Treating anonymous patients: the effectiveness, costs, and strategies of promoting the use of expedited partner therapy

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TREATING ANONYMOUS PATIENTS: THE EFFECTIVENESS, COSTS, AND STRATEGIES OF PROMOTING THE USE OF EXPEDITED PARTNER THERAPY

by

André S. Kiesel

A Dissertation
Submitted to the University at Albany, State University of New York
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Nelson A. Rockefeller College of Public Affairs and Policy
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ABSTRACT

Despite decades of concerted efforts to prevent their spread, chlamydia and gonorrhea remain two of the most prevalent sexually transmitted infections in the United States (U.S.) — exacting a high toll in terms of human health and healthcare expenditure. Though easily cured with antibiotics, both infections may lead to damaging secondary health conditions – known as sequelae – if untreated, including infertility among females. However, treating diagnosed individuals (known as “index patients”) is not enough—it is critical to also care for their recent sex partners as well, lest they reinfect the treated patient. Partner referral is the traditional approach to partner treatment that has been used since at least the 1970s. Under partner referral, patients are recruited to ask their sex partners to present themselves for testing, which puts a burden on the partner to seek out care and may therefore contribute to undertreatment. By contrast, expedited partner therapy (EPT) is a promising newer clinical practice whereby healthcare practitioners provide treatment, without prior clinical examination or diagnosis, to exposed sex partners of index patients—reducing barriers to treatment. EPT may be given as a prescription or as a medicine (med-in-hand) for index patients to deliver to their sex partners. However, EPT is not without its potential downsides. These include EPT’s potential to leave females with pelvic inflammatory disease (PID) and other sequelae undiagnosed (and untreated) and to treat individuals who are not infected (exacting a financial cost).

The three papers of this dissertation explore different aspects of EPT promotion and its impact. The first paper seeks to model the effectiveness of increasing EPT use relative to partner referral on total annual chlamydia diagnoses and underlying chlamydia prevalence
among young adults 18-24 years old with sex partners of the opposite sex using a system dynamics simulation model. Building upon the simulation model constructed in the first paper, the second paper conducts a cost-effectiveness analysis comparing EPT to partner referral and estimates the total societal costs of EPT use versus partner referral. The third paper uses an inductive qualitative approach to document the experiences and perspectives of state health department directors and staff who worked to implement EPT policies and promote EPT use in their states.

Paper 1 finds that increased EPT use would lead to a decrease in the number of annual diagnoses of chlamydia compared with partner referral (the standard of care). Additionally, the overall number of females with PID in the modeled population would be lower due to a decrease in underlying chlamydia prevalence when EPT use increases. Paper 2 finds that EPT use is cost-effective compared to partner referral, especially when used to treat male sex partners of female index patients. The third paper identifies strategies used by state health departments to promote EPT use, as well as the barriers and facilitators of these strategies.

These papers together make valuable contributions to a comprehensive understanding of the implementation of EPT. These papers also contribute to the theoretical literature on implementation science and policy implementation by demystifying why EPT (a seemingly more effective practice of partner treatment) has not been more widely adopted and whether greater adoption ought to be pursued.
ACKNOWLEDGEMENTS

My dissertation was a difficult project for many reasons, which was made possible due to the support and help of many people. First and foremost are the members of my doctoral committee. Dr. Erika Martin was instrumental in driving my focus on proofreading and writing clarity. Dr. Rachel Hart-Malloy brought her extensive knowledge about the mechanisms at play and her precise understanding of key definitions. Dr. Ashley Fox guided my deepening understanding of theory and the big picture surrounding my work. Last but certainly not least was Dr. Luis Luna-Reyes, who watched over my development as a simulation modeler and helped me to keep a outlook positive. From helping with the technical details of modelling and interview synthesis to helping me better tell the story of sexually transmitted infections, I thank my committee members.

My lab members and colleagues were also a constant source of support – both in the feedback they provided but also in their friendship. In absolutely no order, thank you to Sunyoung Pyo, Wenhui Feng, Phil Gigliotti, Bahareh Ansari, Heeun Kim, Maggie Fiacchi, Dina Maloney, and Roland Poirier.

Finally, the support of my friends and family was indispensable. Thank you to Fei Tang, Cody Waugh, Min-jian Liu, Shi Wen, and of course my parents Donna and Eckhart and wife Yi.
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### Table 1. Glossary of key terms used

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<th>Key Term</th>
<th>Definition used in this study</th>
<th>Notes</th>
</tr>
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<tr>
<td><strong>Infection</strong></td>
<td>A clinically diagnosable infection of chlamydia is present in a person when there are enough bacteria at any given anatomical site (e.g., urogenital, anorectal, pharyngeal) to detect using a clinical diagnostic exam. If a clinical diagnostic exam is administered, a diagnosis will occur unless a false negative occurs.</td>
<td>An infection may or may not be diagnosed. A single person may have multiple infections at different anatomical sites. The word “infection” does not refer to people, although “infected individuals” does. Infections may be treated using antibiotics and they may spontaneously clear without treatment. Infections may or may not be symptomatic.</td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
<td>A diagnosis occurs when a clinical exam returns a positive result for chlamydia. Individual patients may be diagnosed multiple times for the same infection or for different infections. A diagnosis may also be due to a false positive with no infection present.</td>
<td>A diagnosis may not occur if a patient is not tested. A “diagnosis’ is an event and does not refer to the patient.</td>
</tr>
<tr>
<td><strong>Underlying prevalence</strong></td>
<td>The proportion of any population that is infected at any given time.</td>
<td>Underlying prevalence will always be higher than the proportion of the population that has been diagnosed because not every person may be tested at once. Underlying prevalence is always a function of incidence (the occurrence of new infections), treatment, and spontaneous clearing.</td>
</tr>
<tr>
<td><strong>Incident cases</strong></td>
<td>Individual people who become infected over time. These individuals may or may not be diagnosed.</td>
<td>If the number of incident cases is greater than the number of individuals who are cured, than</td>
</tr>
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</table>

vi
<table>
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<tr>
<th>Key Term</th>
<th>Definition used in this study</th>
<th>Notes</th>
</tr>
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<tr>
<td>Sequelae</td>
<td>Health conditions which are the consequence of a current or previous infection. Both chlamydia and gonorrhea may lead to sequelae.</td>
<td>underlying prevalence will increase.</td>
</tr>
<tr>
<td>PID</td>
<td>Pelvic inflammatory disease; a major sequela of chlamydia and often a precursor to other chlamydia sequelae.</td>
<td>PID may only occur among females, and it may lead to other sequela.</td>
</tr>
<tr>
<td>Infertility</td>
<td>A major sequela of chlamydia and gonorrhea, which is often though not always, preceded by PID. Females with infertility may not become pregnant.</td>
<td></td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
<td>A major sequela of chlamydia and gonorrhea, which is often though not always preceded by PID. Ectopic pregnancy occurs when a fertilized egg implants outside of the womb, causing damage to surrounding organs.</td>
<td></td>
</tr>
<tr>
<td>Chronic pelvic pain</td>
<td>A major sequela of chlamydia and gonorrhea, which is often though not always preceded by PID. Chronic pelvic pain is pain in the pelvic area that lasts for 6 months or longer. It may intermittent.</td>
<td></td>
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INTRODUCTION
Chlamydia and gonorrhea are two of the most widespread reportable sexually transmitted infections (STI) in the United States (U.S.) and each exerts significant costs on society. There were an estimated 4.0 million chlamydia and 1.6 million gonorrhea infections in 2018 alone (K. M. Kreisel et al., 2021). However, many males and females with chlamydia and gonorrhea show no symptoms, and therefore have no immediate incentive to get tested and therefore do not know that they are infected or that they can infect others (Chacko et al., 2004; Chlamydia Screening in Women (CHL), 2019; Farley et al., 2003; Handsfield et al., 1974; Korenromp et al., 2002; Schillinger et al., 2005). Chlamydia is sometimes referred to a “silent” infection for this reason. Consequently, despite the high estimated infection rates, only roughly 1.8 million chlamydia and 600,000 gonorrhea infections were diagnosed in the US in 2019 (Chlamydia National Profile - Overview, 2020; Gonorrhea National Profile - Overview, 2020). Moreover, rates of chlamydia and gonorrhea infection have also been increasing over time: nationally in the US, the estimated underlying prevalence (the proportion of a population that is infected at any given time) of chlamydia and gonorrhea increased until at least 2019, when the most recent data became available (K. M. Kreisel et al., 2021). While some of the increase from 2018 to 2019 in diagnoses may be due to improved screening efforts many cases still go untreated due to difficulties in case detection and treatment.

Chlamydia and gonorrhea are both easily cured using antibiotic treatment regimens (Gonorrhea Treatment and Cure, 2019; Workowski & Bolan, 2015). If left untreated, though, both infections can have devastating effects on females of reproductive age (Haggerty et al., 2010; Ong et al., 2017). Several downstream health conditions (sequelae) are significantly
more likely among females with untreated infections. An estimated 2.5 million females aged 18-44 have suffered from pelvic inflammatory disease (PID) in their lifetimes, of which an estimated 35% were caused by a chlamydia infection (K. Kreisel et al., 2017; Price et al., 2016). PID may lead to other sequelae, including infertility, chronic pelvic pain, and ectopic pregnancy. Chlamydia and gonorrhea infections also place a significant financial burden on the health systems in the U.S. The lifetime medical costs (the sum total of all private, public, and out-of-pocket medical payments across the entire lifespan) of chlamydia in the U.S. totaled an estimated $691.3 million in 2018, of which $616.8 million was among females and $74.6 million was among males (Chesson et al., 2021). This difference between sexes is partly due to the extra cost burden of sequelae among females, but also because more females are screened and diagnosed—especially for chlamydia. This is for two reasons. First, females may be more likely to be symptomatic and to seek care (Farley et al., 2003; Korenromp et al., 2002). Second, screening recommendations do not include males who have sex with women. Consequently, of the 1.8 million reported chlamydia cases and 0.6 million reported gonorrhea cases, some 64% and 41% were of females, respectively (Gonorrhea National Profile - Overview, 2020; Table 2. Chlamydia — Reported Cases and Rates of Reported Cases by State, Ranked by Rates, United States, 2019, 2021).

To reduce transmission rates and care for individuals with untreated infections before they result in PID or other sequelae, it is important to treat both the symptomatic patients that come in for treatment as well as any sex partners of those patients. This is because treated patients may be quickly reinfected by their untreated sex partners.
Additionally, the treatment of sex partners directly reduces underlying prevalence by curing infected individuals. It also reduces future incidence by preventing any transmission from the treated sex partners—both back to the recently cured index patient and to any other of their own sex partners.

**Approaches to caring for sex partners**

The most comprehensive approach to caring for sex partners is contact tracing, whereby recent sex partners are identified and contacted by disease intervention specialists. However, this approach is used less often for chlamydia or gonorrhea (see below). The more commonly used traditional approach to treating sex partners has been partner referral—in use by this name since at least the 1970s (Kissinger et al., 1998; Ramstedt et al., 1991). Under partner referral, diagnosed patients (referred to as “index” patients) are asked to voluntarily refer their recent sex partners for testing and treatment. Having patients refer their recent sex partners negates the need for disease intervention specialists to conduct contact tracing. However, partner referral has several challenges and limitations that contribute to sub-optimal levels of treatment. These challenges include patients not wanting to inform their sex partners of their diagnosis, sex partners not coming in for testing, and privacy concerns (Chlamydial Infections, 2015).

An alternative strategy aimed at improving some of these shortcomings is known as expedited partner therapy (EPT). EPT involves providing treatment to recent sex partners without clinically examining them or requiring their diagnoses (Expedited Partner Therapy, 2021). Benefits of EPT include the potential to treat sex partners faster and, potentially,
anonymously (Ferreira et al., 2013; Hogben et al., 2005). Faster treatment of sex partners may prevent the reinfection of index patients and reduce onward transmission. However, while EPT appears to be a promising alternative to partner referral, it has been criticized as well. For instance, healthcare practitioners often oppose EPT because it denies them an opportunity to examine and diagnose the sex partners for chlamydia and gonorrhea (and other STIs) and their sequelae before treating them (Rosenfeld et al., 2015). Additionally, much is not known about the benefits and downsides of using EPT versus partner referral (Expedited Partner Therapy, 2021; Ferreira et al., 2013).

To shed better light on the relative merits/demerits of EPT as well as how U.S. states may promote the use of EPT, the three papers included in this dissertation investigate key aspects of the impact of increased EPT use and the methods that may be used to promote it. Paper 1 estimates the change in the number of chlamydia diagnoses among 18-24-year-old males and females that may result from increased EPT use in a state-based case study. Paper 2 examined the cost-effectiveness of EPT use versus partner referral for chlamydia - also in a state-based case study. Papers 1 and 2 only examined chlamydia primarily to control study scope, although both chlamydia and gonorrhea are treated using EPT. Paper 3 qualitatively investigated the various strategies that state health departments in the U.S. have utilized to promote and facilitate EPT use for both chlamydia and gonorrhea.
BACKGROUND

**History of STI Reporting and Contact Tracing**

Chlamydia and gonorrhea are each among a handful of STIs for which diagnoses must be reported (mandatory reporting) to state health departments to monitor outbreaks and to help coordinate the government response. However, case reporting of these STIs has not always been standard practice (Fairchild et al., 2003). Gonorrhea—caused by the bacterium *Neisseria gonorrhoeae*—has been known to medical practitioners since the late 1800s, long before modern testing and treatment regimens became available. Chlamydia, in contrast to gonorrhea, was long classified simply as “not gonorrhea” (Worboys, 2019). It wasn’t until the 1970s that chlamydia was identified as being caused by the bacterium *Chlamydia trachomatis*.

In the early 20th century, having an STI was considered a private matter. Government oversight was not welcomed, especially among the upper classes (Fairchild et al., 2003). However, by 1919, all U.S. states required case reporting for STIs —although anonymous identification numbers were sometimes used instead of names to protect privacy. It wasn’t until 1943, with the introduction of penicillin, that gonorrhea control efforts began to shift from case monitoring (i.e., caring for known cases) to case identification (efforts to detect and treat new infections) (Fairchild et al., 2003). As tests for both chlamydia and gonorrhea became cheaper, more sensitive, and more specific, it became easier to diagnose infections (Fairchild et al., 2003). These improvements have led to a dramatic increase in the number of diagnosed cases over previous decades, making it all but impossible for healthcare practitioners to contact trace and care for each infected
individual (Fairchild et al., 2003; Worboys, 2019). It quickly became apparent that chlamydia, especially, was extremely widespread — today it is thought to be the most prevalent infectious disease in the U.S. (K. M. Kreisel et al., 2021).

To facilitate testing and treatment, governments launched an aggressive strategy combining case reporting and contact tracing to control STI epidemics starting in the 1950’s (Fairchild et al., 2003). Contact tracing involves identifying all sex partners who may have been exposed to the infection to examine and diagnose them. Each diagnosed individual may reveal additional sex partners, and so contact tracing may extend through multiple degrees of separation (i.e., relationship connections). However, because of the resource intensity and infeasibility of contact tracing for prevalent STIs, the 1950’s and subsequent decades were characterized by a gradual divestment of federal funding for chlamydia and gonorrhea control (Fairchild et al., 2003). As testing methodologies improved and their costs declined, it became easier to diagnose infected individuals, leading to growing case counts (Fairchild et al., 2003). Additionally, public health attention shifted to the human immunodeficiency disease (HIV) in the 1980’s and later to syphilis. From a cost-effectiveness standpoint, it is typically more valuable to focus contact tracing on syphilis and HIV (Pultorak et al., 2009), because it is valuable to focus limited resources to prevent more significant comorbidities (e.g., congenital syphilis) (G. L. Oxman & Doyle, 1996; Ramstedt et al., 1991). By the time of writing, contact tracing was only rarely conducted for chlamydia and gonorrhea index patients except when the index patient is a pregnant female or has been diagnosed with other STIs (Cooper & Sánchez, 2018; Golden et al., 2003; Workowski et al., 2021).
Contemporary Approaches to STI Control

Contemporary policies meant to control the spread of chlamydia and gonorrhea have centered on screening, partner referral, and, more recently, EPT. The Centers for Disease Control and Prevention (CDC) instituted screening recommendations focusing on young adult (aged 25 years old or younger) females and men who have sex with men beginning in 1972 for gonorrhea and 1988 for chlamydia (Peterman et al., 2016; Screening Recommendations and Considerations Referenced in Treatment Guidelines and Original Sources, 2021; “Sexually Transmitted Disease Surveillance 2004 Supplement, Chlamydia Prevalence Monitoring Project,” 2005; Walsh & Irwin, 2002; Workowski & Berman, 2002). Screening is the practice of testing individuals based on their individual characteristics (i.e., sex of sex partners, age, sex) rather than the presence of clinical symptoms. Screening leads to diagnosing infected individuals, especially asymptomatic individuals who are unlikely to seek treatment directly. This provides opportunities to utilize contact tracing, partner referral, or EPT to care for any sex partners.

Partner Referral

In addition to screening, it is important to care for sex partners (De et al., 2004). Though the societal context has changed, the fundamentals of partner referral have been in use since at least the 1970s, when the term “partner referral” came into use (the practice may be older still) (Kissinger et al., 1998; Ramstedt et al., 1991). Partner referral still involved case reporting, but instead of contact tracers reaching out directly to exposed partners, index patients would be asked to refer their sex partners to receive testing (Workowski & Bolan, 2015). The advantage of this shift was the lower resources required...
to reach sex partners. Additionally, index patients may be able to contact their sex partners faster than a contact tracer, especially if contact tracers have high caseloads.

However, there are drawbacks to partner referral. Requiring sex partners to be diagnosed before treatment adds time, with the mean time to treatment under partner referral estimated above 2 weeks (Estcourt et al., 2015; Menon-Johansson et al., 2006). This may allow for the index patient to be reinfected before their sex partner(s) are cured (Low et al., 2014). Estimates vary, but some 14% of index patients who are given partner referrals have been found to be reinfected within four months of their treatment (Cameron et al., 2010; Golden et al., 2005; Kissinger et al., 2005). Additionally, sex partners must make and keep an appointment for a diagnostic exam, which does not always occur. Estimates range from 13% to 49% of index patients reporting that all their sex partners were “very likely to have been treated” when given partner referral (Golden et al., 2005; Hogben et al., 2005). Finally, partner referral may fail to treat sex partners who are unwilling to visit a clinic due to various concerns such as privacy and lack of access to care centers (Temkin et al., 2011; Termoreshuizen, 1997).

**Expedited Partner Therapy**

Recognizing these limitations, as early as the late 1970s, some healthcare practitioners began issuing extra prescriptions or medications to index patients for their partners, even though the legality of issuing treatment to individuals not in the direct care of the healthcare practitioner was uncertain (Kissinger et al., 1998; Ramstedt et al., 1991). Public health agencies and practitioners in the late 1990s began seriously looking at EPT as
an alternative to partner referral. California was the first state to pass legislation legalizing EPT in 2001. The CDC began recommending using EPT for both chlamydia and gonorrhea for both males and females when other management strategies are impractical or unsuccessful in 2006 (Guidance on the Use of Expedited Partner Therapy in the Treatment of Gonorrhea, 2021; Handsfield et al., 2006).

There are a few key advantages to using EPT over partner referral. By removing the need to diagnose sex partners, treatment may be rendered sooner. This may prevent reinfection of the index patient and prevent further transmission from any infected sex partners. Additionally, it is possible that some sex partners may accept an EPT treatment when they would not have accepted a partner referral. EPT, therefore, may increase the number of sex partners treated relative to partner referral (Shiely et al., 2010). By improving treatment for sex partners, future transmission of infections may be prevented. Given these advantages, there is speculation that EPT use may drive down underlying prevalence and incidence in the population. This has some support in previous research. One study found that gonorrhea incidence and chlamydia test positivity (the proportion of diagnostic tests that return a positive result) both decreased by approximately 10% after EPT was provided at no charge. However, these changes were not statistically significant (Golden et al., 2015).

There are also some potential downsides of EPT use. By omitting the diagnostic exam, EPT use represents a retreat from an emphasis on case reporting because infected sex partners are not identified (and thereby not reported to a state or jurisdictional
database). This may diminish surveillance capability when EPT is used (Expedited Partner Therapy, 2021). Additionally, any other sex partners of sex partners (not the index patient) are left beyond the reach of healthcare practitioners. EPT trades the healthcare system’s ability to contact trace in exchange for faster and possibly more reliable treatment of recent sex partners.

**Med-in-hand vs. Prescription EPT**

There are two options for delivering EPT to sex partners. Much of EPT is given as a prescription (i.e., the index patient delivers a script to their sex partners) (Kissinger, 2017; Oliver et al., 2016; Slutsker et al., 2020). However, EPT may also be given as a medication—hereafter described as "med-in-hand" EPT (Note: some older studies used the term "patient delivered partner therapy", or PDPT, to refer to med-in-hand EPT). By giving EPT as med-in-hand, recipient sex partners need not attend a pharmacy to fill a prescription. This may increase the probability that sex partners will take the treatment. It may also shorten the time to treatment for sex partners because they have access to the medication sooner. Thus, med-in-hand EPT potentially strengthens the advantages of EPT overall in terms of time to treatment and probability of treatment (Kissinger & Hogben, 2011; Schillinger et al., 2016).

**EPT Legalization and Uptake**

The CDC currently recommends using EPT for both chlamydia and gonorrhea and both males and females when other management strategies are impractical or unsuccessful (Expedited Partner Therapy, 2021). The CDC has also provided guidance to states looking to
legalize EPT, giving specific attention to the features of EPT legalization that are valuable in practice (O’Connor, 2011). The majority of states in the U.S. have adopted legislation to legalize the practice of using EPT to treat sex partners of index patients diagnosed with chlamydia (Legal Status of Expedited Partner Therapy (EPT), 2021). California was the first state to pass such legislation in 2001, followed five years later by 24 states between 2006 and 2010. By 2022, nearly all states had legalized EPT use (Legal Status of Expedited Partner Therapy (EPT), 2021). Table 2 lists the year that US states legalized EPT for the first time.

Table 2. List of U.S. states according to the year in which EPT use was initially legalized in that state.

<table>
<thead>
<tr>
<th>Year</th>
<th>States that legalized EPT in each year</th>
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<tbody>
<tr>
<td>2001</td>
<td>California</td>
</tr>
<tr>
<td>2002</td>
<td>-</td>
</tr>
<tr>
<td>2003</td>
<td>-</td>
</tr>
<tr>
<td>2004</td>
<td>-</td>
</tr>
<tr>
<td>2005</td>
<td>-</td>
</tr>
<tr>
<td>2007</td>
<td>Colorado, New Mexico</td>
</tr>
<tr>
<td>2008</td>
<td>Arizona, Louisiana</td>
</tr>
<tr>
<td>2009</td>
<td>Minnesota, New York, North Carolina, North Dakota, Texas, Utah, Vermont</td>
</tr>
<tr>
<td>2010</td>
<td>Alaska, Illinois, Maine, Missouri, Oregon, Rhode Island, Wisconsin</td>
</tr>
<tr>
<td>2011</td>
<td>Connecticut, Indiana, Massachusetts</td>
</tr>
<tr>
<td>2012</td>
<td>Arkansas, Hawaii</td>
</tr>
<tr>
<td>2013</td>
<td>Nebraska</td>
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<tr>
<td>2014</td>
<td>Idaho</td>
</tr>
<tr>
<td>2015</td>
<td>Michigan, Montana</td>
</tr>
<tr>
<td>2016</td>
<td>Florida, Ohio, West Virginia</td>
</tr>
<tr>
<td>2017</td>
<td>Maryland, New Hampshire</td>
</tr>
<tr>
<td>2018</td>
<td>Delaware, Georgia, Iowa, Virginia</td>
</tr>
<tr>
<td>2019</td>
<td>Kentucky, New Jersey</td>
</tr>
</tbody>
</table>

Source: Centers for Disease Control and Prevention (https://www.cdc.gov/std/ept/legal/default.htm)
The current rate of healthcare practitioner EPT use varies among the states as well as healthcare facilities, ranging from 23% to 77% (Hogben et al., 2005; Hsii et al., 2012; Jotblad et al., 2012; Packel et al., 2006; M. E. Rogers et al., 2007; Rosenfeld et al., 2015; Taylor et al., 2011). Higher EPT use by healthcare practitioners was associated with affiliation with a clinic that provided pre-packaged medications (Jotblad et al., 2012), and with being in a jurisdiction with active EPT promotion (Hsii et al., 2012; Rosenfeld et al., 2015; Taylor et al., 2011). The rate of EPT use is typically measured using surveys of healthcare practitioners, which often differentiate whether practitioners have “ever used” EPT or whether they use EPT “routinely” or “frequently”. The difference between reported “Routine” use of EPT and “ever using” EPT suggests that many healthcare practitioners use EPT only in limited circumstances (e.g., the healthcare practitioner already knows the sex partner) (Hsii et al., 2012; Jotblad et al., 2012; M. E. Rogers et al., 2007). Additionally, this indicates that many more healthcare practitioners are aware of EPT than are using it in routine practice. Some states and city jurisdictions have higher rates of routine EPT use, including California and New York City (Jotblad et al., 2012; Packel et al., 2006). However, the most recently available survey of healthcare practitioners’ use of EPT was published in 2015, and EPT use rates may have changed in the intervening years (Rosenfeld et al., 2015).

States have different regulations governing the use of EPT. For instance, they vary on whether they permit the use of EPT prescriptions which do not include the name of the
sex partner to be treated (so-called "no-name EPT prescriptions"), and whether they exempt healthcare practitioners from medical liability in the event of any adverse outcomes among sex partners that may result from an EPT use (liability protections) (Legal Status of Expedited Partner Therapy (EPT), 2021). Additionally, states vary over which STI's may be treated using EPT. EPT use is almost always allowed for chlamydia, usually allowed for gonorrhea, and sometimes allowed for trichomoniasis (Burstein et al., 2009; Khan et al., 2005; Kissinger et al., 2006; Peterman et al., 2016). States also differ in whether they engage in efforts to lower the cost of using EPT medications by using the Health Resources and Services Administration's 340B Drug Pricing Program for certain patients or by buying the medications in bulk using state funds (Kissinger, 2014). Additionally, there is an ongoing debate about the benefits and drawbacks of providing EPT to index patients with sex partners of the same sex (Clark et al., 2017; Weiss et al., 2019). At the time of writing, the CDC did not recommend that EPT be used to care for men-who-have-sex-with-men, primarily due to concerns about comorbid syphilis and HIV (Guidance on the Use of Expedited Partner Therapy in the Treatment of Gonorrhea, 2021). However, some jurisdictions favor expansion of EPT use to treat men-who-have-sex-with-men (MSM), primarily because there is a lack of scientific evidence to support the concerns about comorbidities (Andre Kiesel, 2022).

**Current Evidence on EPT versus Partner Referral**

A large evidence base has emerged examining the relative effectiveness of EPT versus partner referral across several lines of inquiry. These include investigating whether index patients that receive EPT have a lower probability of becoming reinfected than if they
had received partner referral (Golden et al., 2005; Kissinger et al., 2006), estimating whether there is a change in the probability of treatment for sex partners (Cameron et al., 2010; Oliver et al., 2016), and cost-effectiveness estimates (Gift et al., 2011). However, several questions remain. Though it has been theorized that increased EPT use may reduce population-wide diagnoses and underlying prevalence, this has not been empirically estimated. Additionally, previous cost-effectiveness analyses (Gift et al., 2011) have not accounted for all the possible cost impacts of switching to EPT and therefore an analysis estimating total societal cost has yet to be conducted.

The first—also largest—body of evidence is in evaluating whether EPT recipient index patients have significantly different reinfection rates compared to their partner referral counterparts (Handsfield et al., 2006; Hogben et al., 2005; Kissinger et al., 2006; Stephens et al., 2010; Teplow-Phipps et al., 2015). There is a mix of randomized control trials and observational research that have assessed reinfection with varying results (Cameron et al., 2010; DiClemente et al., 2014a; Golden et al., 2005; Kerns et al., 2011; Kissinger et al., 2005, 2006; Schillinger et al., 2003; Schwebke & Desmond, 2010; Stephens et al., 2010; Taylor et al., 2013; Teplow-Phipps et al., 2015; Vacca et al., 2019; J. Yu et al., 2008; Zofkie et al., 2021). The differences in results warrant some discussion below. The second line of inquiry is in estimating whether sex partners who receive EPT are more likely to be treated than if they had gotten partner referral instead (Cameron et al., 2010; Clark et al., 2017; Golden et al., 2005, 2007; Kissinger et al., 2005, 2006; Schillinger et al., 2003; Schwebke & Desmond, 2010; Vacca et al., 2019). The third major line of inquiry is made up by a limited number of studies that have investigated whether EPT use is more
cost-effective than partner referral (Estcourt et al., 2015; Gift et al., 2011; Roberts et al., 2012; Williams et al., 2021). Remaining questions include what the impact of EPT use is on overall population outcomes, including the total number of diagnoses and underlying chlamydia prevalence. Additionally, it is unclear whether EPT is more cost-effective than partner referral after adjusting for EPT’s potential to treat uninfected sex partners and the varied costs of sequelae.

Several studies previously found reduced reinfection rates when EPT was used instead of partner referral (Cameron et al., 2010; DiClemente et al., 2014a; Golden et al., 2005; Kerns et al., 2011; Kissinger et al., 2005, 2006; Schillinger et al., 2003; Schwebke & Desmond, 2010; Stephens et al., 2010; Taylor et al., 2013; Teplow-Phipps et al., 2015; Vacca et al., 2019; J. Yu et al., 2008; Zofkie et al., 2021). Seven randomized control trials comparing EPT to partner referral were conducted in the US—all but one published between 2003 and 2010 (Cameron et al., 2010; Golden et al., 2005; Kissinger et al., 2005, 2006; Schillinger et al., 2003; Schwebke & Desmond, 2010). Of these randomized control trials, five found significantly lower reinfection rates when index patients received EPT instead of partner referral (Golden et al., 2005, 2015; Kissinger et al., 2005; Nuwaha et al., 2001; Schwebke & Desmond, 2010). However, two randomized control trials found no significant difference in reinfection rates (Kissinger et al., 2006; Schillinger et al., 2003). None of the seven randomized control trials found that increased EPT use led to increased reinfection rates among index patients compared to partner referral. A more recent series of observational studies mostly found that EPT had no significant impact on reinfection rates among index patients (DiClemente et al., 2014a; Kerns et al., 2011; Stephens et al., 2019).
Like the randomized control trials, none of these observational studies found that EPT use increased reinfection rates among index patients.

The discrepancy between the randomized control trials (the initial evaluations of EPT) and observational studies hint at the gap between the evidence for EPT’s potential effectiveness and EPT use in the real world. First, it is important to note a few methodological factors when considering research on EPT. The practice guidelines surrounding EPT use encourage healthcare practitioners to attempt partner referrals before using EPT. This may lead to selection bias whereby sex partners who are more difficult to reach are treated using EPT as a last resort—lessening the measured effectiveness of EPT relative to partner referral in some studies (Expedited Partner Therapy, 2021). Additionally, study power may also be a concern in studies with smaller sample sizes (DiClemente et al., 2014a; Teplow-Phipps et al., 2015; Vacca et al., 2019).

However, in addition to the methodological differences described above, how EPT was used varied. Some randomized control trials included enhancements that may have improved health outcomes for EPT. For example, one study had staff follow up with index patients by phone to remind them to deliver EPT packets to their sex partners (Golden et al., 2005). Of the 14 identified studies (both randomized control trials and observation studies) that evaluated reinfection of index patients, 12 used med-in-hand EPT rather than prescription EPT. These included more than half of the observational studies identified and all but one of the seven randomized control trials (DiClemente et al., 2014a; Gift et al.,
Med-in-hand EPT and prescription EPT may be different because prescription EPT requires additional steps, which delay treatment (Kissinger, 2017; Okah et al., 2017). The proportion of all EPT uses that are given as med-in-hand vs. prescription is understudied (no studies were identified which estimated this proportion). Nevertheless, the different modes of EPT delivery (med-in-hand and prescription) may help explain the evidence-practice gap between the early and later studies.

Another important line of research has investigated whether EPT use was more likely to result in the treatment of sex partners than if they had received a partner referral. This research question is inherently difficult to answer because direct contact with sex partners does not occur when EPT is used. Several studies have followed up with index patients after their healthcare facility visit to ask them whether their sex partners were successfully treated with EPT (Cameron et al., 2010; Clark et al., 2017; Golden et al., 2005, 2007; Kissinger et al., 2005, 2006; Schillinger et al., 2003; Schwebke & Desmond, 2010; Vacca et al., 2019). These studies, in most cases, found that EPT improved treatment rates among sex partners when compared with partner referral, and are the best indication that med-in-hand EPT results in more treatments compared to partner referral. Two studies from New York City aimed to measure treatment rates of sex partners receiving EPT prescriptions. The first study examined two clinics and found that 33% and 55% of prescriptions respectively were filled at nearby pharmacies (Okah et al., 2017; Slutsker et al., 2020). The second study found that 41% of prescriptions were filled at nearby pharmacies. These discrepant findings, including different findings among two clinics in
the same study (with the same methodology), suggest that there may be wide variation in prescription fill rates between clinics (Kissinger, 2017; Okah et al., 2017). Neither of these studies compared EPT to partner referral directly. Overall, previous research suggests that EPT likely increases the probability that sex partners receive treatment relative to partner referral.

Finally, some limited research has assessed the cost-effectiveness of EPT versus partner referral. Most such studies were conducted in the United Kingdom (UK), limiting generalizability to the United States because of the differences in medical insurance and purchasing systems used in the two countries could result in different treatment and payment patterns (Estcourt et al., 2015; Roberts et al., 2012; Williams et al., 2021). One study in the United States assessed the cost-effectiveness and the societal costs of treating sex partners with a chlamydia infection in three cities. The authors of that study considered EPT’s propensity to leave females with undiagnosed sequelae. However, they did not fully assess the impact of testing uninfected sex partners under partner referral or treating uninfected sex partners using EPT (Gift et al., 2011). Another study from the UK found that increasing the efficacy of partner treatment using accelerated partner therapy (APT – the UK equivalent to EPT) was more cost-effective than increasing screening for chlamydia. However, this study did not provide a detailed cost-effectiveness analysis compared to partner referral (Althaus et al., 2014). Still, another study from the UK found that partner referral was more cost-effective than APT. However, the authors only considered the clinical costs when providing partner referral or APT to index patients (Roberts et al., 2012). Finally, a recent study from the UK found that APT was more cost-effective than
partner referral while assuming that APT increased the number of sex partners treated by a flat rate of 25% (Williams et al., 2021). It is not clear that this assumption is valid, especially in different populations with very different payment systems such as in the US.

**Theory: Why Promising Policies Fail to Catch On**

**Dissertation Overview: Contribution to Policy Studies Theory and Practice**

This dissertation addresses whether it is valuable to increase EPT use and investigates how to promote it. The three studies included here focus on the impact of increased EPT use on key epidemiological outcomes used by policymakers, the cost-effectiveness of EPT use from the perspective of society and identifying the promotion strategies that policymakers may use to promote increased EPT. Together, these studies provide critical information to decide how to promote EPT, how much to promote EPT, and how much increased EPT use might cost from a societal perspective.

In addition to the practical contributions, the three papers that comprise this dissertation contribute to the field of policy studies in several distinct ways. In their influential work, Smith, and Larimer (2016) discussed the “fracturing” of policy sciences among the empirical fields of policy evaluation (what have we accomplished?) and policy process studies (explaining how policy is made and implemented), and the more normative field of policy analysis (what should we do?) (K. B. Smith & Larimer, 2016). As seen in Figure 1, Papers 1 and 2 performed policy evaluations of different aspects of increased EPT use, while also contributing to policy analysis. Paper 3 investigates the promotion and implementation of EPT in practice, which incorporated elements of both policy evaluation
and policy process. All three studies contribute to the two overarching questions: can we increase EPT use, and should we increase EPT use?

*Figure 1. The relationship between the three papers of this dissertation*

More broadly, Papers 1 & 2 contribute to the fields of policy evaluation and policy design, and Paper 3 contributes to the emerging field of implementation science in public health. Below I briefly describe each of these areas of policy studies and discuss how each paper contributes to these traditions.

*Policy evaluation and evidence-based policy*

The field of policy evaluation draws centrally on the notion that policy is improved when it is based on scientific evidence. An "evidence-based policy" is a policy that has been informed by rigorous objective data and evaluation (Sanderson, 2002). Adherents of the evidence-based policy paradigm argue that policies that have scientific and quantitative support ought to be implemented (Sanderson, 2002). Modeling studies and cost-effectiveness research are two frequently used approaches to generating credible and rigorous evidence.
Modeling studies in policy studies and public health

One aspect of evidence-based policy is in finding the best ways to provide the evidence needed to inform policy decisions. In many cases, powerful quantitative research designs are utilized to evaluate potential interventions, either in small trials or after their full implementation (Golden et al., 2015; Kissinger et al., 2005). However, there are some interventions which are more difficult to evaluate with direct measurement of outcomes. It is in these instances that modeling methods become valuable because they may use imperfect data so long as they make safe assumptions about these data (Sterman, 2002). In the case of EPT, the measurement of certain outcomes would inherently invalidate the premise of the intervention. This is because EPT precludes any contact with sex partners. Additionally, it is impossible to separate the effects of infection incidence and screening rates when assessing the number of diagnoses of any infectious disease. Modeling can cut through this uncertainty and separate screening from incidence and underlying prevalence. Using existing evidence and making safe assumptions about what is unknown, a model can provide therefore provide critical information to policymakers hoping to interpret an observed change in the number of diagnoses.

