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The Dangers of Introspection: A Systematic Review of Economic Studies of Chlamydia Trachomatis Screening

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Abstract:
Chlamydia Trachomatis is a highly infectious sexually transmitted disease and the most commonly sexually transmitted infection in developed countries. Different approaches to screening are currently being considered by policy makers internationally. A systematic review of economic evaluations of screening for Chlamydia Trachomatis has been carried out as part of the ClaSS (Chlamydia Screening studies). The appropriate modelling approach to use in the analysis of any infectious disease has long been identified in the epidemiological literature. The application to the modelling of sexually transmitted diseases became apparent in the late 1980s (Kretschmar et al). Only 2 out of 24 economic evaluations identified in our review and which used modelling to evaluate a screening programme for Chlamydia used an appropriate modelling approach such as Discrete Event Simulation or System Dynamics. Studies that used other modelling approaches to evaluate the impact of screening on the disease, are likely to incorrectly estimate the cost effectiveness of screening. This is because they fail to incorporate the potential for re-infection and the population effects (eg. impact of transmission) as a result of screening, the contributing effects of which may work in opposing directions. The use inappropriate modelling approaches in the evaluation of Chlamydia, as indeed in any economic evaluation, may lead to the provision of misleading results to policy makers which in turn will lead to decisions that do not make an efficient use of resources. This highlights the importance of wide literature searches and acknowledging the methodological advances of other disciplines

Acknowledgements

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1. Introduction

Chlamydia trachomatis is the most commonly sexually transmitted infection in developed countries and different approaches to screening are currently being considered by policy makers internationally. If left untreated Chlamydia can cause serious complications. For women these include pelvic inflammatory disease, ectopic pregnancy and infertility, which require complex health care. In 1998 the Chief Medical Officer's Expert Advisory Group on *Chlamydia trachomatis* recommended action to reduce the prevalence and morbidity associated with chlamydia infection in the UK.

This paper reports the preliminary results from a systematic review of the economic studies that have evaluated screening programmes for Chlamydia Trachomatis and forms part of the economic evaluation alongside the ClaSS study.

ClaSS is a large population-based study of genital Chlamydia infections. It is funded by the NHS Health Technology Assessment Programme and represents a collaboration between the University of Bristol, the University of Birmingham, The Public Health Laboratory Service, Genitourinary clinics and 27 GP practices in Bristol and Birmingham.

The overall project comprises a number of components which are presented in Figure 1

The objective of the economic evaluation is to determine the relative cost effectiveness of (i) population screening for Chlamydia compared to the current strategy of routine screening only in genitourinary medicine clinics; (ii) the two partner notification strategies; (iii) the different laboratory tests. The evaluation will be carried out from a societal perspective based on 'major outcome averted', defined as the occurrence of at least one of: pelvic inflammatory disease, ectopic pregnancy, and infertility. We will use a modelling approach to estimate cost effectiveness because of the time lag between implementation and any future benefits of Chlamydia screening and the number of possible scenarios.

A review of the published economic evaluations of Chlamydia screening had a number of objectives. First it was apparent that all the data required for our model would not all be available from the ClaSS study. Second we were aware that a variety of different modelling approaches had been used in previously published evaluations. Our review was

required to assess published modelling approaches and identify data requirements and areas of exploration for our sensitivity analysis.

2. Methods

Inclusion criteria

To be included in this study, reports had to meet the following criteria.

Participants*:* Males and females aged 14 years and above

Interventions*:* Any form of screening for Chlamydia Trachomatis. Screening methods could include opportunistic, population and targeted screening. We also included studies that reported on diagnostic tests that were used in screening programmes and studies that reported on contact tracing associated with Chlamydia Trachomatis.

Studies: Formal economic evaluations, cost studies. Cost studies included studies reporting primary research on the costs and utilisation of screening. Modelling studies for Chlamydia and other sexually transmitted diseases, and studies that had discussed costs and may provide useful primary or secondary cost or utilisation data.

Studies were identified using a comprehensive search strategy that is not presented because of space constraints. It was deliberately wide in order not to exclude relevant studies from other disciplines that provide important information for the construction of our own model. The selection of papers followed a two stage review process, based on the work of Mugford (refs) and which has been used by one of the current authors in a previous systematic review of economic studies (Roberts et al, BJOG 2001). This process is not presented here for space reasons. Stage I of the process categorises papers on the basis of title and abstract and coded them with the letter ‘A’. Potentially relevant papers were reviewed in full and further classified in Stage II. Only those papers confirmed as economic evaluations were included in the final review. Confirmed economic evlautions had the final classification ‘A1’.

Stage III- classification of papers by primary focus

All studies were categorised according to their primary focus. Studies that focused on more than one aspect of the screening process were assigned to the category that

appeared to be appropriate for the main focus of that paper. The other aspect of the paper that were relevant to other categories were also considered and compared in the other appropriate category

The primary foci of the papers were categorised follows:

- Screening
- Partner notification
- Diagnostic testing
- Treatment

Stage IV- quality criteria

We used a two-stage quality assessment approach to the evaluations. The first criteria used to assess the quality of the papers were based largely on the quality criteria that had been used by one of the authors in two previous reviews of economic studies (Roberts et al (2002)). These were short-listed from 35 criteria in the checklist in the *BMJ* for reviewing economic evaluations and this discussion regarding their justification is presented elsewhere (Roberts et al (2002)).

