |

Appendix Table 2. Risk of developing complications following acute chlamydial infection

| Complication | Probability | Probability applied to: | Distribution type |
|----------------------------------|--------------------|-----------------------------------------|---------------------------|
| Symptomatic PID (women) | 1%, 10%, 30% | Asymptomatic chlamydia infection | Scenario analysis |
| Ectopic pregnancy (women) | 7.6% | Symptomatic PID | Beta (constrained by 0,1) |
| Tubal factor infertility (women) | 10.8% | Symptomatic PID (exclude those with EP) | Beta (constrained by 0,1) |
| Neonatal conjunctivitis | 14.8% | Infected women giving birth vaginally | Beta (constrained by 0,1) |
| Neonatal pneumonia | 7.0% | Infected women giving birth vaginally | Beta (constrained by 0,1) |
| Epididymitis (men) | 2% | Asymptomatic chlamydial infection | Fixed |

(Source: Adams et al [6])

Appendix B. Costing Methodology

A healthcare system perspective was adopted with respect to costs, with two broad components included in the analysis: (i) the cost of screening, and (ii) the costs of complications arising from untreated infections.

Appendix B.1. Screening Programme Costing Methodology

| <i>Clinical Setting Screening Programme</i> | |
|---------------------------------------------|------|
| Base-Case Analysis | |
| Cost per Offer | €26 |
| Cost per Negative Case | €66 |
| Cost per Positive Case | €152 |
| Partner Notification | €74 |
| GP Led Programme Analysis | |
| Cost per Offer | €38 |
| Cost per Negative Case | €91 |
| Cost per Positive Case | €177 |
| Partner Notification | €74 |
| Nurse Led Programme Analysis | |
| Cost per Offer | €15 |
| Cost per Negative Case | €42 |
| Cost per Positive Case | €128 |
| Partner Notification | €74 |

| <i>'Pee-in-a-pot' Screening Programme</i> | |
|-------------------------------------------|------|
| Cost per Negative Case | €39 |
| Cost per Positive Case | €125 |
| Partner Notification | €74 |

A: Clinical Setting Screening Programme

1. Cost per Offer

| <u>Item</u> | <u>Measure</u> | <u>Unit</u> | <u>Unit Cost</u> |
|-------------------------------------|-----------------|-------------|------------------|
| A. Overhead Costs | | | €11.21 |
| Personnel (Research Health Advisor) | | | €6.84 |
| Telephone | | | €0.15 |
| Computer Equipment | | | €0.65 |
| Stationary | | | €0.61 |
| Printing & Photocopying | | | €0.62 |
| Travel | | | €0.59 |
| Provider Pack | | | €1.75 |
| B. Variables Costs | | | |
| (1) Test Offer | | | €15.13 |
| % of GP Offers | 50 | % | |
| % of PN Offers | 50 | % | |
| GP Time | 6.68 | Minute | €3.97 |
| PN Time | 6.68 | Minute | €0.53 |
| Information Leaflet | 1 | Per Item | €0.10 |
| Estimated Cost per Offer | <i>[A+B(1)]</i> | | €26.34 |
| Other Screening Models: | | | |
| GP Led Programme | | | €37.83 |
| Nurse Led Programme | | | €14.85 |

2. Cost per Negative Case

| <u>Item</u> | <u>Measure</u> | <u>Unit</u> | <u>Unit Cost</u> |
|----------------------------------------|----------------|-------------|------------------|
| A. Overhead Costs | | | €11.21 |
| Personnel (Research Health Advisor) | | | €6.84 |
| Telephone | | | €0.15 |
| Computer Equipment | | | €0.65 |
| Stationary | | | €0.61 |
| Printing & Photocopying | | | €0.62 |
| Travel | | | €0.59 |
| Provider Pack | | | €1.75 |
| B. Variable Costs | | | |
| (1) Accepting the Test Offer | | | €16.63 |
| % of GP Offers | 50 | % | |
| % of PN Offers | 50 | % | |
| GP Time | 6.68 | Minute | €3.97 |
| PN Time | 6.68 | Minute | €0.53 |
| Information Leaflet | 1 | Per Person | €0.10 |
| Request Form | 1 | Per Person | €0.50 |
| Sample Container | 1 | Per Person | €0.50 |
| Transport bag | 1 | Per Person | €0.50 |
| (2) Testing and final diagnosis | | | €38.34 |
| Laboratory testing | 1 | Per Person | €20.38 |
| % of GP Notifications | 50 | % | |
| % of PN Notifications | 50 | % | |
| GP time | 7.64 | Minute | €3.97 |
| PN time | 8.67 | Minute | €0.53 |
| Phone Call | 1 | Per Person | €0.50 |

| | | |
|-----------------------------------------|---------------------|---------------|
| Estimated Cost per Negative Case | $[A + B(1) + B(2)]$ | €66.18 |
|-----------------------------------------|---------------------|---------------|