Cost-effectiveness research in policy studies and public health.

Cost-effectiveness research is highly valued in the field of public health because it can provide the evidence needed by policymakers seeking to maximize the return on investment of their limited available resources. When public resources are limited, it is useful to know which intervention can have the greatest impact given their cost of implementation. By standardizing outcomes from different interventions into single
effectiveness measures, cost-effectiveness analysis can comparatively evaluate such interventions. In the field of public health, this does not typically require converting outcomes into cost estimates, as is done in cost-benefit analysis. This is because of concern about the validity of methods that assign monetary value to health outcomes (Neumann, 2004). Instead, outcomes are converted (if necessary) into more health-relevant values, like quality adjusted life years, or deaths averted. In some cases, a standard measure is used which is specific to that research question, such as successful treatments—used as an outcome in one of the papers of this dissertation.

*Policy design and policy research*

This dissertation also addresses the issue of policy design in policy studies by examining what the most effective way is to design policies aimed at reducing transmission of STIs. Policy design is important to consider as not all policies are equally likely to produce the intended effect. A shift in policy implementation research that occurred from the 1970s to the 1990s was to increase focus on policy instruments and policy design (Sanderson, 2002; K. B. Smith & Larimer, 2016). A focus on policy design suggests that researchers should shift away from the raw content of policies and instead consider public policies as larger packages of policy instruments and identify components of public policies to evaluate separately (Sanderson, 2002; K. B. Smith & Larimer, 2016). These include options like government provided insurance, public information campaigns, loan guarantees, and others (Sanderson, 2002; K. B. Smith & Larimer, 2016). Policy instruments may be thought of as the levers of government action—the strategies which public actors utilize to produce the intended result (e.g., mandates, incentives, penalties). A focus on
research design as it pertains to STIs might therefore focus on what the best policy instruments are to deliver treatment to the public and drive down STI infections e.g., partner referral vs EPT; med-in-hand vs script. One of the papers of this dissertation investigates EPT promotion strategies of state health departments to uncover the policy design that has been used in practice.

Policy Implementation Studies

If evidence-based policies do not realize their promised potential after implementation, an opportunity is created to investigate the reasons for that failure and to identify possible alternative implementation strategies. Doing so may provide a deeper understanding of policy implementation and the ways to get the most out of promising new interventions in healthcare and beyond. This dissertation is situated in the fields of policy implementation and implementation science, and it is linked to several areas of ongoing academic discussion. Implementation theory aims to shed light on why promising policies fail to be adopted in practice or the outcomes do not live up to expectations. Pressman and Wildavsky pioneered this field in 1973, and it is chiefly concerned with exploring and explaining the process and consequences of policy implementation (Pressman & Wildavsky, 1984). Major contributions by scholars like Derthick and Mazmanian and Sabatier expanded our understanding (Derthick, 2013; Sabatier & Mazmanian, 1980). But over time it became clear that a unified theory of implementation was beyond reach (K. B. Smith & Larimer, 2016). Instead, the field fractured into subfields concerned with explaining implementation in different contexts (Nilsen et al., 2013).
Diffusion Theory

The question of why promising policies fail to be adopted in practice has also been taken up by scholars interested in the Diffusion of Innovations (i.e., why and how promising policies “catch-on” or not). Diffusion of Innovation theories posit that governments may learn from each other (E. Rogers, 1971). More broadly, Diffusion of Innovation may refer to the spread of evidence-based practices, particularly in medicine (Greenhalgh et al., 2004). Research in this field has highlighted that cultural factors such as acceptance and a change in attitudes about the new practice can facilitate or hinder the implementation of new practices (Granados et al., 1997). In other words, it is not enough for an innovation to be more effective than the current practice—it must be accepted by the individuals who are implementing the change. In the case of EPT, this refers primarily to healthcare practitioners. Evidence based practices are not automatically adopted in a linear fashion, and promotion requires careful consideration of the context in which a practice is promoted (Grimshaw et al., 2004). Previous survey research has highlighted that the uptake of EPT by healthcare practitioners remains low, and a lack of acceptance may explain why state efforts to promote EPT have floundered (Hsii et al., 2012; McCool-Myers et al., 2020). Paper 1 explores the impact of increased acceptance and use of EPT by healthcare practitioners. Diffusion Theory may also help explain how EPT promotion spread between states, which is one avenue of inquiry of Paper 3.

Implementation Science

Much like the fields of policy implementation and diffusion theory, the field of implementation science is focused on the question of why promising, evidence-based
interventions fail to catch-on and is concerned with how to ensure the take-up of best practices. However, in contrast with policy implementation and diffusion of innovation theory, implementation science did not originate in the field of public administration nor the social sciences. Rather, implementation science came from unconnected research efforts in public health that were aimed at understanding why interventions failed to realize the gains predicted by early clinical trials (Nilsen et al., 2013). Implementation science is concerned with evaluating methods to promote the uptake of evidence-based practices and thereby improve the quality of (predominantly health and healthcare) outcomes (Eccles & Mittman, 2006). A critical area of discussion within implementation science is the “evidence-practice gap”, which is the difference between the findings of early evaluations (the evidence) and the findings of evaluations of the same interventions in their real-world implementation environment (the practice). If implementation fails to produce the expected outcomes, it may be called “implementation failure”. In their seminal study, Oxman et al. (1995) reviewed evaluations of various public health interventions and found that strategies with strong empirical support for their effectiveness rarely achieved the same outcomes after their implementation (A. D. Oxman et al., 1995). Fixsen et al. (2005) conducted a literature review to identify and standardize terminology and foster understanding about what further research was needed to develop the field (Fixsen et al., 2005). Further synthesis was conducted more recently, for example, by Handley et al. (Handley et al., 2016). Their research identified factors that may help to lessen the evidence-practice gap. These included strong leadership, flexibility, the participation of
diverse stakeholders throughout implementation, and minimizing of the behavior change necessary for implementation to be successful (Fixsen et al., 2005; Handley et al., 2016).

To address the evidence-practice gap, researchers have developed frameworks to provide structure for future research. Two theoretical frameworks are relevant to this dissertation: the Reach, Efficacy – Adoption, Implementation, and Maintenance (RE-AIM) framework developed by Glasgow et al. (1999), and the Capability, Opportunity, Motivation, and Behavior (COM-B) framework developed by Michie et al. (2011). The RE-AIM framework predicts that the public health impact of a given intervention depends on the five factors for which it is named. For example, Reach is the number of individuals using the intervention while Efficacy is the difference between the old practice and the new intervention. Applied to EPT, RE-AIM implies that the impact on health outcomes of EPT depends on the number of healthcare practitioners using EPT and EPT’s effectiveness at treating sex partners. Additionally, the implementation of EPT depends on whether EPT is used as intended by the original designers and whether maintenance efforts keep EPT in use after its initial promotion lapses. However, the RE-AIM framework is more descriptive than it is causal. The COM-B framework, by contrast, predicts that a behavioral change (the adoption of a new practice) may occur when the individuals are capable (i.e., legally, and mentally), motivated, and have opportunities to engage in that behavior. Regarding EPT, both RE-AIM and COM-B can be used to describe the uptake of EPT and to assist in understanding why EPT use by healthcare practitioners has not increased as hoped. Paper 3 explores qualitative insights into the barriers to wider uptake of EPT. Future research
could design interventions based on implementation science frameworks that could address these barriers.

Additionally, there has been interest in modelling methodology to study implementation science. Early studies of the evidence-practice gap revealed the complex and interactive nature of the causes of implementation failure. This stimulated interest in efforts to improve implementation through modeling approaches because these methods might be able to untangle this complexity. For example, Zimmerman et al. (2016) used system dynamics modelling to improve implementation. System dynamics is a methodological approach that uses feedback loops between variables to better comprehend complex systems. The practice of participatory system dynamics emphasized the involvement of stakeholders in the design of system dynamics simulations to better identify barriers to implementation (Zimmerman et al., 2016). Participatory system dynamics emphasized that the perspectives of various stakeholders are not necessarily incorrect, but that individual views may be incomplete (Zimmerman et al., 2016). Thus, diverse stakeholders need to be involved in the design of system dynamics models to take advantage of their various perspectives and experiences.

In this dissertation, experts and stakeholders were interviewed extensively throughout model development and testing for the simulation used in Papers 1 and 2. Additionally, these papers investigated practical concerns expressed by healthcare practitioners with the discretion to use EPT that had been described in previous research, including concerns about treating the female sex partners who receive EPT who might
remain with undiagnosed and untreated sequelae (Ferreira et al., 2013; Schillinger et al., 2016). Paper 3 included interviews with directors and staff at state, local, and federal health departments and elicits their perspectives on the strategies to promote EPT and the barriers and facilitators to EPT promotion.

The questions and challenges that have been identified in previous policy implementation and implementation science literature are apparent in the implementation of EPT. EPT is known to be effective from empirical research (particularly early randomized control trials), appears easy to use because it streamlines treatment of sex partners, and is intuitively cost-effective because it allows treatment without the use of relatively costly diagnostic exams. Yet despite these advantages, the uptake of EPT varies widely and remains low in many jurisdictions (demonstrating a lack of expected behavior change) (Kissinger, 2017). Additionally, the improvements promised by early evaluations of EPT have, at least in some cases, failed to materialize in real-world practice when considering the difference between early random control trials and later observational research findings. Improving our understanding of the overall evidence base as it pertains to EPT, as well as the evidence-practice gap, is a central focus of this dissertation.

Dissertation Overview: Aims and Design

This dissertation provides new insight to untangle the mystery of why EPT—a promising intervention—has not accomplished its expected reach or efficacy in implementation. The dissertation also seeks to clarify key remaining scientific questions regarding the efficacy, cost-effectiveness, and promotion of EPT. Finally, it may inform
policy actors hoping to promote the use of EPT. Papers 1 and 2 make use of the extensive literature that previously estimated the impact of increased EPT use on outcomes including the probability of reinfection of index patients and the likelihood of treatment of sex partners who receive EPT rather than partner referral. These papers also expand the implications of existing research by estimating the population-level impact on the number of annual diagnoses of chlamydia, underlying chlamydia prevalence in the population, and the cost-effectiveness of EPT treatment as compared to partner referral. Paper 3 offered valuable theoretical contributions to the field of implementation science by simultaneously examining the bottom-up and top-down perspectives of EPT policy implementation and promotion. Policymakers in state health departments provided the top-down perspective on the promotion strategies they used to promote EPT. The perspectives of healthcare practitioners were also represented, both through interviews with local health department staff and by identifying what aspects of street-level practice policymakers were aware of. Paper 3 also investigated how certain policymakers understood and used scientific evaluations of EPT from across the evidence-practice gap (with wide ranging outcomes).

There were some differences in the focus of each paper as well as in the comparisons made in the two modeling papers. Table 3 provides an overview of these differences between each paper in this dissertation. All papers discussed the use of EPT for chlamydia, but Paper 3 also considers EPT for gonorrhea. This is largely because the promotion strategies identified in Paper 3 could be used for either infection, while the modeling papers needed to control their scope. Additionally, while both modeling papers compared EPT to partner referral, Paper 1 also compared prescription EPT to med-in-hand
EPT. Paper 2 did not make this comparison to control scope and because the cost-effectiveness of med-in-hand relative to prescription EPT is a forgone conclusion. First, by omitting the need for a pharmacy visit, med-in-hand is highly likely to be more cost-efficient than prescription EPT. Second, med-in-hand is typically provided with very low-cost medicine, meaning the extra spending on treating uninfected sex partners is likely minimal under med-in-hand. Both modeling papers investigated the impact of EPT on PID, but Paper 2 additionally looked at other sequelae that are associated with chlamydia and PID (including infertility, ectopic pregnancy, and chronic pelvic pain). This addition was important for Paper 2 because these other sequelae had high-cost burdens and thereby significant consequences for EPT’s cost-effectiveness outcomes. Paper 1, meanwhile, included only PID.

Table 3. Focus areas and comparisons by paper.

<table>
<thead>
<tr>
<th></th>
<th>Paper 1</th>
<th>Paper 2</th>
<th>Paper 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlamydia</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Model comparisons</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Med-in-hand vs.</td>
<td>Yes</td>
<td>No</td>
<td>-</td>
</tr>
<tr>
<td>prescription EPT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EPT vs. partner referral</td>
<td>Yes</td>
<td>Yes</td>
<td>-</td>
</tr>
<tr>
<td>PID</td>
<td>Yes</td>
<td>Yes</td>
<td>-</td>
</tr>
<tr>
<td>Other sequelae</td>
<td>No</td>
<td>Yes</td>
<td>-</td>
</tr>
</tbody>
</table>

Note: EPT = expedited partner therapy; PID = pelvic inflammatory disease; med-in-hand = EPT given as a medication.
Paper 1: Simulating the potential impact of expedited partner therapy on chlamydia diagnoses in New York State

Paper 1 estimates the impact of increased EPT use on the number of cumulative annual chlamydia diagnoses five years after implementation among heterosexual active males and females aged 18–24 years living in New York State (NYS). Two components of EPT use were investigated as strategies to improve EPT use. These included increasing the proportion of sex partners receiving EPT and increasing the proportion of EPT recipients that receive med-in-hand EPT rather than prescription EPT. In addition, the number of diagnoses that resulted from partner referrals, underlying chlamydia prevalence, and undiagnosed PID infections among female sex partners that resulted from each strategy were estimated as secondary outcomes. Using a simulation model to evaluate EPT is valuable for two reasons. First, EPT is a practice that cannot be easily measured via administrative data because EPT recipient sex partners are (almost by definition) not contacted. However, the most used indicator of effectiveness at the societal level—diagnoses of chlamydia—is determined primarily by the number of individuals who are tested and the prevalence of infections among tested individuals (test sensitivity and specificity and anatomical site of testing also play a small role). It is difficult for observational studies to separate these factors when assessing diagnoses as an outcome. Similarly, EPT use may alter diagnoses via two mechanisms. First, EPT leads to less testing of sex partners and may therefore drive down diagnoses as fewer patients are referred for clinical examination and testing. Alternatively, EPT may lead to a decrease in underlying prevalence through improved treatment outcomes, which would also drive down
diagnoses as incident cases decrease. This makes it difficult to interpret the number of diagnoses, even though this is the primary indicator used by policymakers to assess infection spread and control. It is therefore valuable to separate out the sources of change in the number of diagnoses. A simulation model can separate these two mechanisms and estimate the impact of EPT use on diagnoses, which is an important indicator for policymakers. Extensive empirical evidence of EPT’s effectiveness has been published, which provided an evidence base for the simulation model. One study from 2015 measured gonorrhea incidence and chlamydia test positivity (the probability that a diagnostic exam will result in a diagnosis) at the community level after randomizing local health jurisdiction to use EPT med-in-hand packets. The authors reported statistically non-significant improvements of around 10% for each measure (Schillinger et al., 2016). However, this study did not report the total number of diagnoses, was likely limited in statistical power, and could not measure changes in underlying infection prevalence. The expected impact of EPT use on the number of diagnoses, underlying chlamydia prevalence, prevalence of PID, and the number of females with PID among sex partners is summarized in Table 4.

Table 4. Breakdown of outcome measures and the expected direction change relative to the base scenario with no change in EPT or med-in-hand EPT use.

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Expected Direction (Increase/Decrease)</th>
<th>Favors EPT or Partner Referral?</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnoses</td>
<td>Decrease</td>
<td>Partner referral</td>
<td>Fewer cases are diagnosed because partners are never tested; decline in prevalence could lead to decrease in diagnoses</td>
</tr>
</tbody>
</table>
Underlying prevalence of Chlamydia

Decrease

EPT

More treated infections lower overall prevalence

Diagnoses of PID among sex partners

Increase

Partner referral

PID will go undetected since no need for a clinical visit

Prevalence of PID

Decrease

EPT

PID cases decrease due to lower overall prevalence

Note: EPT = expedited partner therapy; PID = pelvic inflammatory disease.

Paper 2: The cost-effectiveness of expedited partner therapy for chlamydia compared to partner referral among young adults: A state-based case study

Paper 2 estimates the cost-effectiveness of EPT and partner referral, total societal costs, and the number of treatments of chlamydia infected and uninfected sex partners using a simulation model specified for young adults living in NYS. The simulation model used in Paper 1 was expanded to include cost outcomes, which meant that the cost effectiveness analysis also incorporated the epidemiological consequences of EPT use (i.e., changes in underlying prevalence). As in Paper 1, NYS provided an excellent case study to study EPT using a simulation model, with good availability of previous literature and population data to serve as model inputs.

Previous research has found that EPT is cost-effective compared to partner referral for chlamydia (Owusu-Edusei Jr et al., 2010). However, no identified previous research has estimated the cost-effectiveness and total societal expenditure accounting for two important consequences of EPT use. The first consequence is that EPT may reduce the
number of needed treatments by decreasing the underlying prevalence. The second is the unnecessary spending incurred by EPT when uninfected sex partners are treated. Total societal costs may be divided into three overall categories: treatment costs (money spent for antibiotic treatments used by both partner referral and EPT), clinical costs (including the time and money spent to test for infections), and sequelae costs (lifetime expenditure for treatment to care for any sequelae). Treatment costs are likely to increase with EPT use because EPT may treat uninfected sex partners, whereas partner referral would not have done so. Clinical costs are expected to decrease with EPT use because EPT eliminates the requirement for sex partners to visit a clinic before treatment. Finally, it is not clear whether costs for the treatment of any sequelae would increase or decrease with EPT use. By not bringing female sex partners into clinics to be examined, EPT may delay treatment for females who have already developed a sequela. On the other hand, if EPT were to reduce the underlying prevalence of chlamydia in the population, it may prevent the onset of sequelae in the first place. There remains a question of whether the impact through underlying prevalence can compensate for the delay in treatment for females who already have a sequela. The cost impact of EPT use expected from Paper 2 are summarized in Table 5, separately for treatment costs, clinical costs, sequelae costs, and total costs.

Table 5. Breakdown of cost categories and the expected societal expenditure on each cost category under EPT and partner referral for chlamydia.

<table>
<thead>
<tr>
<th>Type of cost</th>
<th>Expected impact of EPT</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment costs</td>
<td>Increase</td>
<td>EPT may treat uninfected sex partners</td>
</tr>
<tr>
<td>Clinical costs (e.g., clinical visit and diagnosis)</td>
<td>Decrease</td>
<td>EPT does not require a diagnostic test</td>
</tr>
<tr>
<td>Cost Category</td>
<td>Status</td>
<td>Description</td>
</tr>
<tr>
<td>---------------------------------------------------</td>
<td>--------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Sequelae costs (including PID and others)</td>
<td>Unclear</td>
<td>EPT may delay treatment of sequelae, allowing infections to worsen; EPT may reduce underlying prevalence, reducing sequelae incidence.</td>
</tr>
<tr>
<td>Total societal costs (the sum of all costs)</td>
<td>Unclear</td>
<td>Depends on the relative magnitude of each of the above.</td>
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Note: EPT = expedited partner therapy; PID = pelvic inflammatory disease.

**Paper 3: Promoting expedited partner therapy for chlamydia and gonorrhea to treat exposed sex partners: strategies, facilitators, and barriers to promotion activities by US state health departments**

Paper 3 aims to fill the gaps in our current knowledge of EPT promotion strategies for chlamydia and gonorrhea, barriers, and facilitators using qualitative interviews of US state health department staff and directors throughout the US and inductive analysis. Additionally, one respondent from a federal agency and several local health department staff and directors were also interviewed to provide additional context into how state-level promotion activities impacted their jurisdictions. This study focused on understudied health department staff and their efforts to promote EPT and identified key areas where health departments have opportunities to improve EPT implementation in their states. The findings added to the existing literature by offering additional explanations for variation in EPT use and a better understanding of critical barriers to EPT promotion.
Previous qualitative research has focused on the experiences of healthcare practitioners and patients receiving EPT and barriers to the use of EPT as a practice (Cramer et al., 2013; Rosenfeld et al., 2015). These studies have given little attention to the health department staff and directors responsible for implementing and promoting EPT. One recent study highlighted the barriers in EPT implementation as described by "EPT experts." The authors identified liability and concerns about adverse events, funding, awareness, and electronic medical records (due to technical difficulties in recording treatments for anonymous patients) as "primary barriers" to EPT use (McCool-Myers et al., 2020). However, very little research has focused on the health department staff and directors responsible for implementing and promoting EPT, or the types of promotion strategies and their success at addressing barriers to EPT implementation. Paper 3 fills this gap by investigating policy-level facilitators and barriers to successful EPT adoption and use.
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PAPER ONE

SIMULATING THE POTENTIAL IMPACT OF EXPEDITED PARTNER THERAPY ON

CHLAMYDIA DIAGNOSES: A STATE-BASED CASE STUDY
ABSTRACT

Introduction

Untreated chlamydia infections may lead to pelvic inflammatory disease (PID). Expedited partner therapy (EPT) is a clinical practice of treating – without clinical examination - exposed sex partners of patients diagnosed with chlamydia. Increase EPT use could decrease underlying chlamydia prevalence, diagnoses, and cases of PID.

Methods

A system dynamics model estimated the change in cumulative annual chlamydia diagnoses, underlying prevalence, and the number of cases of PID when EPT use or med-in-hand EPT use increased. The model included 1,004,753 males and 978,764 females aged 18–24 years living in NYS in 2010, unpublished NYS surveillance data on the number of chlamydia diagnoses from 2014-2018 (Years -4 through 0 in the model), and scientific literature. The model estimated the change in the total number of diagnoses of heterosexually acquired chlamydia infections during Year 5. Monte Carlo sensitivity analysis was used.

Results

Increasing EPT use from 25% of index patients to 30% reduced the cumulative number of chlamydia diagnoses during Year 5 by 2.3% (2.5% female, 2.1% male). There were 3.6% fewer women with PID due to a drop in underlying prevalence among females. Increasing the proportion of EPT recipients given med-in-hand EPT from 30% to 45% resulted in 1.0% fewer annual diagnoses (1.2% female, 0.9% male) during Year 5.
Conclusion

Of the two strategies, increasing the proportion of index patients given EPT resulted in the greatest reduction in overall diagnoses. The overall number of females with PID was found to decrease with increased EPT use. It is recommended that EPT use be promoted to help control the spread of chlamydia.
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INTRODUCTION

Chlamydia is one of the most prevalent and costly sexually transmitted infections (STIs) in the United States (U.S.), especially among young adults. In 2020, 1.6 million cases of chlamydia were reported to the CDC, making it the most common notifiable condition in the U.S. as recorded by the CDC in that year (Chlamydia National Profile - Overview, 2020). However, the underlying burden of chlamydia is believed to be much higher due to the high number of asymptomatic infections, with an estimated 4 million new infections of chlamydia occurring in 2018 alone (K. M. Kreisel et al., 2021). While contact tracing and the use of new medications have helped control the spread of the human immunodeficiency virus, chlamydia is increasing (Centers for Disease Control and Prevention, 2021b; DiClemente et al., 2014b). Rates of reported chlamydia are highest among adolescents and young adults aged 15–24 years, with almost two-thirds (61.0%) of all reported chlamydia cases among this age group in 2019 in the U.S. (Chlamydia National Profile - Overview, 2020). Most chlamydia infections do not produce severe morbidity and are easily cured using antibiotics (Golden et al., 2000). However, untreated infections may lead to serious downstream health effects, especially among females (Chlamydial Infections, 2015). Additionally, when index patients (individuals diagnosed through screening efforts) are treated, there remains a risk that they will be immediately reinfected by any infected sex partners (Expedited Partner Therapy, 2021). Therefore, effective chlamydia disease control requires caring for sex partners of index patients to prevent reinfection of index patients and further transmission (Ferreira et al., 2013; Screening Recommendations and
Considerations Referenced in Treatment Guidelines and Original Sources, 2021; Workowski & Bolan, 2015).

There are several options available to healthcare practitioners caring for sex partners of diagnosed index patients. Two prominently used clinical practices are partner referral and expedited partner therapy (EPT) (Expedited Partner Therapy, 2021; Ferreira et al., 2013). Partner referral is the traditional practice whereby sex partners are referred for testing and subsequent treatment if they are diagnosed. EPT is the practice of treating sex partners without clinical consultation or diagnosis. EPT may result in faster treatment of sex partners than partner referral (Ferreira et al., 2013). By improving these treatment outcomes, EPT use may drive down underlying prevalence and future incidence. This would drive down the number of diagnoses, assuming constant screening rates. However, EPT use also artificially reduces the number of sex partners that are diagnosed, diminishing surveillance capacity. Therefore, evaluations of EPT must look beyond diagnoses alone and consider underlying prevalence as well. In addition to this complication, the lack of clinical examination under EPT may have the unintended consequence of some female sex partners with pelvic inflammatory disease (PID) remaining undiagnosed, which may lead to devastating medical complications. On the other hand, if EPT use reduces underlying prevalence by a great enough margin, the overall number of females with PID might decline regardless. The Centers for Disease Control and Prevention (CDC) currently recommends the use of EPT to treat both male and female sex partners of index patients diagnosed with chlamydia when other partner management strategies are impractical or unsuccessful (Expedited Partner Therapy, 2021). EPT may be given either as a prescription to be filled
by sex partners or as medication (med-in-hand) to be delivered to sex partners by index
patients (Hogben & Kissinger, 2008).

Healthcare practitioners have two important decisions to make concerning EPT. The
first is whether they will use EPT or a partner referral to care for any sex partners. This
depends on their awareness of EPT legality, beliefs about EPT, and other factors (Rosenfeld et al., 2015). EPT use remains low in many clinics according to survey research, especially “routine” EPT use (Hogben et al., 2005; Hsii et al., 2012; Jotblad et al., 2012; Packel et al., 2006; M. E. Rogers et al., 2007; Rosenfeld et al., 2015; Taylor et al., 2011). Two identified studies of EPT uptake included New York City or national samples (which included New York State - NYS) of healthcare practitioners in their samples (Hogben et al., 2005; M. E. Rogers et al., 2007). The percentage of healthcare practitioners who had ever used EPT in these two studies was between 39.0% and 49.2% (Hogben et al., 2005; M. E. Rogers et al., 2007). Meanwhile, the percentage of healthcare practitioners who used EPT “half or more than half of the time” or “frequently” was between 24.0% and 27.1% (Hogben et al., 2005; M. E. Rogers et al., 2007). Note that both studies were conducted before EPT was formally legalized in NYS in 2009 and in a city that has made significant efforts to promote EPT use (Andre Kiesel, 2022; Oliver et al., 2016). The current rate of EPT use by healthcare practitioners (i.e., the proportion of index patients who are given EPT for their sex partners) throughout NYS remains somewhat unclear but is likely around or above 25.0% given the previous literature (Hogben et al., 2005; M. E. Rogers et al., 2007) and consultation with experts (see methods). Once healthcare practitioners have decided to use EPT, the second decision is whether to provide med-in-hand EPT or a prescription. It is not
clear whether med-in-hand EPT is superior to prescription EPT based on current evidence (Oliver et al., 2016). However, because prescription EPT requires an additional pharmacy visit (by the index patient or sex partner), it is likely that med-in-hand EPT is able to treat sex partners faster than prescription EPT (Nemeth & Schillinger, 2019; Oliver et al., 2016; Schillinger, 2018). It allows sex partners to take treatment without going to a pharmacy first, potentially increasing the probability of treatment and decreasing the time to treatment. As such, med-in-hand EPT is likely used instead of prescription EPT whenever it is available (Ferreira et al., 2013; Hsii et al., 2012; Kissinger, 2014). Therefore, the choice to use med-in-hand EPT depends more on availability. This typically depends on whether a payer is present (to pay for the medication) since the recipient sex partner is not present to pay for themselves (Andre Kiesel, 2022).

Studies show that using EPT rather than partner referral may reduce the probability of reinfection among index patients and increase the probability of treatment of sex partners (Ferreira et al., 2013; Gannon-Loew et al., 2017; Kissinger & Hogben, 2011; Schillinger et al., 2016; Shiely et al., 2010). Omitting the testing requirement for sex partners reduces the time between index patient diagnosis and sex partner treatment, and it may result in treatment for sex partners who would otherwise not have been tested at all (Ferreira et al., 2013; Golden et al., 2015; Kissinger et al., 2005). However, there remains an opportunity to estimate the change in the number of diagnoses alongside underlying chlamydia prevalence (the proportion of the population infected at a given time) that may result from an increase in EPT use relative to partner referral use. There is also a need to quantify other consequences of changes in EPT use, such as a potential increase in the
number of females with undiagnosed pelvic inflammatory disease (PID) from missed opportunities for clinical examination when given EPT rather than partner referral and whether this might offset the benefits derived from EPT.

This study used a simulation model to investigate these related questions. The model estimated the impact of two strategies aimed at strengthening EPT implementation on the total number of annual chlamydia diagnoses over a one-year period compared with a base run assuming no change in EPT use among young adult males and females living in NYS. In NYS, the number of chlamydia diagnoses increased 15.0% from 2012 to 2019 across all ages (Sexually Transmitted Infections Surveillance Report, 2019). As of 2019, NYS ranked 9th in terms of rate of chlamydia cases per 100,000 population (Table 2. Chlamydia—Reported Cases and Rates of Reported Cases by State, Ranked by Rates, United States, 2019, 2021)17. NYS was selected for this study due to its large study population and the availability of data and inputs needed to simulate the model. This included scientific literature regarding EPT set in New York City (Oliver et al., 2016; Slutsker et al., 2020). It was also possible to request publicly unavailable surveillance data on diagnoses (needed for calibration of the model) from the NYS Department of Health Office of Sexual Health & Epidemiology. In addition, NYS is similar to most states in the US in terms of its past EPT promotion activities, which do not include expensive statewide programs like California’s medication purchase program, or extensive promotion of EPT as seen in Washington state (Andre Kiesel, 2022; Gift et al., 2011; Kovaleski et al., 2016). Therefore, strategies to strengthen EPT implementation in NYS and their impact on diagnoses and underlying
prevalence are likely to be generalizable to many other states where similar efforts are also being considered.

The model used in this study examined two strategies to strengthen EPT implementation. The first strategy was to increase the proportion of sex partners given EPT rather than partner referral. The second strategy was to increase the proportion of EPT recipients that are given med-in-hand rather than prescription EPT. The primary outcome was the number of overall diagnoses that resulted from each strategy. Secondary outcomes included the number of diagnoses of sex partners due to partner referrals, underlying chlamydia prevalence, and the number of undiagnosed PID infections among females.
METHODS

Analytical Overview

A system dynamics simulation model was used to estimate the impact of two strategies that changed the proportion of EPT use versus partner referral and med-in-hand EPT use versus prescription EPT use. Outcomes were measured with each strategy and compared to the base case with no change in EPT use or med-in-hand EPT use. This study utilized a 10-year system dynamics model. The model used aggregate data from New York State on the number of chlamydia diagnoses for the years 2013-2017 to simulate outcomes for the period 2018-2023. The model estimated the change in the total number of diagnoses of heterosexually acquired chlamydia infections during Year 5 with each of two strategies to strengthen EPT implementation. The first five years [Year -5 (2014) through the end of Year 0 (2018)], were for calibration and modeling the system absent any policy interventions. The latter five years, [Year 1 (2019) through Year 5 (2023)], comprised the strategy phase-in period. The number of cumulative annual diagnoses during Year 5 was compared to the baseline scenario, which simulated current conditions with no change in inputs. Year 5 was assessed alone because this provided an evaluation window far removed from any unintended feedback effects and because policymakers frequently consider outcomes in one-year increments (see Time Structure of Model, below). The model was run once in the base run and once with altered inputs to represent the start of the two strategies to strengthen EPT implementation.

Numerous experts were consulted during several stages of this study, including 18 key informants to inform decisions about model development. First, individuals with an
understanding of treatment options for sex partners of index patients diagnosed with chlamydia helped to identify the probability of EPT use versus partner referral and med-in-hand EPT use versus prescription EPT use as possible options for improving EPT effectiveness at reducing diagnoses and prevalence. Second, experts with knowledge of past promotion efforts to increase EPT use helped to quantify the feasible increase in these aspects that was possible for these two strategies. Third, these same experts were asked to weigh in on the appropriate phase-in period for each strategy. Fourth, experts with knowledge of EPT and chlamydia treatment options reviewed the structure of the model. Finally, individuals with a methodological understanding of system dynamics and stock and flow modeling provided invaluable input during structural design, validation, and calibration of the model.

Population

The model was built to simulate the spread and control of chlamydia among the entire young adult population of NYS. It included 1,983,517 individuals aged 18-24 years, residing in NYS and regardless of sexual activity and sex of sex partner (males=1,004,753 and females=978,764) (2010: Populations and People, 2011). Population counts were derived from the 2010 US Census counts for these ages and by biological sex. The model included individuals aged 18–24 years because this age group is most impacted by chlamydia infection, and there is rich literature investigating chlamydia transmission and treatment among this age cohort within and outside NYS (Chlamydia Screening in Women (CHL), 2019; Schillinger et al., 2005; Ueda et al., 2020). Several groups were not accounted for in this model. First, all modeled individuals were assumed to be exclusively sexually
active with members of the opposite sex. This assumption was made because individuals with same-sex sex partners are likely to have lower rates of EPT use. The Centers for Disease Control and Prevention (CDC) treatment guidelines previously recommended that men who have sex with men (MSM) be referred for clinical examination whenever possible (Expedited Partner Therapy, 2021). The CDC released updated guidance in 2021 to recommend that “shared clinical decision-making regarding EPT for MSM” be used (Guidance on the Use of Expedited Partner Therapy in the Treatment of Gonorrhea, 2021).

There is no guidance or research to date available regarding the use of EPT for women who have sex with women. Additionally, females with same-sex sex partners likely make up a small proportion of individuals at risk of becoming infected with chlamydia, although this group is in need of further study (Gorgos & Marrazzo, 2011; Singh et al., 2011). Transgender individuals were not specifically accounted for in the model because the surveillance data used to calibrate input values included only binary sex at birth. This meant that calibration of a model with transgender individuals would have been highly speculative. For all these reasons and to control the scope of this study, individuals with same-sex sex partners and transgender individuals were not modeled.

**Model Outcomes**

The primary outcome for each strategy was the total number and percentage change in the number of cumulative annual chlamydia diagnoses that occurred in the 52 weeks of Year 5 with each strategy (see below for details on EPT improvement strategies), as compared to the base run with no strategies. A diagnosis was defined as a positive diagnostic exam, regardless of whether it was a true or false positive. Modeled individuals
could have multiple diagnoses. Secondary outcomes included the number of female sex partners with undiagnosed PID (both overall and specifically due to having been given EPT and missing a chance for clinical evaluation), the number of diagnoses due to partner referrals (a subset of all diagnoses), and the change in underlying chlamydia prevalence (the proportion of all modeled individuals in the *Infected* health state).

**EPT Strategies**

The first strategy was to increase the probability that EPT was used by healthcare practitioners rather than partner referral to treat sex partners. This involved a 5%-point increase in the proportion of index partners given EPT from 25% to 30% over a 1-year phase-in period (Year 1 to 2). A 5%-point increase was determined to be a realistic target for an EPT increase for all NYS over a one-year phase-in period in consultation with experts. However, this may be a conservative estimate since studies in other states have found larger increases in EPT where EPT use has been actively promoted by the state. For example, EPT use increased from 30.6% to 55.9% when intensive one-on-one training sessions with healthcare practitioners were provided in Maryland (Milkovich et al., 2021).

The second strategy involved increasing the probability that EPT was offered as med-in-hand rather than as prescription EPT from a base proportion of 30% to 45% over a six-month phase-in period. This input, also derived from expert recommendations, was more in line with estimates from national studies. For instance, when promotion was mixed with prepared med-in-hand EPT packets in Washington state it increased providers’ use of med-in-hand EPT from 39.0% to 65.0% (Golden et al., 2015). Med-in-hand EPT
involves direct delivery of medication to sex partners by the index patient, which further streamlines EPT by not requiring sex partners to visit a pharmacy to fill a prescription. Giving med-in-hand EPT rather than prescription EPT is believed to increase the probability of treatment before reinfection could occur, thereby increasing EPT's effectiveness without diverting any patients from partner referral (Expedited Partner Therapy, 2021; Ferreira et al., 2013; Schillinger, 2018). The shorter phase-in period for the second strategy was due to the nature of the policy changes required to increase EPT med-in-hand. This assumption was made in consultation with two experts as well as analysis of interviews with state health department staff and directors who had implemented similar policies (Andre Kiesel, 2022). Such policy changes might involve a shift in insurance rules or an update to the patient definition used to determine eligibility for the Health Resources and Services Administration's 340B Drug Pricing Program. These changes could occur more suddenly than EPT promotion among healthcare practitioners, although the process to adopt these initial policy changes might take longer (Andre Kiesel, 2022).