The second stage of our quality assessment included criteria from the BMJ checklist about details and choice of any model used. This is because the economic evaluation of any screening programme is only fully evaluated by including estimations about what would have happened in the absence of the screening programme. The purpose of any screening programme is typically to identify disease early to avoid any long term complications and in the absence of a long term follow up study, a modelling approach is typically required to evaluate the cost effectiveness of averting long term outcomes. The CMO report illustrated the appropriate model for Chlamydia screening was one which could accommodate the effect of re-infection and the population effects of screening on the incidence and prevalence of the disease.

Thus the model used in the evaluation needs to be critically appraised to ensure it was appropriate for the task. This item was not used as a hanging offence to reject the study since other useful information may be missed that would be required for our own

modelling approach. However, the results drawn from evaluations that had used the wrong modelling approach could be misleading.

Economic Evaluations

Quality - Stage1

- The research question is stated, implied or apparent (provision of comparative options);
- The viewpoints(s) of the analysis are stated or implied;
- The source(s) of effectiveness estimates used are stated, implied or apparent and appropriate***;
- The primary outcome measure(s) are stated, implied or apparent;
- Quantities of resources are reported separately from their unit costs, or can be derived;
- Currency and price data are recorded;
- Details of currency or price adjustments for inflation or currency conversion are given (if appropriate);
- The discount rate is stated or is apparent, and is justified (if relevant).

Quality Check – Stage 2

- Details of model used are given
- The choice of model used and the key parameters on which it is based are justified/appropriate***

The BMJ guidelines suggest that the model used should explicit and clear. However our use of these guidelines to assess the quality of a study requires us to use explore whether or not the model used is appropriate for the task.

No study was rejected at this stage on the basis of an inappropriate modelling approach.

Stage IV- Data extraction

The data extraction sheets are available from the authors. Data were extracted then converted from their respective currencies to UK £ *Sterling*, using Purchasing Power Parities published by the Organisation for Economic Co-operation and Development. Once converted to UK *Sterling* the cost data were inflated to 2003 prices using the NHS Executive Hospital & Community Health Services Pay and Prices inflation index.

3. Results

A total of 556 papers were identified by the literature search. Two reviewers (TR, SR) reviewed their titles and abstracts independently. The initial and subsequent classification of these studies together with the categorisation by primary focus is presented in Figure 1. The diagram shows that 190 papers were reviewed in full. 57 of the papers were considered to be full economic evaluations

The studies were reviewed according to their primary focus. We report here on a subset of 24 papers from the 57 confirmed economic evaluations that had the primary focus of Screening:

We included any definition of screening programme in this group namely

- Population,
- Opportunistic
- Selective

In terms of the first stage of our quality check one study failed because currency and price data were not recorded and the source of effectiveness data was not clear and a further 5 were considered of dubious quality. The most common reason for failing the quality check was failure to report the price year of the cost data or currency details. We did not extract the cost data used in these evaluations but the characteristics of some of these studies proved to have very important messages with respect to other aspects of quality and thus they were not eliminated from the review. These studies were marked with a query.

3.1 Opportunistic screening

Eleven out of the 24 economic evaluations of screening programmes were analysing the cost effectiveness of opportunistic screening. See Appendix 1

Economic outcome and Model used

All but one of the studies was based on an outcome of sequelae avoided (similar to major outcome averted). The only study using a different outcome used cost per case detected and treated as the main outcome. Seven of the studies used a static decision model, one used a Markov Model two used unspecified simulation models. Only one study used a discrete event simulation approach to the modelling. See Table 2.

Comment

Nine out of 11 studies suggested that opportunistic screening can be cost effective under particular circumstances or for a certain age group. Four studies specify a range for which screening is cost effective, typically under 30 years or in the age group 18-24 years. 2 did not directly suggest that opportunistic screening was cost effective and stated that the cost effectiveness depends on the test used and the prevalence of infection and one specifies a cut-off cost for the test.

One of these two studies that did not directly assert that screening was cost effective, was by Postma et al, was based on a static decision model. It suggested that introducing partner notification significantly improves the cost effective ratio and that future studies should also include re-infection and that a static model was a first step. The study by Welte at al which was the only study to use Discrete Event Simulation in the modelling approach and included re-infection and partner notification suggested that screening would be cost effective in the long run but that cost effectiveness would not be clear in the short run. The authors argued that the results of this analysis depended upon the prevalence of the disease and the success of Partner referral. Rather than focussing on the actual results, this paper highlighted the point that a dynamic model best determines the cost effectiveness of a Chlamydia screening programme

3.2 Selective Screening

Ten studies evaluated selective or targeted screening. These studies were typically targeting individuals by risk status, age group or characteristics which could be demographic, occupational or sex related. For example one study targeted pregnant women (refs), another targeted abortion seeking women (refs) while another study

targeted female army recruits(ref). Six of these evaluations were based on their own primary study.