Other Screening Models:

| | | |
|------------------|--|---------------|
| GP Led Programme | | €90.54 |
|------------------|--|---------------|

| | | |
|---------------------|--|---------------|
| Nurse Led Programme | | €41.83 |
|---------------------|--|---------------|

3. Cost per Positive Case

| <u>Item</u> | <u>Measure</u> | <u>Unit</u> | <u>Unit Cost</u> |
|----------------------------------------|-----------------------|--------------------|-------------------------|
| A. Overhead Costs | | | €11.21 |
| Personnel (Research Health Advisor) | | | €6.84 |
| Telephone | | | €0.15 |
| Computer Equipment | | | €0.65 |
| Stationary | | | €0.61 |
| Printing & Photocopying | | | €0.62 |
| Travel | | | €0.59 |
| Provider Pack | | | €1.75 |
| B. Variable Costs | | | |
| (1) Accepting the Test Offer | | | €16.63 |
| % of GP Offers | 50 | % | |
| % of PN Offers | 50 | % | |
| GP Time | 6.68 | Minute | €3.97 |
| PN Time | 6.68 | Minute | €0.53 |
| Information Leaflet | 1 | Per Person | €0.10 |
| Request Form | 1 | Per Person | €0.50 |
| Sample Container | 1 | Per Person | €0.50 |
| Transport bag | 1 | Per Person | €0.50 |
| (2) Testing and final diagnosis | | | €38.34 |
| Laboratory testing | 1 | Per Person | €20.38 |
| % of GP Notifications | 50 | % | |
| % of PN Notifications | 50 | % | |
| GP time | 7.64 | Minute | €3.97 |
| PN time | 8.67 | Minute | €0.53 |
| Phone Call | 1 | Per Person | €0.50 |

| | | | |
|-----------------------------------------|-----------------------------------|------------|----------------|
| (3) Treatment | | | €69.78 |
| % of consultations by GP | 100 | % | |
| GP time | 14.71 | Minute | €3.97 |
| Receptionist time | 2.5 | Minute | €0.21 |
| Information Leaflet | 1 | Per Person | €0.10 |
| Consent Form | 1 | Per Person | €0.10 |
| PN Form | 1 | Per Person | €0.10 |
| % treated with Azithromycin | 97 | % | |
| % treated with Doxycycline | 3 | % | |
| Azithromycin | 1 | Per Dose | €10.70 |
| Doxycycline | 1 | Per Dose | €5.77 |
| (4) Retesting | | | €16.15 |
| % of Individuals retested | 60 | % | |
| PN/HA time | 7.6 | Minute | €0.53 |
| Phone Call | 2 | Per Person | €0.50 |
| Sample Container | 1 | Per Person | €0.50 |
| Transport Bag | 1 | Per Person | €0.50 |
| Request Form | 1 | Per Person | €0.50 |
| Laboratory testing | 1 | Per Person | €20.38 |
| Estimated Cost per Positive Case | $[A + B(1) + B(2) + B(3) + B(4)]$ | | €152.10 |
| Other Screening Models: | | | |
| GP Led Programme | | | €176.46 |
| Nurse Led Programme | | | €127.75 |