**Model Structure**

The model used in this study was a “stock and flow” simulation. This modeling approach is distinct from agent-based simulation models, which track individual autonomous agents (modeled individuals who make decisions independent of other agents) through their interactions (Rahmandad & Sterman, 2008). Behavioral choices made by agents are based on a set of rules that guide their decisions (Garcia, 2005). Agent-based models allow researchers to include different types of agents in their models, which are modeled individuals in agent-based models. For example, a model could include agents
with multiple concurrent sex partners and other agents who have only monogamous relationships. Study outcomes for each type of agent can therefore be assessed in agent-based simulations (Garcia, 2005). In contrast, stock and flow simulations categorize modeled individuals into aggregate “stocks” (these may be thought of as containers or buckets with modeled individuals inside) (Anderson et al., 1991; Blower et al., 1991; Rahmandad & Sterman, 2008). A stock holds modeled individuals to represent that these individuals are of a certain status – for example, a stock may contain all infected individuals. Modeled individuals within stocks are assumed to be homogeneous in every way and to adhere to the population average (regardless of whether such individuals could exist in real life). Instead of modeling specific behavioral choices, stock and flow models include mathematical formulas that use variables to calculate the rate of flow (via transition states) between different stocks (also known as health states). This presents a change in the status of modeled individuals as they transition (e.g., from infected to uninfected). Because individuals in stocks are presumed to be homogeneous, they also share the same average propensity for all transitions between stocks (Rahmandad & Sterman, 2008).

There were a few key advantages to using a stock and flow model rather than an agent-based simulation in this study. First, using a stock and flow model allowed for efficient calculations of a complex system with more feedback effects and a broader scope than would be possible using an agent-based model given the same computational resources (Rahmandad & Sterman, 2008). Second, stock and flow models allowed for easy calculation of the aggregate outcomes that this study aimed to estimate, including total
diagnoses and underlying chlamydia prevalence. Finally, using a stock and flow model allowed for extensive sensitivity analysis with thousands of runs using randomized input variable values because of the negligible computational power required for each run.

Figure 1 displays the relationship between the three health states in the model, which are depicted as boxes with borders. Also included in the figure are transition states, which are the pathways between health states depicted as double-sided lines with arrows denoting the direction in which modeled individuals could transition. Finally, variables controlled the probability of any transition occurring and are depicted in Figure 1 as labels without borders that connect to transition states with blue arrows.

The model structure was based on the susceptible-infected-susceptible (SIS) model of infectious disease, which describes the epidemiological transmission of infections as a system in which recovered individuals are not immune and return to a susceptible status (i.e., uninfected and able to become infected) (Anderson et al., 1991; Hethcote, 1989; Stekler et al., 2005). The model was divided into three sections: incidence, screening, and treatment. The section for incidence is visible at the top of the model in Figure 1. It included variables for the transmission among sex partners of modeled individuals moving from Susceptible unexposed to Susceptible exposed, as well as variables to define how Susceptible exposed individuals transitioned to the Infected health state when they contracted chlamydia from their infected sex partners. The screening section is visible on the upper right side of Figure 1. It calculated the overall probability that individuals in the Infected health state would be screened and diagnosed to become index patients. Finally, the
treatment section of the model is visible at the bottom of Figure 1. This section calculated the probability of treatment for index patients given a diagnosis via screening, as well as the probability of treatment among sex partners using either partner referral or EPT. The treatment of index patients and sex partners in the treatment section was also tied to the \textit{Become unexposed} transition pathway shown in the top left of Figure 1. In this way, chlamydia control efforts (screening, partner referral, and EPT) pushed modeled individuals towards the left-hand side of the model, while the transmission of chlamydia between sex partners pushed modeled individuals to the right-hand side.

\textit{Time Structure of Model}

The model had a time period of ten years, which included Years -4 through 0 (before implementation of two strategies to improve EPT) and Years 1 through 5 (after implementation). Years -4 through 0 were for calibration to the historical data and corresponded to the years 2014-2018 (see \textit{Data Source and Model Inputs}). Years 1 through 4 (corresponding to 2019-2022) provided time for the impact of each strategy to be realized in the model before assessing the outcomes. All outcomes were assessed during Year 5 (corresponding to 2023). This allowed for comparison between the two strategies and the base run after feedback effects had been resolved. Feedback effects are shifts in the distribution of modeled individuals in the model which occur in response to changes in input variables. While the model was carefully calibrated to produce realistic outcomes in the long term, the external validity of these immediate feedback effects could not be verified. Therefore, model outcomes were assessed far removed from these possibly unrealistic feedback effects. Outcomes were assessed during a single year (Year 5) because
policymakers typically consider year end performance measures, and it was decided in consultation with an expert that such an estimation would be valuable. The model had a time step of one week for a total of 520 weeks. A one-week time step was chosen because it was deemed unlikely that more than one event (i.e., diagnosis of index patients and treatment of sex partners) in the model could occur within one week. The two strategies were implemented starting in week 261, which was the first week of Year 1. Each strategy also had a phase-in period during which the relevant inputs transitioned linearly from their base values to their final implementation values. The phase-in periods reflected the likely real-world implementation of the two strategies, which could not feasibly occur instantaneously according to expert conversations (see EPT Improvement Strategies for an explanation of the specific phase-in periods). Measuring outcomes in Year 5 also allowed comparisons to be made far removed from the phase-in periods and any potentially unrealistic feedback effects.

Model Validation

The model was validated according to best practices, as previously established in predictive modeling and system dynamics literature (Oliva, 2003; Sterman, 2002; Weinstein et al., 2003). To assess behavioral anomalies and structural validity, key inputs were assessed using a range of possible values in Monte Carlo sensitivity analysis (Oliva, 2003; Sterman, 2002). Additionally, experts (n = 16) with an understanding of the progression of health states of individuals infected with chlamydia reviewed the model during development. These experts helped to establish whether the necessary health states were sufficient to assess transition probabilities independently, a key assumption of
Markov chain models (Caro et al., 2012; Gilks et al., 1996; Siebert et al., 2012). The model was also tested under extreme inputs from every input variable (see Table 6) to ensure that the model behaved realistically. For example, significantly increasing the probability of screening eliminated chlamydia from the population, along with a dramatic decrease in condom use (one of the input variables that influences transmission between sex partners), caused a significant increase in chlamydia prevalence and diagnoses.

Data Source and Model Inputs

The model was calibrated using historical data provided by the NYS Department of Health Office of Sexual Health and Epidemiology (De-Identified Aggregated NYS STI Surveillance Data. (December 4th, 2020). Office of Sexual Health & Epidemiology. Sent by Request; Data Not Publicly Available., n.d.). The data were unpublished aggregate data provided by request. These data included the number of chlamydia diagnoses for males and females aged 18-24 in NYS and were used to calibrate the model's input values. The historical data used for calibration were for the years 2014-2018, which corresponded to Years -4 through Year 0 in the model. Years 1 through 5 corresponded to 2019 through 2023. All other inputs were derived using a combination of previous literature, expert interviews, and assumptions by the author. Table 6 includes a list of inputs used in the model, values used for each input for males and females with lower and upper bounds for sensitivity analysis, and references for each input. The appendix includes further details about model inputs and sources as well as the aggregate data used for calibration. Calibration was completed while keeping all inputs at or within a 0.05 absolute value
difference (for inputs that were probabilities) of their respective values identified in the existing literature.

Integration of Sex Differences in the Model

The model used different inputs for males and females to account for sex differences in certain variables. This separation allowed for estimating outcomes separately for males and females in the model. Females had fewer sex partners on average (Drumright et al., 2004; Gift et al., 2011; Niccolai et al., 2011), a lower probability of asymptomatic chlamydia infection (Barbee et al., 2014; Chacko et al., 2004; Chan et al., 2016; Chlamydia Screening in Women (CHL), 2019; Screening Recommendations and Considerations Referenced in Treatment Guidelines and Original Sources, 2021; De Vries et al., 2006; Farley et al., 2003; Golden et al., 2005; Kissinger et al., 2005; Korenromp et al., 2002; Ku et al., 2002; Miller et al., 2004; Mosure et al., 1997; Patel et al., 2018; Paxton et al., 1998; Schillinger et al., 2005), a lower probability of extragenital infection (anorectal and oropharyngeal) (Chan et al., 2016; Danby et al., 2016; Jones et al., 2019; Patton et al., 2014; Trebach et al., 2015), and a higher probability of getting screening for chlamydia because males were not targeted in national screening guidelines by the CDC (Chacko et al., 2004; Chlamydia Screening in Women (CHL), 2019; Farley et al., 2003; Hengel et al., 2013). Additionally, females were susceptible to PID, while males were not (Haggerty et al., 2010; Kumar et al., 2021; Ong et al., 2017). The probability of PID development was based on the time a female remained infected and untreated, regardless of whether she was given EPT or partner referral. It was assumed that males never developed PID because previous research had established that this was unlikely or poorly understood (Y.-S. Lee & Lee, 2013; Westrom, 1996).
Sensitivity Analysis

Monte Carlo sensitivity analysis was used, which involved simultaneously varying all input variables across their lower and upper bounds as listed in Table 6. This was done to assess the robustness of the study results against uncertainty in these input values. The minimum and maximum values of the outputs were calculated, along with the standard deviation of the 10,000 sensitivity-run output values.
RESULTS

Table 7 presents the values and percentage changes from the base run for primary and secondary outcomes during Year 5 with the two strategies in place to strengthen EPT implementation. All outcomes were reported for the base run (without intervention) and once for each of the two strategies. In the base run, a total of 4,751 female and 8,334 male sex partners were diagnosed from partner referrals during Year 5 of the simulation. This was 18.0% of all diagnoses in the base run during Year 5 (the remaining diagnoses were due to screening efforts). In the base run, EPT use was associated with 167 female sex partners with PID left undiagnosed due to missed opportunities for clinical examination, and there were 1,206 PID cases overall during Year 5.

Figure 2 displays trendlines for the number of total annual diagnoses during each year in the base run and each of the two strategies from the beginning of Year -4 to the end of Year 5. In the base run, the number of cumulative annual diagnoses during Year 5 increased 0.1% from 66,468 to 72,765 from the number of diagnoses during Year 1 (the first year during which the strategies to improve EPT were implemented), with 6,297 additional annual diagnoses (Figure 2 and Table 7).

Compared to the base run, an increase in the proportion of index patients given EPT from 25% to 30% over a one-year phase-in period in the first strategy was associated with a decrease in cumulative annual chlamydia diagnoses during Year 5 of 2.6% to 36,978 and 1.9% to 21,236 among female and male sex partners, respectively (Table 7). Meanwhile, the number of sex partners diagnosed from partner referrals was 6.0% lower at 4,468
among female sex partners and 6.6% lower at 7,780 among male sex partners as compared to the base run.

Increasing the proportion of EPT use also resulted in 205 females with PID left undiagnosed due to missed opportunities for clinical examination, an increase of 22.6% from the base run in Year 5 (Table 7). However, the overall number of females with newly acquired PID decreased by 3.8% in Year 5 relative to the base run. This was due to a reduction in untreated females with chlamydia. Underlying prevalence (taking the average of 52 weekly values in Year 5) was 2.6% lower among females and 1.8% lower among males in Year 5 compared to the base run. This change in underlying prevalence was less than the associated decrease in the number of annual diagnoses for each sex during Year 5.

In the second strategy, increasing the proportion of EPT recipient index patients given med-in-hand EPT from 30% to 45% over a six-month phase-in period resulted in a 1.1% and 0.8% decrease in chlamydia diagnoses among female and male sex partners, respectively (Table 7). A total of 172 females with PID were left undiagnosed after being given EPT in the second strategy during Year 5, which was a slight increase of 3.2% compared to the base run.
DISCUSSION

This study investigated two strategies that may strengthen EPT implementation and estimated the degree of change in chlamydia diagnoses and other outcomes associated with each strategy among young adults aged 18-24 years with heterosexually acquired chlamydia infections in NYS. Increasing the proportion of index patients who were given EPT rather than partner referral by 5%-points was associated with a decrease in the number of cumulative annual diagnoses in Year 5. This decrease was greater compared to the decrease resulting from increasing the proportion of EPT recipient index patients who were given med-in-hand EPT rather than prescription EPT by 15%-points. Previous literature had demonstrated that EPT could improve treatment outcomes for sex partners and reduce the probability of reinfection for index patients (Ferreira et al., 2013; Golden et al., 2015). This study expanded on these findings by showing how these improvements in treatment outcomes might impact chlamydia diagnoses at the population level for a large and populous state.

This study also provided additional insight into the unintended consequences of two strategies to strengthen EPT implementation, such as a reduction in diagnoses from fewer partner referrals and changes in incidence of PID. Past systematic reviews have noted that further research was needed into the impact of increased EPT use on the number of females who might have undiagnosed PID due to a missed opportunity for clinical examination (Expedited Partner Therapy, 2021; Ferreira et al., 2013). This study found that, while the specific number of females treated with EPT saw an increase in undiagnosed PID, the overall benefits of reducing chlamydia prevalence resulted in fewer cases of PID in
the entire population under the first strategy of increasing EPT use. This means that the concerns of healthcare practitioners regarding using EPT identified in previous research are supported by this study. Specifically, healthcare practitioners in survey research have stated that they may avoid using EPT because it may miss potential PID among female sex partners (Gannon-Loew et al., 2017). However, this study also found that increased EPT use may result in a lower incidence of PID in the overall population due to the lower underlying prevalence of chlamydia. In other words, the reduction in the prevalence of PID in the overall population was enough to make up for the increase in PID prevalence specifically among sex partners. This means that state health department staff hoping to increase EPT use are also correct in saying that the benefits would outweigh the unintended consequences (Andre Kiesel, 2022).

Of the two strategies tested, increasing the proportion of sex partners given EPT instead of partner referral had a greater impact on diagnoses than increasing the proportion of EPT recipients who were given med-in-hand instead of prescription EPT. In other words, the improvements in time to treatment and the probability of treatment brought by EPT alone (compared to partner referral) were more impactful than the incremental increase in these factors going from prescription EPT to med-in-hand EPT. However, this was partly due to the reduction in the number of sex partners diagnosed after being referred for testing rather than a drop in underlying prevalence. The sex partners who would have been diagnosed along with their treatment when given a partner referral would have been treated regardless, and therefore do not represent a reduction in diagnoses that reflects a drop in underlying prevalence. Policymakers who observe only
the overall number of diagnoses should be aware that some of the decrease in diagnoses brought by increased EPT use may result from fewer tests given because of fewer partner referrals. However, the difference between the decrease in diagnoses and the decrease in underlying prevalence was small and increasing EPT use had the bigger impact of the two strategies on both diagnoses and prevalence. In addition, the decrease in the total number of annual diagnoses of sex partners in the first strategy compared to the base run was proportionately greater for male sex partners than for female sex partners. This difference was because a greater proportion of male diagnoses were due to partner referrals, while females were more likely to be diagnosed because of chlamydia screening relative to males.

Shifting EPT to using med-in-hand rather than prescriptions represented an improvement in EPT effectiveness in terms of reducing the number of diagnoses and underlying prevalence. While this improvement in effectiveness was smaller than in the first strategy, the second strategy did have a benefit. Unlike in the first strategy, increasing med-in-hand use improved the number of diagnoses and underlying prevalence without a significant increase in undiagnosed PID among females. This was because increasing med-in-hand use improved the treatment effectiveness of EPT without reducing the number of partner referrals (and clinical visits by female sex partners). The small increase in the number of females with PID was due to a decrease in the probability that female sex partners would seek treatment when they were given med-in-hand EPT rather than a prescription. However, the reduction in diagnoses that resulted from this strategy was less than that resulting from increasing the proportion of index patients given EPT. This study found that increasing med-in-hand relative to prescription EPT would also lead to a
decrease in diagnoses, but that this decrease would be smaller than simply increasing the use of EPT relative to partner referral. This finding helps to clarify a gap in previous EPT literature in which the intervention was often studied using med-in-hand rather than prescription EPT, and these two types of EPT use were rarely considered separately (Ferreira et al., 2013).

This analysis had several limitations. By relying on previous literature to supply inputs for analysis, it was possible these inputs could not be applied specifically to the NYS population. This study utilized sensitivity analysis to provide estimates robust to variations in the inputs to mitigate this limitation. This study also assumed only heterosexual activity among young adults aged 18–24 living in NYS, limiting generalizability to those outside this age range, location, or with same-sex sex partners. The assumption about sex of sex partners was made for three reasons. First, practice guidance in effect at the time of analysis emphasized that EPT should not be considered a routine partner management strategy for individuals not exclusively engaged in heterosexual activity (Expedited Partner Therapy, 2021; Handsfield et al., 2006). These guidelines existed because there were concerns that same-sex sex partners have a heightened risk of comorbidities (Expedited Partner Therapy, 2021). As a result of those guidelines, the number of same-sex sex partners given EPT was deemed to be low. Second, it is important to limit the scope of any model wherever possible while allowing the central research question to be answered. Third, the methodology employed by this study relied heavily on previous research for model inputs. There was very little research on EPT use for individuals with same-sex sex partners, and several significant assumptions would have been necessary to study this
population. Transgender individuals were also not specifically accounted for in the model because the surveillance data used to calibrate input values included only binary sex at birth. Future research is needed to replicate this study with more diverse sex, individuals with sex partners of the same sex, and age groupings. These vulnerable populations are sorely understudied. Another limitation was that sequelae other than PID were not considered in this analysis because untreated infections of chlamydia have the same propensity to lead to downstream health conditions, regardless of whether the failure to treat occurred after an attempted partner referral or an attempted EPT treatment. Therefore, estimating the impact of increased EPT use on more than one type of sequelae would not have been meaningful, but readers may infer that sequela other than PID would have the same proportionate changes in their changing prevalence as those estimated for PID.

CONCLUSION

This study utilized a modeling approach to investigate two different strategies to strengthen EPT implementation. The impact of the two strategies on annual chlamydia diagnoses, underlying prevalence, and the number of females with PID in Year 5 (five years after the start of implementation) were estimated. The results provide important insights into the value of different targets for policies meant to strengthen EPT implementation so that policymakers may make informed decisions. This study demonstrated that EPT is likely superior to partner referral in terms of population-wide outcomes, including the total number of diagnoses and underlying chlamydia prevalence. While giving EPT to some index patients may delay diagnosis of PID among their female sex partners, the reduction in
underlying chlamydia prevalence brought by increased EPT use is expected to reduce the overall number of females with PID. Therefore, policymakers seeking to promote EPT should focus on promoting its use over partner referral, although it is beneficial to provide EPT as med-in-hand rather than a prescription if that is feasible as well.
TABLES AND FIGURES

Table 6. Input variable values for chlamydia infection and sources with lower and upper bounds used in the sensitivity analysis

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Susceptible unexposed</td>
<td>831,081</td>
<td>853,148</td>
<td>Calibration</td>
</tr>
<tr>
<td>Susceptible exposed</td>
<td>41,533</td>
<td>42,636</td>
<td>Calibration</td>
</tr>
<tr>
<td>Infected</td>
<td>106,150</td>
<td>108,969</td>
<td>Calibration</td>
</tr>
<tr>
<td>Condom use probability</td>
<td>0.38 (0.33, 0.43)</td>
<td>0.48 (0.43, 0.53)</td>
<td>(Chlamydia Screening in Women (CHL), 2019)</td>
</tr>
<tr>
<td>Probability of screening if asymptomatic</td>
<td>0.00 (0.00, 0.00)</td>
<td>0.00 (0.00, 0.00)</td>
<td>(Chlamydia Screening in Women (CHL), 2019)</td>
</tr>
<tr>
<td>Mean number of sex partners given diagnosis</td>
<td>1.20 (1.15, 1.25)</td>
<td>1.25 (1.20, 1.30)</td>
<td>(Gift et al., 2011)</td>
</tr>
<tr>
<td>Probability of partner change</td>
<td>0.02 (0.00, 0.03)</td>
<td>0.02 (0.00, 0.03)</td>
<td>(De Vries et al., 2006; Glick et al., 2012)</td>
</tr>
<tr>
<td>Proportion asymptomatic</td>
<td>0.75 (0.70, 0.80)</td>
<td>0.85 (0.80, 0.90)</td>
<td>(Chlamydia Screening in Women (CHL), 2019; Farley et al., 2003; Schillinger et al., 2005)</td>
</tr>
<tr>
<td>Probability sexually active</td>
<td>0.80 (0.75, 0.85)</td>
<td>0.65 (0.60, 0.70)</td>
<td>(Ueda et al., 2020)</td>
</tr>
<tr>
<td>Prevalence</td>
<td>0.05 (0.00, 0.10)</td>
<td>0.03 (0.00, 0.08)</td>
<td>(K. M. Kreisel et al., 2021; Schillinger et al., 2005)</td>
</tr>
<tr>
<td>Incidence with infected partner</td>
<td>0.10 (0.05, 0.15)</td>
<td>0.10 (0.05, 0.15)</td>
<td>(Althaus, Heijne, et al., 2012; Althaus, Turner, et al., 2012; Lin et al., 1998; Quinn et al., 1996; Tu et al., 2011)</td>
</tr>
<tr>
<td>Sensitivity of screening exam</td>
<td>0.97 (0.85, 1.00)</td>
<td>0.97 (0.85, 1.00)</td>
<td>(Gaydos, 2005; Watson et al., 2002)</td>
</tr>
<tr>
<td>EPT prescription treatment probability</td>
<td>0.41 (0.36, 0.77)</td>
<td>0.41 (0.36, 0.77)</td>
<td>(Oliver et al., 2016; Slutsker et al., 2020)</td>
</tr>
<tr>
<td>Input name</td>
<td>Female (low, high)</td>
<td>Male (low, high)</td>
<td>Source</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>--------------------</td>
<td>------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>EPT med-in-hand treatment probability</td>
<td>0.53 (0.48, 0.80)</td>
<td>0.53 (0.48, 0.80)</td>
<td>(Kissinger et al., 2005, 2006; Oliver et al., 2016)</td>
</tr>
<tr>
<td>Prevalence among sex partners</td>
<td>0.60 (0.55, 0.65)</td>
<td>0.60 (0.55, 0.65)</td>
<td>(Khan et al., 2005)</td>
</tr>
<tr>
<td>Probability infection clears when untreated</td>
<td>0.09 (0.04, 0.14)</td>
<td>0.09 (0.04, 0.14)</td>
<td>(Geisler et al., 2013a; Golden et al., 2000; Korenromp et al., 2002)</td>
</tr>
<tr>
<td>Proportion opposite sex</td>
<td>0.96 (0.91, 1.00)</td>
<td>0.96 (0.91, 1.00)</td>
<td>(Lansky et al., 2015)</td>
</tr>
<tr>
<td>Mean time to treatment partner referral</td>
<td>2.75 (2.70, 2.80)</td>
<td>2.75 (2.70, 2.80)</td>
<td>(Estcourt et al., 2015; Menon-Johansson et al., 2006)</td>
</tr>
<tr>
<td>Mean time to treatment EPT</td>
<td>1.70 (1.65, 1.75)</td>
<td>1.70 (1.65, 1.75)</td>
<td></td>
</tr>
<tr>
<td>Probability of screening if partner referral</td>
<td>0.60 (0.55, 0.65)</td>
<td>0.60 (0.55, 0.65)</td>
<td>(Gift et al., 2011; Golden et al., 2005; Hogben &amp; Kissinger, 2008; Kissinger et al., 2005; Termoreshuizen, 1997)</td>
</tr>
<tr>
<td>Probability of treatment if diagnosed</td>
<td>0.60 (0.55, 0.65)</td>
<td>0.60 (0.55, 0.65)</td>
<td>(Gift et al., 2011; Golden et al., 2005; Hogben &amp; Kissinger, 2008; Kissinger et al., 2005; Termoreshuizen, 1997)</td>
</tr>
<tr>
<td>Probability of screening (symptomatic)</td>
<td>0.07 (0.06, 0.07)</td>
<td>0.07 (0.06, 0.07)</td>
<td>(Chacko et al., 2004; Datta et al., 2007; Farley et al., 2003; Torrone et al., 2014)</td>
</tr>
<tr>
<td>Proportion med-in-hand</td>
<td>0.30 (0.25, 0.35)</td>
<td>0.30 (0.25, 0.35)</td>
<td>Assumption</td>
</tr>
<tr>
<td>Probability of infection among EPT treated</td>
<td>0.60 (0.55, 0.65)</td>
<td>0.60 (0.55, 0.65)</td>
<td>Assumption</td>
</tr>
<tr>
<td>Prevalence</td>
<td>0.04 (0.00, 0.09)</td>
<td>0.04 (0.00, 0.09)</td>
<td>(Chacko et al., 2004; Datta et al., 2007; Termoreshuizen, 1997)</td>
</tr>
<tr>
<td>Input name</td>
<td>Female (low, high)</td>
<td>Male (low, high)</td>
<td>Source</td>
</tr>
<tr>
<td>--------------------------------------------------------</td>
<td>--------------------</td>
<td>-----------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Proportion EPT use</td>
<td>0.50 (0.45, 0.55)</td>
<td>0.50 (0.45, 0.55)</td>
<td>Farley et al., 2003; Torrone et al., 2014)</td>
</tr>
<tr>
<td>Probability of PID if untreated</td>
<td>0.12 (0.02, 0.24)</td>
<td>-</td>
<td>Assumption (Haggerty et al., 2010; Kumar et al., 2021; Price et al., 2013)</td>
</tr>
<tr>
<td>Probability of infertility within 1 year given PID</td>
<td>0.10 (0.05, 0.15)</td>
<td>-</td>
<td>(Chesson et al., 2021; Haggerty et al., 2010; Kumar et al., 2021)</td>
</tr>
<tr>
<td>Extragenital testing given extragenital infection and testing at any site</td>
<td>-</td>
<td>0.55 (0.50, 0.60)</td>
<td>(Patton et al., 2014)</td>
</tr>
<tr>
<td>Prevalence of extragenital infection</td>
<td>-</td>
<td>0.09 (0.04, 0.14)</td>
<td>(Jones et al., 2019)</td>
</tr>
</tbody>
</table>

Notes: EPT = expedited partner therapy. Med-in-hand = medicine in hand. PID = pelvic inflammatory disease. MSM = men who have sex with men. Population parameters with their source given as “calibration” (number of individuals in the population and each health state) refer to the NYS population of males and females aged 18–24 years old. Population parameters do not have lower and upper bounds because these were not varied in the sensitivity analysis.
Table 7. Results of the simulation model with the number and percent change from the base run in the number of diagnoses during Year 5 resulting from each strategy, diagnoses due to partner referral, prevalence, and PID among females for chlamydia, with lower and upper bounds of sensitivity analysis

<table>
<thead>
<tr>
<th></th>
<th>Base run (Low, High)</th>
<th>Strategy 1: EPT use (Low, High)</th>
<th>EPT use % - change</th>
<th>Strategy 2: Med-in-hand (Low, High)</th>
<th>Med-in-hand % - change</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening diagnoses</td>
<td>21,652 (9,593, 33,823)</td>
<td>21,236 (9,120, 32,821)</td>
<td>-1.9%</td>
<td>21,471 (9,583, 33,316)</td>
<td>-0.8%</td>
</tr>
<tr>
<td>Partner referral</td>
<td>8,334 (3,378, 12,250)</td>
<td>7,780 (3,018, 11,320)</td>
<td>-6.6%</td>
<td>8,241 (3,373, 12,134)</td>
<td>-1.1%</td>
</tr>
<tr>
<td></td>
<td>Prevalence</td>
<td>0.036 (0.017, 0.061)</td>
<td>-1.8%</td>
<td>0.036 (0.017, 0.060)</td>
<td>-0.3%</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening diagnoses</td>
<td>37,978 (13,911, 62,299)</td>
<td>36,978 (12,989, 59,859)</td>
<td>-2.6%</td>
<td>37,554 (13,891, 61,092)</td>
<td>-1.1%</td>
</tr>
<tr>
<td>Partner referral</td>
<td>4,751 (2,329, 6,696)</td>
<td>4,468 (2,119, 6,247)</td>
<td>-6.0%</td>
<td>4,711 (2,327, 6,647)</td>
<td>-0.8%</td>
</tr>
<tr>
<td></td>
<td>Prevalence</td>
<td>0.046 (0.018, 0.080)</td>
<td>-2.6%</td>
<td>0.045 (0.018, 0.078)</td>
<td>-1.1%</td>
</tr>
<tr>
<td>PID cases</td>
<td>1,206 (366, 2,450)</td>
<td>1,160 (345, 2,331)</td>
<td>-3.8%</td>
<td>1,203 (366, 2,410)</td>
<td>-0.3%</td>
</tr>
<tr>
<td>PID cases due to EPT</td>
<td>167 (47, 391)</td>
<td>205 (57, 461)</td>
<td>22.6%</td>
<td>172 (49, 396)</td>
<td>3.2%</td>
</tr>
</tbody>
</table>
Notes: EPT = expedited partner therapy. Med-in-hand = medicine in hand. PID = pelvic inflammatory disease. This table presents the number of diagnoses, the number of diagnoses due to partner referral, prevalence during Year 5 (an average of 52 weekly values), and the number of females with PID that resulted from the base run and each of the two strategies during the fifth year after implementation (which is the final year of the simulation). “PID cases” refers to cases among sex partners only and does not include PID cases among unscreened sexual networks. “PID cases due to EPT” refers to incident cases of PID that occurred within the two weeks after EPT was given to an index patient and the point at which it was assumed female sex partners would seek treatment for symptoms of PID. This is a subset of all PID cases. The percent change is also given and is the difference between the value of each outcome when a strategy was used and the base run. Values in parentheses include the upper (0.95) and lower (0.05) bounds of each variable in the Monte Carlo simulation. The simulation was run repeatedly while varying all inputs simultaneously and randomly across their upper and lower bounds (Table 6) to estimate a distribution of possible values for each outcome.
Figure 2. Simplified Markov chain stock-and-flow diagram.

Notes: This figure presents the three health states in the model as well as the relationship between them, which represents the core of the simulation model. Health states or "stocks" (boxes with borders) represent different health and exposure statuses of modeled individuals. All input variables ultimately influence the probability that individuals in the model moved between health states. Individuals moved between health states by crossing through transition states via "flows" (double-sided straight lines with black arrowheads). Variables connected to blue arrows may count individuals to serve as outputs or (more commonly) represent probability inputs.

Individuals in the *Infected* health state could be screened and tested positive to become *Diagnoses from screening*, and their sex partners became eligible for partner management (EPT or partner referral). If any infected sex partner was left untreated (*Cure without partner treatment*), reinfection could occur (via *Contract infection from partner*). If instead, all partners lost their infection status by any means (EPT, partner referral, or a spontaneous loss of infection), simulated individuals transitioned back to the low-risk *Susceptible unexposed* health state via the *Network cured together* transition state. Individuals infected but unexposed were not explicitly modeled because they could not receive EPT. Individuals went through the *Become exposed* transition state when their sex partners contracted an infection, or when they changed sex partners to a partner who had an infection.
Figure 3. Projected chlamydia diagnoses among males and females over ten years including the base run, increasing EPT use and increasing the use of med-in-hand EPT using state-based case study.
Notes: This figure presents the total number of diagnoses per year from screening between the start of the simulation through the start of the interventions at year 5 and the end of the simulation at year 10. One panel represents diagnoses of females and the other diagnoses of males. A vertical line marks the start of the interventions and is labeled “Intervention start.” Each intervention has a unique phase-in period that begins after the start of the intervention.
References


reduction intervention for African American adolescent girls in juvenile detention centers: a randomized controlled trial. Women & Health, 54(8), 726–749.


Ferreira, A., Young, T., Mathews, C., Zunza, M., & Low, N. (2013). Strategies for partner notification for sexually transmitted infections, including HIV. Cochrane Database of Systematic Reviews, 10.


*Screening recommendations and considerations referenced in treatment guidelines and original sources.* (2021). Centers for Disease Control and Prevention.
https://www.cdc.gov/std/treatment-guidelines/screening-recommendations.htm


1. Overview

This appendix provides details on the health states, transition states, input variables, and intermediate variables (see definitions below) used in the model for my dissertation papers 1 and 2. The reasoning used to estimate the values of input variables based on previous literature is described. Additionally, the mathematical formulas used to determine intermediate variables and to calculate the transition probabilities are provided. This technical appendix may be used to reconstruct the model in Vensim or other simulation software.

The health states and transition states used in the model are described in Section 2 of this appendix. Section 3 is organized into four parts according to the model’s four arms. Three of the arms (Incidence, Screening, and Treatment) estimated the impact of increased expedited partner therapy (EPT) use on chlamydia diagnoses in paper 1. The fourth arm of the model (Cost-effectiveness) uses outputs from the Treatment arm to calculate the cost outcomes for paper 2.

Sections 3.1, 3.2, 3.3, and 3.4 are further divided into two subsections (e.g., 3.1.1 and 3.1.2) detailing each arm’s input and intermediate variables. Input variables have fixed values (unaffected by any other variables in the model) and were determined using previous literature, expert interviews, and assumptions based on known values. The exception is the variable Prevalence. The previous literature estimate (a fixed value presented in Table 8) was used to calibrate the model variable Prevalence during the calibration period (see 3.1.1.5 Prevalence). After the calibration period had elapsed, the
model variable *Prevalence* (no longer fixed to the previous literature estimate) and was allowed to vary freely as an outcome variable. Intermediate variables used the fixed values of the input variables to calculate values needed for further calculation and eventual estimation of transition probabilities. Transition variables determine what proportion of modeled individuals (or the probability that a modeled individual) in one health state transition to another health state in each time step (which was one week). While it would be possible to perform all calculations in the variables that provide the probability that modeled individuals would switch health states using transition states, such formulas would be complex and prone to error from incorporating all input variables in their respective sections. Intermediate variables thus serve to simplify the translation from fixed input variables to the final transition probabilities. They may also incorporate other intermediate variables into their calculations to make different model parts responsive to each other. Finally, section 4 of this appendix includes the number of annual chlamydia diagnoses of males and females aged 18-24 years in New York State (NYS). These data were provided by the NYS Department of Health and were used to calibrate the model along with other values from previous literature.