Outcome and model used

Five studies used a static decision analytic model, 1 used a Markov model and the remaining four did not use a modelling approach at all. The four that did not use a model all used an outcome of cost per case of Chlamydia detected. The six studies that used a static decision analytic model were all based on an outcome of major sequelae avoided. See Table 2

Comment

The six studies that used a decision model all made some recommendation about the cost effectiveness of screening based on their targeted population and the question being explored. For example, the results of Goree et al, suggested that screening all women aged 15 to 24 is considerably more cost effective than screening only high risk women. This analysis was carried out using a Markov model based on an outcome of PID and related sequelae avoided. The appropriateness of any recommendations based on a static model are discussed below.

Of the four papers that didn't use any modelling approach 3 didn't make any conclusion about whether or not screening was cost effective . For example Gunn et al, estimated the cost per specimen obtained and the cost per case of Chlamydia identified. This could be seen as a valid first step to evaluating a screening programme. On the other hand the study by Begely et al, which didn't use a model and used an outcome of cost per test, concluded that screening asymptomatic patients in a Family Planning Clinic is cost effective.

3.3 Population screening:

Only 3 papers evaluated the potential economic effects of a population screening programme based on outcomes of Major Outcome Averted. The models used and the subsequent analysis resulting from these papers differed significantly and they each give conflicting results about the cost effectiveness of the screening programme.

Comment

The study by Van Valkengoed et al, (2001) is the study that has the closest resemblance to the ClaSS study but with the exception that it focuses on women only. The economic analysis is based on *major outcome averted* where major outcome is defined as one or more of PID, Ectopic pregnancy, infertility etc. The model used was a static decision analytic approach. The study concluded that population screening for 15 to 40 year olds is not cost effective. We discuss validity of such conclusions based on a static model below.

On the other hand Paavonen et al (1998) evaluated a population screening programme for women only, using PCR test on urine and an EIA test for Swabs. The outcomes were cost per case detected and cost per case cured but the analysis also considered the outcomes such as PID, ectopic pregnancy and infertility which would occur in the absence of screening. The model used was also a static decision analytic model on a hypothetical cohort. This study concluded that screening using PCR was cost effective even at low prevalence. Again we question the validity of this recommendation.

In contrast, Townshend and Turner evaluated the population screening on for men and women in the age of 20 to 40 years using a hypothetical cohort and literature based cost and effectiveness data. The analysis was based on an outcome of *major outcome averted* for men, women and neonates. In terms of quality this study was marked with a query on the basis of Stage 1 of the quality assessment criteria but the paper was written to illustrate the use of their modelling approach as opposed to their economic evaluation technique. The authors used a System Dynamic modelling approach. It showed that the proposed screening programme would prevent significant numbers of infertility cases annually (but this depends on the probability of infertility following an episode of PID) and that the screening programme could be paying for itself after 4 years and recouping the initial outlay after 12. The quality of the economic evaluation in this paper leads us to question the results but the modelling approach illustrates very important issues.

These conflicting conclusions are likely to based on a number of reasons: data used, costs used, prevalence and the probability of PID having been infective with Chlamydia and the probability of long term outcomes such as infertility being related to PID. However, we would argue that a fundamental flaw of the studies by Van Valkengoed and Paavonen is that they used the wrong model for the evaluation. The discussion of how these factor affect the results will be discussed further below.

Finally, our systematic review highlighted another recently published systematic review of economic studies for Chlamydia screening by Honey et al (2002). This review had a more restricted focus than our own, studies were eligible for inclusion if it assessed screening for Chlamydia trachomatis in Primary Care which was defined as the first point of contact for health care provision or Family Planning clinics. The outcomes assessed in this review were cases of Pelvic Inflammatory Disease (PID) prevented or cases of Chlamydia detected. We are critical of this review for two main reasons. First, the review included studies and assessed them even though the outcome was restricted. There was no discussion of the limitations of this outcome in a screening evaluation. Secondly, the authors did not review the studies on the basis of the modelling approach that was used. We discuss these issues below.

4. Discussion

4.1 Outcome used for screening

Table 2 presents the results of studies in terms of the principle outcome and the model used. We show that six out of the 24 studies used Cost per Case Detected as their outcome. 4 of these used no model and 2 used a decision analytic model.

Cost per case detected as an outcome may be appropriate as a first step or preliminary analysis but based on this outcome, policy decisions about whether or not a screening programme should be implemented should not be made. A short-term outcome such as cost per case detected or treated will not give any indication of the final success of the screening programme. Chlamydia is an infectious disease, cases detected and treated can

be re-infected as soon as they return to their infected partners and the importance of partner notification is crucially important.