B: 'Pee-in-a-pot' Screening

1. Cost per Negative Case

| <u>Item</u> | <u>Measure</u> | <u>Unit</u> | <u>Unit Cost</u> |
|--------------------------------------------|-----------------------------------|-------------|------------------|
| A. Overhead Costs | | | €12.10 |
| Personnel (Research Health Advisor) | | | €6.84 |
| Telephone | | | €0.15 |
| Computer Equipment | | | €0.65 |
| Stationary | | | €0.61 |
| Printing & Photocopying | | | €0.62 |
| Travel | | | €0.59 |
| Consumables, Materials, Volunteer Payments | | | €2.64 |
| B. Variable Costs | | | |
| (1) Test | | | €1.60 |
| Information Leaflet | 1 | Per Person | €0.10 |
| Urine Container | 1 | Per Person | €0.50 |
| Transport bag | 1 | Per Person | €0.50 |
| Request Form | 1 | Per Person | €0.50 |
| (2) Testing and final diagnosis | | | €25.48 |
| Laboratory testing | 1 | Per Person | €20.38 |
| PN time | 8.67 | Minute | €0.53 |
| Phone Call | 1 | Per Person | €0.50 |
| Estimated Cost per Negative Case | $[A+B(1)+B(2)]$ | | €39.18 |

2. Cost per Positive Case

| <u>Item</u> | <u>Measure</u> | <u>Unit</u> | <u>Unit Cost</u> |
|--------------------------------------------|----------------|-------------|------------------|
| A. Overhead Costs | | | €12.10 |
| Personnel (Research Health Advisor) | | | €6.84 |
| Telephone | | | €0.15 |
| Computer Equipment | | | €0.65 |
| Stationary | | | €0.61 |
| Printing & Photocopying | | | €0.62 |
| Travel | | | €0.59 |
| Consumables, Materials, Volunteer Payments | | | €2.64 |
| B. Variable Costs | | | |
| (1) Accepting the Test Offer | | | €1.60 |
| Information Leaflet | 1 | Per Person | €0.10 |
| Urine Container | 1 | Per Person | €0.50 |
| Transport bag | 1 | Per Person | €0.50 |
| Request Form | 1 | Per Person | €0.50 |
| (2) Testing and final diagnosis | | | €25.48 |
| Laboratory testing | 1 | Per Person | €20.38 |
| % of PN Notifications | 100 | % | |
| PN time | 8.67 | Minute | €0.53 |
| Phone Call | 1 | Per Person | €0.50 |
| (3) Treatment | | | €69.78 |
| % of consultations by GP | 100 | % | |
| GP time | 14.71 | Minute | €3.97 |
| Receptionist time | 2.5 | Minute | €0.21 |

| | | | |
|-----------------------------------------|-----------------------------------|------------|----------------|
| Information Leaflet | 1 | Per Person | €0.10 |
| Consent Form | 1 | Per Person | €0.10 |
| PN Form | 1 | Per Person | €0.10 |
| % treated with Azithromycin | 97 | % | |
| % treated with Doxycycline | 3 | % | |
| Azithromycin | 1 | Per Dose | €10.70 |
| Doxycycline | 1 | Per Dose | €5.77 |
| (4) Retesting | | | €16.15 |
| % of Individuals retested | 60 | % | |
| PN/HA time | 7.6 | Minute | €0.53 |
| Phone Call | 2 | Per Person | €0.50 |
| Sample Container | 1 | Per Person | €0.50 |
| Transport Bag | 1 | Per Person | €0.50 |
| Request Form | 1 | Per Person | €0.50 |
| Laboratory testing | 1 | Per Person | €20.38 |
| Estimated Cost per Positive Case | $[A + B(1) + B(2) + B(3) + B(4)]$ | | €125.10 |

C: Partner Notification & Treatment

| | | | |
|------------------------------------------------------------|-------|------------|---------------|
| A. Contacting Partners | | | €1.97 |
| % of Partners contacted by Patient | 89 | % | |
| % of Partners contacted by PN/HA | 11 | % | |
| Nurse/Research Health Advisor Time | 11.67 | Minute | €0.53 |
| Phone Calls | 1 | Per Person | €0.50 |
| Contact Cards | 1 | Per Person | €0.79 |
| B. Partner Treatment | | | €67.94 |
| % of Partners Treated | 65 | % | |
| % of Primary Care | 69 | % | |
| % of GUM Consultations | 31 | % | |
| GP time | 14.5 | Minute | €3.97 |
| GUM Clinic Visit | 1 | Per Visit | €173 |
| Receptionist time | 2.5 | Minute | €0.21 |
| Information Leaflet | 1 | Per Person | €0.10 |
| % treated with Azithromycin | 97 | % | |
| % treated with Doxycycline | 3 | % | |
| Azithromycin | 1 | Per Dose | €10.70 |
| Doxycycline | 1 | Per Dose | €5.77 |
| C. Partner Testing | | | 3.84 |
| % of Treated Partners Tested | 20 | % | |
| Sample Container | 1 | Per Person | €0.50 |
| Transport Bag | 1 | Per Person | €0.50 |
| Request Form | 1 | Per Person | €0.50 |
| Laboratory testing | 1 | Per Person | €20.38 |
| Cost of Partner Notification, Treatment and Testing | | | |