Table 8 provides the calibrated values of each input variable which were used in the model. Input variables in each of the four sections (3.1.1, 3.2.1, 3.3.1, and 3.4.1) of this technical appendix may be cross-referenced with the *Input Name* column in Table 8. Excerpts from Table 8 are presented with the description of each variable and each of the health states for easy referencing.
Table 8. Input values and sources with lower and upper bounds used in the sensitivity analysis

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Susceptible unexposed</td>
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<td>Infected</td>
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<td>108,969</td>
<td>Calibration</td>
</tr>
<tr>
<td>Condom use probability</td>
<td>0.38 (0.33, 0.43)</td>
<td>0.48 (0.43, 0.53)</td>
<td>(Copen, 2017)</td>
</tr>
<tr>
<td>Probability of screening if asymptomatic</td>
<td>0.00 (0.00, 0.00)</td>
<td>0.00 (0.00, 0.00)</td>
<td>(Chlamydia Screening in Women (CHL), 2019)</td>
</tr>
<tr>
<td>Mean number of sex partners given diagnosis</td>
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<td>1.25 (1.20, 1.30)</td>
<td>(Gift et al., 2011)</td>
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<td>0.02 (0.00, 0.03)</td>
<td>(De Vries et al., 2006; Glick et al., 2012)</td>
</tr>
<tr>
<td>Proportion asymptomatic</td>
<td>0.75 (0.70, 0.80)</td>
<td>0.85 (0.80, 0.90)</td>
<td>(Chlamydia Screening in Women (CHL), 2019; Farley et al., 2003; Schillinger et al., 2005)</td>
</tr>
<tr>
<td>Probability sexually active</td>
<td>0.80 (0.75, 0.85)</td>
<td>0.65 (0.60, 0.70)</td>
<td>(Ueda et al., 2020)</td>
</tr>
<tr>
<td>Input Prevalence</td>
<td>0.05 (0.00, 0.10)</td>
<td>0.03 (0.00, 0.08)</td>
<td>(K. M. Kreisel et al., 2021; Schillinger et al., 2005)</td>
</tr>
<tr>
<td>Incidence with infected partner</td>
<td>0.10 (0.05, 0.15)</td>
<td>0.10 (0.05, 0.15)</td>
<td>(Althaus, Heijne, et al., 2012; Althaus, Turner, et al., 2012; Lin et al., 1998; Quinn et al., 1996; Tu et al., 2011)</td>
</tr>
<tr>
<td>Sensitivity of screening exam</td>
<td>0.97 (0.85, 1.00)</td>
<td>0.97 (0.85, 1.00)</td>
<td>(Gaydos, 2005; Watson et al., 2002)</td>
</tr>
<tr>
<td>EPT prescription treatment probability</td>
<td>0.41 (0.36, 0.77)</td>
<td>0.41 (0.36, 0.77)</td>
<td>(Oliver et al., 2016; Slutsker et al., 2020)</td>
</tr>
<tr>
<td>EPT med-in-hand treatment probability</td>
<td>0.53 (0.48, 0.80)</td>
<td>0.53 (0.48, 0.80)</td>
<td>(Kissinger et al., 2005, 2006; Oliver et al., 2016)</td>
</tr>
<tr>
<td>Prevalence among sex partners</td>
<td>0.60 (0.55, 0.65)</td>
<td>0.60 (0.55, 0.65)</td>
<td>(Khan et al., 2005)</td>
</tr>
<tr>
<td>Probability infection clears when untreated</td>
<td>0.09 (0.04, 0.14)</td>
<td>0.09 (0.04, 0.14)</td>
<td>(Geisler et al., 2013a; Golden et al., 2000;</td>
</tr>
<tr>
<td>Input name</td>
<td>Female (low, high)</td>
<td>Male (low, high)</td>
<td>Source</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>--------------------</td>
<td>------------------</td>
<td>---------------------------------------------</td>
</tr>
<tr>
<td>Proportion opposite sex</td>
<td>0.96 (0.91, 1.00)</td>
<td>0.96 (0.91, 1.00)</td>
<td>Korenromp et al., 2002)</td>
</tr>
<tr>
<td>Mean time to treatment partner referral</td>
<td>2.75 (2.70, 2.80)</td>
<td>2.75 (2.70, 2.80)</td>
<td>(Lansky et al., 2015)</td>
</tr>
<tr>
<td>Mean time to treatment EPT</td>
<td>1.70 (1.65, 1.75)</td>
<td>1.70 (1.65, 1.75)</td>
<td>(Estcourt et al., 2015; Menon-Johansson et al., 2006)</td>
</tr>
<tr>
<td>Probability of screening if partner referral</td>
<td>0.60 (0.55, 0.65)</td>
<td>0.60 (0.55, 0.65)</td>
<td>(Gift et al., 2011; Golden et al., 2005; Hogben &amp; Kissinger, 2008; Kissinger et al., 2005; Termoreshuizen, 1997)</td>
</tr>
<tr>
<td>Probability of treatment if diagnosed</td>
<td>0.60 (0.55, 0.65)</td>
<td>0.60 (0.55, 0.65)</td>
<td>(Gift et al., 2011; Golden et al., 2005; Hogben &amp; Kissinger, 2008; Kissinger et al., 2005; Termoreshuizen, 1997)</td>
</tr>
<tr>
<td>Probability of screening (symptomatic)</td>
<td>0.07 (0.06, 0.07)</td>
<td>0.07 (0.06, 0.07)</td>
<td>(Chacko et al., 2004; Datta et al., 2007; Farley et al., 2003; Torrone et al., 2014)</td>
</tr>
<tr>
<td>Proportion med-in-hand</td>
<td>0.30 (0.25, 0.35)</td>
<td>0.30 (0.25, 0.35)</td>
<td>Assumption</td>
</tr>
<tr>
<td>Proportion subsidized</td>
<td>0.30 (0.25, 0.35)</td>
<td>0.30 (0.25, 0.35)</td>
<td>Assumption</td>
</tr>
<tr>
<td>Probability of infection among EPT treated</td>
<td>0.60 (0.55, 0.65)</td>
<td>0.60 (0.55, 0.65)</td>
<td>Assumption</td>
</tr>
<tr>
<td>Proportion EPT use</td>
<td>0.50 (0.45, 0.55)</td>
<td>0.50 (0.45, 0.55)</td>
<td>Assumption</td>
</tr>
<tr>
<td>Cost of chlamydia treatment (2020 dollars)</td>
<td>26.00 (20.80, 31.20)</td>
<td>26.00 (20.80, 31.20)</td>
<td>(Gift et al., 2011)</td>
</tr>
<tr>
<td>Cost of chlamydia treatment if subsidized (2020 dollars)</td>
<td>0.30 (0.24, 0.36)</td>
<td>0.30 (0.24, 0.36)</td>
<td>(Gift et al., 2011)</td>
</tr>
<tr>
<td>Cost of clinical appointment (2020 dollars)</td>
<td>45.00 (36.00, 54.00)</td>
<td>45.00 (36.00, 54.00)</td>
<td>(Gift et al., 2011)</td>
</tr>
<tr>
<td>Input name</td>
<td>Female (low, high)</td>
<td>Male (low, high)</td>
<td>Source</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>-----------------------------------</td>
<td>--------------------------------</td>
<td>---------------------------------------------</td>
</tr>
<tr>
<td>Cost of time of clinical visit (2020 dollars)</td>
<td>30.00 (24.00, 36.00)</td>
<td>30.00 (24.00, 36.00)</td>
<td>(Gift et al., 2011)</td>
</tr>
<tr>
<td>Cost of PID treatment (2020 dollars)</td>
<td>380.00</td>
<td>-</td>
<td>(Yeh et al., 2003)</td>
</tr>
<tr>
<td>Cost of chronic pelvic pain treatment (2020 dollars)</td>
<td>800.00</td>
<td>-</td>
<td>(Yeh et al., 2003)</td>
</tr>
<tr>
<td>Cost of ectopic pregnancy (2020 dollars)</td>
<td>4,000.00</td>
<td>-</td>
<td>(Yeh et al., 2003)</td>
</tr>
<tr>
<td>Cost of infertility (2020 dollars)</td>
<td>8,000.00</td>
<td>-</td>
<td>(Yeh et al., 2003)</td>
</tr>
<tr>
<td>Probability of PID if untreated</td>
<td>0.12 (0.02, 0.24)</td>
<td>-</td>
<td>(Haggerty et al., 2010; Kumar et al., 2021; Price et al., 2013)</td>
</tr>
<tr>
<td>Probability of infertility given PID</td>
<td>0.10 (0.05, 0.15)</td>
<td>-</td>
<td>(Chesson et al., 2021; Haggerty et al., 2010; Kumar et al., 2021)</td>
</tr>
<tr>
<td>Probability of chronic pelvic pain given PID</td>
<td>0.18 (0.13, 0.23)</td>
<td>-</td>
<td>(Haggerty et al., 2010; Ong et al., 2017)</td>
</tr>
<tr>
<td>Probability of ectopic pregnancy given PID</td>
<td>0.08 (0.03, 0.13)</td>
<td>-</td>
<td>(Haggerty et al., 2010; Ong et al., 2017)</td>
</tr>
<tr>
<td>Extragenital testing rate given extragenital infection</td>
<td>-</td>
<td>0.55 (0.50, 0.60)</td>
<td>(Patton et al., 2014)</td>
</tr>
<tr>
<td>Prevalence of extragenital infection</td>
<td>-</td>
<td>0.09 (0.04, 0.14)</td>
<td>(Jones et al., 2019)</td>
</tr>
</tbody>
</table>

Notes: PR = partner referral; EPT = expedited partner therapy; Med-in-hand = medicine in hand EPT (providing medication to deliver to sex partners rather than a prescription); PID = pelvic inflammatory disease.

All probability values are given for one week, the simulation time step, unless otherwise stated.

Inputs listed as “Calibration” were the initial inputs for the three health states. These values were calibrated using the population of males and females aged 18-24 years living in New York State according to the 2010 United States (U.S.) census. For example, the model estimated the number of infected individuals using the total population, screening rates, prevalence estimates, and diagnoses totals. These values do not have ranges because they were not assessed in the sensitivity analysis. They also do not have specific sources because they were derived during calibration.
Sources listed as "Assumption" were values estimated after consultations with experts in the field. No literature was identified which could provide values for these inputs.

Table 9 lists all intermediate variables in the simulation model used for papers 1 and 2 and the equations used to calculate each intermediate variable. This table is separated into four sections, with one section for each of the four arms of the model. Note that some of the equations reference variables (either input or intermediate) in other arms.
Table 9. List of intermediate variables used in the simulation model with the equations used to calculate each variable, organized by model arm

<table>
<thead>
<tr>
<th>Intermediate variable name</th>
<th>Equation used to calculate intermediate variable</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence arm</strong></td>
<td></td>
</tr>
<tr>
<td>Probability partner receives EPT</td>
<td>EPT treatment rate * Prevalence among sex partners</td>
</tr>
<tr>
<td>Probability partner receives partner referral treated</td>
<td>PR treatment rate * Prevalence</td>
</tr>
<tr>
<td>Probability partner treated</td>
<td>Prob Partner receives EPT + Prob Partner receives partner referral</td>
</tr>
<tr>
<td>Probability partner becomes uninfected without treatment</td>
<td>Prob change partner to uninfected only + Infection clears untreated – (Infection clears untreated * Prob Change partner to uninfected only)</td>
</tr>
<tr>
<td>Probability changing partner to uninfected only</td>
<td>Partner change * (1 – Partner Infected)</td>
</tr>
<tr>
<td>Probability become unexposed</td>
<td>Prob Partner treated + Prob Partner becomes uninfected without treatment – (Prob Partner treated * Prob. Partner becomes uninfected without treatment)</td>
</tr>
<tr>
<td>Probability of switching infected partner</td>
<td>Partner change * Partner Infected</td>
</tr>
<tr>
<td>Probability partner becomes infected</td>
<td>Partner Infected * Prob of infection from partner * Avg. number of partners</td>
</tr>
<tr>
<td>Probability of becoming exposed</td>
<td>Prob Partner becomes infected + Prob Switching partner infected – Prob Partner becomes infected * Prob Switching partner infected)</td>
</tr>
<tr>
<td><strong>Screening arm</strong></td>
<td></td>
</tr>
<tr>
<td>Probability of diagnosis</td>
<td>Sensitivity * (1-Prop Partners of opposite sex) * 3-site/extragenital testing * Prevalence extragenital chlamydia</td>
</tr>
<tr>
<td>Screening rate</td>
<td>(Prob of screening (asymptomatic * (1-Proportion symptomatic)) + (Prob of screening (symptomatic * Prop symptomatic))</td>
</tr>
<tr>
<td>Screening and diagnosis rate</td>
<td>Prob of diagnosis * Screening rate + Sensitivity * Prop. Partners of opposite sex</td>
</tr>
<tr>
<td><strong>Treatment arm</strong></td>
<td></td>
</tr>
<tr>
<td>EPT success</td>
<td>(Prob EPT that is med-in-hand * Med-in-hand success prob) + (Prescription EPT success prob * (1-Prop EPT that is med-in-hand))</td>
</tr>
<tr>
<td>EPT treatment rate</td>
<td>EPT success * Prop EPT use</td>
</tr>
<tr>
<td>Probability of partner treatment</td>
<td>((EPT \text{ treatment rate}) \times \text{Prevalence among sex partners EPT} + (\text{PR treatment rate}))</td>
</tr>
<tr>
<td>PR treatment rate</td>
<td>(\text{Prop PR use} \times \text{Prob of treatment if diagnosed} \times \text{Prob. of diagnosis} \times \text{Prob of screening if referred} )</td>
</tr>
<tr>
<td>PR diagnoses</td>
<td>(\text{Number of partners attempted PR} \times \text{Prob of diagnosis} \times \text{Prob of screening if referred} \times \text{Prevalence among sex partners PR} )</td>
</tr>
</tbody>
</table>

**Cost-effectiveness arm**

| Average cost of medication | \(\text{Price of medication if subsidized} \times \text{Prop 340b} + \text{Price of medication if not subsidized} \times (1-\text{Prop 340b})\) |
| Total EPT treatments | EPT treatments of infected + EPT treatments of uninfected |
| Total medication costs | \(\text{Total EPT treatments} \times \text{Average price of medication}\) |
| Total EPT costs | \(\text{Total EPT medication costs} + \text{EPT sequelae cost}\) |
| Total PR clinic costs | \(\text{Clinical visit costs} \times \text{Total PR clinic visits}\) |
| Total PR costs | \(\text{Total PR clinic costs} + \text{Total PR medication costs} + \text{PR sequelae cost}\) |
| Mean cost of sequelae | \(\text{PID cost} + \text{CPP cost} \times \text{Prob. chronic pelvic pain given PID} + \text{EP cost} \times \text{Prob. ectopic pregnancy given PID} + \text{Infertility cost} \times \text{Prob infertility given PID} + \text{Added sequelae cost for sensitivity}\) |
| EPT cost per sex partner | \(\text{Total EPT Costs} / \text{Total EPT treatments}\) |
| PR cost per sex partners | \(\text{Total PR Costs} / \text{Number of partners attempted PR}\) |
| Incremental cost (c1-c2) | \(\text{PR cost per sex partner} - \text{EPT cost per sex partner}\) |
| EPT effectiveness score | \(\text{EPT treatments of infected} / \text{Total EPT treatments}\) |
| PR effectiveness score | \(\text{Total PR Treatments} / \text{Number of partners attempted PR}\) |
| Incremental effectiveness (e1-e2) | \(\text{PR effectiveness score} - \text{EPT effectiveness score}\) |
| ICER | \(\text{Incremental cost (c1-c2)} / \text{Incremental effectiveness (e1-e2)}\) |

Notes: \(\text{Prob} = \text{probability}; \text{Prop} = \text{proportion}; \text{EPT} = \text{Expedited partner therapy}; \text{PR} = \text{partner referral}; \text{ICER} = \text{incremental cost effectiveness ratio}; \text{PID} = \text{pelvic inflammatory disease}\)
2. Health States and Transition States

Figure 4 provides an overview of the three health states in the model and the five transition states that allowed modeled individuals to transition between the three health states.

*Figure 4: Simplified Markov chain stock and flow diagram including health states and transition states*

Note: This figure displays the three health states (boxes with borders) and five transition states (labels with black-headed arrows) used in the simulation model. The four arms of the model detailed in this appendix calculated the probability of that modeled individuals in each health state would move between health states via the transition states.
### 2.1 Health States

#### 2.1.1 Susceptible unexposed

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Susceptible unexposed</td>
<td>831,081</td>
<td>853,148</td>
<td>Calibration</td>
</tr>
</tbody>
</table>

This health state included modeled individuals who were not exposed to chlamydia via sexual activity with any individual with an infection. This health state included individuals who had no sex partner and individuals who were sexually active but only with sex partners that had no infection among them. Modeled individuals could leave this health state to transition to the Susceptible exposed health state but could not transition directly to the Infected health state from the Susceptible unexposed health state. Modeled individuals could transition to the Susceptible unexposed health state from either of the other two health states.

#### 2.1.2 Susceptible exposed

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Susceptible exposed</td>
<td>41,533</td>
<td>42,636</td>
<td>Calibration</td>
</tr>
</tbody>
</table>

This health state included any modeled individuals exposed to at least one individual with a current chlamydia infection via sexual activity within the last two weeks. Modeled individuals could become exposed either because their existing sex partners became infected or because they switched sex partners to a new sex partner with an ongoing infection. Modeled individuals in this health state could transition either to the
Susceptible unexposed health state by becoming unexposed or to the Infected health state if an infection transmitted from a sex partner.

2.1.3 Infected

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infected</td>
<td>106,150</td>
<td>108,969</td>
<td>Calibration</td>
</tr>
</tbody>
</table>

This health state included modeled individuals that had a chlamydia infection at any anatomical infection site. To move to the Infected health state, modeled individuals had to first become exposed by transitioning to the Susceptible exposed health state. Individuals in the Infected health state could transition back to either of the other two health states. If the modeled individual was treated without their partners receiving treatment or if the modeled individual became uninfected by an immune response (with one or more sex partners left infected), the modeled individuals transitioned to the Susceptible exposed health state. If the modeled individual and all their sex partners became uninfected together (through treatment or immune response), they transitioned to the Susceptible unexposed health state.

2.2 Transition States

2.2.1 Become exposed

This transition state moved modeled individuals from the Susceptible unexposed health state to the Susceptible exposed health state. This could occur either by switching sex partners to an individual with an existing infection or by having existing sex partners becoming infected.
2.2.2 Become unexposed

This transition state moved modeled individuals from the *Susceptible exposed* health state to the *Susceptible unexposed* health state. This transition could occur either by changing sex partners such that no current sex partners have an infection or by having any sex partners with an infection receiving treatment or becoming uninfected without treatment (through an immune response).

2.2.3 Contract infection from partner

This transition state moved modeled individuals from the *Susceptible exposed* health state to the *Infected* health state. This transition used the probability of chlamydia transmission between sex partners, given one sex partner was infected (being exposed) while adjusting for condom use.

2.2.4 Cure without partner treatment

This transition state moved modeled individuals from the *Infected* health state to the *Susceptible exposed* health state. This transition occurred whenever a modeled individual was treated without treating all sex partners who had an infection. As a result, the modeled individual became uninfected (and susceptible to reinfection) and returned to the *Susceptible exposed* health state.

2.2.5 Network cured together

This transition state moved modeled individuals from the *Infected* to the *Susceptible unexposed* health state. This transition represented the success of treatment efforts and natural immune responses, leaving the index patient and all currently infected sex partners uninfected. The index patient and any sex partners could become uninfected either by
treatment or through becoming uninfected by a natural immune response. If any sex partners failed to become uninfected when the index patient became uninfected, the modeled individual instead transitioned alone to the Susceptible exposed health state via the Cured without partner treatment transition state. When an index patient and all their infected sex partners became uninfected, both the index patient and the sex partners that became uninfected would transition to the Susceptible unexposed health state using the Network cured together transition state. This is because all infected individuals in any specific sexual network are in the Infected health state. In this way, a single diagnosis of an index patient could lead to curing multiple individuals, and modeled individuals in the Infected health state did not need to be diagnosed by screening to become uninfected. When multiple individuals became uninfected in this way, a time delay was used depending on the time to treatment for sex partners treated with either EPT or partner referral. The index patient used this transition state first, and any infected sex partners used this transition state only after they became uninfected (through treatment or immune response).

3. Model variables and structure

The following sections detail the four arms of the model, including incidence in section 3.1, screening in section 3.2, treatment in section 3.3, and cost-effectiveness in section 3.4. Each section has a figure (Figures A3-A6) that provides an overview of that arm of the model and how input and intermediate variables relate to each other. Each section also includes subsections for input and intermediate variables. Input variables are listed in Table 8 and are fixed inputs used to calculate the intermediate variables. In the sections describing input variables (section 3.1.1, 3.2.1, 3.3.1, and 3.4.1), the literature and any
assumptions used to define each variable’s value are described. Intermediate variables are listed in Table 9 and are defined by calculations that use either input variables or other intermediate variables. In the sections describing intermediate variables (sections 3.1.2, 3.2.2, 3.3.2, and 3.4.2), each variable includes the equation used to calculate that intermediate variable.

3.1 Incidence Arm

The incidence arm controls the rate at which uninfected individuals gain infected sex partners (become exposed) and the rate at which exposed individuals themselves become infected when an infection is transmitted from one of their infected sex partners. Figure A3 displays variables and their interactions in the Incidence arm. Key variables included the number of sex partners of males and females, the probability of sexual activity, and the probability of infection transmission between sex partners. The incidence arm interacts with a section of the treatment arm, which allows for the treatment of sex partners to prevent the transmission of infection to modeled individuals in the incidence section. Variables from the treatment arm used in the Incidence arm appear in grey at the top of Figure A3.
Notes: Variables appear as black text labels or as grey text labels. Variables with blue backgrounds are input variables that provide the probability values needed to calculate intermediate variables. The variables in the incidence arm control the rate of flow from the leftmost health state Susceptible unexposed towards the rightmost health state Infected.
3.1.1 Input variables of the incidence arm

3.1.1.1 Incidence with infected partner

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence with infected partner</td>
<td>0.10 (0.05, 0.15)</td>
<td>0.10 (0.05, 0.15)</td>
<td>(Althaus, Heijne, et al., 2012; Althaus, Turner, et al., 2012; Lin et al., 1998; Quinn et al., 1996; Tu et al., 2011)</td>
</tr>
</tbody>
</table>

This variable, along with the condom use variable, was used to calculate the probability that modeled individuals transitioned from the Susceptible exposed to the Infected health state. It is defined as the probability of transmission from one infected sex partner to one uninfected sex partner within one week, given average sexual activity. This variable is unlikely to be different over time because it is fundamentally about the biological probability of an infection occurring. Research that estimates this variable is ethically problematic. It involves diagnosing individuals to confirm their infection status and not treating them (ideally, not even telling them they are infected to ensure they maintain their normal behavior).

Four published articles were identified. Lin et al. (1998) estimated this value at 0.129 for transmission from an infected partner by clinically examining women who had been (exclusively) exposed to infected male partners in the Boston area (Lin et al., 1998). This study was limited to females only. Tu et al. (2011) used a Markov model to estimate transmission probability on a per act basis. They provided multiple estimates depending on
the actual chlamydia prevalence to account for uncertainty in the value of the prevalence variable used in their model. Given a value of chlamydia prevalence of 0.04 (most similar to the prevalence value used in this study – see 3.1.1.5 Input Prevalence) and without condom use, the per act transmission was estimated to be 0.22 (Tu et al., 2011). Althaus et al. (2012) compared different methods of estimating transmission probability by assessing vulnerability to different inputs (Althaus, Turner, et al., 2012). Quinn (1996) evaluated transmission rates by testing members of both sexes and found that transmission was similar between male-female and female-male transmission (Quinn et al., 1996).

3.1.1.2 Probability of partner change

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of partner change</td>
<td>0.02 (0.00, 0.03)</td>
<td>0.02 (0.00, 0.03)</td>
<td>(De Vries et al., 2006; Glick et al., 2012)</td>
</tr>
</tbody>
</table>

This variable defines the probability that any individual in the model will change to a new sex partner in one week. This variable includes the probability that individuals with no sex partner will gain a sex partner, as well as the probability that individuals with an existing partner(s) get a different or additional sex partner(s). This variable is essential for setting the transition from the Susceptible unexposed to the Susceptible exposed health states. This move makes modeled individuals eligible for diagnosis and treatment. This variable also played a role in modeled individuals becoming unexposed when they changed to sex partners without an infection.
De Vries et al. (2006) conducted a cost-effectiveness analysis and reported that the number of sex partners per year was 4.23 for males and 3.89 for females (in a Dutch population) (De Vries et al., 2006). Glick used four United States (U.S.) wide surveys and two Seattle-based surveys to estimate differences in sexual behaviors between males, females, and men who have sex with men (MSM). They found that the number of sex partners had a median of one sex partner for males and females aged 18-24 years but that this ranged from 0-5 for females and from 0-99 for males (Glick et al., 2012). Dividing these values into one-week increments, a range between 0.0127 and 0.813 new partners per week can be established. The base value used in the model was 0.015 partners per week for both males and females after calibration.

3.1.1.3 Probability sexually active

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability sexually active</td>
<td>0.80 (0.75, 0.85)</td>
<td>0.65 (0.60, 0.70)</td>
<td>(Ueda et al., 2020)</td>
</tr>
</tbody>
</table>

This variable is defined as the probability that any individual in the model was sexually active in the previous week. It acts as a gate for modeled individuals into the model’s right side, where exposure, infection, and treatment occur. Individuals who are not sexually active could not become susceptible or infected in this model. This variable is disaggregated by sex. Ueda et al. (2020) estimated this value separately for males and females aged 18-24 years. Values reported in that paper are pasted below (Lei & South, 2021; Ueda et al., 2020).
Table 10. Distribution of males and females in different frequency of sex acts as provided by Ueda (2020)

<table>
<thead>
<tr>
<th>Sexual activity frequency</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not sexually active</td>
<td>30.9</td>
<td>19.1</td>
</tr>
<tr>
<td>1-2 sex acts per yr.</td>
<td>8.9</td>
<td>10.1</td>
</tr>
<tr>
<td>1-3 sex acts per month</td>
<td>22.7</td>
<td>18.6</td>
</tr>
<tr>
<td>Weekly sex acts or more</td>
<td>37.4</td>
<td>52.1</td>
</tr>
</tbody>
</table>

Table 10 presents the proportion of males and females aged 18-24 years that fell into each category of sexual act frequency in Ueda et al. (2020). For example, 30.9% of males in Ueda et al. (2020) were not sexually active within the previous year. There is a minimum and maximum probability of sexual activity when calculating the number of sex acts per week because the authors provided ranges for two of their categories. For example, individuals who engaged in 1-2 sex acts per year had their proportion (8.9 for males and 10.1 for females) either divided by 52 (once per year) at the minimum or of 26 (twice per year) at the maximum. For the category listed weekly sex acts or more, it was assumed that the maximum number of weekly sex acts was seven. After calculations, the minimum probability of sexual activity per week from Ueda et al. (2020) for males was 0.43, and the maximum was 0.68. The minimum possible probability value for females was 0.57, and the maximum was 0.77. Given this finding, setting the probability of sexual activity per week near 0.60, with females higher than males, was deemed plausible. This value was used after calibration.

3.1.1.4 Condom use probability

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
</table>
This variable defines the probability that condoms are used and used correctly for all sex acts in the previous week. Condom use was included in this model to allow for a change in behavior over time to explain changes in incidence. Condom use protected against transmission at a flat rate – modeled individuals who used condoms correctly could not become infected. This variable was disaggregated by sex because males and females report different condom use patterns. The citation given is likely an overestimate because it was not adjusted down for failures (condom broke, condom used for only part of the time during sex acts, etc.). The included table did not break out effective condom use completely. This variable could be as low as 0.19 (males), and 0.10 (females), and these values were used to define condom use by males and females aged 18-24 years (Copen, 2017).

3.1.1.5 Input Prevalence

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Input Prevalence</td>
<td>0.05 (0.00, 0.10)</td>
<td>0.03 (0.00, 0.08)</td>
<td>(K. M. Kreisel et al., 2021; Schillinger et al., 2005)</td>
</tr>
</tbody>
</table>

There were two variables for prevalence, including the input variable *Input Prevalence* (described here and included in Table 8) and *Prevalence* (described below in section 4.1 Calibration). *Input Prevalence* was based on previous literature estimates of the underlying chlamydia prevalence (see below). *Input Prevalence* was used as the target...
value of the model variable *Prevalence*. In other words, *Input Prevalence* was not used directly as a model parameter, and it was not used in any calculations directly.

Two literature sources were used to estimate *Input Prevalence*, separately among males and females (K. M. Kreisel et al., 2021; Schillinger et al., 2005). The following citations differed in their exact values. However, underlying chlamydia prevalence appears to be higher among females and is likely below a value of 0.10 for both sexes. The most recent estimate with the best methodology was by Kreisel et al. (2021), who estimated male prevalence at 0.026 and female prevalence at 0.048 (K. M. Kreisel et al., 2021). These values for prevalence were used to set the starting health state distribution and in calibration.

3.1.1.6 Probability of PID if untreated

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of PID if untreated</td>
<td>0.12 (0.02, 0.24)</td>
<td>-</td>
<td>(Haggerty et al., 2010; Kumar et al., 2021; Price et al., 2013)</td>
</tr>
</tbody>
</table>

This variable defines the probability that a prevalent female will develop pelvic inflammatory disease (PID) in a week if not treated. This variable works together with the time to treatment variables and *Prevalence* in the model to determine the number of females who develop PID in a time step. Haggerty et al. (2010) conducted a literature review and found that a proportion of between 0.02 and 0.05 of females developed PID within a 2-week period between diagnosis and treatment (Haggerty et al., 2010). Price et al. (2013) provided another literature review with different follow-up periods and
calculated a probability of developing PID between 0.12 and 0.16 per chlamydia infection (within six months of the chlamydia infection) (Price et al., 2013). The rate of PID incidence within one week for untreated females is therefore below 0.10 and likely below 0.05. In this study, sensitivity analysis considers a wide range for this variable between 0.02 and 0.16 per chlamydia infection (Kumar et al., 2021).

3.1.2 Intermediate variables of the incidence arm

3.1.2.1 Probability partner receives EPT

This variable gives the probability that any sex partner of a diagnosed index patient will receive EPT for treatment in one week, either in med-in-hand or prescription form. The equation used to calculate this variable multiplies the input Proportion EPT use (input in the treatment arm) with Prevalence to calculate the probability that a sex partner who is exposed but themselves uninfected will have their partners treated by EPT. Combined with other intermediate variables, this variable serves to boost the probability that modeled individuals will become unexposed.

Equation: EPT treatment rate * Prevalence among sex partners

3.1.2.2 Probability partner receives partner referral

This variable was used to determine the probability of becoming unexposed for modeled individuals due to the treatment of their sex partners using partner referral. It utilized a variable from the treatment arm and Prevalence to determine the probability that an infected individual would be treated using partner referral. Combined with other intermediate variables, this variable boosts the probability that modeled individuals will become unexposed.
Equation: P.R. treatment rate*Prevalence

3.1.2.3 Probability partner treated

Given possible EPT treatment or partner referral treatment, this variable calculates the probability that sex partners could be treated, causing the modeled individual to become unexposed. This variable added these two probabilities to a total probability because these are non-sequential mutually exclusive events (sex partners either receive EPT or partner referral).

Equation: Prob partner receives EPT + Prob partner receives partner referral

3.1.2.4 Probability partner becomes uninfected without treatment

This variable encodes the probability that an infected sex partner will become uninfected without treatment in a week through an immune response. Together with the probability of partner treatment, this variable helps define the overall probability that modeled individuals will become unexposed.

Equation: Probability change partner to uninfected only + Infection clears untreated - (Infection clears untreated * Prob. change partner to uninfected only)

3.1.2.5 Probability changing partner to uninfected only

This variable calculated the probability that a modeled individual with an infected sex partner changed sex partners to an uninfected partner. Combined with other intermediate variables, this variable boosts the probability that modeled individuals will become unexposed.

Equation: Partner change * (1 - Prevalence)
3.1.2.5 Probability become unexposed

This variable calculated the probability that a modeled individual became unexposed (moving from *Susceptible exposed* to *Susceptible unexposed*) for any of 3 reasons. These reasons included their sex partners becoming uninfected without treatment, their sex partners becoming uninfected with treatment, and the modeled individual changing sex partners to either have no sex partners or to having only partner(s) with no infections (counted in the variable *Partner becomes uninfected without treatment*). The equation calculates the probability of each event happening individually and subtracts the multiple of both event probabilities to allow partners to become unexposed for any combination of reasons (allowing modeled individuals to become unexposed if any one or more than one of these events occurred).

Equation: Prob. partner treated + Prob. partner becomes uninfected without treatment - (Prob. partner treated * Prob. partner becomes uninfected without treatment)

3.1.2.6 Probability of switching infected partner

This variable calculated the probability that modeled individuals changed or added sex partners to having an infected sex partner(s). It considers the probability of partner change (which is different for males and females) and the probability that a new sex partner is infected (which is the population prevalence of chlamydia).

Equation: Partner change * Prevalence

3.1.2.7 Probability partner becomes infected

This variable provided the probability that an existing uninfected sex partner became infected, thereby exposing the modeled individual. It is tied to the probability that the sex partners of modeled individuals have other sex partners of their own and that the
sex partners of the modeled individual become infected from exposure to their other sex partners. Therefore, three separate events must occur. First, the sex partner must have additional sex partners beyond the modeled individual (subtracting one from the average number of sex partners). Second, those sex partners must already be infected with chlamydia. Third, there must be a transmission of the infection to the sex partner of the modeled individual.

Equation: Prevalence * Prob of infection from partner * (Mean number of partners – 1)

3.1.2.8 Probability of becoming exposed

This variable combines the previous two variables (3.1.2.6 Probability of switching partner infected and 3.1.2.7 Probability of partner becomes infected) to calculate the final probability that a modeled individual will become exposed to chlamydia in one week.

Equation: Prob partner becomes infected + Prob switching partner infected – (Prob. partner becomes infected * Prob switching partner infected)

3.2 Screening Arm

The screening arm controls the rate at which infected individuals receive screening and diagnoses of chlamydia. Figure A4 displays the variables and their interactions in the screening arm. Important variables in this arm include the screening rates for males and females with symptomatic or asymptomatic infections. Additionally, the screening sensitivity controls whether individuals who are both infected and screened are diagnosed. The final variable in this section is Screen and diagnosis rate, which is then multiplied by the number of individuals in the Infected health state to determine the number of diagnoses from screening. Diagnosed individuals are then passed to the treatment arm, where the
probability that they and their partner(s) receive treatment is calculated. The screening arm also controls the emergence of sequelae among untreated sex partners.

Figure 6. Screening Arm Overview

3.2.1 Input variables of the screening arm

3.2.1.1 Extragenital testing given extragenital infection

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extranagenital testing rate given extragenital infection</td>
<td>-</td>
<td>0.55 (0.50, 0.60)</td>
<td>(Patton et al. 2014, Chan et al., 2016)</td>
</tr>
</tbody>
</table>

This variable is defined as the probability of extragenital (infections at anatomical sites other than at the urogenital site) testing given a male has only an extragenital
infection (anorectal and pharyngeal) with no urogenital infection. This variable serves to depress the successful screening rate by incorporating a probability that an extragenital infection will be missed (given the infection was only present at an extragenital site and no testing was conducted at any extragenital site). Patton et al. (2014) used the STD Surveillance Network and found that 0.317 of men who have sex with men (MSM) were tested for pharyngeal chlamydia and 0.459 for anorectal chlamydia (Patton et al., 2014). Chan et al. (2016) provided valuable prevalence estimates at extragenital sites for males and females (Chan et al., 2016).

3.2.1.2 Proportion asymptomatic

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion asymptomatic</td>
<td>0.75 (0.70, 0.80)</td>
<td>0.85 (0.80, 0.90)</td>
<td>(Chlamydia Screening in Women (CHL), 2019; Farley et al., 2003; Schillinger et al., 2005)</td>
</tr>
</tbody>
</table>

This variable is defined as the proportion of individuals with an infection who have no symptoms. This variable has a powerful influence on the screening rate for individuals in the model because having symptoms makes individuals much more likely to get screening. Individuals without symptoms are subject to general screening recommendations, while those with symptoms may get tested to diagnose the cause. Previous literature has established that females are more likely to show symptoms of a chlamydia infection than males in most cases. Still, the degree of difference between the two sexes in their probability of showing symptoms varies by source. Farley et al. (2003)
estimated that 0.609 and 0.877 of males and females were asymptomatic (Farley et al., 2003). Schillinger et al. (2005) noted that 0.06 of their all-male sample had no symptoms (Schillinger et al., 2005). De Vries et al. (2006) gave a value of 0.3 for males and 0.5 for males for symptomatic infections (De Vries et al., 2006). After calibration, this study used a value of 0.85 for this variable for males and 0.75 for females.

3.2.1.3 Probability of screening symptomatic

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of screening</td>
<td>0.07 (0.06, 0.07)</td>
<td>0.07 (0.06, 0.07)</td>
<td>(Chacko et al., 2004; Datta et al., 2007; Farley et al., 2003; Torrone et al., 2014)</td>
</tr>
</tbody>
</table>

This variable defines the probability that individuals with symptomatic infection (symptoms present) will get testing. This variable is disaggregated by sex – males and females with symptoms are assumed to have the same probability of getting testing if symptomatic. Together with the Probability of screening asymptomatic and the Proportion asymptomatic variables, this variable determines the overall screening rates for males and females in the model. No literature was identified that estimated the probability of testing given symptomatic infection, but some published results did provide the overall screening rate for females regardless of symptoms. Given the estimates for the probability that infections are symptomatic, it is possible to calculate a possible value for the screening rate among symptomatic individuals from the overall screening rate. After calibration, the average screening rate for females (regardless of the presence of symptoms) had to match
the estimates for the proportion of females tested for chlamydia every week. The Healthcare Effectiveness Data and Information Set (HEDIS) includes a measure of screening among females aged 16-24 years, which was between 0.48 and 0.53 females tested within one year (Chlamydia Screening in Women (CHL), 2019). Dividing by 52 weeks, a value around 0.0096 per week may be accurate. This value was used in calibration for the overall screening rate. The probability of testing symptomatic individuals was assumed to be 0.065 per week.

3.2.1.4 Probability of screening asymptomatic

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of screening if asymptomatic</td>
<td>0.00 (0.00, 0.00)</td>
<td>0.00 (0.00, 0.00)</td>
<td>(Chlamydia Screening in Women (CHL), 2019)</td>
</tr>
</tbody>
</table>

Individuals who had an infection that was not symptomatic were still able to receive chlamydia screening. This variable interacts with the Proportion asymptomatic variable and the Probability of screening symptomatic variable to set the overall screening rates. This variable is disaggregated by sex because females are subject to a stronger general screening recommendation than males. For females, there are indicators to show the percentage of females screened each year. This variable is harder to quantify for males, given the lack of research or published estimates. However, it stands to reason that the asymptomatic screening rate for males is very small because males are not subject to the same general screening recommendation (Chlamydia Screening in Women (CHL), 2019; Hoover et al., 2014). Given that the overall screening rate for females is likely around
0.0096 per week, that a proportion of 0.75 of females are likely asymptomatic (see 3.2.1.2 Proportion symptomatic) and assuming that symptomatic females are tested at a rate of 0.065 per week (see 3.2.1.3 Probability of screening symptomatic), it is possible to calculate the screening rate for asymptomatic females. This variable was given a value of 0.002 for the proportion of females screened per week after calibration. No source was found to estimate this variable for males, and it was assumed that asymptomatic males were screened at a rate of one-quarter that of females at 0.0005 screened per week. Note that males were tested at a higher rate in the model from partner referrals, which ignored the presence of symptoms.

3.2.1.5 Sensitivity of screening

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity of screening exam</td>
<td>0.97 (0.85, 1.00)</td>
<td>0.97 (0.85, 1.00)</td>
<td>(Gaydos, 2005; Watson et al., 2002)</td>
</tr>
</tbody>
</table>

This variable was defined as the probability that an individual with a chlamydia infection will test positive if they are tested. This study’s model does not differentiate between different testing methodologies (polymerase chain reaction, nucleic acid amplification tests, etc.), so this variable is given as an average sensitivity of all testing methods given their proportion of use. The estimates from two studies varied from 0.85 to 0.97 (Gaydos, 2005; Watson et al., 2002). A value of 0.90 was used after calibration.
3.2.2 Intermediate variables of the screening arm

These variables use the values provided by the input variables in section 3.2.1 to calculate the number of infected individuals diagnosed by screening eventually. The number of diagnoses is calculated as a separate variable (rather than being directly calculated in the transition state) for calibration purposes. The number of diagnoses from screening was matched to the annual historical data provided by the New York State Department of Health (see Section 4 of this appendix).