Related to the issue is the importance of the sensitivity and specificity of the tests. Another section of this review, not reported here, is focused on papers that evaluated the relative cost effectiveness of different tests. Cost per case detected, even when evaluating the efficacy of the different tests is an inadequate outcome. It is well recognised in most screening programmes, within the number of positive cases identified there will be a proportion of false positive cases identified who will receive treatment un-necessarily when the specificity of the test is not 100%. This always has an impact. In Chlamydia screening, a false positive result will lead to unnecessary treatment as well as the distress and anxiety associated with notifying partners and the associated fall-out from this such as accusations of infidelity etc. (This has been shown in the Social research arm of the ClaSS study). While a false negative will lead to a woman being re-assured in the short term only to endure potentially serious longer term outcomes such as infertility. But also because of the infectious nature of the disease, the individual will also remain infectious and consequences will arise for other potential partners who may become infected. None of these outcomes can be captured sufficiently by evaluating a screening programme based on a short-term outcome. Where possible, the programme should be evaluated to the full extent of its consequences. When possible the inadequacy of the short term outcome should be highlighted. The study may still represent a valuable first step, but policy decisions are not possible on such an outcome.

Honey et al (2002) used the Drummond Criteria (refs) to quality assess their economic evaluations. The authors interpretation of one of the criteria (Point 4) “Were all the important and relevant costs and consequences for each alternative identified” did not alert them to the fact that ‘cost per case detected’ is an inadequate outcome to use in the evaluation of a screening programme.

4.2 Use of Modelling

The correct model to use in the evaluation of an infectious disease should be capable of encompassing as far as possible all the effects that will arise especially the transmission

of disease between individuals. The correct model used in the evaluation of an infectious disease was realized in the epidemiological literature in the 18th Century (Bernoulli (1760)). For many infectious diseases, screening and treatment do not often imply a lifetime cure or immunity. For some infectious diseases it is possible to get re-infected again after treatment. This is also the case for an infectious sexually transmitted disease such as Chlamydia Trachomatis.

Models that do not incorporate all the potential effects of screening will neglect a number of important effects. One the one hand, individuals who are screened and successfully treated should not further infect other individuals. But, on the other hand, these individuals will risk re-infection if they go back to the same partner or another partner who is infected. In addition, because the sensitivity of the test is not 100% there will always be a small proportion of individuals who are given a false negative result. These individuals can un-intentionally infect others. The overall effect of these opposing forces cannot be determined in a 'static' model. Therefore the results of static models cannot be used to make any assumptions about the cost effectiveness of screening. The results will be wrong and the direction of the bias cannot be determined.

The Criteria used to assess quality in the review by Honey et al (2002) did not include any reference to the modelling approach. So the models used in the evaluations that were reviewed in their study were not assessed for appropriateness. The guidelines for economic evaluations, by Drummond et al, recommended for reviewers (and Authors) published by the BMJ do include two criteria with regard the justification of the model used. Although there much debate about the suitability of the BMJ guidelines for assessing the quality of economic evaluations because it was not their objective, we believe that some adaptation and re-interpretation of the BMJ guidelines can help to review the quality of an economic study. One item in the criteria asks if "the choice of the model used and the key parameters on which it are based are justified". A slight re-interpretation of this criterion replacing justified by "appropriate" (as we did) makes it a suitable question for quality assessment.

Two papers in our review highlighted the appropriate models to use in the economic evaluation of screening for Chlamydia Trachomatis.

Townshend and Turner (2000) used a System Dynamic approach to evaluate population screening. *System dynamics* and similar models allow for some forms of interaction between individuals. For example, the risk of an infection can be made to depend on the number already infected. This paper was found by searching the non- economic literature for models used to evaluate Chlamydia Screening and was found in the operational research literature.

Welte et al (2001) used a Discrete Event Simulation model based on individual level data from the Amsterdam Pilot study to evaluate opportunistic screening. *Discrete event simulation* models allow full representation of individuals' history and interaction between specific individuals. For example, the risk of an individual acquiring a sexually transmitted disease can be made to depend on the status of a sexual partner. However, the price that must be paid for the ability to model in such detail is that these models require specialist software or programming skill to construct and running times are very much longer than for other types of model. This paper was found as part of our main economic search but the principles and papers upon which it was based, namely the work of Mirjam Kretzschmar, was found in our search of the non economic literature for models used to evaluate Chlamydia Screening. The additional evidence by Kretzschmar re-enforced the message about the modelling.

Unusually for Health Technology Assessment, there are many economic evaluations published on the subject of screening for Chlamydia trachomatis. The justification for yet another economic evaluation of Chlamydia screening which was one of the objectives of the ClaSS study is simple. Our systematic review of the literature highlighted key principles for the construction of our own model. The cost and effectiveness data that we extracted from our review will help us to identify potentially sensitive areas in our own model and highlight gaps where better information is required. The model used to evaluate the cost effectiveness of Chlamydia screening in the ClaSS study will be the first to use individual level data on both screening and partner notification from primary

research using a Discrete Event Simulation model. Our model will be based on the work of Kretzschmar et al and Welte et al. But where their evaluation was done in two stages, an epidemiological component followed by a separate cost effectiveness component, we aim to construct a new model which will combine epidemiology and economics into one comprehensive model. (See Barton et al, HESG 2003).