| | | |
|---------------------------------|------------------------------|----------------|
| A. Cost of Notification | Per Person | €1.97 |
| B. Cost of Treatment | Per Person | €104.53 |
| C. Cost of Testing | Per Person | €21.28 |
| Total | $[A+B+C]$ | €128.38 |
| 65 % of Partners Treated | | |
| 20 % of Treated Partners Tested | | |
| Estimated Cost of PNTT | $[A+(0.65*B)+(0.65*0.20*C)]$ | €73.75 |

Appendix B.2. Cost Analysis: Screening Unit Cost Data

Appendix Table 3. Unit costs of materials, consumables, drugs and tests

| Item | Baseline (SD) € 2008 | Source |
|---------------------------|-------------------------|----------------------|
| Sample container | 0.50 (0.2) | Pilot Study Accounts |
| Transport bag | 0.50 (0.2) | Pilot Study Accounts |
| Request form | 0.50 (0.2) | Pilot Study Accounts |
| Information leaflets | 0.10 (0.04) | Pilot Study Accounts |
| Contact cards | 0.79 (0.32) | Pilot Study Accounts |
| Consent form | 0.10 (0.04) | Pilot Study Accounts |
| Partner notification form | 0.10 (0.04) | Pilot Study Accounts |
| Phone call | 0.50 (0.2) | Eircom |
| Azithromycin | 10.70 (4.28) | MIMS Ireland |
| Doxycycline | 5.77 (2.31) | MIMS Ireland |
| Laboratory testing | 20.38 (8.15) | Laboratory, DOHC |
| Pregnancy test | 14.00 (5.60) | Pilot Study Accounts |

SD - standard deviation. All cost items assumed to be normally distributed

Appendix Table 4. Unit costs of personnel input

| Item | Baseline (SD) € 2008 | Source |
|----------------------------------|-------------------------|---------------------------------------|
| General Practitioner, per minute | 3.97 (1.59) | Office of Revenue Commissioner Report |
| Practice Nurse, per minute | 0.53 (0.21) | Irish Nurses Organisation |
| GUM Clinic Visit | 173.00 (69.20) | Case-mix, DOHC |
| Receptionist, per minute | 0.21 (0.08) | IrishJobs.ie |

SD - standard deviation. All cost items assumed to be normally distributed

Appendix Table 5. Screening process time input

| Screening step | Minutes (SD) | Source |
|-----------------------------------------------|--------------|-------------|
| Practice Nurse time (test offer) | 6.68 (2.9) | Pilot Study |
| General Practitioner time (test offer) | 6.68 (2.9) | Pilot Study |
| Practice Nurse time (notification) | 8.67 (3.3) | Pilot Study |
| General Practitioner time (notification) | 7.64 (5.1) | Pilot Study |
| General Practitioner time (treatment) | 14.71 (4.7) | Pilot Study |
| Receptionist time (treatment) | 2.5 (1.7) | Pilot Study |
| Practice Nurse/HA time (retesting) | 7.6 (4.9) | Pilot Study |
| Practice Nurse/HA time (contacting partners) | 11.67 (2.9) | Pilot Study |
| General Practitioner time (partner treatment) | 14.5 (4.7) | Pilot Study |

| | | |
|---------------------------------------|-----------|-------------|
| Receptionist time (partner treatment) | 2.5 (1.7) | Pilot Study |
|---------------------------------------|-----------|-------------|