3.2.2.1 Probability of diagnosis

This variable calculates the probability that an individual that is infected and screened will be diagnosed. It incorporates the average sensitivity input (3.2.1.5 Sensitivity of screening) and three variables to control for extragenital testing. This inclusion accounted for the fact that a screening test may miss infections if they are exclusively at extragenital (oropharyngeal or anorectal) sites, and the individual is not tested at those sites. The incorporation of extragenital testing variables depresses the diagnosis rate.

Equation: Sensitivity*(1-Prop. extragenital) *Extragenital testing * Prevalence extragenital chlamydia

3.2.2.2 Screening rate

The screening rate variable calculates the probability that an infected individual will be screened. This variable is disaggregated for males and females. Symptomatic individuals are more likely to receive screening, and females are much more likely to be screened if they have an asymptomatic infection relative to males.

Equation: (Probability of screening (asymptomatic * (1-Proportion symptomatic)) + (Probability of screening (symptomatic * Proportion symptomatic)
3.2.2.3 Screening and diagnosis rate

This variable multiplies the previous two intermediate variables (3.2.2.1 Screening rate and 3.2.2.2 Probability of diagnosis) together to calculate the probability that any individual infected with chlamydia will be both screened and diagnosed. This variable does not include diagnoses from partner referrals, which are added to the total number of diagnoses in the treatment arm. This variable is calculated separately for males and females.

Equation: Probability of diagnosis * Screening rate

3.3 Treatment Arm

The treatment arm of the model controls the treatment of index patients and their sex partners. Figure A4 presents the variables and their interactions in the treatment arm. Input variables are used to calculate the number of index patients who are treated with and without their sex partner(s) as well as the number of sex partners treated with and without their index patient. In this way, index patients either move along the Cure without partner treatment transition state or the Network cured together transition state. It is also possible in the treatment arm for index patients and sex partners to become uninfected without treatment through an immune response.
3.3.1 Input variables of the treatment arm

3.3.1.1 EPT med-in-hand treatment probability

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPT med-in-hand treatment</td>
<td>0.53 (0.48, 0.80)</td>
<td>0.53 (0.48, 0.80)</td>
<td>(Kissinger et al., 2005, 2006; Oliver et al., 2016)</td>
</tr>
</tbody>
</table>

This variable is defined as the probability of successful eventual treatment of any sex partner after an index patient is given med-in-hand EPT for that sex partner. Med-in-hand success probability is hard to estimate because the sex partner may never present
themselves at a pharmacy to pick up their medication. Estimates varied from 0.558 to 0.795 from different self-report studies. A compelling estimate around 0.558 came from Kissinger et al. (2005) and Kissinger et al. (2006) as their samples were aged under 24 (Kissinger et al., 2005; Oliver et al., 2016). It is reasonable to assume that sex partners receiving med-in-hand are more likely to take any medication than are sex partners who must first fill a prescription. Therefore, we may also compare this variable to EPT prescription success probability, which should be smaller.

3.3.1.2 EPT prescription treatment probability

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPT prescription treatment probability</td>
<td>0.41 (0.36, 0.77)</td>
<td>0.41 (0.36, 0.77)</td>
<td>(Oliver et al., 2016; Slutsker et al., 2020)</td>
</tr>
</tbody>
</table>

This variable was defined as the probability, given a diagnosed index patient is provided with an EPT prescription for their sex partner, that the sex partner will be treated using medications filled by that EPT prescription. Recent research projects estimated this probability by attaching claim identifiers to the EPT prescriptions to determine what proportion of prescriptions were filled. Slutsker et al. (2020) estimated this value at 0.41 using claim I.D.s (providing index patients an I.D. number that their sex partners report to their pharmacy to confirm that the prescription was filled), while in Oliver et al. (2016) 0.77 of index patients reported treatment of their sex partners (Oliver et al., 2016; Slutsker et al., 2020). Self-reports by index patients may not reflect the true probability of sex partner treatment. It is also possible this value is different in different populations.
3.3.1.3 Mean number of sex partners given diagnosis

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean number of sex partners given diagnosis</td>
<td>1.20 (1.15, 1.25)</td>
<td>1.25 (1.20, 1.30)</td>
<td>(Gift et al., 2011)</td>
</tr>
</tbody>
</table>

This variable defines the average number of sex partners for diagnosed index patients, which sets the number of sex partners treated by partner referral or EPT. This variable is related to the probability of partner change and the probability that individuals are sexually active. Literature investigating the treatment of sex partners has estimated this value. For example, Gift et al. (2011) used an estimated value of 1.4 sex partners for females and 1.9 sex partners for males diagnosed with chlamydia (note these values are higher than the average number of partners in the general population) (Gift et al., 2011). For this study, the average number of partners is the same for partner referral and EPT. Hence, it influences both partner treatment strategies’ overall effectiveness but does not differentiate between EPT and partner referral.

3.3.1.4 Mean time to treatment partner referral

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean time to treatment partner referral</td>
<td>2.75 (2.70, 2.80)</td>
<td>2.75 (2.70, 2.80)</td>
<td>(Estcourt et al., 2015; Menon-Johansson et al., 2006)</td>
</tr>
</tbody>
</table>

This variable gave the time delay between index patient clinic visit (diagnosis) and final treatment of any sex partners treated with partner referral. This variable did not influence the success of partner referral, but it did influence the probability that an index
patient would become reinfected by their sex partners, and it did allow females to develop sequelae before treatment. Estcourt et al. (2015) found that a proportion of 0.450 of sex partners was treated within six weeks (this study was conducted in the United Kingdom) (Estcourt et al., 2015). Menon-Johansson et al. (2006) were not evaluating the time to treatment for sex partners, but rather the time saving from utilizing a text messaging notification system for diagnosed index patients. But the authors did provide an estimated median of 15 days to treatment for the regular arm and 8.5 days for the text messaging arm. The present study’s model used a value of 2.0 weeks for this variable (Menon-Johansson et al., 2006).

3.3.1.5 Mean time to treatment EPT

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean time to treatment</td>
<td>1.70 (1.65, 1.75)</td>
<td>1.70 (1.65, 1.75)</td>
<td>(Estcourt et al., 2015; Menon-Johansson et al., 2006)</td>
</tr>
</tbody>
</table>

This variable is defined as the time from diagnosis of an index patient to final treatment of any sex partners treated using EPT. There is very little research measuring this time directly. Some research has provided the percent of partners treated by a certain time after the index patient received EPT (prescription or med-in-hand). For example, Kissinger et al. (2005) reported that a proportion of 0.558 of heterosexual males reported treatment of their sex partners within one month (the exact follow-up period is unclear in this paper) (Kissinger et al., 2005). However, this estimate includes individuals who did not accept EPT, while the current study’s model includes a failure rate separately. It stands to
reason that the time to treatment is lower for EPT than for partner referral (because sex partners must not visit a clinic for testing). The model used a value of 1.7 weeks.

3.3.1.6 Probability of screening if partner referral

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of screening if partner referral</td>
<td>0.60 (0.55, 0.65)</td>
<td>0.60 (0.55, 0.65)</td>
<td>(Gift et al., 2011; Golden et al., 2005; Hogben &amp; Kissinger, 2008; Kissinger et al., 2005; Termoreshuizen, 1997)</td>
</tr>
</tbody>
</table>

This variable defined the probability that sex partners of index patients treated with partner referral would get tested for chlamydia. While limited research has estimated this value directly, the probability of eventual treatment for sex partners receiving partner referral is well researched. Together with the variable Probability of treatment if diagnosed (described in 3.3.1.7), it is possible to calculate a value for the Probability of screening if referred because both events must occur for partner treatment. Hogben & Kissinger (2008) conducted a literature review and found a range between 0.30 and 0.55 for the treatment of sex partners (Hogben & Kissinger, 2008). In Golden et al. (2005), 0.52 of sex partners treated with partner referral reported that treatment was “very likely” or better, while Kissinger et al. (2005) estimated this value at 0.35 (Golden et al., 2005; Kissinger et al., 2005). Gift et al. (2011) combined these previous studies and used a value of 0.49 for their simulation study (Gift et al., 2011). Given a probability of treatment of 0.60, a value of 0.60 for this variable produces a probability of treatment given partner referral of 0.36. This is
on the low end of previous estimates, but it is important to note that a one-week time period is used in this model. Assuming that the treatment rate decays over time after initial diagnosis, a probability value of 0.36 is plausible.

3.3.1.7 Probability of treatment if diagnosed

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of treatment if diagnosed</td>
<td>0.60 (0.55, 0.65)</td>
<td>0.60 (0.55, 0.65)</td>
<td>(Gift et al., 2011; Golden et al., 2005; Hogben &amp; Kissinger, 2008; Kissinger et al., 2005; Termoreshuizen, 1997)</td>
</tr>
</tbody>
</table>

This variable defines the probability that any modeled individual will be treated within one week after their diagnosis. This variable was used for index patients diagnosed through screening and sex partners tested and diagnosed with a partner referral. Four previous studies estimated the probability of treatment given partner referral. Together with the Probability of screening if referred these were used to estimate the probability of treatment if diagnosed at 0.60 (see 3.3.1.6 Probability of screening if referred above).

3.3.1.8 Probability infection clears when untreated

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability infection clears when untreated</td>
<td>0.09 (0.04, 0.14)</td>
<td>0.09 (0.04, 0.14)</td>
<td>(Geisler et al., 2013a; Golden et al., 2000; Korenromp et al., 2002)</td>
</tr>
</tbody>
</table>
This variable defined the probability that individuals who have an infection that remains untreated will become uninfected without treatment. This variable applies to individuals in the *Infected* health state, as well as sex partners of modelled individuals in the *Uninfected exposed* health state. Research estimating this variable involves leaving infections untreated to see how long chlamydia infection persists. It stands to reason that the year of study is not important, because this probability is determined by the biology of chlamydia infection. Geisler et al. (2013) found that a proportion of 0.22 of infected individuals did not have an infection after 15 days (Geisler et al., 2013b). Golden et al. (2000) conducted a literature review finding that infected females were generally culture-negative after 60 days, which provides a cut-off point after which female infections must clear in the model (Golden et al., 2000). Korenromp et al. (2002) conducted a literature review to estimate the proportion of infections that are symptomatic but included a mean duration of infection in days which ranged from 26 days among males with chlamydia to 1,112 days among females with chlamydia at the extremes (Korenromp et al., 2002). While studies from any year were assessed, there is high variability in the results and little research to draw on for this variable.

### 3.3.1.9 Prevalence among sex partners

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence among sex partners</td>
<td>0.60 (0.55, 0.65)</td>
<td>0.60 (0.55, 0.65)</td>
<td>(Khan et al., 2005)</td>
</tr>
</tbody>
</table>

This variable is defined as the probability of infection (*Prevalence*) among the sex partners of diagnosed index patients. This variable plays a key role in calculating the
effectiveness of both partner referral and EPT in the model. It is used to calculate both the probability that an EPT treatment will treat an infected sex partner and the probability that partner referral testing will return positive (which may or may not lead to a treatment).

The estimated overall sex partner prevalence of diagnosed index patients is given by Khan et al. (2005) at 0.57 (Khan et al., 2005).

In the model, the overall probability of infection is kept constant, but the prevalence among sex partners eligible for EPT and treated sex partners via partner referral may diverge. The formula to connect the variables for prevalence among sex partners for EPT and partner referral is:

\[
\text{Partner referral partner prev.} = \frac{\text{Overall partner prev.} - \text{EPT partner prev.} \times \text{Proportion of partners EPT}}{1 - \text{Prop. of partners treated EPT}}
\]

Thus, increasing the prevalence among sex partners targeted for EPT is possible without increasing the overall partner prevalence. Similarly, targeting sex partners with a higher probability of infection for EPT reduces the probability of infection among partners given partner referral.

3.3.1.10 Proportion of EPT that is med-in-hand

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion med-in-hand</td>
<td>0.30 (0.25, 0.35)</td>
<td>0.30 (0.25, 0.35)</td>
<td>Assumption</td>
</tr>
</tbody>
</table>

This variable provides the proportion of EPT recipient sex partners who receive med-in-hand EPT rather than partner referral. This variable is subject to modification in one of the strategies examined in paper 1. This variable is also important for calculating the
overall probability that sex partners who receive EPT will eventually be treated because the treatment probabilities are different for med-in-hand and prescription EPT. Discussions with experts in the field helped to estimate that a proportion of 0.30 of EPT recipient sex partners receive med-in-hand, and this was used as the base value for this variable.

3.3.1.11 Proportion EPT use

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion EPT use</td>
<td>0.50 (0.45, 0.55)</td>
<td>0.50 (0.45, 0.55)</td>
<td>Assumption</td>
</tr>
</tbody>
</table>

This variable is the proportion of index patients that receive EPT for their sex partners. One of the strategies to improve EPT implementation evaluated in paper 1 alters this variable to assess the impact of an increase. Discussions with experts in the field estimated that a proportion of 0.25 of index patients receive EPT for their sex partners, and this is used as the base value for this variable. Index patients that do not receive EPT for their sex partners received partner referral instead.

3.3.2 Intermediate variables of the treatment section

3.3.2.1 EPT success

This variable uses the probability of successful treatment for med-in-hand EPT and prescription EPT to calculate an average treatment probability for each sex partner given EPT was used to treat sex partners. This variable also incorporates the estimated proportion of EPT recipient sex partners that receive med-in-hand EPT rather than prescription EPT.
Equation: (Prob EPT that is med-in-hand * Med-in-hand success prob) + (Prescription EPT success prob * (1-Prop. EPT that is med-in-hand))

3.3.2.2 EPT treatment rate

This variable incorporates the probability of EPT being used rather than partner referral to calculate the proportion of all sex partners treated using EPT within one week.

Equation: EPT success*Proportion EPT use

3.3.2.3 Probability of partner treatment

This variable uses the treatment rates for EPT and partner referral (PR) and the prevalence of chlamydia among sex partners to determine the probability of treatment for any infected sex partners using either EPT or partner referral within one week. This variable is an important determinant of the transition state Network cured together (see 2.2.5), which moves modeled individuals from the Infected health state to the Susceptible unexposed health state.

Equation: EPT treatment rate * Prevalence among sex partners EPT + P.R. treatment rate

3.3.2.4 Partner Referral (PR) treatment rate

Like EPT treatment rate, this variable calculates the proportion of all sex partners who are treated with partner referral. In this instance, treatment by partner referral is conceptualized as a referral accepted by the index patient, delivered to their sex partner(s), followed by a prescription being filled by those sex partners, and finally, medication was taken. All these events must occur before a sex partner is treated, and so these variables are multiplied together.

Equation: Proportion PR use * Probability of treatment if diagnosed * Probability of diagnosis * Probability of screening if referred
3.3.2.5 PR diagnoses

This variable is one of few variables in the model which calculates a numerical value rather than a probability. *PR diagnoses* (PR = partner referral) is the number of sex partners diagnosed due to a partner referral from their sex partners (index patients diagnosed in the screening arm of the model). This variable is counted as an output for paper 1. Typically, it is best practice in stock and flow models to calculate the number of individuals only within health states or transition states. However, a numerical value is calculated in this intermediate variable to provide this output. This variable is also added to the total number of diagnoses from screening. In this way, the variable *PR diagnoses* allows sex partners to become index patients themselves, thereby allowing their other sex partners to be treated using partner management (whether EPT or partner referral). This variable is disaggregated for males and females.

Equation: Number of partners attempted PR * Probability of diagnosis * Probability of screening if referred * Prevalence among sex partners PR

3.3.2.6 Time to sex partner treatment

This variable calculated the mean time difference between the index patient visiting a clinic and the treatment of the index patient and all infected sex partners (if partner treatment efforts are successful). The equation of this variable incorporates the proportion of sex partners that receive EPT instead of partner referral to calculate the mean time (in weeks) to the treatment of any sex partners.

Equation: \((\text{Mean time to treat EPT} \times \text{Prop treated by EPT} + \text{Mean time to treat PR} \times (1 - \text{Prop treated by EPT})) / 2\)
3.3.2.7 Index patients treated

This variable is one of few variables in the model which calculates a numerical value rather than a probability. This variable calculated the number of index patients treated in each time step. The Vensim function DELAY1 causes the output from this calculation (the first clause before the comma within the parentheses) to be executed after the delay time has elapsed (defined by the second clause after the comma within the parentheses). This function meant a time delay of \textit{Mean time to treat after diagnosis} between an index patient’s diagnosis and their treatment. The number of index patients treated is calculated immediately after diagnosis. However, these modeled individuals do not transition through the transition states \textit{Cure without partner treatment}, and \textit{Network cured together} until after the time delay has elapsed.

Equation: \text{DELAY1} (\text{Diagnoses including partner referrals*Prob of treatment if diagnosed, Mean time to treat after diagnosis})

3.3.2.8 Partner treated

This variable is also one of few variables in the model which calculates a numerical value rather than a probability. This variable calculated the number of sex partners treated either by EPT or by partner referrals. The Vensim function DELAY1 causes the output from this calculation (the first clause before the comma within the parentheses) to be executed after the delay time has elapsed (defined by the second clause after the comma within the parentheses). There was a time delay (set by the variable \textit{Time to sex partner treatment}) that determined the time between index patient diagnosis and when any sex partners would transition via the \textit{Network cured together} transition state. This time delay
incorporated the proportion of sex partners that receive EPT (see 3.3.2.6 Time to sex partner treatment).

Equation: \( \text{DELAY1} (\text{Diagnoses including partner referrals} \times \text{Prob of partner treatment} \times \text{Mean num partners, Time to sex partner treatment}) \)

3.4 Cost-effectiveness Arm

The Cost-effectiveness arm of the model calculates the incremental cost-effectiveness ratio (ICER), cost-effectiveness ratios, and total societal costs of EPT and partner referral. The number of treatments of infected and uninfected individuals from the treatment arm serves as the basis of the calculations in the cost-effectiveness arm. Also used is the incidence of PID, which occurs in the incidence arm of the model. Figure A5 displays all the variables in the cost-effectiveness arm and their interactions. Three panels display the calculations of the cost-effectiveness ratios, sequelae costs, and ICER separately. Note the variables in grey, which are the same as their black counterparts of the same name, only transposed to serve in calculating an intermediate variable in a different area of the model.
Figure 8. Cost-effectiveness arm overview
3.4.1 Input variables of the cost-effectiveness section

3.4.1.1 Clinic appointment costs

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of clinical appointment (2020</td>
<td>45.00 (36.00,</td>
<td>45.00 (36.00,</td>
<td>(Gift et al.,</td>
</tr>
<tr>
<td>dollars)</td>
<td>54.00)</td>
<td>54.00)</td>
<td>2011)</td>
</tr>
</tbody>
</table>

Whenever a modeled individual received testing, it was assumed they also made a clinical appointment for a consultation. This variable includes both the out-of-pocket expense for a clinical visit as well as testing. Gift et al. (2011) had an estimate for this variable from surveys and previous literature (Gift et al., 2011). This value was adjusted for inflation to 2020 inflation-adjusted United States dollars.

3.4.1.2 Cost of time for clinical visit

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of time of clinical visit (2020</td>
<td>30.00 (24.00,</td>
<td>30.00 (24.00,</td>
<td>(Gift et al.,</td>
</tr>
<tr>
<td>dollars)</td>
<td>36.00)</td>
<td>36.00)</td>
<td>2011)</td>
</tr>
</tbody>
</table>

A clinical visit requires time in transportation to the clinic and to complete the consultation and any testing. This variable is the estimated value for this time component. It is added to the Clinic appointment costs to make an overall cost of consultation and testing for recipients of partner referral. Gift et al. (2011) included an estimate for this variable from surveys and previous literature (Gift et al., 2011). This value was adjusted for inflation to 2020 U.S. dollars.
3.4.1.3 Ectopic Pregnancy cost

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of ectopic pregnancy (2020</td>
<td>4,000.00</td>
<td>-</td>
<td>(Yeh et al.,</td>
</tr>
<tr>
<td>(2020 dollars)</td>
<td>(3,200.00, 4,800.00)</td>
<td></td>
<td>2003)</td>
</tr>
</tbody>
</table>

The cost of ectopic pregnancy used the estimates from Gift (2011), adjusted for inflation to 2020 United States dollars (Gift et al., 2011).

3.4.1.4 Infertility cost

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of infertility (2020 dollars)</td>
<td>8,000.00</td>
<td>-</td>
<td>(Yeh et al.,</td>
</tr>
<tr>
<td></td>
<td>(6,400.00, 9,600.00)</td>
<td></td>
<td>2003)</td>
</tr>
</tbody>
</table>

The cost of infertility used the estimates from Gift (2011), adjusted for inflation to 2020 United States dollars (Gift et al., 2011).

3.4.1.5 Price of medication with 340B

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of chlamydia treatment if</td>
<td>0.30 (0.24, 0.36)</td>
<td>0.30 (0.24, 0.36)</td>
<td>(Gift et al.,</td>
</tr>
<tr>
<td>subsidized (2020 dollars)</td>
<td></td>
<td></td>
<td>2011)</td>
</tr>
</tbody>
</table>

This variable provides the estimated price of chlamydia medications if the 340B reduced pricing program was used. This variable and the variable *Price of medication without 340B* (see 3.4.1.6) assumes a standard dose of the recommended regimens of Doxycycline. However, the cost of the alternative regimens of Azithromycin was also
considered in the sensitivity analysis. The value of this variable was determined in consultation with experts in the field and cross-referenced with existing literature. This variable works together with Proportion 340B (see 3.4.1.7) to depress the cost of chlamydia treatment overall because the average cost of treatment (see 3.4.2.1) thereby considers the price controls of the 340B program.

3.4.1.6 Price of medication without 340B

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of chlamydia treatment (2020 dollars)</td>
<td>26.00 (20.80, 31.20)</td>
<td>26.00 (20.80, 31.20)</td>
<td>(Gift et al., 2011)</td>
</tr>
</tbody>
</table>

This variable estimates the average cost of a chlamydia treatment (Doxycycline) as an out-of-pocket expense. Insurance compensation is not considered. Gift et al. (2011) provided an estimate in 2010 dollars based on surveys of four clinics in different U.S. cities. Additionally, online price listings at various online retailers (including Wal-Mart, Target, and CVS) for chlamydia treatment in New York State were considered. A cost of $26 was used (in 2020 inflation-adjusted dollars), with a wide sensitivity bound. This variable was adjusted down for the final average medication price by the variable Price of medication with 340B.

3.4.1.7 Proportion 340b

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion subsidized</td>
<td>0.30 (0.25, 0.35)</td>
<td>0.30 (0.25, 0.35)</td>
<td>Assumption</td>
</tr>
</tbody>
</table>
This variable provided the proportion of EPT recipients and index patients (note: sex partners diagnosed because of a partner referral from an index patient became index patients themselves) that received price-controlled 340B medications. This variable was estimated at 0.30 in consultation with experts.

3.4.1.8 PID cost

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of PID treatment (2020 dollars)</td>
<td>380.00</td>
<td>-</td>
<td>(Yeh et al., 2003)</td>
</tr>
<tr>
<td></td>
<td>(88.00, 3,500.00)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The cost of PID included testing, treatment, time, and consultation costs as estimated by previous literature. In contrast to other cost variables, PID and the other sequelae are counted in terms of lifetime costs for any female that develops one or more of these sequelae. Yeh, Hook, & Goldie (2003) provided one estimate for the cost of each sequela. However, it is important to note that this study occurred before significant revisions to the healthcare system in the United States (Yeh et al., 2003). It is therefore likely out of date. Thus, an average of all costs of chlamydia infections (including chlamydia infection and any sequelae) was compared with a more recent estimate by Chesson et al. (2021) (Chesson et al., 2021). The authors of that study aggregated all lifetime costs and found that females incurred an average cost of $616.75 (2020 dollars). The average cost for all females in the model for this study who became infected was $704.00 (2020 dollars). This finding provided some confidence that older literature was still relevant for more specific costs once adjusted for inflation. Nevertheless, wide confidence intervals were
used in the sensitivity analysis for this variable and other cost variables for chlamydia sequelae.

3.4.1.9 Prob ectopic pregnancy given PID

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of ectopic pregnancy given PID</td>
<td>0.08 (0.03, 0.13)</td>
<td>-</td>
<td>(Haggerty et al., 2010; Ong et al., 2017)</td>
</tr>
</tbody>
</table>

Two studies provided estimates for the probability of ectopic pregnancy, infertility, and chronic pelvic pain occurring, given existing PID. The studies used to determine this variable were Haggerty et al. (2010) and Ong et al. (2017) (Haggerty et al., 2010; Ong et al., 2017). For the probability of ectopic pregnancy, Haggerty et al.’s literature review described previous findings ranging from 9.1% to 16.4%. In comparison, Ong et al.’s study used a value of 0.08% of females developing ectopic pregnancy given chlamydia infection only (no PID infection). After calibration given the probability of PID, this study used a probability value of 0.08 for this variable because Ong et al.’s study was more recent with a more robust methodology.

3.4.1.10 Prob chronic pelvic pain given PID

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of chronic pelvic pain given PID</td>
<td>0.18 (0.13, 0.23)</td>
<td>-</td>
<td>(Haggerty et al., 2010; Ong et al., 2017)</td>
</tr>
</tbody>
</table>
Two studies provided estimates for the probability of chronic pelvic pain given a PID infection. The studies used to define this variable included Haggerty et al. (2010) and Ong et al. (2017) (Haggerty et al., 2010; Ong et al., 2017). Ong et al.’s paper is the more recent, listing a lower probability for this variable with a proportion of 0.18 of women with chlamydia, which was used after calibration in this study.

3.4.1.11 Chronic Pelvic Pain cost

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of chronic pelvic pain treatment</td>
<td>800.00</td>
<td>-</td>
<td>(Yeh et al., 2003)</td>
</tr>
<tr>
<td>(2020 dollars)</td>
<td>(640.00, 960.00)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The cost of chronic pelvic pain used the estimates from previous literature adjusted for inflation to 2020 United States dollars (Gift et al., 2011).

3.4.1.12 Probability of infertility within 1 year given PID

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of infertility</td>
<td>0.10 (0.05, 0.15)</td>
<td>-</td>
<td>(Chesson et al., 2021; Haggerty et al., 2010; Kumar et al., 2021)</td>
</tr>
<tr>
<td>given PID</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

This variable defines the probability that a female will become infertile, given she has already developed PID. It is not necessarily true that all infertility stems from PID or even that PID occurs first, but PID is a significant risk factor for infertility (Haggerty et al., 2010). It was valuable to use PID as a gateway probability for all sequelae because previous literature had estimated the probability of infertility and other sequelae given PID.
Haggerty et al. (2010) reported an estimate of 0.18 for infertility given symptomatic PID (Haggerty et al., 2010). Adams et al. (2007) included an estimate of 0.108 for tubular infertility as a complication given a PID infection (Adams et al., 2007). Though this last paper was based in the United Kingdom, infection dynamics are assumed to be the same regardless of population (Ong et al., 2017).

3.4.1.13 Probability of chronic pelvic pain given PID

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of chronic pelvic pain given PID</td>
<td>0.18 (0.13, 0.23)</td>
<td>-</td>
<td>(Haggerty et al., 2010; Ong et al., 2017)</td>
</tr>
</tbody>
</table>

Like the variable *Probability of infertility within 1 year given PID*, this variable is also a probability of chronic pelvic pain given an existing PID infection. Ong et al. (2017) reported a probability of 0.18 for this variable (Ong et al., 2017). Haggerty et al. (2010) listed several studies ranging from 0.29 to 0.56 for chronic pelvic pain given PID (Haggerty et al., 2010).

3.4.1.14 Probability of ectopic pregnancy given PID

Excerpt from Table 8:

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of ectopic pregnancy given PID</td>
<td>0.08 (0.03, 0.13)</td>
<td>-</td>
<td>(Haggerty et al., 2010; Ong et al., 2017)</td>
</tr>
</tbody>
</table>

The last of the sequelae considered was an ectopic pregnancy, and it is also calculated using a probability assuming a prior PID infection. Ong et al. (2017) reported an
estimated probability of 0.076 for this variable (Ong et al., 2017). Haggerty et al. (2010) listed previous research which found that 0.091 of first pregnancies were ectopic with PID as compared to 0.014 with no PID (Haggerty et al., 2010).

3.4.2 Intermediate variables of the cost-effectiveness section

3.4.2.1 Average cost of medication

This variable provides an average of the cost of medications for treating one modeled individual for chlamydia. It uses the price of medication without price controls under the 340B drug pricing program, the price of medications with price control, and the proportion of patients that may receive reduced pricing.

Equation: Price of medication with 340B*Prop 340b+Price of medication without 340B*(1-Prop 340b)

3.4.2.2 Total EPT treatments

This variable calculated the total number of treatments due to EPT use. EPT may be used to treat sex partners who are not infected, which helps determine the cost-effectiveness ratio for EPT based on the prevalence among sex partners receiving EPT. This variable adds all EPT treatments, regardless of infection status.

Equation: EPT treatments of infected + EPT treatments of uninfected

3.4.2.3 Total medication costs

This variable adds the total costs for EPT medications, including infected and uninfected sex partners, and price-controlled and uncontrolled medications.

Equation: Total EPT treatments*Average price of medication
3.4.2.4 Total EPT costs

This variable calculated the total societal costs of EPT use, which includes the price of medications and the cost of sequelae.

Equation: Total EPT medication costs + EPT sequelae cost

3.4.2.5 Total PR clinic costs

This variable calculated the total clinic costs due to partner referral by multiplying the total clinic visits (regardless of infected status) with the cost of each clinic visit.

Equation: Clinical visit costs*Total PR clinic visits

3.4.2.6 Total PR costs

This variable added the three cost components of partner referral, including the clinic costs (labeled consultation and testing costs in Paper 2), the total partner referral medication costs, and the total partner referral sequelae costs.

Equation: Total PR clinic costs + Total PR medication costs + PR sequelae cost

3.4.2.7 Mean cost of sequelae

For both partner referral and EPT, it is necessary to calculate the average cost of sequelae. The probabilities and costs may be added directly since chronic pelvic pain, ectopic pregnancy, and infertility are contingent on a preexisting PID infection in this model.

Equation: PID cost + CPP cost*Prob chronic pelvic pain given PID + EP cost*Prob ectopic pregnancy given PID + Infertility cost*Prob infertility given PID
3.4.2.8 EPT cost per sex partner

This variable calculated the average cost of each EPT treatment, regardless of infection status. This included both medication and sequelae costs.

Equation: Total EPT Costs/Total EPT treatments

3.4.2.9 PR cost per sex partner

This variable calculated the average cost of each partner’s referral treatment, regardless of infection status. This variable included medication, consultation, and testing, and sequelae.

Equation: Total PR Costs/Number of partners attempted P.R.

3.4.2.10 Incremental cost (c1-c2)

The incremental cost is a formula component of the ICER formula, and it is the difference between the cost per treatment of partner referral and EPT.

Equation: P.R. cost per sex partner-EPT cost per sex partner

3.4.2.11 EPT effectiveness score

The EPT effectiveness score is a component of the ICER formula. It is calculated as the number of EPT treatments of infected individuals divided by the total number of EPT treatments.

Equation: EPT treatments of infected/Total EPT treatments

3.4.2.12 PR effectiveness score

The partner referral effectiveness score is a component of the ICER formula. It calculated the number of partner referral treatments (all partner referral treatments are
assumed to be of infected individuals) divided by the total number of partners who attempted partner referrals (including uninfected sex partners who received EPT but were not treated).

Equation: Total PR Treatments/Number of partners attempted P.R.

3.4.2.13 Incremental effectiveness (e1-e2)

The incremental effectiveness score is a formula component of the ICER formula, and it is the difference between the effectiveness scores of partner referral and EPT.

Equation: P.R. effectiveness score-EPT effectiveness score

3.4.2.14 ICER

The ICER is the primary outcome of paper 2 and is calculated as the incremental cost divided by the incremental effectiveness. It may be thought of as the cost of each additional treatment given as EPT rather than a partner referral.

Equation: Incremental cost (c1-c2)/Incremental effectiveness (e1-e2)

4. Additional Tables

Table 11 presents the number of annual chlamydia diagnoses for NYS for males and females aged 18-24 years, including reporting from New York City and the rest of the state (these have separate reporting systems). The NYS Department of Health provided these data by request and these data are not available publicly (De-Identified Aggregated NYS STI Surveillance Data. (December 4th, 2020). Office of Sexual Health & Epidemiology. Sent by Request; Data Not Publicly Available., n.d.). The annual totals include both individuals diagnosed by screening and sex partners diagnosed because of partner referrals. Because
these data were aggregated to the total number of diagnoses per year, it was necessary to calculate the average weekly diagnoses for each sex and year for modeling purposes. These weekly averages were assigned to the start of each year and were calculated as the total number of annual diagnoses divided by 52 weeks. The weekly averages are not reflective of the actual weekly averages and were calculated for modeling purposes.

4.1 Calibration

Once the structure of the model was finalized (see Figures A3, A4, A5, and A6 for detailed views of the model structure), it was necessary to calibrate the input variables (listed in Table 8). This meant fine tuning their values to balance the model such that outcomes would match historical values. All input variables had literature-derived confidence intervals, and their calibration values were required to fall within these confidence intervals. The Vensim software included automatic calibration functions, which tested all variables randomly across their confidence intervals to see which combination of input variable values produced the expected outcomes. In some situations, multiple input values could produce the same result, though this was rare. Calibration was conducted during the calibration phase, which included the first five years of the simulation (Years -5 through the end of Year 4). Prevalence and Diagnoses were both outputs of the model and were calibrated during the calibration phase.

4.1.1 Prevalence

The model variable Prevalence was free to change over time within the model and had two phases: the calibration phase and the outputting stage. This variable was distinct from the input variable, Input Prevalence, discussed in section 3.1.1.5. During the
calibration phase, other input variables were adjusted within their confidence intervals such that the variable Prevalence would fall within its confidence interval (i.e., within 0.05 of the variable Input Prevalence). Vensim’s calibration function was utilized, along with the author’s judgement in setting input variable values (also based in part on expert interviews). All intermediate variables that used Prevalence in their formulas used the model variable Prevalence, and not the input variable Input Prevalence. Input Prevalence was used only to calibrate the model along with the number of diagnoses reported by the New York State Department of Health (see Section 4.1.2, below). Balancing the number of individuals diagnosed using Input Prevalence ensured calibration of the Screening arm of the model. Similarly, calibrating the model to maintain Prevalence ensured that the Treatment and Incidence arms were balanced correctly. Within paper 1, the variable Prevalence is discussed as an indicator of EPT’s effectiveness.

Figure A7 displays the values of the variables Input Prevalence and Prevalence (which was different for males and females). Also shown is the calibration period over which the values of Prevalence were calibrated to match Input Prevalence by adjusting all other input variables.
**Figure 9. Calibration phase, and values of Input Prevalence and Prevalence over time for Years 0 to 10**

![Graph showing calibration phase and prevalence over time for years 0 to 10.](image)

**4.1.2 Diagnoses**

**Table 11. Chlamydia diagnoses of males and females aged 18-24 years in New York State in annual totals from 2013 to 2018 with calculated average weekly totals**

<table>
<thead>
<tr>
<th>Year</th>
<th>Male Total Diagnoses (a)</th>
<th>Female Total Diagnoses (b)</th>
<th>Total Diagnoses (a+b)</th>
<th>Weekly Average Male (a/52)</th>
<th>Weekly Average Female (b/52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>14,347</td>
<td>34,635</td>
<td>48,982</td>
<td>275</td>
<td>664</td>
</tr>
<tr>
<td>2015</td>
<td>15,383</td>
<td>35,059</td>
<td>50,442</td>
<td>294</td>
<td>672</td>
</tr>
<tr>
<td>2016</td>
<td>16,172</td>
<td>35,754</td>
<td>51,926</td>
<td>310</td>
<td>685</td>
</tr>
<tr>
<td>2017</td>
<td>17,720</td>
<td>37,288</td>
<td>55,008</td>
<td>340</td>
<td>715</td>
</tr>
<tr>
<td>2018</td>
<td>18,207</td>
<td>37,519</td>
<td>55,726</td>
<td>349</td>
<td>720</td>
</tr>
</tbody>
</table>
To fill in the number of diagnoses per week for all other weeks, values were interpolated between the weekly average value of each year. Weekly values within each year were calculated using the XLOOKUP function in Microsoft Excel, which fills unknown values between two datapoints using a linear approximation. For example, in the first week of 2016, the number of estimated diagnoses was 310 male diagnoses per week, and this rose linearly each week until it reached 340 in the first week of 2017. Note that these calculated weekly averages do not reflect the true number of diagnoses each week, which are unknown for this study and likely fluctuate significantly throughout a year. However, the weekly average served as an expected value for the number of diagnoses per week with which to compare the number of diagnoses produced by the model (which had no seasonal or weekly variation built in). These weekly values were used in combination with real-world chlamydia prevalence estimates (see 4.1.1 Prevalence, above) to calibrate the model’s other input variable values. This approach allowed for balancing the model’s screening and incidence arms with the model’s treatment arm. The screening arm had to diagnose the correct proportion of infected individuals to match the above calculated weekly diagnoses. Meanwhile, the treatment arm had to treat the correct proportion of diagnosed individuals to maintain the expected value for the variable Prevalence (overtreatment would reduce prevalence over time, and vice versa).
References


treatment of sex partners on recurrent or persistent gonorrhea or chlamydial infection. *New England Journal of Medicine, 352*(7), 676–685.


and neisseria gonorrhoeae among men with urethritis and their female sex partners.