A critical factor in our review was that it was not restricted to economic studies alone. One of the most important messages from our review was discovered by searching the wider literature on the use of modelling for Chlamydia Screening and infectious diseases. What is most striking is that in Epidemiology, unlike in Health Economics, the principles required for modelling infectious diseases are not a recent discovery. The discovery was made in the epidemiology literature by Daniel Bernoulli more than 250 years ago.

“Bernoulli Was Ahead of Modern Epidemiology”, Letter to the Editor from Klaus Dietz and J.A.P. Heesterbeek. *Nature,* 30 November 2000. The writers of this letter commemorate the 300th anniversary of Swiss mathematician Daniel Bernoulli (1700-1782)). They point out that Bernoulli was the “first to express the proportion of susceptible individuals of an endemic infection in terms of the force of the infection and life expectancy." Bernoulli expressed the wish that "...no decision shall be made without all the knowledge which a little analysis and calculation can provide". A wish that still strikes a chord and is relevant today.

Unfortunately, as with so many areas of health economics there is a danger of trying to re-invent the wheel. We have illustrated that it often proves useful to explore concepts from the perspective of other disciplines

This also highlights another point. The construction and use of a model in economic evaluation should not be seen solely the responsibility of the economist. Economists are rarely qualified in epidemiology. We have demonstrated here that before modelling is used in an evaluation the natural history of the disease should be understood. Furthermore the modelling skills required in this area, are to some extent beyond the skills of the majority of main stream economists. Specialist skills in Operational Research are often

required to do the complex modelling that is required in this subject area. Understanding the natural history of an infectious disease such as Chlamydia Trachomatis would have avoided repeating the same ground in evaluations which have added little in terms of beneficial results to the policy makers that need to make decisions.

5. Conclusion

In summary, the impact of any screening programme for Chlamydia trachomatis will depend on the prevalence of the disease, the comprehensiveness of the proposed screening programme and partner referral strategies, the sensitivity and specificity of the test used and the efficacy of treatment. This can only be captured by using the right outcome and the correct modelling approach. Out of the 24 confirmed economic evaluations that had the primary focus of Chlamydia Screening only two papers used the correct approach for modelling disease. In other sections of our review, that focus on different areas and which is not reported here, there were 33 confirmed economic evaluations and only one more paper used a correct approach to modelling the diagnostic tests.

The recent publication of another review of economic studies of Chlamydia screening, by other authors as we were drawing conclusions from our own review, was rather disconcerting. We were not expecting to be critical of this review but found two mains causes of concern to us. First the review did not discuss the inadequacy of cost per case detected as an outcome. Secondly the authors did not critique their studies on the basis of the models used.

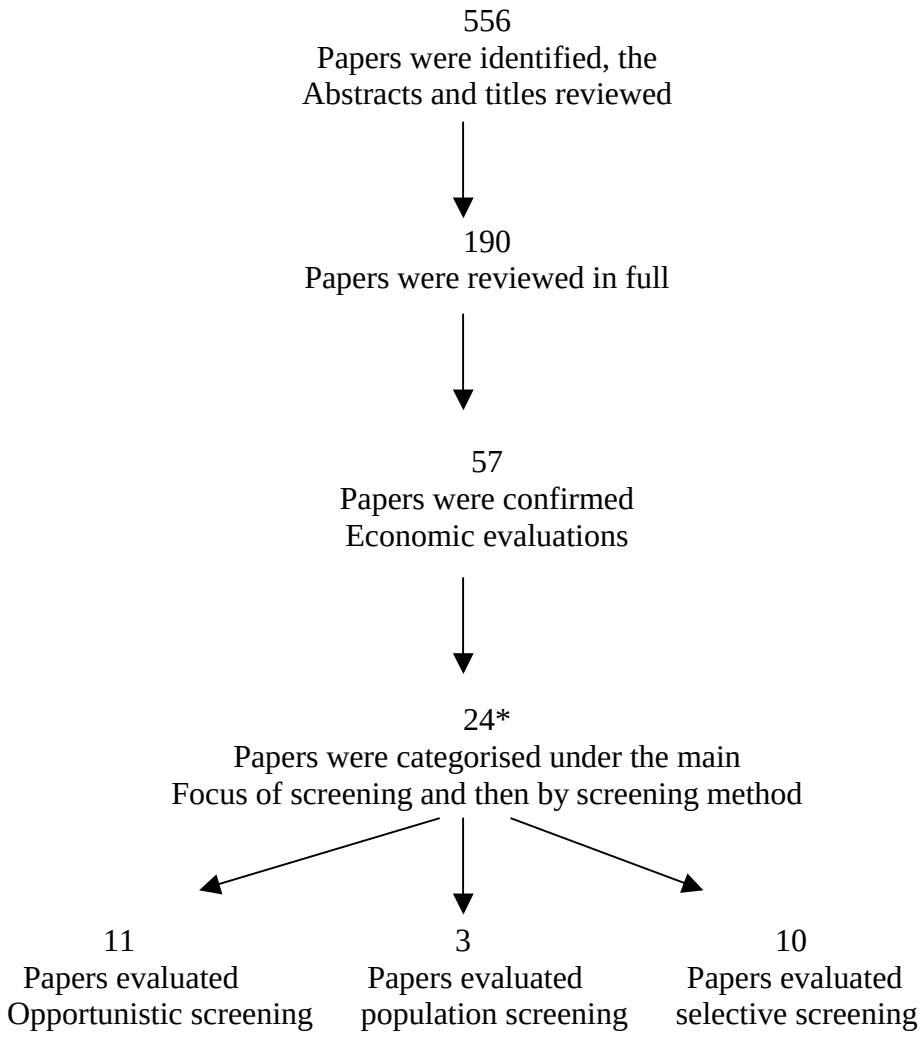
The width and comprehensiveness of our search and review has allowed us to discover the fundamental principles required for the modelling of an infectious disease. A principle which appears to have been missed by many others who have carried out economic evaluations in this area.