SD – standard deviation. All cost items assumed to be normally distributed

Appendix Table 6. Screening Overheads

| Resource Item | Total Cost (€) | Set Up/ Running Ratio | Unit Cost per Offer (€) | Source |
|--------------------------------------------------------------------|----------------|-----------------------|-------------------------|----------------------|
| Telephone Charges | 572.00 | 0.50 | 0.15 | Pilot Study Accounts |
| Computer Equipment | 1,284.70 | 1.00 | 0.65 | Pilot Study Accounts |
| Stationary | 2,414.62 | 0.50 | 0.61 | Pilot Study Accounts |
| Printing and Photocopying | 2,431.00 | 0.50 | 0.62 | Pilot Study Accounts |
| Travel Expenses | 2,326.45 | 0.50 | 0.59 | Pilot Study Accounts |
| Clinical Setting: Provider Pack | 1,150.00 | 1.00 | 1.75 | Pilot Study Accounts |
| 'Pee-in-a-pot' Setting: Consumables, Materials, Volunteer Payments | 3,459.16 | 1.00 | 2.64 | Pilot Study Accounts |
| Programme Administrator (6 month screening period) | 26,886.86 | 0.50 | 6.84 | Pilot Study Accounts |

Cost per offer = (total cost) x (set up/ running ratio) / total screening offers

Total overhead costs were allocated on the basis of the ratio of time/costs dedicated to the **set up** versus the **running** of the screening programmes. A cost per offer was allocated based on the total number of screening offers in the pilot study.

Appendix B.3. Complications of Chlamydia Infection Costing Methodology

The data used to estimate the average cost per complication are presented in the following tables.

Appendix Table 7. Unit costs in the estimation of the costs of infections and complications

| Condition | Baseline cost (SD) | Source |
|-----------------------------------------------------------------------|---------------------|--------------------------------------------------------------------------------------------|
| Symptomatically infected & actively seeking treatment (women/men) | | |
| GP clinic visit | 48.39 (4.36) | Irish Office of Revenue Commissioner |
| GUM clinic visit | 173 (69.20) | Irish Office of Revenue Commissioner |
| Diagnosis | 92.83 (37.13) | Pilot Study Estimate based on treatment protocol from Adams at al [6] and Irish Unit Costs |
| Treatment | 10.55 (2.44) | Monthly Index of Medical Specialities (MIMS) - Ireland |
| Pelvic inflammatory disease | | |
| Diagnosis | 53.34 (21.33) | Pilot Study Estimate based on treatment protocol from Adams at al [6] and Irish Unit Costs |
| Treatment | 42.49 (fixed) | MIMS Ireland |
| Hospital inpatient episode | 2,683.89 | Weighted average based on bed days of diagnoses below |
| Other Uterine & Adnexa Procedures for Non-Malignancy | 4,048.68 (1,619.47) | Case-mix, DOHC |
| Endoscopic and Laparoscopic Procedures for Female Reproductive System | 2,936.40 (1,174.56) | Case-mix, DOHC |
| Infections, Female Reproductive System | 2,134.51 (853.80) | Case-mix, DOHC |
| Hospital outpatient episode | 173 (69.20) | Case-mix, DOHC |
| Epididymitis | | |
| Diagnosis | 92.83 (37.13) | Pilot Study Estimate based on treatment protocol from Adams at al [6] and Irish Unit Costs |
| Treatment | 5.77 (fixed) | MIMS Ireland |
| Hospital inpatient episode | 2,410.32 | Weighted average based on bed days of diagnoses below |
| Testes Procedures W/O CC | 3,008.44 (1,203.38) | Case-mix, DOHC |
| Inflammation of the Male Reproductive System W CC | 4,632.36 (1,852.94) | Case-mix, DOHC |
| Inflammation of the Male Reproductive System W/O CC | 2,087.90 (835.16) | Case-mix, DOHC |

| | | |
|------------------------------------------------------|-------------------------|--------------------------------------------------------------------------------------------|
| Ectopic pregnancy (all hospital inpatient episodes) | | |
| Ectopic Pregnancy | 5,086.80 (2,034.72) | Case-mix, DOHC |
| Antenatal & Other Obstetric Admission | 1,543.41 (617.36) | Case-mix, DOHC |
| Antenatal & Other Obstetric Admission, Same day | 463.98 (185.59) | Case-mix, DOHC |
| Tubal factor infertility | | |
| Other Uterine & Adnexa Procedures for Non-Malignancy | 11,369.35 (4,535.22) | Case-mix, DOHC |
| Neonatal conjunctivitis & pneumonia | | |
| Diagnosis | 20.38 (8.15) | Pilot Study Estimate based on treatment protocol from Adams et al [6] and Irish Unit Costs |
| Treatment | 19.27 (7.71) | MIMS Ireland |
| Pneumonia hospital inpatient episode | 4,379.18 (1,751.67) | Case-mix, DOHC |

GP-general practice, GUM-genitourinary medicine; All costs items assumed to be normally distributed, truncated at 0, and rounded to the nearest £ for presentation; SD - standard deviation.