*The Journal of Infectious Diseases, 178*(6), 1707–1712.


PAPER TWO

THE COST-EFFECTIVENESS OF EXPEDITED PARTNER THERAPY FOR CHLAMYDIA COMPARED TO PARTNER REFERRAL AMONG YOUNG ADULTS: A STATE-BASED CASE STUDY
ABSTRACT

Introduction

Untreated infections may lead to pelvic inflammatory disease (PID). Expedited partner therapy (EPT) is the clinical practice of treating—without clinical examination—exposed sex partners of patients diagnosed with chlamydia.

Methods

This study was a cost-effectiveness analysis comparing EPT to partner referral for heterosexually acquired infections of chlamydia. The model included males and females aged 18-24 years living in New York State (NYS), unpublished NYS surveillance data, and existing scientific literature. Total societal costs, per treatment costs, and the ICER comparing EPT to partner referral were estimated for all treatments. Secondary outcomes included the number of infected and uninfected sex partners treated, total costs related to treatment and clinical utilization, and the costs of PID and other sequelae.

Results

For EPT and partner referral, the total annual societal costs were $1,404,235 and $3,328,526 respectively, when all index patients received either EPT or partner referral for their sex partners. Under the EPT simulation, the cost of treatment for PID and other sequelae among females was $861,903. EPT was estimated to be cost-saving among sex partners compared to partner referral, with an ICER of -13 among females and -83 among males.
**Conclusion**

EPT is a robust intervention from a cost-effectiveness perspective, especially in treating male sex partners of heterosexually active females. Though EPT had significantly higher societal treatment costs, EPT was more cost-saving overall due to having lower clinical and testing costs.
ACKNOWLEDGEMENTS

The simulation model developed in this research project would not have been possible without the contributions and feedback of a few generous individuals, who kindly contributed their time and energy to making this possible. Thank you.
INTRODUCTION

Sexually transmitted infections (STI) include some of the most prevalent and costly infectious diseases in the United States. When implementing policies intended to reduce the burden of STIs, societal costs and cost-effectiveness of different practices are important indicators for policymakers. They can help policymakers and public health practitioners understand the scope of need and inform decision-making. Societal costs (also termed total health spending) include all public, private, and out-of-pocket medical expenses that are paid over a given time period. This aggregation of all costs is an important indicator of the total cost burden of a disease, which is not influenced by any shifts in costs between payers. Cost-effectiveness refers to the ratio between costs and effectiveness outcomes (i.e., number of treatments) for a specific practice. This measure helps compare different practices and assess them on a per treatment level. The annual societal cost of chlamydia in the United States totaled an estimated $691.3 million in 2018, of which $74.6 million was among males and $616.8 million was among females (Chesson et al., 2021). Much of these costs are associated with a small subset of all chlamydia cases that have higher costs than most chlamydia cases. While chlamydia is easily cured with (relatively inexpensive) antibiotics, untreated infections can lead to serious downstream health effects (sequalae). These include pelvic inflammatory disease (PID), ectopic pregnancy, infertility, and chronic pelvic pain (Haggerty et al., 2010; Kumar et al., 2021; Ong et al., 2017; Price et al., 2013). It is critical to treat infected individuals quickly, particularly females, who are more susceptible to sequelae (Haggerty et al., 2010). Therefore, screening efforts have focused on diagnosing female index patients and treating them (Screening Recommendations and Considerations Referenced in Treatment Guidelines and Original Sources, 2021).
Additionally, previous research indicates that females are more likely to have symptomatic chlamydia infections than males (Barbee et al., 2016; Korenromp et al., 2002; Miller et al., 2004; Patel et al., 2018; Paxton et al., 1998), which likely leads to additional testing (Chlamydia Screening in Women (CHL), 2019; Farley et al., 2003; Schillinger et al., 2005). For these reasons, the number of female diagnoses is typically higher than male diagnoses.

A critical component of chlamydia control is treating sex partners of diagnosed index patients because this prevents reinfection and further transmission (Hogben et al., 2005; Schillinger et al., 2016). There are several options available to healthcare practitioners seeking to care for the sex partners of diagnosed index patients. The two most common options are partner referral and EPT. Partner referral is the practice of asking index patients to encourage their sex partners to seek testing. Under partner referral, sex partners are only treated after healthcare practitioners diagnose them with chlamydia, which prevents treatments of uninfected sex partners but incurs the cost of a diagnostic exam regardless of infection status. EPT forgoes the requirement to first diagnose sex partners and allows presumptive treatment by providing either an extra prescription or medication (med-in-hand) to the index patient to deliver to their sex partner(s). EPT saves costs in diagnostic exams, but it may result in expenses incurred from unnecessary treatments of uninfected sex partners. It is possible to miss opportunities to diagnose PID and other sequelae among female sex partners who are given EPT (Althaus et al., 2014; Expedited Partner Therapy, 2021). On the other hand, if EPT is more effective at reducing underlying chlamydia prevalence, the incidence of sequelae may decline. In this way, both partner referral and EPT may result in excessive spending in different aspects of the treatment process.
Previous research has found that EPT is cost-effective compared to partner referral (Althaus et al., 2014; Gift et al., 2011; Roberts et al., 2012; Williams et al., 2021). One study in the United States assessed the cost-effectiveness and the per-treatment (e.g., not aggregate) societal costs of treating infected sex partners in three cities (Gift et al., 2011). The authors of that study found that EPT was cost-effective relative to partner referral, but that the magnitude of EPT’s advantage depended on the payer. The authors did not assess the impact of testing uninfected sex partners under partner referral or treating uninfected sex partners under EPT (Gift et al., 2011). Another UK study found that increasing the efficacy of partner treatment using accelerated partner therapy (APT – the UK equivalent to EPT) was more cost-effective than increasing screening for chlamydia. However, this study was not able to provide a detailed cost-effectiveness analysis compared to partner referral (Althaus et al., 2014). When considering various interventions, it is important to compare them to each other, but also to compare each intervention to current practice. A second UK study found that simple partner referral was more cost-effective than APT. However, the authors considered only the clinical costs when providing partner referral or APT to index patients (Roberts et al., 2012). Such analyses are valuable, but it is important to consider costs beyond clinical costs. EPT has a noted advantage when it comes to reducing clinical costs because it omits the requirement for a diagnostic exam (treatment costs and the costs of any undiagnosed sequelae remain). Finally, another recent UK study found that APT was more cost-effective than partner referral and had lower societal costs than standard contact tracing (Williams et al., 2021). However, this study assumed that APT increased the number of sex partners treated by a flat rate of 25%. It is not clear that the previous literature supports this assumption, and this reduction rate did not consider the effect of
decreased chlamydia prevalence resulting from increased EPT use. In addition to these methodological limitations, the three studies conducted in the UK might not generalize to the US context due to differences in the healthcare funding structure (Estcourt et al., 2015; Roberts et al., 2012; Williams et al., 2021). Three of the four cost-effectiveness analyses identified considered the cost of sequela in their analysis (Althaus et al., 2014; Gift et al., 2011; Williams et al., 2021).

However, there are limits to previous studies and reasons to believe that EPT might not be cost-effective if certain factors are considered. For instance, while EPT may reduce costs by averting the need for a clinical visit, it may also increase costs because treatment may be given to more sex partners, whether it is clinically necessary or not. This increase in treatment costs has the potential to cancel out reductions in clinical costs. It should be noted that these extra societal costs may come in exchange for effectiveness gains, benefiting EPT’s cost-effectiveness ratio in comparison to partner referral. In this way, it may be possible for increased EPT use to result in higher societal costs while simultaneously improving cost-effectiveness. Alternatively, because EPT use has the potential to reduce the underlying prevalence of chlamydia, it is also possible for EPT to reduce total societal spending on chlamydia.

Like with treatment costs, it is unclear whether EPT or partner referral is more cost effective when it comes to treating costly sequelae. PID and other associated sequelae are among the costliest consequences of chlamydia infections (Gift et al., 2008; Yeh et al., 2003). An estimated 2.5 million females aged 18-44 have suffered from pelvic inflammatory disease (PID) in their lifetimes, of which an estimated 35% were caused by a
chlamydia infection (Kreisel et al., 2017; Price et al., 2016). Estimates for the lifetime societal costs associated with a single case of PID vary widely, ranging from $88 U.S. Dollars (USD) to $3,500 USD (year 2000 dollars) (Yeh et al., 2003). Meanwhile, per case lifetime costs of chronic pelvic pain were estimated between $640 USD and $960 USD, ectopic pregnancy from $3,200 to 4,800 USD, and infertility from $6,400 to $9,600 USD in year 2000 (Yeh et al., 2003). On the one hand, PID that has already developed among female sex partners may be more likely to be detected under partner referral. This is because sex partners are clinically examined under partner referral and this examination may lead to diagnosis. However, EPT has the potential to treat more sex partners and to treat them faster, potentially driving down underlying chlamydia prevalence. In this way, EPT use may prevent the incidence of PID and other sequelae and reduce their prevalence relative to partner referral.

Previous studies on the cost-effectiveness of EPT have not considered each of these costs. The relative size of these changes will determine the overall cost-effectiveness and total societal costs of increased EPT use. Moreover, previous studies from the US have focused on costs that accrue to a specific payer (e.g., costs to the state, costs to private insurers, cost to the individual patient), but have not considered the full societal costs of EPT versus partner referral. Cost-effectiveness reveals whether a practice offers more or better treatment at the same cost. Meanwhile, the term societal costs considers the number of treatment events, as cost-effective practices may incur higher societal costs if they are used more frequently. Both measures are valuable.
This study estimated the cost-effectiveness of EPT and partner referral for heterosexually acquired chlamydia, the total societal costs of treating all sex partners with either EPT or partner referral, and the total number of treatments of infected and uninfected sex partners in one year (Year 5 – see below). This was done using a simulation model specific to young adults living in New York State (NYS). Although the population includes all males and females aged 18-24 years irrespective of sex of sex partner, modeled individuals were presumed to be exclusively engaged in heterosexual activity for ease of calculation (Expedited Partner Therapy, 2021; Handsfield et al., 2006). Additionally, women who have sex with women and transgender individuals were not specifically accounted for in the model to control the scope of the model and because it was deemed likely that these groups make up a small proportion of the population. These assumptions are addressed in the limitations section.
METHODS

Analytical Overview

A system dynamics simulation model was used to estimate the cost-effectiveness of EPT compared to partner referral. The societal cost of treating sequelae among female sex partners and the costs of treating (under EPT) or testing (under partner referral) sex partners with no chlamydia infection was considered. This study utilized system dynamics model to track costs and savings for all treatments using either partner referral or EPT during Year 5.

Population

The model included 1,983,517 young adult males (N=1,004,753) and females (N=978,764) aged 18-24 years residing in NYS according to the 2010 US Census (2010: Populations and People, 2011). NYS was selected for this study due to its large study population and the availability of data and inputs needed to simulate the model. This included scientific literature regarding EPT set in New York City (Oliver et al., 2016; Slutsker et al., 2020). Additionally, it was possible to request publicly unavailable surveillance data on diagnoses (needed for calibration of the model) from the NYS Department of Health Office of Sexual Health & Epidemiology. In addition, NYS is similar to most states in the US in terms of its past EPT promotion activities, which do not include expensive statewide programs like California’s medication purchase program, or extensive promotion of EPT as seen in Washington state (Andre Kiesel, 2022; Gift et al., 2011; Kovaleski et al., 2016). Therefore, efforts to increase or improve EPT use in NYS and their results on diagnoses and underlying prevalence are likely to be generalizable to many other states where similar efforts are being considered. Modeled individuals could become
sexually active only with the opposite sex and only heterosexually acquired infections were considered. This assumption was made because individuals with same-sex sex partners are likely to have lower rates of EPT use. The Centers for Disease Control and Prevention (CDC) treatment guidelines previously recommended that men who have sex with men (MSM) be referred for clinical examination whenever possible (Expeditied Partner Therapy, 2021). The CDC released updated guidance in 2021 to recommend that “share clinical decision-making regarding EPT for MSM” be used (Guidance on the Use of Expedited Partner Therapy in the Treatment of Gonorrhea, 2021). There is no guidance or research to date available regarding the use of EPT for women who have sex with women. Additionally, females with same-sex sex partners likely make up a small proportion of individuals at risk of becoming infected with chlamydia, although this group is in need of further study (Gorgos & Marrazzo, 2011; Singh et al., 2011). Transgender individuals were not specifically accounted for in the model because the surveillance data used to calibrate input values included only binary sex at birth.

**Model Outcomes**

The primary outcomes of the model included the total societal costs of EPT and partner referral, the cost-effectiveness ratios of EPT and partner referral, and the incremental cost-effectiveness ratio (ICER) between partner referral and EPT—all measured in Year 5 of the simulation. Cost-effectiveness ratios provided the per-treatment cost of EPT and partner referral of infected sex partners, which allowed independent evaluation of each practice. The cost-effectiveness ratios were calculated as cost $C$ (the total societal cost for EPT or partner referral – see below) divided by effectiveness $E$ (the number of infected sex partners successfully treated by EPT or partner referral in the
The ICER provided the incremental cost of treating one additional sex partner using EPT instead of partner referral. The ICER was calculated as:

\[
\text{ICER} = \frac{C_{PR} - C_{EPT}}{E_{PR} - E_{EPT}}
\]

Where \( C_{PR} \) was the incremental societal cost (societal cost for each additional successful treatment) of treating a sex partner with partner referral, \( C_{EPT} \) was the incremental cost of treating a sex partner with EPT, \( E_{PR} \) was the effectiveness score of partner referral (successful treatments divided by total treatment attempts), and \( E_{EPT} \) was the effectiveness score of EPT. Secondary outcomes included the total treatment costs (in 2020 inflation-adjusted United States dollars), total clinical costs, and total cost of sequelae among females. The last outcomes considered were the numbers of infected and uninfected sex partners treated by EPT and partner referral.

Table 1 includes a list of inputs used in the model, values used for each input for males and females with lower and upper bounds used in the sensitivity analysis, and references for each input. The values in Table 1 were calibrated so that prevalence and the number of diagnosed individuals in the model matched real-world estimates of prevalence and historical data on diagnoses. The historical data used for calibrations were unpublished aggregate data provided by request by the NYS Department of Health Office of Sexual Health and Epidemiology (De-Identified Aggregated NYS STI Surveillance Data, 2020). These data included the number of reported chlamydia diagnoses for males and females aged 18-24 in NYS. The historical data used for calibration were for the years 2014-2018, which corresponded to Years -4 through Year 0 in the model. Years 1 through 5 corresponded to 2019 through 2023 (De-Identified Aggregated NYS STI Surveillance Data).
Laboratories that test for certain communicable diseases (including but not limited to chlamydia) in NYS are mandated to report diagnoses to the NYS Department of Health (New York State Sanitary Code 10NYCRR 2.10; New York City Administrative Code §11). These annual data were interpolated to provide an average number of diagnoses per week used in calibration. Chlamydia prevalence estimates were sourced from the existing literature (K. M. Kreisel et al., 2021). Sensitivity ranges were derived either by considering the spread of findings in previous studies or using a range within 0.05 units of the calibrated input values if the literature values were consistent with each other or if only one literature source was identified.

Model Structure

The aims of this study were to estimate aggregate outcomes, including total diagnoses, which may be calculated easily using a “stock and flow” simulation. This modeling approach is distinct from agent-based simulation models, which track individual autonomous agents (modeled individuals that make decisions and are separate entities from other agents) through their interactions. Agent-based modeling allows researchers to design different types of agents (e.g., agents willing to have multiple concurrent sex partners and other agents who only have one sex partner at a time) and to study outcomes for each type of agent. Stock and flow simulations instead apply mathematical calculations to aggregate "stocks", which include individuals in a specific category. It is assumed that modeled individuals within stocks are homogeneous. Stocks (health states), flows (transition states), and variables in the model interacted directly using mathematical formulas rather than by modeling and then aggregating the outcomes of individual agents.
Using a stock and flow model in this study allowed for efficient calculations of a complex system with more feedback effects and a broader scope than would be possible using an agent-based model (Rahmandad & Sterman, 2008). Stock and flow models also allow for extensive sensitivity analysis, with thousands of runs using randomized input variable values because the computational power required for each run is negligible. However, because individuals in stocks are presumed to be homogeneous, they also share the same average propensity for all transitions between stocks (see below). The only exception made in this study was to separate males and females within each stock. Many of the input and intermediate variables were assigned different values for male- and female-modeled individuals.

Figure 1 displays the three health states (stocks) that served as the core of the simulation model, the transition states between the health states, and select variables that influenced the probability that modeled individuals would use these transitions. Health states are depicted as boxes with borders. Transition states are double-sided lines with arrowheads connecting health states. These arrowheads denote the direction in which modeled individuals could move. Input variables are fixed values derived from previous studies, expert interviews, or assumptions based on known information (see technical appendix for details). Intermediate variables use input variables to perform calculations that eventually determine the probability that the modeled individuals will transition between health states. Input and intermediate variables are represented by blue labels without borders and appear around health states and transition states in Figure 1. Figure 2 displays the relationships between the variables used to calculate the primary outcomes.
(below), including variables for costs of treatment and the total number of treatments for EPT and partner referral.

The model structure was based on the susceptible-infected-susceptible (SIS) model of infectious disease, which describes the epidemiological spread of infections as a system where recovered individuals are not immune and return to a susceptible status (i.e., uninfected and able to become reinfected) (Anderson et al., 1991; Hethcote, 1989; Stekler et al., 2005). The susceptible unexposed health state included susceptible individuals with no exposure (i.e., not sexually active) and is found on the left side of Figure 1. The susceptible exposed health state is located in the middle of the model and includes susceptible individuals with an infected sex partner(s). Finally, the infected health state comprised individuals with a current chlamydia infection and is located on the model’s far-right side. The model calculated the probability of a diagnosis of modeled individuals and the treatment of any sex partners (by partner referral or EPT) to determine the number of modeled individuals moving from the infected health state to either of the two susceptible health states.

The model had a time step of one week over 520 total weeks (spread over 10 years from Year -4 through Year 5). A one-week time step was chosen because it was deemed unlikely that more than one event (i.e., diagnosis of index patients and treatment of sex partners) in the model could occur within one week. All outcomes were assessed during Year 5 (corresponding to 2023). This allowed for comparison between the two strategies and the base run after feedback effects had been resolved. Feedback effects are shifts in the distribution of modeled individuals in the model which occur in response to changes in
input variables. While the model was carefully calibrated to produce realistic outcomes in the long term, the external validity of these immediate feedback effects could not be verified. Therefore, model outcomes were assessed far removed from these possibly unrealistic feedback effects. Outcomes were measured during a single year (Year 5) because policymakers typically consider year end performance measures, and it was decided in consultation with an expert that such an estimation would be valuable.

The simulation was run once with all sex partners treated with EPT and once with all sex partners treated by partner referral. This approach allowed for comparison between the total societal costs of EPT and partner referral at their theoretical maximum use levels. The model—developed to estimate the numbers of treatments, diagnoses, and underlying prevalence changes in response to increased EPT use—calculated the number of treatments of infected and uninfected individuals for both practices. Effectiveness in the cost-effectiveness calculation was measured as the number of treatments of infected individuals.

Costs in this study were counted using three categories to group these costs as needed for each sex partner. These categories included clinical costs (including consultation and testing), treatment costs if an individual was treated with either partner referral or EPT, and sequelae costs for females who developed any sequelae. Clinical costs included the time and financial cost of a consultation and a diagnostic exam to test for chlamydia. Clinical costs also included productivity loss for the time spend to get a consultation, as estimated by Gift et al. (2011) using previous literature. This cost was considered separately from treatment costs because not all sex partners who received
partner referrals received testing. Similarly, not all individuals who received a consultation and testing in the model were treated. Treatment costs explicitly referred to the cost of one dose (according to the standard treatment regimen) of antibiotic medication to treat chlamydia and were the same regardless of sex or whether receiving EPT or partner referral. EPT-treated sex partners incurred treatment costs regardless of infection status, while sex partners receiving partner referrals incurred treatment costs only if they were diagnosed and treated. Consultation and testing costs and treatment costs were counted on a per-treatment episode basis, as the various events could occur over time (e.g., receiving a test, picking up treatment from a pharmacy). In addition, consultation costs for EPT and partner referral use included a sum of all clinical, treatment, and sequelae costs incurred for the use of either practice over the number of treatments estimated by the model.

Finally, sequelae costs included all lifetime testing and treatment costs for any instances of sequelae among females. Four types of sequelae among female sex partners were considered, including PID, chronic pelvic pain, ectopic pregnancy, and infertility. Testing and treatment costs were combined for all sequelae because it was assumed all females who developed sequelae would eventually incur all testing and treatment costs in their lifetimes. Previous studies had not separated component costs related to sequelae treatment (Haggerty et al., 2010). Sequelae costs were considered independently from any clinical and testing costs for any chlamydia infections. The probability of sequelae development was based on the time a female remained infected and untreated, regardless of whether they received screening, EPT or partner referral. It was assumed that males never developed sequelae because previous research had established that this was unlikely or poorly understood (Y.-S. Lee & Lee, 2013; Westrom, 1996). It was further assumed that
PID would occur as a precursor to other types of sequelae because chronic pelvic pain, ectopic pregnancy, and infertility are much more likely if a female develops PID first (Ong et al., 2017; Price et al., 2013). Additionally, existing studies had estimated the probability of forms of sequelae (including infertility, chronic pelvic pain, and ectopic pregnancy) developing given an existing PID infection (Haggerty et al., 2010).

To summarize, sex partners receiving partner referral incurred clinical costs (including clinic fees, test costs, and time expenditures) and treatment costs if tested and diagnosed (including medication costs). Sex partners treated with EPT incurred treatment costs regardless of infection status. For sex partners who received EPT prescriptions, treatment costs included the cost of medication and the time needed to pick up the medication from a pharmacy. If a sex partner received med-in-hand EPT instead, treatment costs included only the cost of medication.

**Model Validation**

The model was validated according to best practices as previously established in the health modeling and system dynamics literature (Oliva, 2003; Sterman, 2002; Weinstein et al., 2003). To assess behavioral anomaly and structural validity, key inputs were assessed with a range of possible values using Monte Carlo sensitivity analysis (see below) (Oliva, 2003; Sterman, 2002). The model was run with extreme values to evaluate its global stability. Finally, throughout model development and calibration, 16 experts were consulted for feedback. These individuals were experts in chlamydia epidemiology, surveillance, and medical treatment and came from epidemiological, system dynamics modeling, and public health practice backgrounds and were consulted via conference call.
Sensitivity Analysis

Sensitivity analysis was conducted to quantify the range of possible output values when assumptions about input values were relaxed. Previous studies established that economic analyses of chlamydia treatment are sensitive to specific inputs, especially the probability of chlamydia transmission between sex partners and cost estimates used for sequelae among females (Gift et al., 2008, 2011). Another critical factor in determining cost-effectiveness for EPT and partner referral is the probability of infection among sex partners, which determines the proportion of all EPT treatments that result in curing an infected individual. Thus, the probability of infection has a strong influence on the cost-effectiveness of EPT. This factor also determines the likelihood of testing uninfected sex partners for partner referral. Therefore, the input values for the cost of sequelae, the probability of sequelae, and the probability of infection among sex partners causing the ICER to switch from negative to positive (or vice versa) were identified. Additionally, Monte Carlo analysis was also used for sensitivity analysis, which simultaneously and randomly varied all input variables across their sensitivity ranges (Table 12) over 10,000 runs to assess variation in outcomes.
RESULTS

Table 13 presents the primary outcomes of this study as estimated by a model that simulated the spread and control of heterosexually acquired chlamydia in a population. These outcomes included: cost-effectiveness ratios; the ICER comparing EPT to partner referral; the total treatment, clinical, and lifetime sequelae costs; and the number of infected and uninfected sex partners treated under EPT and partner referral among males and females aged 18-24 years in NYS. Outputs are given separately for males and females. The percentages of individuals of each sex that were treated by EPT and partner referral are included. Total costs and the number of treatments are given for a one-year time period.

When the model parameters were set such that healthcare practitioners used EPT to treat all sex partners, 29,652 sex partners received treatment annually in Year 5. In comparison, just 7,730 sex partners received treatment when the model parameters were set such that healthcare practitioners treated all partners using partner referral in Year 5. A significant portion of EPT treatments (45.3%) were among uninfected sex partners. Meanwhile, a mere 1.3% of partner referral treatments were for uninfected sex partners due to false positives on the diagnostic exam. A majority (72.8%) of all sex partner treatments were of male sex partners because females were more likely to be screened and diagnosed as index patients.

Total annual estimated societal costs in Year 5 of the simulation were lower when all treatments were given as EPT (female: $1,009,419, male: $394,817) rather than as partner referrals (female: $1,889,201, male: $1,439,324). Annual estimated clinical costs of
partner referral recipients totaled $498,574 among females and $1,337,647 among males. EPT recipient sex partners never incurred clinical costs. Total sequelae treatment costs (counted on a lifetime basis) accruing in one year amounted to $1,352,729 among female sex partners treated using partner referral and $861,903 among female sex partners treated using EPT.

Treatment costs were lower for partner referral compared to EPT. Societal treatment costs for sex partners who received partner referrals totaled $37,898 annually among females and $101,678 annually among males. In contrast, total societal EPT treatment costs amounted to $147,515 annually among female sex partners and $394,817 among male sex partners.

EPT was cost-saving compared to partner referral, with an ICER of -12 for treatment of female sex partners and -83 for the treatment of male sex partners. The cost-effectiveness ratios were also lower for EPT than for partner referral. The estimated societal cost per treatment episode of infected sex partners for EPT was $33 for males and $229 for females. At the same time, these cost-effectiveness ratios for infected sex partners treated by partner referral were higher at $259 and $912 for males and females, respectively. Treatment costs per treatment of each infected sex partner were $18 for both male and female sex partners given partner referral and $33 for both male and female sex partners given EPT. Clinical costs per treatment episode were $241 for sex partners given partner referral. Treatment and clinical costs were the same between males and females because relevant inputs were not differentiated by sex in the previous literature. Sequelae
costs per treatment of infected female sex partners were $653 for partner referral and $195 for EPT in lifetime costs.

**Sensitivity Analysis**

Sensitivity analysis revealed the range in values of outputs that is possible when inputs are altered. This was done because there is uncertainty in the true values of the input variables and because a sensitivity analysis can provide a sense of the reliability of the results. The sensitivity analysis revealed a wide range of possible societal costs, especially for female sex partners. This was because treatments of females using EPT rather than partner referral were not always cost saving. The Monte Carlo sensitivity analysis varied all inputs randomly across their low and high bounds (Table 12) across 10,000 runs to assess the range of possible outcomes. The total estimated societal costs of partner referral varied from $2,210,160 to $6,431,700, while the total estimated societal costs of EPT varied from $958,654 to $3,316,505. The ICER for EPT versus partner referral varied between -244 and 101 among females and between -115 and -60 among males. The wide range in the costs of sequelae was responsible for the cost range for female sex partners.

The sensitivity analysis of specific input variables revealed that even extreme values for prevalence among male sex partners did not result in cost savings for partner referral. Figure 4 displays the change in the ICER between EPT and partner referral given changes in three inputs for female sex partners. For female sex partners, sensitivity analysis revealed that partner referral was more cost-saving compared to EPT when the probability of infection among sex partners treated with EPT decreased from 0.60 to 0.53 among females.
(0.07% decrease), the probability of sequelae among untreated females increased from 0.12 to 0.13 (0.01% increase), or the average cost of sequelae increased from $1,628 to $1,727 (6.08% increase).
DISCUSSION

This study provided estimates of EPT's cost-effectiveness among young adults with presumed heterosexually acquired chlamydia infections living in a highly populous state and found that EPT was cost-saving among male and female sex partners. Estimated societal costs favored the use of EPT over partner referral. The EPT model scenario saw significantly more expenditure on treatments but lower clinical fees, and a moderately lower cost for sequelae treatment. The finding for male sex partners was robust to sensitivity analysis. The sensitivity analysis revealed that the cost-effectiveness of EPT and partner referral among females depended on the input values for the cost and probability of PID. If the probability of PID or if the cost of PID and other associated sequelae increased, EPT became less cost-effective relative to partner referral for female sex partners.

It is important to understand several nuances to contextualize the results of this study better. In this study, EPT use was associated with substantially lower estimated societal consultation and testing costs and sequelae costs than partner referral, which compensated for EPT's higher treatment costs. EPT had higher societal treatment costs than partner referral because EPT treated many more sex partners overall. Under partner referral, sex partners had to get tested and fill prescriptions, making their eventual treatment less likely and with an increased time to heal, which also provided more time for infections to clear without treatment and for sequelae to develop among female sex partners. Additionally, negative tests drastically reduced the number of treatments of uninfected sex partners under partner referral. It should also be noted that treatment costs were higher among males for both EPT and partner referral because more male sex partners received treatment as sex partners, while females were more likely to be screened...
without a referral due to the model’s input parameters. Finally, while the probability of failing to diagnose sequelae among infected females treated with EPT was higher, the prevalence of chlamydia and the number of diagnoses overall was lower in the EPT scenario. This meant that there were fewer females with sequelae overall when healthcare practitioners used EPT to treat all sex partners, even though a small subset of females saw an increase in the probability of untreated sequelae.

One previous study estimated the cost-effectiveness and societal costs of EPT as compared to partner referral in three clinics in different US cities (Gift et al., 2011). The present study agreed with and expanded upon this earlier finding in some respects. Regardless of whether unintended consequences were considered, this study found EPT to be cost-effective compared to partner referral due to the high cost of clinical testing among partner referral recipients. Additionally, the present study provided an estimate of the total societal costs of partner referral and EPT. In addition to being cost-effective, it is important to note that EPT was also a more effective intervention in terms of the probability of treating an infected sex partner, which drove down chlamydia prevalence and reduced societal spending on chlamydia control. This study expands on previous research that estimated the societal costs of individual treatments and within single healthcare facilities (Gift et al., 2011).

EPT remained cost-saving in the sensitivity analysis among males, even when all inputs were simultaneously driven to extreme values. Therefore, it is reasonable to conclude that EPT used to treat male partners will be a cost-saving measure in all realistic scenarios. For females, the cost-savings finding was less robust and highly subject to both
the probability and costs of sequelae development. An option to improve EPT's cost-effectiveness would be to limit its use for male sex partners, as this would reduce costs for undiagnosed PID and other sequelae among female sex partners. However, any option that denies female sex partners the use of an effective treatment option like EPT should be considered with great care and ought to respect the epidemiological consequences in addition to the financial impact.

Future research may be needed to investigate the financial impact of other options for increasing or improving EPT implementation. Apart from increasing the probability of EPT use, efforts to enhance EPT implementation might target sex partners with a higher likelihood of infection with EPT or use med-in-hand EPT rather than prescription EPT. These options might increase EPT's cost-effectiveness over partner referral beyond the findings of this study, as they decrease the costs of EPT treatment for each successful treatment.

Like previous research, this cost-effectiveness analysis was susceptible to the cost inputs for sequelae, partly because estimates for the cost of sequelae literature vary widely (Gift et al., 2011). To account for this uncertainty, this study used wide ranges derived from the existing literature in the sensitivity analysis, which increased the ICER comparing EPT to partner referral to 101 among females at the highest sensitivity values—suggesting that EPT could be significantly less cost-effective relative to partner referral. The wide range in sequelae cost estimates is likely mainly driven by actual variance in the seriousness and costs of sequelae infections, ranging from curable inflammation to permanent infertility (Price et al., 2013; K. J. Smith et al., 2008; Yeh et al., 2003). This study demonstrated that
the cost-effectiveness of EPT use depends on the severity of the sequelae that develop. From a cost perspective, partner referral is preferable when male index patients describe symptoms of their female sex partners that may hint at PID or any other sequelae.

This study has several limitations. First, it was not possible to differentiate among costs to patients, clinics, insurance agencies, and other stakeholders due to the complexity and uncertainty about the inputs needed. Future research is required to untangle the distribution of the total societal costs identified in this study. That said, it is possible to assume that the distribution of costs by payer for EPT would mirror the same costs for partner referral. Under this assumption, increased EPT use would save costs for the payers of diagnostic exams (i.e., Medicaid and insurance agencies), even if these payers also covered treatments. If the payers of diagnostic exams were different from the payer for treatments, then increased EPT use would shift costs from the former to the latter. Similarly, the costs of prepackaged med-in-hand EPT may be incurred by state governments or non-profit clinics, leaving little for recipient index patients to pay. Second, all males and females in the model were assumed to be either sexually inactive or heterosexually active. This is known to be inaccurate as not all sexually active individuals aged 18-24 years are heterosexually active (Weiss et al., 2019). This decision was, however, partially made due to the CDC’s guidance at time of writing which does not routinely recommend EPT to men with current male sex partners (Handsfield et al., 2006). These guidelines exist because there are concerns that same-sex sex partners have a heightened risk of comorbidities (Expedited Partner Therapy, 2021). As a result of these guidelines, the number of same-sex sex partners given EPT was deemed to be low. Transmission between females who report having sex with only females is presumed to be low, although this is
understudied (Bailey et al., 2004; Muzny et al., 2016). Transgender individuals were not specifically accounted for in the model because the surveillance data used to calibrate input values included only binary sex at birth. Third, this study assumed that female sex partners would develop ectopic pregnancy, infertility, and chronic pelvic pain only after first developing PID. This assumption may underestimate the number of female sex partners who develop sequelae by omitting sequelae occurring absent any PID, though this underestimate affected EPT and partner referral recipient female sex partners equally. Finally, this study only considered individuals aged 18-24 years because the relevant literature was most well developed for this age group. Future research could examine the cost-effectiveness of EPT use among MSM, transgender, and older or younger individuals.