The results of our review have served to re-enforce our concerns about limited focus and introspection in economic analyses. The economic studies we reviewed have revealed a lack of awareness about a number of issues. First, the natural history of the disease that

they were analysing; second, the inadequacy of the short- term outcomes in screening; and third, the appropriate model to use in the economic evaluation of Chlamydia screening. Our wide review highlighted the key principles of the modelling approach required for evaluating infectious diseases.

A wider search process and an open mind to the discoveries of other disciplines are the key messages of this paper.

Figure 1



* The remaining 33 economic evaluations did not have screening has their primary focus and are not included in this paper but will be included in the final report.

Table 2:

Model used in papers which had a primary focus evaluating screening			
Model type	Outcome	Number of studies fitting this description	Comment
No model	Cost per case detected	4	Modelling not used which was appropriate for outcome being evaluated
Static decision model	Cost per case detected	2	Correct model given outcome. But outcome inadequate to fully evaluate a screening programme. *Check was this the objective of this study*
Static decision model	Major outcome averted	11 (+1 to check – cervicitis)	Inappropriate model given the outcome being evaluated
Markov	Major outcome averted	2	Inappropriate model given the outcome being evaluated
Simulation	Major outcome averted	1	Inappropriate model given the outcome being evaluated
Computer model unspecified	Sequelae averted	1	Insufficient information to assess appropriateness of model
Discrete event simulation	Major outcome averted	1	Appropriate approach given outcome
System dynamics	Major outcome averted	1	Appropriate approach given outcome

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Appendix 1: Summary Table for Papers Reviewed

Study country Final classification and quality assessment	**Primary Focus;** **Sex; age**	**Viewpoint**	**Effectiveness Data sources**	**Cost data** **(Year and type of currency)**	**Model used**	**Test**	**Treatment**	**Primary Outcome**	**Result**	**Comment**
Postma et al 2001 (Netherlands) Id531 A(1) Pass	Opportunistic in GP; women and male partners; 15-29 years	Societal	Amsterdam Pilot study	Dutch sources and published Literature 1996 Euros	Static Decision analytic model	LCR	Single dose Azithromycin	Net cost per Major Outcome Averted	Partner pharmocotherpay reduces net costs per major outcome averted of the screening program by 50% Partner notification significantly improves cost effectiveness	Model insufficient to make policy decisions but authors argue that this is a justifiable first step and do not attempt to make policy recommendations.
van Valkengoed 2001 (Netherlands) id574 A(1) Pass	Population using – home obtained urine specimen; Women only; 15-40 years	Societal	Amsterdam Pilot study & own primary data	Cites Postma et al (id 671) 1996 US $	Static Decision analytic model	LCR	Single dose Azithromycin (or Erythromycin for pregnant women for 5 days)	2 outcome; Woman cured and Major outcome averted	Population screening of 15-40 yrs is not cost effective	Model insufficient for this result. Policy recommendations should not be made.
Goeree 2001 (Canada) id620 A(1) Pass	Selective screening; High risk women; 15-24 years	Health care system	Literature	Canada Government sources 1999 Canada $	Markov model	7 different test/samples	Not specified	PID & related sequelae	screening all women aged 15 to 24 is considerable more costly and only moderately more effective than screening only high risk women	Model insufficient for this result. Policy recommendations should not be made.
Postma et al 2000 (Netherlands) id671 A(1) Pass	Opportunistic in GP; Women only; 15-34 years	Societal	Own Study: this is the Amsterdam Pilot study	Short term costs from Postma et al (id 671), long term costs from the published litertaure- 1996 US $	Static Decision analytic model	LCR	Single dose Azithromycin	Major outcome averted	Screening sex active women under 30 is cost effective	Model insufficient for this result. Policy recommendations should not be made.