Appendix Table 8. Probability of attending health care settings due to infection and complications

| Condition | Baseline probability (SD) | Distribution* | Source |
|------------------------------------------------------------------|-----------------------------------|---------------|-----------------|
| Symptomatically infected & actively seeking treatment | | | |
| GUM vs. GP clinic | Women: 45% (3%), Men: 77% (2%) | Beta | Adams et al [6] |
| Pelvic inflammatory disease | | | |
| Inpatient hospital admission | 6.5% (1%) | Beta | Adams et al [6] |
| Outpatient hospital treatment | 6.5% (1%) | Beta | Adams et al [6] |
| Epididymitis | | | |
| GP vs. GUM clinic | 50% (20%) | Normal | Adams et al [6] |
| Inpatient hospital admission | 10% (3%) | Normal | Adams et al [6] |
| Tubal factor infertility | | | |
| Diagnosis & treatment | 50% (20%) | Normal | Adams et al [6] |
| Neonatal pneumonia | | | |
| Inpatient hospital admission | 19% (8%) | Beta | Adams et al [6] |

GP-general practice, GUM-genitourinary medicine; *All distributions for probabilities were truncated at 0 and 1; SD - standard deviation.

Note: Data adopted from Adams et al [6] given lack of evidence for the Irish Healthcare Setting.

Appendix C. QALY Methodology

The QALY losses from chlamydia complications were estimated by multiplying the duration in a condition by the valuation for each health state:

Total QALY loss for each state = (1 - quality of life weight) * duration in each state

Estimates of the quality of life weights (health utility index, HUI) were taken from the studies by the Institute of Medicine (2000). Smith *et al* (2008) have more recently published estimates using the time trade off method (TTO) and the visual analogue scale (VAS). The Institute of Medicine (2000) values were based on the consensus of an expert advisory panel, the TTO/VAS were estimated from sampling women who had reported no history of diagnosis with PID or related conditions. The duration of each condition was based on Adams *et al* (2007). Tubal factor infertility was assumed to last longer than a year; therefore QALY loss from this condition was discounted in future years. In probabilistic analysis, for the Institute of Medicine (2000) estimates, the uncertainty around them was unknown and a coefficient of 0.4 was used to estimate the SD. For the TTO/VAS estimates, the distribution was assumed to be normal with a reported SD as per the publication.

Appendix Table 9. Quality of life/utility weights, duration status, and estimated QALY loss from chlamydia complication states

| State | Quality/Utility weight* | Duration (years)** | QALY Loss |
|-----------------------------------------------------|-------------------------|--------------------|-----------|
| Women | | | |
| Pelvic inflammatory disease (PID): overall | 0.90 | 0.077 | 0.008 |
| <i>PID - outpatient</i> [^] | 0.69, 0.87 | 0.27 | 0.006 |
| <i>PID - inpatient</i> [^] | 0.60, 0.84 | 0.005 | 0.001 |
| Ectopic pregnancy (EP): overall | 0.63, 0.87 | 0.038 | 0.010 |
| Tubal factor infertility | 0.66, 0.84 | 3.468 | 0.871 |
| Men | | | |
| Epididymitis – overall | | | 0.011 |
| <i>Epididymitis - outpatient</i> [^] | 0.46 | 0.019 | 0.010 |
| <i>Epididymitis - inpatient</i> [^] | 0.30 | 0.003 | 0.002 |
| Neonatal | | | |
| Neonatal conjunctivitis | 0.97 | 0.042 | 0.001 |
| Neonatal pneumonia –overall | | | 0.037 |
| <i>Neonatal pneumonia - outpatient</i> [^] | 0.79 | 0.167 | 0.035 |
| <i>Neonatal pneumonia - inpatient</i> [^] | 0.55 | 0.022 | 0.010 |

QALY- quality adjusted life year;

*QALY weights were obtained from studies by the Institute of Medicine [19] and Smith et al [20];

[^] Inpatient refers to patients admitted to inpatient hospital care; outpatient is all other hospital and community care.

** Duration data taken from Adams et al [6]