**Conclusions**

This study provided a cost-effectiveness estimate of EPT compared to partner referral among young adults adjusting for the financial impact of EPT’s ability to treat uninfected sex partners. After sensitivity analysis of three inputs—prevalence of chlamydia among sex partners, the probability of sequelae developing, and the cost of sequelae—this study found that EPT was more cost-effective than partner referral and that EPT was cost-saving when used to treat both male and female sex partners. Policymakers may note that increasing the proportion of EPT use among index patients will save societal costs despite EPT’s propensity to treat uninfected individuals. Given this economic analysis from a societal perspective, promotion of EPT is strongly recommended.
### TABLES AND FIGURES

**Table 12. Input variable values for chlamydia infection and sources with lower and upper bounds used in the sensitivity analysis**

<table>
<thead>
<tr>
<th>Input name</th>
<th>Female (low, high)</th>
<th>Male (low, high)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Susceptible unexposed</td>
<td>831,081</td>
<td>853,148</td>
<td>Calibration</td>
</tr>
<tr>
<td>Susceptible exposed</td>
<td>41,533</td>
<td>42,636</td>
<td>Calibration</td>
</tr>
<tr>
<td>Infected</td>
<td>106,150</td>
<td>108,969</td>
<td>Calibration</td>
</tr>
<tr>
<td>Condom use probability</td>
<td>0.38 (0.33, 0.43)</td>
<td>0.48 (0.43, 0.53)</td>
<td>(Copen, 2017)</td>
</tr>
<tr>
<td>Probability of screening if asymptomatic</td>
<td>0.00 (0.00, 0.00)</td>
<td>0.00 (0.00, 0.00)</td>
<td>(Chlamydia Screening in Women (CHL), 2019)</td>
</tr>
<tr>
<td>Mean number of sex partners given diagnosis</td>
<td>1.20 (1.15, 1.25)</td>
<td>1.25 (1.20, 1.30)</td>
<td>(Gift et al., 2011)</td>
</tr>
<tr>
<td>Probability of partner change</td>
<td>0.02 (0.00, 0.03)</td>
<td>0.02 (0.00, 0.03)</td>
<td>(De Vries et al., 2006; Glick et al., 2012)</td>
</tr>
<tr>
<td>Proportion asymptomatic</td>
<td>0.75 (0.70, 0.80)</td>
<td>0.85 (0.80, 0.90)</td>
<td>(Chlamydia Screening in Women (CHL), 2019; Farley et al., 2003; Schillinger et al., 2005)</td>
</tr>
<tr>
<td>Probability sexually active</td>
<td>0.80 (0.75, 0.85)</td>
<td>0.65 (0.60, 0.70)</td>
<td>(Ueda et al., 2020)</td>
</tr>
<tr>
<td>Prevalence</td>
<td>0.05 (0.00, 0.10)</td>
<td>0.03 (0.00, 0.08)</td>
<td>(K. M. Kreisel et al., 2021; Schillinger et al., 2005)</td>
</tr>
<tr>
<td>Incidence with infected partner</td>
<td>0.10 (0.05, 0.15)</td>
<td>0.10 (0.05, 0.15)</td>
<td>(Althaus, Heijne, et al., 2012; Althaus, Turner, et al., 2012; Lin et al., 1998; Quinn et al., 1996; Tu et al., 2011)</td>
</tr>
<tr>
<td>Sensitivity of screening exam</td>
<td>0.97 (0.85, 1.00)</td>
<td>0.97 (0.85, 1.00)</td>
<td>(Gaydos, 2005; Watson et al., 2002)</td>
</tr>
<tr>
<td>Input name</td>
<td>Female (low, high)</td>
<td>Male (low, high)</td>
<td>Source</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>--------------------</td>
<td>------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>EPT prescription treatment probability</td>
<td>0.41 (0.36, 0.77)</td>
<td>0.41 (0.36, 0.77)</td>
<td>(Oliver et al., 2016; Slutsker et al., 2020)</td>
</tr>
<tr>
<td>EPT med-in-hand treatment probability</td>
<td>0.53 (0.48, 0.80)</td>
<td>0.53 (0.48, 0.80)</td>
<td>(Kissinger et al., 2005, 2006; Oliver et al., 2016)</td>
</tr>
<tr>
<td>Prevalence among sex partners</td>
<td>0.60 (0.55, 0.65)</td>
<td>0.60 (0.55, 0.65)</td>
<td>(Khan et al., 2005)</td>
</tr>
<tr>
<td>Probability infection clears when untreated</td>
<td>0.09 (0.04, 0.14)</td>
<td>0.09 (0.04, 0.14)</td>
<td>(Geisler et al., 2013a; Golden et al., 2000; Korenromp et al., 2002)</td>
</tr>
<tr>
<td>Proportion opposite sex</td>
<td>0.96 (0.91, 1.00)</td>
<td>0.96 (0.91, 1.00)</td>
<td>(Lansky et al., 2015)</td>
</tr>
<tr>
<td>Mean time to treatment partner referral</td>
<td>2.75 (2.70, 2.80)</td>
<td>2.75 (2.70, 2.80)</td>
<td>(Estcourt et al., 2015; Menon-Johansson et al., 2006)</td>
</tr>
<tr>
<td>Mean time to treatment EPT</td>
<td>1.70 (1.65, 1.75)</td>
<td>1.70 (1.65, 1.75)</td>
<td>(Estcourt et al., 2015; Menon-Johansson et al., 2006)</td>
</tr>
<tr>
<td>Probability of screening if partner referral</td>
<td>0.60 (0.55, 0.65)</td>
<td>0.60 (0.55, 0.65)</td>
<td>(Gift et al., 2011; Golden et al., 2005; Hogben &amp; Kissinger, 2008;</td>
</tr>
<tr>
<td>Probability of treatment if diagnosed</td>
<td>0.60 (0.55, 0.65)</td>
<td>0.60 (0.55, 0.65)</td>
<td>Kissinger et al., 2005; Kissinger et al., 2005; Termoreshuizen, 1997</td>
</tr>
<tr>
<td>Probability of screening (symptomatic)</td>
<td>0.07 (0.06, 0.07)</td>
<td>0.07 (0.06, 0.07)</td>
<td>(Chacko et al., 2004; Datta et al., 2007; Farley et al., 2003;</td>
</tr>
<tr>
<td>Input name</td>
<td>Female (low, high)</td>
<td>Male (low, high)</td>
<td>Source</td>
</tr>
<tr>
<td>----------------------------------------------------</td>
<td>--------------------</td>
<td>------------------</td>
<td>-------------------------------------</td>
</tr>
<tr>
<td>Proportion med-in-hand</td>
<td>0.30 (0.25, 0.35)</td>
<td>0.30 (0.25, 0.35)</td>
<td>Torrone et al., 2014</td>
</tr>
<tr>
<td>Probability of infection among EPT treated</td>
<td>0.60 (0.55, 0.65)</td>
<td>0.60 (0.55, 0.65)</td>
<td>Assumption</td>
</tr>
<tr>
<td>Prevalence</td>
<td>0.04 (0.00, 0.09)</td>
<td>0.04 (0.00, 0.09)</td>
<td>(Chacko et al., 2004; Datta et al., 2007; Farley et al., 2003; Torrone et al., 2014)</td>
</tr>
<tr>
<td>Proportion EPT use</td>
<td>0.50 (0.45, 0.55)</td>
<td>0.50 (0.45, 0.55)</td>
<td>Assumption</td>
</tr>
<tr>
<td>Cost of chlamydia treatment (2020 dollars)</td>
<td>26.00 (20.80, 31.20)</td>
<td>26.00 (20.80, 31.20)</td>
<td>(Gift et al., 2011)</td>
</tr>
<tr>
<td>Cost of chlamydia treatment if subsidized (2020 dollars)</td>
<td>0.30 (0.24, 0.36)</td>
<td>0.30 (0.24, 0.36)</td>
<td>(Gift et al., 2011)</td>
</tr>
<tr>
<td>Cost of clinical appointment (2020 dollars)</td>
<td>45.00 (36.00, 54.00)</td>
<td>45.00 (36.00, 54.00)</td>
<td>(Gift et al., 2011)</td>
</tr>
<tr>
<td>Cost of time of clinical visit (2020 dollars)</td>
<td>30.00 (24.00, 36.00)</td>
<td>30.00 (24.00, 36.00)</td>
<td>(Gift et al., 2011)</td>
</tr>
<tr>
<td>Cost of PID treatment (2020 dollars)</td>
<td>380.00</td>
<td>-</td>
<td>(Yeh et al., 2003)</td>
</tr>
<tr>
<td>Cost of chronic pelvic pain treatment (2020 dollars)</td>
<td>800.00</td>
<td>-</td>
<td>(Yeh et al., 2003)</td>
</tr>
<tr>
<td>Cost of ectopic pregnancy treatment (2020 dollars)</td>
<td>4,000.00</td>
<td>-</td>
<td>(Yeh et al., 2003)</td>
</tr>
<tr>
<td>Cost of infertility (2020 dollars)</td>
<td>8,000.00</td>
<td>-</td>
<td>(Yeh et al., 2003)</td>
</tr>
<tr>
<td>Probability of PID if untreated</td>
<td>0.12 (0.02, 0.24)</td>
<td>-</td>
<td>(Haggerty et al., 2010; Kumar et al., 2021; Price et al., 2013)</td>
</tr>
<tr>
<td>Probability of infertility given PID</td>
<td>0.10 (0.05, 0.15)</td>
<td>-</td>
<td>(Chesson et al., 2021; Haggerty et al., 2010; Kumar et al., 2021)</td>
</tr>
<tr>
<td>Probability of chronic pelvic pain given PID</td>
<td>0.18 (0.13, 0.23)</td>
<td>-</td>
<td>(Haggerty et al., 2010; Ong et al., 2017)</td>
</tr>
<tr>
<td>Input name</td>
<td>Female (low, high)</td>
<td>Male (low, high)</td>
<td>Source</td>
</tr>
<tr>
<td>--------------------------------------------------------</td>
<td>--------------------</td>
<td>-----------------</td>
<td>-------------------------------------------------</td>
</tr>
<tr>
<td>Probability of ectopic pregnancy given PID</td>
<td>0.08 (0.03, 0.13)</td>
<td>-</td>
<td>(Haggerty et al., 2010; Ong et al., 2017)</td>
</tr>
<tr>
<td>Extragenital testing given exposure and given testing</td>
<td>-</td>
<td>0.55 (0.50, 0.60)</td>
<td>(Patton et al., 2014)</td>
</tr>
<tr>
<td>Prevalence of extragenital infection</td>
<td>-</td>
<td>0.01 (0.01, 0.01)</td>
<td>(Jones et al., 2019)</td>
</tr>
</tbody>
</table>

Notes:

EPT = expedited partner therapy; PID = pelvic inflammatory disease; med-in-hand = EPT given as a medication.

"Treatment costs" refer to the cost of chlamydia antibiotic treatments. "Clinical appointment" costs refer to the dollar cost of per diagnostic exam for chlamydia. "Time costs of clinical visits" include the time taken to attend a healthcare facility as well as the time invested by healthcare practitioners.

All probability values are given for one week, the simulation time step, unless otherwise stated.

Inputs listed as "Calibration" were the initial inputs for the three health states. These values were calibrated using the population of males and females aged 18–24 years living in New York State (NYS) according to the 2010 US census. For example, the model was used to estimate the number of infected individuals using the total population, screening rates, prevalence estimates, and diagnoses totals. These values do not have ranges because they were not assessed in the sensitivity analysis. They also do not have specific sources because they were derived during calibration.

Sources listed as "Assumption" were values estimated after consultations with experts in the field. No literature was identified to provide values for these inputs.
Table 13. Modeled chlamydia-related total treatment and sequelae costs, number of successful treatments, and cost-effectiveness ratio of heterosexually active male and female sex partners aged 18-24 years old given EPT and partner referral use state-based case

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Partner referral</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>Male</td>
<td>Total</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Number of sex partners treated</td>
<td>2,099</td>
<td>5,631</td>
<td>7,730</td>
<td>8,065</td>
<td>21,586</td>
</tr>
<tr>
<td>Number of infected sex partners treated</td>
<td>2,072</td>
<td>5,559</td>
<td>7,631</td>
<td>4,412</td>
<td>11,808</td>
</tr>
<tr>
<td>Number of uninfected sex partners treated</td>
<td>27</td>
<td>71</td>
<td>98</td>
<td>3,653</td>
<td>9,778</td>
</tr>
<tr>
<td>Total societal cost (USD)</td>
<td>1,889,201</td>
<td>1,439,32</td>
<td>3,328,52</td>
<td>1,009,4</td>
<td>394,817</td>
</tr>
<tr>
<td>Total treatment cost (USD)</td>
<td>37,898</td>
<td>101,678</td>
<td>139,575</td>
<td>147,515</td>
<td>394,817</td>
</tr>
<tr>
<td>Total clinical cost (USD)</td>
<td>498,574</td>
<td>1,337,64</td>
<td>1,836,22</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total sequelae cost (USD)</td>
<td>1,352,729</td>
<td>0</td>
<td>1,352,729</td>
<td>861,903</td>
<td>0</td>
</tr>
<tr>
<td>Treatment cost per infected sex partner treated (USD)</td>
<td>18</td>
<td>18</td>
<td>37</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>Clinical cost per infected sex partner treated (USD)</td>
<td>241</td>
<td>241</td>
<td>481</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sequalae cost per infected sex partner treated (USD)</td>
<td>653</td>
<td>0</td>
<td>653</td>
<td>195</td>
<td>0</td>
</tr>
<tr>
<td>CE ratio</td>
<td>912</td>
<td>259</td>
<td>229</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>ICER</td>
<td>-</td>
<td>-</td>
<td>-12</td>
<td>-83</td>
<td></td>
</tr>
</tbody>
</table>

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Notes: Treatment costs are annualized, including all weeks of the last year of the simulation; USD = 2020 United States dollars; CE = cost-effectiveness; ICER = incremental cost-effectiveness ratio; EPT = expedited partner therapy. ICER = incremental cost-effectiveness ratio. CE ratios are given as 2020 dollars spent (all costs summed) per treatment of infected sex partners.
Figure 10. Simplified Markov chain stock and flow diagram including health states, transition states, and input variables

Notes: A Markov chain is a simulation model which uses health states or "stocks" (boxes with borders) to represent modeled individuals' different health and exposure statuses. Modeled individuals may move between health states by crossing through transition states via "pipes" (transition states). Transition states are double-sided straight lines with black arrowheads. Infected individuals who test positive become "Diagnosed Index Patients," and their sex partners become eligible for partner referral or EPT treatment. If any sex partner is left untreated, reinfection may occur after the index patient transitions through Cure without partner treatment to the at-risk Susceptible and exposed health state. If healthcare practitioners successfully treat all partners with any strategy, simulated individuals transition back to the Susceptible and unexposed health state.
Figure 2. Simplified diagram of variables used to calculate the cost-effectiveness ratios for partner referral and EPT displaying which variables were used to calculate each ratio

Notes: PR = partner referral; EPT = expedited partner therapy; CE = cost effectiveness. Partner referral is the practice of asking diagnosed index patients to refer their sex partner(s) for testing and eventual treatment if diagnosed. EPT is the practice of providing a prescription or medication to the index patient to deliver to their sex partner(s). Cost effectiveness refers to the costs in terms of societal costs per treatment of infected sex partner.

All labels in this diagram represent variables. The final cost-effectiveness ratios are displayed in bold and with a border. "Shadow" variables are shown in grey, which are variables calculated in a different section of the model and reused in the section depicted here.

340b refers to the United States Health Resources and Services Administration's 340B Drug Pricing Program.
Notes: PID = pelvic inflammatory disease; CPP = chronic pelvic pain; EP = ectopic pregnancy; PR = partner referral; EPT = expedited partner therapy. This figure displays the variables used to calculate average and totals costs of sequelae for female sex partners who develop PID, ectopic pregnancy, chronic pelvic pain, and infertility. The probability and cost of each sequela are averaged as the *Mean cost of sequelae*, which is the same for EPT and partner referral.
Figure 12. Trend of ICER value given percentage change in the average cost of sequelae, the probability of sequelae, and its prevalence among female sex partners

Notes: ICER = incremental cost-effectiveness ratio. The ICER is the ratio between the incremental cost of each additional treatment given to EPT to the incremental effectiveness return for each treatment. This figure displays the trendline of the ICER comparing expedited partner therapy (EPT) to partner referral given a percentage change in three selected inputs. The inputs are the cost of sequelae, the probability of sequelae, and the probability of infection among sex partners receiving EPT.

An ICER of 0 indicates that EPT and partner referral are in parity in terms of cost-effectiveness. In this figure, the probability of sequelae and prevalence among sex partners cross the ICER = 0 thresholds with only small percentage increases, at 0.13 and $1,628 respectively. In contrast, the cost of sequelae must fall by nearly 20% from 0.60 to 0.53 to cross ICER = 0.

The point labels are not the percent change at that point but rather the input value at that percent change. For example, a -20% change in the probability of sequelae developing was 0.10, which was down from 0.12.
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PAPER THREE

PROMOTING EXPEDITED PARTNER THERAPY FOR CHLAMYDIA AND GONORRHEA TO TREAT EXPOSED SEX PARTNERS: STRATEGIES, FACILITATORS, AND BARRIERS TO PROMOTION ACTIVITIES BY US STATE HEALTH DEPARTMENTS
ABSTRACT

Introduction

Expedited partner therapy (EPT) is the practice whereby healthcare practitioners treat, without a prior diagnosis, the sex partners of index patients diagnosed with certain sexually transmitted infections (STI). EPT effectively prevents reinfection of index patients and improves treatment outcomes for sex partners, particularly if given to index patients as medicine-in-hand instead of as a prescription. Unfortunately, there is limited research about health department strategies to promote EPT or the facilitators and barriers to these efforts.

Methods

EPT promotion strategies, barriers, and facilitators to EPT promotion among health departments were investigated using diversity sampling (sampling states with various characteristics). Twenty-two semi-structured interviews with federal, state, and local health department staff and directors involved with EPT promotion were conducted, including 14 US states and eight local jurisdictions. Inductive line-by-line coding and the constant comparison method were used to synthesize common and divergent themes utilizing grounded theory. Respondent’s support for EPT promotion was also assessed.

Results

Five promotion strategies were identified, including advocacy and education, partnerships, committees of stakeholders, pre-purchasing medication, and conducting research. Commonly reported barriers to EPT promotion included perceptions about adverse outcomes and medical liability, a lack of payment solutions, and interest group
opposition. Barriers limited to certain jurisdictions included legislative landscape, culture, and resource constraints. Facilitators to EPT included individual champions of EPT, interest groups in favor of EPT, and liability protections. An emergent theme was opposing perspectives among respondents on whether to provide EPT to MSM and for gonorrhea. Proponents of EPT for MSM argued that it was important to provide better access to care while opponents expressed concerns about comorbidities.

**Conclusions**

There are a variety of strategies available to state health departments to promote the use of EPT, yet complex structural barriers remain to EPT promotion efforts. However, state governments are uniquely positioned to address these barriers by negotiating with medical and pharmacy boards to unify messaging and coordinating funding for pre-purchasing EPT medications.
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INTRODUCTION

National diagnoses of sexually transmitted infections (STI) in the United States increased from 2015 to 2019, including chlamydia (19%) and gonorrhea (56%) (CDC, 2018; “Centers for Disease Control and Prevention,” 2021a). This underscores the need to promote and improve interventions that may help reduce incidence (K. M. Kreisel et al., 2021). One strategy to address the rising number of diagnoses is to ensure treatment of the sex partners of diagnosed index patients (the first individuals in a sexual network to be diagnosed by screening). This is because sex partners are at high risk of infection and can reinfect their partners if left untreated. In the clinical setting, options to manage sexual partners include partner referral and expedited partner therapy (EPT) (Expedited Partner Therapy, 2021; Jamison et al., 2018). Partner referral is the traditional practice of enlisting index patients to refer their sex partners for testing (and treatment if diagnosed) (Kissinger & Hogben, 2011). EPT is the practice of, without a prior diagnosis, providing either prescriptions or prepackaged medicines (med-in-hand) to index patients to deliver to their sex partner(s) (Ferreira et al., 2013). Evaluations of EPT's effectiveness at reducing reinfections among index patients and reducing time to treatment for sex partners are positive compared to partner referral (Ferreira et al., 2013; Handsfield et al., 2006; Oliver et al., 2016).

Since 2006, the Centers for Disease Control and Prevention (CDC) has included information and guidance on EPT legalization and implementation and recommended EPT use for partner management (Gannon-Loew et al., 2017; Legal Status of Expedited Partner Therapy (EPT), 2021; O'Connor, 2011). By 2021, EPT use was "permissible" in all but four states and "potentially allowable" in all remaining states (Legal Status of Expedited Partner ...
Therapy (EPT), 2021). Initial legalization of EPT in most states involved allowing healthcare practitioners to legally consider the sex partners of index patients diagnosed with certain STIs as 'patients' in their care (Legal Status of Expedited Partner Therapy (EPT), 2021). The use of EPT varies significantly between states, and differences in the policies and promotion efforts may explain this (Kissinger, 2014; McCool-Myers et al., 2020). While documentation of the variation in state policies is available from 2019, there has not been a scientific summary of EPT promotion strategies used by states (Cramer et al., 2013).

Previous qualitative research has focused on the experiences of healthcare practitioners and patients receiving EPT and barriers to the use of EPT as a practice (Cramer et al., 2013; Rosenfeld et al., 2015). However, little research has focused on the health department staff and directors responsible for implementing and promoting EPT. One recent study identified liability and concern about adverse events, funding, awareness, and electronic medical records as barriers to EPT implementation by practitioners and researchers (Legal Status of Expedited Partner Therapy (EPT), 2021; McCool-Myers et al., 2020). However, the types of promotion strategies and their success at addressing obstacles to EPT implementation remain understudied.

This present study aims to fill the gaps in our current knowledge of EPT promotion strategies, barriers, and facilitators using both qualitative interviews of state health department staff and directors involved with EPT throughout the US, and inductive analysis. Additionally, interviews were conducted with one respondent from a federal agency and several local health department staff and directors to provide additional
context about how state-level promotion activities impact their jurisdictions. This study focused on understudied health department staff and their efforts to promote EPT and identified key areas where health departments have opportunities to improve EPT implementation in their states. The findings add to the existing literature by offering additional explanations for variation in EPT use and a better understanding of critical barriers to EPT promotion.
METHODS

Analytical Overview

Semi-structured interviews of health department staff and directors were conducted to gather information about strategies used to promote EPT and the facilitators and barriers to promoting EPT. Transcripts were inductively coded using grounded theory to identify codes, categories, and themes (Glaser, 1965).

Sampling, Recruitment, and Respondents

This study utilized diversity sampling (selecting respondents to obtain representation on specific factors) to select initial targets and recruit successive respondents. Public information (hosted on state health department websites) about each state’s EPT policies and promotion efforts was used to identify states from different regions (northeast, south, and west), diverse legislative (whether the health department has control over EPT legalization), and STI epidemiology. An effort was also made to sample states that had legalized EPT both before and after 2010, in case states that had legalized EPT earlier had different promotion strategies from those with more recent legalization.

Finally, states with different legal permissions for EPT were sampled according to the CDC’s legalization tracker (Legal Status of Expedited Partner Therapy (EPT), 2021). The sampling strategy evolved, including abandoning consideration of the year of legalization (respondents’ answers did not differ meaningfully). A small group of initial interviews was secured using a listserv posting (n=4) and direct outreach to specific individuals. Subsequent interviews were secured using snowball sampling (n=10) and direct outreach to state health department public contact emails (n=5). Three respondents declined to participate, one responded initially but did not follow up, and a further five state health
departments gave no response. Recruitment continued after code saturation (final themes were identified) after 12 interviews and until meaning saturation (final themes were fully developed with all codes) was obtained after 20 interviews (Hennink et al., 2017). Table 1 gives characteristics of respondents, which included 22 health department directors and staff from 18 unique jurisdictions, including federal, state, and local health departments. Directors were individuals who headed STI control branches within their respective state or local health departments, which handled the state or local response to STIs (including chlamydia, gonorrhea, trichomoniasis, and syphilis). Staff members were generally more specialized in chlamydia and gonorrhea control, or even EPT implementation specifically. Three interviews included two respondents, while all other interviews were one-on-one. A majority of respondents had more than five years of experience working with EPT.

**Data Collection**

A semi-structured interview guide was used, with a series of broad questions and unscripted probing questions to add detail (see Appendix 2). In this way, every respondent answered a set of core questions about their background working with EPT, their jurisdiction’s STI challenges, and the strategies, barriers, and facilitators to EPT promotion that they had encountered. Probing questions explored the unique context of EPT promotion in each jurisdiction. Interviews ranged between 30 minutes and one hour in length and were conducted by phone or video conference calling. Interviews were recorded with respondents’ permission and transcribed using automatic audio-to-text transcription software. The author manually reviewed transcriptions, and synthesized interviews were member-checked to ensure respondents agreed with the authors’ interpretation of their answers as presented in point-by-point summaries (Birt et al., 2016). Coding started
immediately after the first interview, and themes identified in early interviews were used to inform subsequent questioning (Bradley et al., 2007; Brod et al., 2009; Glaser, 1965).

**Data Analysis**

Grounded theory was used to guide the interpretation and analysis of interviews. All codes were emergent codes identified using line-by-line coding after the first interview. Similar codes were grouped and refined further into concepts and into themes. Some themes were later determined to be limited to early respondents and were removed, and two themes were eventually combined due to overlap in their coverage of codes. The themes identified during earlier analysis were expanded and modified as additional interviews were completed. NVivo 12.1.0 was used for coding and theme development. See Appendix 2 for the list of codes and their definitions.
RESULTS

Table 14 includes characteristics of respondents' jurisdictions, including the type of jurisdiction (federal, state, or local) and how EPT was used. Regarding the states surveyed, the state's differed in the statutes that governed EPT use, including whether they required that names be included on EPT prescriptions, which infections they could treat using EPT (ranging from chlamydia alone to chlamydia, gonorrhea, and/or trichomoniasis), and whether healthcare providers are free from liability in the event of adverse (i.e., allergic) reactions (Table 14). Further, EPT was actively promoted in nearly all states surveyed, regardless of political leaning. States utilized a variety of strategies to promote EPT, each with specific strengths and limitations. Also identified were barriers and facilitators to EPT implementation, which were not specific to promotion strategies.

**EPT promotion strategies**

Table 15 lists five strategy themes that were identified along with the strengths and limitations of each strategy. These themes included advocacy and education for healthcare practitioners, forming partnerships, using stakeholder subcommittees, medication pre-purchasing, and research.

*Advocacy and education*

Many respondents engaged in presentations, workshops, and webinars to promote EPT among healthcare practitioners and pharmacists. The purpose of these efforts was typically to explain to healthcare providers what EPT was, when it was appropriate to use, and (if applicable) that they were protected from liability when administering it. In some cases, proponents started advocacy before EPT legalization. One respondent explained:
"We did webinars. I presented - I don't know how many grand rounds on the topic. We invited ourselves to come give round - grand rounds on it... We held focus groups. I mean, it was before it was legalized, we had focus groups with providers and with pharmacists to try to anticipate what messaging would work and what they viewed as obstacles." - Local administrator

There was concern among several respondents that pharmacists might not fill EPT prescriptions, typically because pharmacists might be unaware EPT was legal. Many health departments had also developed information sheets with crucial information about EPT for patients and healthcare practitioners.

**Forming partnerships**

A central theme in many interviews was various partnerships between their health department and individuals in influential positions, other state health departments, and non-government organizations. Partnerships of all types strengthened the promotion of EPT by reaching important audiences and gaining allies to help promote EPT without health department resource expenditure.

A few respondents described partnerships with individuals who served as "champions" of EPT promotion using their unique positions to help promote EPT. For example, it was valuable to partner with state pharmacy, nursing, and medical boards in many states. The professionals in these fields were more receptive to promotional messaging from their professional boards than the health department.

"That [promotion to physicians] is best received when the person saying it is a medical physician themselves, which I am not... partnering with [a] medical director, is one of the things that I would recommend to other states." - State department head

In addition to professional boards, a few states had partnered with medical schools to ensure that graduating students would be familiar with EPT. Finally, a few states partnered
with non-profits to help with direct promotion to healthcare facilities, survey distribution and analysis, and the distribution of pre-purchased EPT medications (see below).

A few respondents described cooperation between themselves and other state health departments aiming to promote EPT. In some cases, they shared pieces of advice regarding the value of liability protections and how best to utilize the Federal 340B reduced pricing program (described in more detail below).

Committees of stakeholders

In several states, committees of stakeholders were formed before EPT implementation to ensure that stakeholders accepted important aspects of EPT. The exact make-up (for example, healthcare providers, pharmacists, legal professionals) and timing of committees (before or after EPT legalization) varied, but respondents described these efforts as beneficial in every instance. Expressly, they noted how committees revealed resolvable conflicts between stakeholders. In this way, forming stakeholder committees averted conflicts during implementation and invited other organizations to aid state efforts to promote EPT.

Pre-purchasing medications for EPT med-in-hand

Another strategy was to pre-purchase medications to facilitate easier use of EPT med-in-hand. Most states that pre-purchased EPT medications for public health department clinics used the Health Resources and Services Administration's (HRSA) 340B Drug Pricing Program. This program requires pharmaceutical manufacturers participating in Medicaid to sell medications at discounted prices to health care providers caring for uninsured and low-income patients. In practice, the 340B program significantly reduced
the cost of EPT med-in-hand for patients at public and non-profit clinics. In describing the low costs of discounted medications, one participant explained:

"Very, very inexpensive. Yep, it's like a pack of gum or less to treat somebody for chlamydia." - State department staff

A few respondents described changes in public health departments in recent years to increase capacity to treat patients, which indirectly benefited EPT implementation because these clinics could use state pre-purchased medications. However, using the 340B program required considering EPT treatments of sex partners as treating index patients, because EPT treatments may prevent the reinfection of index patients. Considering EPT as a treatment of index patients was necessary to satisfy the 340B patient definition (a specific section of the law governing 340B use), which defined patients as individuals with an established relationship and healthcare records at the healthcare facility treating them using 340B medications (Notice Regarding Section 602 of the Veterans Health Care Act of 1992 Patient and Entity Eligibility, 1996). Respondents from two states reported an inability or hesitation by their leadership to make this interpretation, and a lack of state funding available to purchase med-in-hand medications without 340B’s price reduction. These states, therefore, did not pre-purchase EPT med-in-hand. This hesitance was out of concern that using 340B in this way could jeopardize the states’ use of 340B for other (often more expensive) purchasing programs. A few states either implemented or were considering pre-purchasing medications outside of 340B pricing. This option required significant state funding.
Conducting research

Respondents rarely described research on EPT by health departments and were usually contingent on having scientifically trained staff or a partnership with a research university. EPT-focused research improved implementation efforts by evaluating the impact of promotion efforts. For example, some health departments evaluated the reception of EPT materials they distributed using surveys and other feedback mechanisms.

Barriers and Facilitators

Respondents identified seven barriers to EPT promotion, which are presented in Table 16. Some barriers were described by nearly all respondents, including a lack of payment solutions and perceptions about adverse outcomes and medical liability. Other barriers were specific to certain jurisdictions, including legislative landscape, cultural factors, and funding availability.

Adverse outcomes and liability

Nearly all respondents described a barrier stemming from concerns of healthcare practitioners about adverse outcomes, the potential for medical malpractice lawsuits, and liability protections. Respondents described liability protections as a facilitator to promotion efforts. Liability protections were included in the laws of half of the conservative states and all but one of the progressive states in this study. Remarking about their state’s liability protections, one respondent stated:

"Believe it or not, for our conservative, very red state. We have wonderful legislation in place around EPT." - State department head
In some cases, even with liability protections, it remained a challenge to educate healthcare practitioners. Additionally, state liability protections do not cover federally insured healthcare practitioners, as explained by one respondent:

"We've had to deal a lot with the FQHCs [Federally Qualified Health Centers] because their liability insurance is actually covered by HRSA. And so, there's complications around whether they would be supported if they were sued around EPT. That's not a state's issue – it's a federal issue." - Non-government agent

Respondents who frequently met with healthcare practitioners to promote EPT noted that the concern for adverse events was persistent and pervasive, despite extremely rare adverse reactions to medications. Three respondents had tracked adverse reactions to EPT in their state with no cases found, while others noted that no case had ever occurred to their knowledge. Many respondents expressed frustration that the concern about liability was so prevalent given the apparent absence of adverse outcomes, including the following individual:

"We didn’t find [adverse reactions] with the first hundred thousand episodes - maybe it’s okay. Not only that, the liability cuts two ways. Right? I mean, no one knows how this works out. So, you could easily say that you are liable for not offering an intervention which is in the STD Treatment Guidelines, as you are liable for offering a treatment if there was an adverse event." - State department staff

One respondent in a state without liability protections stated that over time this concern eventually diminished with persistent messaging to healthcare practitioners to recognize that liability is unlikely to materialize in practice.

Paying for EPT

Many respondents described a key barrier as difficulty in paying for EPT whenever pre-purchased medications were not available. This barrier occurred in states where no
pre-purchasing was done and was cited as a barrier for patients who are not low income or who go to private clinics. In addition, payment for med-in-hand was left either to be paid by the index patient or the healthcare provider because insurance providers and Medicaid may not reimburse index patients for EPT medications for their sex partners. One state and one local health department respondent described the issue as follows:

“Otherwise, it’s going to be up to the patient or their insurance company, but I don’t think the insurance companies are going to pay in general. For you to treat someone else [sex partners].” - State department head

“But I think a funding issue has been to have to buy those medications and then give them away for free... or how can they charge the patient for medications that aren’t actually the patient’s medications.” - Local department head

While the 340B program enabled pre-purchasing of med-in-hand EPT in several states, two states rejected this option due to concerns about its legality. Namely, these respondents identified uncertainty in the definition of “patients” for the 340B program, which may be interpreted to exclude the use of 340B medications to treat sex partners of index patients. One respondent explained:

“What would help tremendously is if there was a way to go on a federal level to the 340B program and say, “look if you can redefine what a patient is for STD medications, that would eliminate a lot of barriers because right now we only give prescriptions”.” - State department head

Regarding EPT prescriptions, respondents described different payment barriers. For example, insurance companies may not cover sex partners who bring their prescriptions to a pharmacy, especially if the prescription did not include their name. According to one respondent:

“I know that there are situations where patients have received the generic or unnamed prescriptions and have encountered very strong barriers – inability to just
convert those to their own name [for the purpose of insurance claiming].” - State department head

Therefore, private healthcare providers may be limited to writing prescriptions with sex partner names included, even when the law in that state permits the use of prescriptions without names.

Resource constraints

In most states, respondents described health department programs as struggling to face the combined challenge of various public health crises with their limited resources. One respondent stated bleakly:

“We’ve had to make really difficult decisions in the last few years about, you know, okay, we have to do less with less.” - State department head

These challenges included COVID-19, human immunodeficiency virus (HIV) management, and the reemergence of congenital syphilis. While chlamydia and gonorrhea were prevalent, controlling these infections (and promoting EPT specifically) were rarely described as priority activities for surveyed health department offices, particularly among directors. Larger states were likely to have more staff dedicated to STI control and even to EPT specifically. But even for these states, resources available for EPT promotion have reportedly diminished in recent years.

Local culture and legal landscape

The legal and cultural landscape in some states presented barriers to EPT promotion and STI control more generally. These impacted both the willingness of legislatures to adopt or modify EPT policy and the willingness of patients to seek care for
Respondents from conservative states described difficulty controlling STIs given local culture. One respondent described the situation in these terms:

“And I will tell you that many clients return with the same infection every three months. And it doesn’t matter how much education... we’ve given them on prevention... And so that is one of our challenges - it’s repeat and there's not really anything you can do. “Just give me the medicine, it’ll cure it”. - State department head

Culture often paralleled the legal landscape with conservative legislatures unwilling to address STI-related public problems. As a result, while respondents in several conservative states reported easy adoption of EPT legislation, it was difficult to make amendments after adoption in many cases.

**Interest group involvement**

In several states, interest groups conflicted with aspects of EPT implementation. One source of resistance originated from trial lawyers, whose respondents described resisting the adoption of liability protections. One example was provided by the following remark:

“But the concern is that [the State’s] trial lawyers might, you know, really balk at having any liability protection written into the statute. You know, medical malpractice is probably their bread and butter so they would oppose any protections against, you know, medical malpractice lawsuits against pharmacists or physicians.” - State department head

This concern was reported by three respondents in different states, though two of these noted that their concern was speculation. When faced with trial lawyer opposition to liability protections, one successful strategy was to partner and negotiate with a legal professional to enlist a spokesperson who could communicate with other lawyers on behalf of the health department. In addition to trial lawyer opposition, a few respondents
reported that pharmacy boards and medical boards disagreed with the exact wording used in the EPT statute. However, resistance to EPT from interest groups other than trial lawyers was uncommon.

**Perceived limits of EPT**

Respondents varied widely in their beliefs about to what extent EPT should replace partner referral. In some cases, this limited their promotion of EPT. Some respondents felt EPT should be considered a standard of care and that healthcare practitioners should be held liable for not using EPT (rather than being concerned about liability for an adverse reaction). Proponents of EPT use cited the improved time to treatment for sex partners, reductions in reinfections among index patients, and the convenience that EPT offered to sex partners who would not need to visit a healthcare provider for testing (and possibly a pharmacy as well if given med-in-hand). Most respondents held a middling position, considering EPT an option of last resort if the “gold standard” (direct care through partner referral) was unobtainable. One respondent remarked:

“So, while some states, promoting EPT as just, you know, another tool in the toolbox, which we do too. We really do try to urge that it be seen as an intervention, as, of last resort.” - State department head

Finally, a few respondents themselves rejected any use of EPT and refused to promote EPT for any infection. The stated concerns of opponents of EPT were the emergence of antimicrobial resistance and failing to care for sex partners who receive EPT.

Among respondents who did support EPT use, there were also concerns about treating patients with gonorrhea and men who have sex with men (MSM) using EPT. Several respondents opposed using EPT for gonorrhea, citing concerns about the greater
potential for extragenital infections, the lack of availability of oral medication needed for the treatment regime for gonorrhea if EPT is used (Gonorrhea Treatment and Cure, 2019), or a belief that CDC guidelines advise against using EPT for gonorrhea. Some respondents stated great concern for emerging antimicrobial resistance, especially for gonorrhea. Others were less concerned, citing a belief that the CDC would monitor this issue of gonorrheal antimicrobial resistance. Respondents who favored using EPT on index patients with gonorrhea also argued that EPT was too valuable as a treatment option to not use for gonorrhea, despite concerns.

Respondents also disagreed on offering EPT to MSM index patients. Those who opposed using EPT to treat MSM expressed concerns about the presence of extragenital (anorectal or pharyngeal) infections, cited evidence that extragenital infections were more prevalent among MSM, and noted that MSM are at increased risk of HIV and syphilis comorbidity. These respondents believed MSM had greater need of individualized personal care and ought not be treated anonymously using EPT. Respondents who supported using EPT for MSM noted the lack of scientific evidence supporting the concern that MSM treated with EPT had worse health outcomes as a result of their EPT treatment. Supporters of EPT for MSM also noted that not using an effective treatment option like EPT, despite a lack of scientific evidence, was likely perpetuating longstanding stigma against MSM.

*Influence of individuals in positions with discretionary power*

One factor that served as a barrier or facilitator to EPT implementation was specific individuals in professional positions with discretion about EPT policy and the power to shape policy according to their beliefs. In some cases, respondents described single
individuals as having prevented any implementation of EPT. A description of one such powerful individual was as follows:

“There was an instance where there was someone who was influential who was opposed [to EPT]. And it was only when that person retired that it became possible to move forward.” - State department head

In other instances, individuals in key roles were described as “champions” of EPT and worked as allies of the health department to promote EPT, as described by this respondent:

“There were certain champions that just sort of popped up and we started to partner.” - State department head

These individuals served as connections between the health department and other organizations, providing opportunities to promote EPT or introduce education about EPT to professional schools or practicing healthcare practitioners.
DISCUSSION

This study revealed several strategies, barriers, and facilitators of EPT promotion reported by state and local health department staff members promoting and using EPT. This research adds to existing literature, which has not focused on the specific strategies used by health departments to promote EPT in different states. While efforts to promote EPT were widespread, several barriers repeatedly appeared, requiring structural changes to the system surrounding EPT.