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Study country Final classification and quality assessment	**Primary Focus;** **Sex; age**	**Viewpoint**	**Effectiveness Data sources**	**Cost data** **(Year and type of currency)**	**Model used**	**Test**	**Treatment**	**Primary Outcome**	**Result**	**Comment**
Welte et a 2000 (Netherlands) id42 A(1) Pass	Opportunistic in GP; Men and women 15-65 years	Societal	Amsterdam Pilot study & literature	Short term costs from Postma et al (id 671), long term costs estimated using a breakdown of resource use 1997 US $	Discrete Event Simulation	LCR	Single dose Azithromycin	Major outcome averted	Say it may save costs in the long run, but not short run, but really highlighting dynamic model	Correct model. Paper highlighting use of model and suggesting some conclusions.
Townshend 2000 (UK) id41 A1?	Population screening; Men and women; 12-40 years	NHS	Literature	Literature UK £ no year	System Dynamics model	Not specified	Not specified	PID and related sequelae for men, women and neonates	Suggests that proposed screening programme would prevent significant numbers of infertility cases annually. Additionally it could be paying for itself after about 4 years and re-couping the initial outlay after about 12.	Correct model. Paper highlighting use of model and suggesting some conclusions
Howell et al 2000 (US) id479 A(1) Pass	Selective screening; Female US army recruits; All recruits – age focus<25 years	Military and civilian	Own primary study (id3)	TRADOC & Own costs 1998 US $	Static Decision analytic model	LCR	Single dose Azithromycin	Sequelae avoided	Basically screening army recruits is C/E. From military perspective screening under 25yrs provides greatest cost saving	Wrong model. Results may be wrong. Model insufficient to make policy recommendations
Shafer 1999 (US) id183 A(1) Pass	Selective screening; Adolescent female; 15-19 years	Health care system	Literature	Government charges deflated to reflect cost 1995 US $	Decision analysis	LCR & PCR	Azithromycin 1g & I/m Ceftriaxone 1g	PID prevented	1283 cases of PID would be prevented at a mean cost of $5093	Wrong model. Results may be wrong. Model insufficient to make policy recommendations

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Howell et al 1999 (US) id3 A(1) Pass	Selective screening; Female army recruits; 17-39 years	Military (modified payer)	Own primary study	TRADOC & Own costs 1995 US $	Static Decision analytic model implied (but not presented or made explicit)	LCR	Single dose Azithromycin	PID avoided	Screening by age provided a cost saving to the Army over a 1 year period	Wrong model. Results may be wrong. Model insufficient to make policy recommendations
Howell et al 1998 (US) id4 A(1) Pass	Opportunistic screening in Family planning clinic; Women; 11-68 years (Median 25 years, focus age<30 years)	Health care system	Own primary study	Baltimore City hospital and literature 1995 US $	Static Decision analytic model	PCR tests on cervical swab, and or urine	Doxycycline	Sequelae prevented in men, women and infants but considers consequences of longer term sequelae	Age based screening provides the greatest cost saving of the three strategies examined. Universal screening is cots effective at a prev greater than 10.2%	Wrong model. Results may be wrong. Model insufficient to make policy recommendations
Gunn 1998 (US) id366 A(2)	Selective – outreach clinic; High risk adolescent males; teenage	Health care system	n/a	Own primary study 1996 US $	No model	LCR	Single dose Azithromycin	cost per specimen obtained and cost per case identified	cost per specimen obtained $103; cost per case identified was $1677	Correct result for this approach
Paavonen 1998 (Finland) id2 A(1) ?check	Population; Women; Not specified	Health care system	Literature and expert opinion	National Research and development Centre for Welfare and Health Finland US $ (year & exchange rate not specified)	Static Decision analytic model	PCR on urine; EIA on swabs	Single dose Azithromycin	cure? Cost per case detected, but does look at longer term outcomes	Population screening for Chlamydia trachomatis using PCR is cost effective even in low prevalence populations. net saving for pop screening in Finland $3.5 m	Wrong model. Results may be wrong. Model insufficient to make policy recommendations

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Genc 1996 (Uppsala, Sweden) id25 A(1) ?	Opportunistic at youth clinic, GP, family planning; Women and male partners; Age not specified – but sexually active, non pregnant and reproductive age	Health care system	literature	Own costs from id26 US $ no year	Static Decision analytic model	Tissue cell culture / EIA & DNA amplification	Single dose Azithromycin	Cost per case identified and treated	screening with DNA amp assay combined with the single does azithromycin treatment of the positive patients is the most cost effective strategy when the prevalence is 6%.	Outcome is right for this model but study is trying to suggests that individuals will be cured and does not take into account re-infection
Marrazzo et al 1996 (US) id7 A(1) Pass	Selective and universal screening in Family planning and STD clinics; Women; Mean age in FP – 22 years, mean age in STD – 25 years	Societal	Own primary study	Own costs from region office of family planning 1993 US$	Static Decision analytic model	DFA/ Cell culture /EIA/ DNA probe	Doxycycline (compliance estimated at 70-100%, see Washington '87)	Sequelae avoided	at the given prev, it would be cost saving to screen universally in FP clinics and selectively in STD clinics	Wrong model. Results may be wrong. Model insufficient to make policy recommendations
Genc 1993 (Uppsala, Sweden) id26 A(1) ?	Opportunistic during routine health check, Men; Adolescent age	Health care system	Literature	Own primary costs US $ no year (1SKr =7$)	Static Decision analytic model	LE-EIA & EIA	Single dose Azithromycin	cure for males, but does include contact tracing and the costs associated with PID and ectopic infertility	compared with no screening, screening adult males reduced the overall costs when the prevalence of CT infection is above 2% for le-EIA and 10% for EIA.	Wrong model. Results may be wrong. Model insufficient to make policy recommendations
Sellors 1992 (USA) id162 A(1) Pass	Universal vs Selective; Women; Mean 21.5 years	Health care system	Own primary study	Own costs Can $ 1989 (1CAN$=US$0.85)	No model	EIA and/or culture	Not specified	CT infection	Selective versus population screening in low prevalence setting is efficient	Explorative study. Correct conclusion reached.

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Nettleman 1991 (US) id6 A(1) ?	Selective screening - pregnant; Women; Not specified but pregnant	Health care system	Literature	Literature Not stated	Static Decision Analysis	culturing and direct antigen test	Erythromycin 7 days	cost per complication eg. Salpingitis. Neoenatal pneumonia	screening all preg women is not cost effective although depends on the test?	Model insufficient for this result. Policy recommendations should not be made.
Buhaug 1990 (Norway) id1 A(1) Pass	Opportunistic - during FP or routine gynae visits to a GP; Women; 15-35 years	Societal (implied not stated)	Own primary study	Own costs from GP and University of Trondheim 1987 NKr & £ Sterling	Simulation Model	? No info	lymecycline (7 days)	Sequelae avoided	testing was cost effective for 18-24 yr olds only	Limited information provided on

All papers after 1990 had data extracted and were cost effectiveness analysis – none were cost utility analysis

Study country *Final classification and quality assessment*	**Primary Focus;** **Sex; age**	**Viewpoint**	**Effectiveness Data sources**	**Cost data Year and type of currency**	**Model used**	**Test**	**Treatment**	**Primary Outcome**	**Result**	**Comment**
Buhaug 1989 (Norway) id 17 A(1) Pass	Opportunistic during FP or routine gynae visit to GP; Women; 15-39 years	Societal (implied not stated)	Own primary study	Own costs from GP and university of Trondheim 1987 NOK & £ Sterling	Markov Model	Not specified	7 day treatment but drug not specified	Sequelae avoided	Testing was cost effective for 18-24 yr olds only	Wrong model. Results may be wrong. Model insufficient to make policy recommendations

Study country *Final classification and quality assessment*	**Primary Focus; Sex; age**	**Viewpoint**	**Effectiveness Data sources**	**Cost data Year and type of currency**	**Model used**	**Test**	**Treatment**	**Primary Outcome**	**Result**	**Comment**
Begley 1989 (US) id181 A(1) Pass	Routine testing ; Adolescents; Mean 16 years (12-19 years)	Health Care System	Own primary study	Own primary study 1987 US $	No Model	Not specified	Oral tetracycline QDS -7 days	cost per test/ screen/treatment	say CT screening of asymptomatic patients in FP clinic is Cost effective	No model - analysis insufficient to make policy recommendations
Skjeldestad 1988 (Norway) id24 A(1) Pass	Targeted - abortion seeking; Women; Not specified	Health Care System	Own primary study	Local cost data 1985 US$ & NOK	No Model	Culturing - but not specified	Lymecycline (7 days)	Salpingitis	abortion seeking women should be screened and treated for CT for the abortion is carried out - otherwise salpingitis is a risk.	No model and no attempt to make policy decisions. Acceptable conclusion
Trachtenberg 1988 (US) id22 A(1) Pass	Opportunistic in Family Planning clinic; Women; Not specified	Health Care System	Based on study by Handsfield JAMA 86 - 2 Seattle FP clinics	Based on data used by Washington (ref) Not stated in this study - but cites Washington	Static Decision Analysis	Direct smear flourescein labelled antibody method	Doxycline (7 days)	Sequelae avoided	screening asymptomatic women is cost effective	Wrong model. Results may be wrong. Model insufficient to make policy recommendations

Study country *Final classification and quality assessment*	**Primary Focus; Sex; age**	**Viewpoint**	**Effectiveness Data sources**	**Cost data Year and type of currency**	**Model used**	**Test**	**Treatment**	**Primary Outcome**	**Result**	**Comment**
Nettleman 1988 (US) id20 A(1) Fail	Opportunistic at STD clinics; Women; Not specified	Health Care System	Literature	Local cost data US $ 1985	Computer Model – unspecified	Direct Antigen	N/a	PID avoided	Screening would be cost effective if the county and state jointly funded it using the DA test costing under 7$	Insufficient information on model to accept result
Philips 1987 (US) id23 A(1) Pass	Opportunistic during gynae visit; Women; Not specified	Health Care System	Literature	Local Charges US $ 1984	Static Decision Analysis	Direct smear flourescein labelled antibody method or EIA	Tetracycline QDS (7 days)	Cervicitis	Testing women for cervical infection with CT is cost effective	Wrong model. Results may be wrong. Model insufficient to make policy recommendations

These are studies from which data are not extracted because they are too old – pre 1990