Previous literature had identified wide variation in EPT uptake in different states (Cramer et al., 2013; Introcaso et al., 2013; S. Lee et al., 2015). It was well established that liability protections and the ability to issue “no-name” prescriptions facilitated easier EPT use by healthcare practitioners (Cramer et al., 2013). In addition, the concerns that healthcare practitioners harbor about adverse outcomes, healthcare practitioners’ desire to directly care for each of their patients, and problems with reporting requirements had been documented (Legal Status of Expedited Partner Therapy (EPT), 2021; McCool-Myers et al., 2020).

In addition to these previously identified factors, two new factors arose as explanations for variation in EPT uptake in this study. First, there is wide variation in the opportunities (or lack thereof) for promotion strategies available to health departments. Of the five strategic themes identified, only advocacy and education were feasible to implement in all states that were included in this study. The other four strategies (forming partnerships, committees of stakeholders, pre-purchasing medications for med-in-hand, and conducting research) were only feasible to implement in states with certain conditions.
Research efforts required that health departments had scientifically trained staff or that the health department had a collaborative relationship with a university. Stakeholder committees and partnerships required cooperation between groups with often opposing objectives. Finally, pre-purchasing medications with 340B pricing required interpreting the legal language defining patients for the 340B program.

The second factor not previously identified that may explain variation in EPT uptake by healthcare practitioners is the support for EPT by health departments. The respondents of this study demonstrated a wide range of support for EPT. The reasons respondents cited to support their position included directly referencing scientific research, different interpretations of the CDC’s guidance on EPT, and their own professional experience. It seems likely that information about EPT is conflicting and that this conflict is impacting health department staff as much as it is impacting healthcare practitioners. Some health departments were highly active in promoting EPT, while on the other extreme, some respondents reported avoiding all EPT promotion.

A lack of payment options was a significant barrier that inhibited EPT use and promotion. This observation expands on previous qualitative research and provides insight into complications that persist despite the established cost-effectiveness of EPT (Gift et al., 2011; McCool-Myers et al., 2020). When it comes to cost, interpretation of payment barriers suggests two scenarios that would facilitate EPT use. The first scenario is when the index patient may receive a 340B priced med-in-hand packet dispensed at a healthcare facility (in states that utilize the 340B program for med-in-hand EPT and in the clinic that services low-income patients). The second scenario is when sex partners fill prescriptions
at a pharmacy using their own Medicaid or insurance coverage (possibly requiring their name on the prescription). Though EPT is more convenient for sex partners by omitting a diagnostic exam, it remains challenging to pay for in all other situations.

The policy implication of the payment barrier is that enabling EPT use requires modifying payment and reimbursement to facilitate payment when the direct beneficiaries of treatment (sex partners) are not present to pay for the medication. It would be valuable for HRSA to publish guidance for the 340B program or update the patient definition to make it compatible with EPT legalization statutes. For private clinics, it would be valuable for policymakers to encourage or require insurance providers and Medicaid to cover sex partners of their members in cases of STI partner treatment. Requiring coverage would enable index patients to receive medications for their partners for med-in-hand (at healthcare facilities and pharmacies), even when low-cost prepaid drugs are unavailable.

This study included several respondents from conservative states who actively promoted EPT. Support for EPT promotion in health departments was unrelated to the political climate in states. In some cases, respondents described that their states adopted a very progressive EPT policy. This fact contrasted with other policies related to sexual health described by respondents, such as comprehensive sex education and expanding abortion access; both were described as politically infeasible. This contrast may suggest that EPT policy is treated as routine or institutional policy in some cases, which remain somewhat separated from party politics in agenda-setting (Howlett, 1998). However, some conservative states in this study faced difficulty in adopting or updating EPT legislation and faced challenges related to local culture.
The results of this study also connect to existing policy theory. First, the communication and cooperation between states aligned with the diffusion of innovation theory. Successful implementation of public health policies depends on the effectiveness of the innovation, communication channels, time, leadership, and social systems (E. Rogers, 1971). Several health department directors shared essential ideas, demonstrating a vital communication channel between the states with earlier adoption of EPT legalization and those that legalized EPT more recently. Additionally, identifying key structural barriers that impede healthcare practitioners' decision to use EPT aligns with street-level bureaucracy theory (Lipsky, 2010). Successful promotion efforts benefited from making changes that facilitated easier EPT use by healthcare practitioners, by, for example, streamlining payment options. Several respondents recognized the value of making EPT the “path of least resistance” rather than promoting EPT without changing the system around EPT use (Cramer et al., 2013). This is related to the discretionary options available to healthcare practitioners.

There were limitations in this study. First, while states with diverse legal and cultural features were selected, more states were invited than accepted. It is possible that respondents who accepted the invitation were systematically different from those who did not, although there was no reason to suspect that this was the case. It is also likely that respondents had recall bias, particularly for states with long histories of EPT promotion. The oldest promotion efforts discussed by respondents dated 16 years before the time of the interview. Still, the experiences related by these respondents were not meaningfully different from respondents who described more recent promotion efforts (although states
that legalized EPT more recently did have respondents that were noticeably more excited about promoting EPT).

The results imply a few critical areas of potential future research. First, it is essential to investigate various payment methods that facilitate easier payment for EPT and to what extent these efforts expand or modify EPT use. Additionally, a few of the strategies identified in this study have not been evaluated scientifically. For example, it may be valuable to evaluate the impact of EPT education for healthcare practitioners in training, which resulted from some state partnerships described in this study. Another aspect of EPT legalization that may warrant deeper study is the impact professional organization support may have on EPT use patterns in a state. Several respondents highlighted the influence that these organizations have on their respective professionals (including nurses, physicians, and pharmacists), but no quantitative research has investigated this research avenue.

**Conclusions**

This study highlighted the key strategies used by health departments and identified the barriers to increased EPT use. EPT use is underutilized due to structural barriers that may inhibit EPT use when it would otherwise be a valuable treatment option. State health departments are in a unique position to address several obstacles, and fortunately, the ability to address these obstacles may exist independent of political barriers. These include forming partnerships to help streamline EPT use, finding ways to prepackage med-in-hand EPT, and negotiating with insurance providers and Medicaid to cover sex partners of their members.
### Table 14. Sample characteristics of respondents’ home jurisdictions

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Type</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jurisdiction type</td>
<td>State</td>
<td>13 (59.1)</td>
</tr>
<tr>
<td></td>
<td>Local</td>
<td>7 (31.8)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>2 (9.1)</td>
</tr>
<tr>
<td>Region</td>
<td>Northeast</td>
<td>5 (22.7)</td>
</tr>
<tr>
<td></td>
<td>South</td>
<td>6 (27.3)</td>
</tr>
<tr>
<td></td>
<td>Pacific West</td>
<td>4 (18.2)</td>
</tr>
<tr>
<td></td>
<td>Midwest</td>
<td>6 (27.3)</td>
</tr>
<tr>
<td></td>
<td>National Perspective</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Infections for which EPT use was promoted</td>
<td>Chlamydia only</td>
<td>2 (9.1)</td>
</tr>
<tr>
<td></td>
<td>Both chlamydia and gonorrhea</td>
<td>17 (77.3)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>2 (9.1)</td>
</tr>
<tr>
<td>Infections for which EPT use was legalized</td>
<td>Chlamydia only</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td></td>
<td>Both chlamydia and gonorrhea</td>
<td>17 (77.3)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>3 (13.6)</td>
</tr>
<tr>
<td>EPT medication pre-purchasing coordinated by health department</td>
<td>Yes</td>
<td>14 (63.6)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>7 (31.8)</td>
</tr>
<tr>
<td>No-name EPT prescriptions legal</td>
<td>Yes</td>
<td>16 (72.7)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>5 (22.7)</td>
</tr>
<tr>
<td>Medical liability protection for clinicians</td>
<td>Yes</td>
<td>14 (63.6)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>7 (31.8)</td>
</tr>
</tbody>
</table>
Notes: EPT=expedited partner therapy. “No-name EPT prescription” refers to the legality of writing EPT prescriptions for anonymous sex partners, for example, by prescribing medication to recipients named “EPT”. Percentages in this table do not sum to 100 because respondents with a national focus did not apply for several characteristics.
Table 15. EPT promotion strategies reported by respondents, the frequency of mention of each strategy, and the strengths and limitations for each strategy

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Frequency of mention</th>
<th>Strengths</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advocacy and education</td>
<td>Most</td>
<td>Low resource requirement; can assuage concerns about EPT being used improperly</td>
<td>May not have the desired impact; time for the benefit to materialize; requires connections with hosting organizations</td>
</tr>
<tr>
<td>Forming partnerships</td>
<td>Most</td>
<td>Minimal resources required for payoff</td>
<td>Not always an option; subject to partners’ objectives</td>
</tr>
<tr>
<td>Committees of stakeholders</td>
<td>Medium</td>
<td>Resolving conflicts between stakeholders is valuable throughout the promotion</td>
<td>May require a compromise between participating organizations; coordination with nongovernment stakeholders best to start early</td>
</tr>
<tr>
<td>Pre-purchasing medications for EPT med-in-hand</td>
<td>Medium</td>
<td>Eliminates payment barrier for recipient patients</td>
<td>Funding is rarely available at the required scale to implement without 340B program pricing</td>
</tr>
<tr>
<td>Conducting research</td>
<td>Least</td>
<td>May improve local EPT promotion</td>
<td>The perception that no further research was needed; EPT challenging to research; access to collaborating research centers or in-house research</td>
</tr>
</tbody>
</table>

Notes: “med-in-hand” refers to EPT use in which the medication is provided to the index patient to deliver to their sex partners, rather than a prescription.
Table 16. Barriers and facilitators to EPT implementation described by respondents, frequency of mention, whether each was a barrier or facilitator, and any strategies which were identified that could address the barrier

<table>
<thead>
<tr>
<th>Barriers/Facilitator</th>
<th>Frequency of mention</th>
<th>Type</th>
<th>Strategies to address barriers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse outcomes and liability</td>
<td>Most</td>
<td>Barrier or Facilitator</td>
<td>None</td>
</tr>
<tr>
<td>Paying for EPT</td>
<td>Most</td>
<td>Barrier</td>
<td>Pre-purchase EPT medications for med-in-hand and partnering with insurance/Medicaid</td>
</tr>
<tr>
<td>Resource constraints</td>
<td>Medium</td>
<td>Barrier</td>
<td>None</td>
</tr>
<tr>
<td>Local culture and legal landscape</td>
<td>Medium</td>
<td>Barrier</td>
<td>Information outreach, advocacy, and education may be effective</td>
</tr>
<tr>
<td>Interest group involvement</td>
<td>Least</td>
<td>Barrier or Facilitator</td>
<td>Partnerships and committees of stakeholders can find a compromise</td>
</tr>
<tr>
<td>Perceived limits of EPT</td>
<td>Least</td>
<td>Barrier</td>
<td>Information outreach; advocacy and education</td>
</tr>
<tr>
<td>Influence of individuals in positions with discretionary power</td>
<td>Least</td>
<td>Barrier or Facilitator</td>
<td>No strategies for barriers; it is valuable to partner with potential “champions” of EPT</td>
</tr>
</tbody>
</table>

Notes: Some themes were barriers for some states but were facilitators in other states. For example, interest groups could align with or oppose state promotion efforts. No themes were identified that were facilitators only.
References


https://www.cdc.gov/std/statistics/2020/overview.htm#Chlamydia


Ferreira, A., Young, T., Mathews, C., Zunza, M., & Low, N. (2013). Strategies for partner notification for sexually transmitted infections, including HIV. *Cochrane Database of Systematic Reviews, 10*.


*Legal Status of Expedited Partner Therapy (EPT).* (2021).


**APPENDIX**

*Table 17. List of codes developed in NVivo 12.6.0 and definitions for each code.*

<table>
<thead>
<tr>
<th>Name of code</th>
<th>Description of code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ability to clinically examine sex</td>
<td>References to partner referral’s advantage for clinically examining sex partners. EPT is a great policy, but partner referral is the gold standard because we can examine each patient.</td>
</tr>
<tr>
<td>partners</td>
<td></td>
</tr>
<tr>
<td>Administrative barriers</td>
<td>References to administrative difficulties promoting EPT. For example, needing to clear social media packages for release.</td>
</tr>
<tr>
<td>Adverse reactions</td>
<td>Educating providers about adverse reactions to medications and navigating this issue. References to the fact that adverse reactions are rare, and it is hard to persuade healthcare practitioners.</td>
</tr>
<tr>
<td>Advocacy &amp; listening tours</td>
<td>Descriptions of advocacy and listening tours by health department staff (or the respondent themselves). Efforts to educate health practitioners about EPT.</td>
</tr>
<tr>
<td>Asymptomatic infections</td>
<td>References to chlamydia and gonorrhea being asymptomatic and requiring screening to diagnose prevalent individuals.</td>
</tr>
<tr>
<td>Barriers to promotion</td>
<td>Any comments related to barriers to promotion of EPT.</td>
</tr>
<tr>
<td>Challenge of volume of cases</td>
<td>References to the challenge posed by the sheer volume of cases overwhelming capacity to control STIs.</td>
</tr>
<tr>
<td>Challenges to jurisdiction</td>
<td>Discussions about the specific issues faced by the jurisdiction. Issues which are not specific to EPT but provide context.</td>
</tr>
<tr>
<td>Clinicians receptive to EPT</td>
<td>Mention of reasons why EPT might be favored by some providers outside local health departments.</td>
</tr>
<tr>
<td>Clinicians’ willingness to have</td>
<td>References to difficulties getting healthcare practitioners to have conversations about sex partners and relationships – not necessarily specific to EPT.</td>
</tr>
<tr>
<td>partner conversations</td>
<td></td>
</tr>
<tr>
<td>Conflict</td>
<td>References to the value of involving stakeholders with opposing views and the value of that conflict for improving EPT promotion.</td>
</tr>
<tr>
<td>Connecting to the right people</td>
<td>References to the importance of forming and having connections with the right people who can help. Relates to champions of EPT.</td>
</tr>
<tr>
<td>COVID-19 related</td>
<td>Challenges related to the COVID-19 pandemic. For example, epidemiological expertise being relegated to pandemic control instead of STIs.</td>
</tr>
</tbody>
</table>

265
<table>
<thead>
<tr>
<th>Topic</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>De-stigmatizing</td>
<td>Comments related to efforts to reduce stigma around STIs, MSM, and EPT.</td>
</tr>
<tr>
<td>Educating and partnering with pharmacists</td>
<td>Discussions about how to educate pharmacists or how to partner with professional associations - for example how to fill no-name prescriptions.</td>
</tr>
<tr>
<td>Educating providers</td>
<td>Discussions about how to educate healthcare providers about the legality of EPT, the benefits of EPT use, and the liability protections connected to EPT.</td>
</tr>
<tr>
<td>Emails and notifications to clinics</td>
<td>Descriptions of email or listserv notification programs for healthcare practitioners.</td>
</tr>
<tr>
<td>EPT for gonorrhea</td>
<td>Discussions about whether and to what extent to use EPT to treat gonorrhea.</td>
</tr>
<tr>
<td>EPT for MSM</td>
<td>Reasons to give or not give EPT to MSM, and discussions about MSM.</td>
</tr>
<tr>
<td>EPT med-in-hand vs. prescription</td>
<td>Discussions about the value of having EPT med-in-hand available, or the challenges related to prescription EPT.</td>
</tr>
<tr>
<td>EPT willingness depends on relationship with partner</td>
<td>Discussions about how index patients may be unwilling to use EPT (and partner referral) depending on their relationship with their sex partners.</td>
</tr>
<tr>
<td>EPT prescriptions with no name</td>
<td>Comments related to the use of EPT with no name for the recipient sex partner.</td>
</tr>
<tr>
<td>Evaluations of and research about EPT</td>
<td>References to efforts to evaluate or study EPT using research or health department surveys, including the difficulties and benefits of these efforts.</td>
</tr>
<tr>
<td>Facilitators</td>
<td>Discussions about facilitators to EPT promotion.</td>
</tr>
<tr>
<td>Factsheets and Information</td>
<td>Comments about writing and providing fact sheets or guides - to providers, patients, and pharmacists.</td>
</tr>
<tr>
<td>Federal 340B program</td>
<td>Specific mentions of the 340B program, including benefits and barriers to use.</td>
</tr>
<tr>
<td>Financial issues</td>
<td>Answers which refer to any financial complication with using EPT. For example, index patients being unwilling to use EPT if they had to pay for their partners’ medication.</td>
</tr>
<tr>
<td>Free or low-cost EPT</td>
<td>Discussions about ways to make EPT low cost or free, and comments about the benefits of using these strategies.</td>
</tr>
<tr>
<td>Funding and grants</td>
<td>Money and grants used to promote EPT, or the search for money to help promote EPT.</td>
</tr>
<tr>
<td>Topic</td>
<td>Description</td>
</tr>
<tr>
<td>-------</td>
<td>-------------</td>
</tr>
<tr>
<td>General benefits of EPT use</td>
<td>General comments about the value of EPT which don't categorize neatly into other codes.</td>
</tr>
<tr>
<td>Include stakeholders</td>
<td>Discussions to the value of including stakeholders, particularly early in the process.</td>
</tr>
<tr>
<td>Independent champions of EPT</td>
<td>Description of key allies to health departments who helped to promote EPT or streamlines a key aspect of EPT use or enabled broader education about EPT.</td>
</tr>
<tr>
<td>Individuals opposed to EPT</td>
<td>Descriptions by respondents of specific individuals who blocked EPT promotion or use using their discretionary powers.</td>
</tr>
<tr>
<td>Legal considerations</td>
<td>Issues where the law was constraining and made it difficult to promote EPT.</td>
</tr>
<tr>
<td>Legal strengths</td>
<td>Comments related to the advantage of certain legal decisions which streamline or enable EPT promotion.</td>
</tr>
<tr>
<td>Legality perception among providers</td>
<td>References to the lack of knowledge among healthcare practitioners about EPT's legality or legal status. Discussions about how to educate healthcare practitioners.</td>
</tr>
<tr>
<td>Lessons learned</td>
<td>Answers to the question of what lessons the respondent has learned or what they would do differently if they had the chance.</td>
</tr>
<tr>
<td>Liability protection</td>
<td>Discussions about liability protections for EPT. The benefits of having liability protections, problems if no protections exist, how to educate healthcare practitioners or persuade them to use EPT despite not having protections.</td>
</tr>
<tr>
<td>Liberal vs. conservative</td>
<td>Discussions about political affiliation on the legislature, health department, or the population.</td>
</tr>
<tr>
<td>Local health departments</td>
<td>Comments about how to negotiate with local health departments to promote EPT in their district.</td>
</tr>
<tr>
<td>Low-income patients</td>
<td>Comments related to low-income patients needing help to get care, and the challenges related to caring for low-income patients.</td>
</tr>
<tr>
<td>Medicine for gonorrhea</td>
<td>Specific comments related to the availability or lack of availability of medications needed to treat gonorrhea with EPT.</td>
</tr>
<tr>
<td>Messaging to public</td>
<td>Descriptions of efforts to educate the public about EPT.</td>
</tr>
<tr>
<td>Patient behaviors</td>
<td>Comments identifying specific behaviors by people which increases the spread or makes STI control difficult.</td>
</tr>
<tr>
<td>Patients going private</td>
<td>Answers identifying or discussing the shift of patients away from public health clinics towards private facilities. Private healthcare providers were described as less interested in treating sex partners.</td>
</tr>
<tr>
<td>Topic</td>
<td>Description</td>
</tr>
<tr>
<td>--------------------------------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Patients requesting EPT</td>
<td>Comments about patients requesting EPT or preferring EPT for its convenience.</td>
</tr>
<tr>
<td>Personal experience</td>
<td>Answers to questions about respondent’s experience and history with EPT promotion efforts.</td>
</tr>
<tr>
<td>Power of money</td>
<td>It is valuable to have money attached to EPT use as an incentive.</td>
</tr>
<tr>
<td>Prepackaging EPT for med-in-hand</td>
<td>Discussions about ways to prepackage EPT for med-in-hand.</td>
</tr>
<tr>
<td>Pull people in and use assets</td>
<td>Descriptions of efforts to make use of connections between the respondent and individuals who could help promote EPT.</td>
</tr>
<tr>
<td>Reach of state health department</td>
<td>References to the limits of state health department power/authority to make meaningful changes.</td>
</tr>
<tr>
<td>Reasons to give to MSM</td>
<td>Comments in favor of providing EPT to MSM.</td>
</tr>
<tr>
<td>Reasons to not offer EPT to MSM</td>
<td>Comments about barriers to providing EPT to MSM.</td>
</tr>
<tr>
<td>Reduction in diagnoses due to EPT use</td>
<td>Comments related to the reduction in diagnoses that come from a loss of partner referrals when EPT is used. Concern or lack of concern about this effect.</td>
</tr>
<tr>
<td>Reporting requirements</td>
<td>Discussions about reporting requirements, particularly surrounding electronic reporting and how EPT may not be compatible with patient-based systems which must assign treatment to individuals.</td>
</tr>
<tr>
<td>Reputation</td>
<td>Participant’s statements about how to utilize health department reputation to promote EPT, or how to enhance that reputation to strengthen the policy efforts.</td>
</tr>
<tr>
<td>Resistance to change and time</td>
<td>Comments relating to a resistance to change among healthcare practitioners and administrators. People seemingly opposed to using EPT because partner referral is standard.</td>
</tr>
<tr>
<td>Resource constrains</td>
<td>References to a lack of department resources to control STIs.</td>
</tr>
<tr>
<td>Stigma</td>
<td>Comments related to the stigma against STIs and difficulties in controlling infections which are taboo.</td>
</tr>
<tr>
<td>Strategies</td>
<td>Discussions about the various promotion strategies that states have attempted.</td>
</tr>
<tr>
<td>Streamline payment</td>
<td>It is important to streamline ways to pay for EPT and find ways to pay for EPT.</td>
</tr>
<tr>
<td>Study and evaluate EPT</td>
<td>Related to research efforts to study or evaluate the effectiveness or implementation of EPT.</td>
</tr>
<tr>
<td>Subcommittee to promote EPT</td>
<td>Descriptions of subcommittees formed to help promote EPT or to resolve specific issues. Points about the value of these efforts.</td>
</tr>
<tr>
<td>----------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>The power of individuals</td>
<td>Any reference to specific individuals who were particularly influential as barriers or facilitators to EPT promotion.</td>
</tr>
<tr>
<td>Transportation</td>
<td>References to transportation as a barrier to providing care - the large distance between patients and healthcare facilities.</td>
</tr>
<tr>
<td>Trust in patients to fill EPT</td>
<td>Comments about whether healthcare practitioners trust index patients to deliver EPT to their sex partners.</td>
</tr>
<tr>
<td>Urban vs. rural</td>
<td>Discussions about the difficulties of controlling STI is rural areas, or the impact of urbanicity.</td>
</tr>
<tr>
<td>Use of apps and tech</td>
<td>Discussions about the value of technology to help control STIs, or generally modernizing communication with patients.</td>
</tr>
<tr>
<td>Value of clarity</td>
<td>It is important to be very clear, precise, and specific in writing and communicating EPT guidelines and information.</td>
</tr>
</tbody>
</table>

Notes: EPT = expedited partner therapy. MSM = men who have sex with men. 340B refers to the Federal program, which provides low-cost medications to eligible healthcare facilities to treat low-income patients. Med-in-hand refers to EPT medicine in hand, as opposed to prescription EPT.
CONCLUSION
Overview of Dissertation Results

This dissertation provided insights into the effectiveness, cost-effectiveness, and strategies used to promote EPT use at population scale. Paper 1 demonstrated that EPT’s ability to treat sex partners at a higher rate might lead to an overall reduction in the number of diagnoses of chlamydia, given a constant screening rate. This reduction was not explained by a decrease in testing due to partner referrals when EPT was used instead and was driven primarily by a reduction in underlying prevalence. Furthermore, the reduction in chlamydia prevalence in the modeled population led to an overall decrease in the number of females that developed pelvic inflammatory disease (PID). This was true even though the female sex partners treated with EPT in the model had higher rates of untreated PID than their counterparts treated with partner referral. Paper 2 revealed that EPT use was cost-effective relative to partner referral by expanding upon the simulation model developed for Paper 1. The clinical costs of diagnostic exams for sex partners that were averted by EPT use exceeded the additional treatment costs of EPT. Finally, Paper 3 revealed several strategies that policymakers in US states have utilized to promote EPT use by healthcare practitioners, such as forming committees of stakeholders and pre-purchasing medications for med-in-hand EPT.

Contributions to Existing Empirical Literature

Paper 1 provided the first estimates of EPT’s impact on the total number of annual chlamydia diagnoses in a population, which is an important indicator used by policymakers to assess the effectiveness of the implementation of chlamydia control policies. This paper expanded upon previous literature investigating the effectiveness of EPT use on individual index patients and sex partners (Gannon-Loew et al., 2017; Hodge Jr et al., 2008; Schillinger
et al., 2016; Shiely et al., 2010). Paper 1 also included the development of a system dynamics simulation model that could be adapted to other states or populations in future research. Paper 2 expanded upon studies that had previously investigated EPT’s cost-effectiveness relative to partner referral (Gift et al., 2011; Kissinger et al., 2006). This paper provided an estimate for the cost-effectiveness of EPT use, accounting for EPT’s potential to treat uninfected individuals and considering the reduction in underlying prevalence that was estimated in Paper 1. Paper 2 revealed that sequelae costs could result in higher per treatment spending among a minority of all the female sex partners who received EPT. However, the paper demonstrated that overall societal spending would decrease regardless.

**Contributions to Theory**

**Contributions to Policy Implementation Literature**

This dissertation makes several contributions to the theoretical literature in the Policy Implementation field. First, Paper 3 provides a valuable dual perspective by focusing both on the top-down perspective of state health department directors and the bottom-up perspective of the local health department staff members. Staff in government public health clinics are direct recipients of EPT promotion efforts, especially the prepackaged medications for med-in-hand, which was available to some (but not all) public health clinics where respondents were based. It should be noted that this dual perspective did not include healthcare practitioners at private health clinics, which would be valuable. This said, private healthcare practitioners have been interviewed about EPT in previous literature (McCool-Myers et al., 2020). This dual perspective contributed to the old debate
between the supporters of theories including Lipsky’s street-level bureaucracy and Pressman and Wildavsky’s work on implementation of federal policies (Lipsky, 2010; E. Rogers, 1971). The final decision on whether to use EPT and whether to offer med-in-hand EPT depends on the discretion of local healthcare practitioners. These individuals described various factors that they consider in exercising this discretion, such as considering the convenience of using EPT and concern for sex partners who might not receive necessary care if they received EPT. In this way, Paper 3 offers support for Lipsky’s framework of street-level bureaucrats determining the shape of policy implementation. On the other hand, interviews with the state-level health department directors who promoted EPT made clear that the decisions made at higher levels of government had a significant impact on the options available to local health department staff. For example, the option to make med-in-hand EPT available was primarily determined by state-level directors.

The findings of Paper 3 also align with the predictions of the Diffusion of Innovation theory (E. Rogers, 1971). Diffusion of Innovation was pioneered by Rogers in 1971 and posited that innovations spread depending on the effectiveness of the innovation, communication channels, time, leadership, and social systems (E. Rogers, 1971). The policy diffusion literature has suggested that the adoption of innovative policies and practices tend to cluster in time and space as states may learn from the experience of other states (early adopters) and take-up effective solutions based on real-world evidence of effectiveness (Shipan & Volden, 2008). The effectiveness of EPT is well established in the previously described public health literature, and many of the respondents in Paper 3 were knowledgeable about these evaluations. Additionally, several of the state health department section directors interviewed as part of Paper 3 reported that they examined
other state policies and communicated with directors in other states. This included seeking advice on how to design legislation to legalize EPT use, as well as ideas for the promotion of its use. The time component can be observed in the pattern of EPT legalization by state legislatures over time, although Paper 3 did not specifically examine this aspect of EPT implementation. Finally, the leadership component was well demonstrated by Paper 3 respondents. In several instances, respondents reported that the contribution of leaders who guided EPT implementation was critical to the success of EPT implementation. Paper 3 could not demonstrate causality that these components were necessary for EPT implementation to be successful, but it revealed that these factors were present in many states and were identified by respondents as important.

Contributions to Implementation Science Literature

Each of the three papers made important contributions to the existing literature in the field of implementation science. Implementation science is concerned – among other questions – with evaluating policies after their implementation in their real-world use settings and identifying factors that explain the evidence-practice gap. This is the gap between research evaluations in highly structured research settings and those conducted in real-world settings (Nilsen et al., 2013).

First, Paper 1 expanded upon existing range in evaluation outcomes found in empirical research in public health, which may be understood as an evidence-practice gap as described in implementation science (Eccles & Mittman, 2006; Hogben et al., 2005; Vacca et al., 2019). Previous evaluations of EPT focused on estimating the impact of EPT use on reinfection rates among index patients and treatment probabilities for sex partners treated using EPT (Ferreira et al., 2013; Handsfield et al., 2006). Paper 1 uses previous
estimates (of reinfection of index patients and treatment of sex partners) from both the low and high end of the evidence-practice gap and translates these known patient-level outcomes into percent change in total diagnoses at the population level. This expands upon existing research and provides an estimate of the evidence-policy gap that policymakers may use. In addition, Paper 1 separately estimates the impact of EPT on total diagnoses as well as underlying prevalence. This is important because EPT may reduce the overall number of diagnoses in two ways: by treating sex partners more effectively thus driving down underlying prevalence, and by not diagnosing infected sex partners when they receive EPT instead of partner referral. Policymakers may use the estimates of Paper 1 to better interpret changes in diagnoses that accompany an increase in EPT use. If EPT use expands, it is expected that the number of diagnoses will fall, and this change is primarily due to a decline in underlying prevalence and not a decline in testing. Second, there is growing recognition that the cost-effectiveness of an intervention is critical to its long-term sustainability in implementation (Eisman et al., 2020; Krebs & Nosyk, 2021). Policymakers benefit from a greater understanding of the cost-effectiveness characteristics of EPT, and Paper 2 helps to fill this gap for EPT. Finally, Paper 3 identified several facilitators to EPT implementation which align with the findings of previous implementation science research. For example, the value of involving diverse sets of stakeholders early in the implementation process to address their concerns was reaffirmed (Handley et al., 2016; Zimmerman et al., 2016).

Two other theories of implementation were supported by Paper 3. The RE-AIM framework predicts that the public health impact of a given intervention depends on Reach, Efficiency, Adoption, Implementation, and Maintenance (Glasgow et al., 1999). Meanwhile,
the COM-B framework predicts that a behavioral change (the adoption of a new practice) may occur when the individuals are capable (i.e., legally, and mentally), motivated, and have opportunities to engage in that behavior (Michie et al., 2011). The RE-AIM and COM-B frameworks may serve as a basis for future research on EPT, considering the findings in this dissertation. RE-AIM’s focus on maintenance aligns with a major finding of Paper 3 concerning facilitators to EPT use. Promotion efforts that make EPT easy to use and which simplify the financial uncertainty surrounding EPT use were revealed to be important in Paper 3. An opportunity exists to measure the impact of such promotion efforts on long term routine use of EPT. Additionally, the COM-B framework might imply that motivating healthcare practitioners to use EPT may be the most important target for future promotion efforts, given that the capability and opportunity prerequisites of behavior change are largely met (EPT is legal - awareness of its legality is quite high, and healthcare practitioners have an opportunity to use it every time an index patient is diagnosed). Accordingly, evaluating options to motivate healthcare practitioners to use EPT may be valuable at this stage on EPT's implementation. RE-AIM may also help to explain why EPT's health impact remains lower than hoped. Previous research has highlighted the difference between the rate of healthcare practitioners who have ever used EPT and those who routinely use EPT (Hsii et al., 2012; Jotblad et al., 2012; M. E. Rogers et al., 2007).

**Policy Implications**

These three papers contain valuable information to be considered by policy actors, particularly in state health departments. First, Paper 1 supported the promotion of EPT as effective and found that increased EPT use was associated with a decrease in total annual diagnoses in NYS among males and females aged 18-24 years old with sex partners of the
opposite sex. Policy actors considering whether to promote EPT use or invest state resources in other efforts may use the findings from Paper 1 to help anticipate the health benefits from promoting EPT. Paper 1 showed that it may be more valuable to promote the use of EPT to reach more sex partners rather than promoting the use of med-in-hand EPT. Finally, Paper 1 provided an estimate for policymakers in the change in the number of annual diagnoses that could result from an increase in EPT use. This estimation also included a calculation of the proportion of the reduction in diagnoses that was attributable to a decrease in underlying prevalence (rather than a reduction in testing among sex partners induced by EPT use). This estimation is important because policy actors monitor diagnoses closely as an indicator of underlying prevalence.

Paper 2 provided valuable insights into the cost-effectiveness of promoting EPT relative to partner referral among males and females aged 18-24 years old with sex partners of the opposite sex. Cost-effectiveness is a critical consideration during policy implementation and promotion. Policymakers may know that promoting EPT use, particularly for male sex partners of diagnosed female index patients, is a highly cost-effective policy from a societal perspective. Among female sex partners, the cost-effectiveness of replacing partner referrals with EPT is less clear, as it depends largely on the probability of sequelae (such as PID) occurring among female sex partners before they receive treatment for chlamydia. However, it should be noted that Paper 1 also found that the overall number of females with PID is likely to fall with increased EPT use because of the decrease in the underlying prevalence of chlamydia. In combination with Paper 2’s findings, this suggests that increased EPT use may be a robust intervention from a cost-effectiveness perspective even for female sex partners.
Finally, Paper 3 documented and described the strategies used by US state health departments to promote EPT use, including discussions about the barriers and facilitators to each of the strategies employed. This Paper may serve policymakers seeking to promote EPT in their jurisdiction to understand better what has been tried and how to address the barriers to EPT promotion. Several respondents in Paper 3 described the efforts in their states to promote EPT or implement EPT for the first time. Documentation of the various strategies employed by policymakers in the past as well as the strengths and limitations of these strategies may be invaluable for policymakers who are considering EPT promotion in their states. 89

**Remaining Literature Gaps**

The papers presented in this dissertation helped to identify several important directions for future research on EPT, with possible theoretical implications in on implementation science, diffusion of innovation, evidence-based policy, and more (Eccles & Mittman, 2006; E. Rogers, 1971; Sanderson, 2002). Future research could evaluate the impact of stakeholder involvement during the implementation of EPT by comparing states with stakeholder committees with those that lacked them. Additionally, it would be valuable to estimate the remaining evidence-practice gap by answering two key questions regarding EPT. The first is measuring the difference in treatment probabilities for sex partners given med-in-hand EPT and prescription EPT. Second, it is important to separate the impact of EPT use from any other enhancements that may have inadvertently been evaluated alongside EPT in earlier research (for example, calling sex partners to remind them to deliver EPT medications) (Ferreira et al., 2013). Answering these questions would help to identify the behavior changes necessary to realize the expected improvements in
sex partner treatment probability and index patient reinfection rates promised by the early evaluations of EPT.

Papers 1 and 2 made valuable contributions to understanding the impact of increased EPT use on various outcomes, but they were limited in their scope. For example, these studies considered only young adults aged 18–24 years old with sex partners of the opposite sex living in NYS. Therefore, these papers have limited generalizability to individuals outside this age range or location. Furthermore, it was assumed that MSM would never receive EPT, in part because the current recommendation by the CDC considers EPT an option of last resort when treating MSM (Workowski & Berman, 2006). Furthermore, transgender individuals were not included in the model because the surveillance data used for calibration did not distinguish transgender individuals. As a result, both transgender individuals and MSM are understudied in the existing EPT literature and future research should replicate the studies with more diverse sex and sexual orientation populations. Moreover, an active discussion has begun among policy actors about the use of EPT to treat MSM, and future research would provide valuable evidence to inform this discussion (Andre Kiesel, 2022; Weiss et al., 2019). In addition to these considerations, Paper 2 also relied on previous literature to provide estimates for the cost of PID and other sequelae. While these cost estimates included many indirect costs (i.e., loss of productivity), none of the previous literature considered quality of life impacts in their cost estimates (Yeh et al., 2003). Paper 2 therefore does not account for these additional costs and may underestimate the true cost of these sequelae, and future research could investigate this possibility.
Conclusion

Together, the three studies in this dissertation provide important information to add to the existing literature and to inform policymakers engaged in promoting the use of EPT. Paper 1 demonstrated that increasing EPT use could lead to a decrease in both chlamydia diagnoses and underlying chlamydia prevalence. Paper 2 showed that EPT was a cost-effective alternative to partner referral for heterosexually acquired chlamydia infections, especially for male sex partners. Finally, Paper 3 documented the strategies used by health department staff and directors to promote EPT. With the rise in chlamydia and gonorrhea diagnoses along with their underlying prevalence in recent years, this dissertation offers insights into the impacts of a promising clinical practice that may help to control these sexually transmitted infections.
Reference


Ferreira, A., Young, T., Mathews, C., Zunza, M., & Low, N. (2013). Strategies for partner notification for sexually transmitted infections, including HIV. *Cochrane Database of Systematic Reviews, 10*.


