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Evaluation of an internet-accessed STI testing (e-STI testing) and results service in two London boroughs

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Funded by Guy's and St. Thomas' Charity

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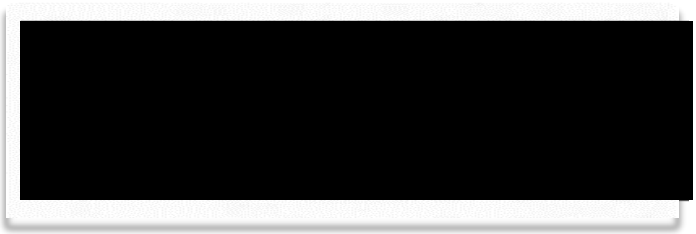
'I, Emma Kathleen Wilson, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis'.



Abstract

Background

Internet-accessed STI (e-STI) testing is recommended in England to expand access to STI testing services, particularly among high-risk groups. Yet the evidence for the effectiveness of this testing modality is limited. This thesis aimed to address this evidence gap, by evaluating the effects of an e-STI testing and results service (SH:24) on STI diagnoses and STI testing uptake, when delivered alongside usual care in two London boroughs.

Theoretical premise of thesis

In line with theory-driven approaches to evaluation, I developed an explanatory framework outlining hypothesised change processes that may be triggered by the intervention. I adopted a critical realist conceptualisation of causal mechanisms and I drew on the 'candidacy' lens to conceptualise change processes in relation to access and utilisation of STI testing services. I then used this framework to situate the evaluation findings.

Methods

This evaluation was based on a randomised controlled trial (RCT). 2,072 individuals aged 16–30 years, resident in Lambeth and Southwark, with at least one sexual partner in the previous 12 months and willing to take an STI test, were recruited in community settings. Participants were allocated to an e-STI testing service (intervention) or to a website with signposting to local sexual health clinics (control). The e-STI testing service provided postal self-sampling kits for chlamydia, gonorrhoea, HIV and syphilis. Results were delivered via text message or phone, and participants were signposted to local clinics for confirmatory testing and treatment as necessary.

Results

The published trial results are as follows: 1,031 participants in the intervention group and 1,032 control group were included in the analyses. At 6 weeks, 50.0% of the intervention group completed an STI test compared to 26.6% in the control group (relative risk, RR 1.87, 95% confidence interval 1.63 to 2.15, p<0.001). 2.8% of the intervention *v* 1.4% in the control were diagnosed with an STI (RR 2.10, 95% confidence interval 0.94 to 4.70, p=0.079). The effect on the proportion of participants treated was 1.1% in the intervention *v* 0.7% in the control (RR 1.72, 95% confidence interval 0.71 to 4.16, p=0.231).

Secondary analyses (unpublished at the time of writing) demonstrated that the intervention was effective for uptake of STI testing among a subsample of participants who had never previously tested for STIs.

Conclusions

The findings lend weight to national policies in England, which promote e-STI testing as a means to increase utilisation of STI testing services, particularly among groups who do not use conventional services. While the results support the candidacy model's processual framing of health care utilisation, further research is required to understand how the construct of candidacy is recognised and negotiated within a digital service environment by different socio-demographic groups. In addition, larger trials are needed to assess outcomes later in the cascade of care.

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I also thank Brook Young People and the many GP surgeries in London who conducted patient record checks.

List of Abbreviations

AIDS	Acquired immune deficiency syndrome
ART	Anti-retroviral therapy
BASHH	British Association for Sexual Health and HIV
BME	Black and Minority Ethnic
CCG	Clinical Commissioning Group
CI	Confidence interval
CrI	Credible interval
DoH	United Kingdom Department of Health
GP	General Practitioner
GUM	Genito-urinary medicine
HIV	Human immunodeficiency virus
KCL	Kings College London
MAR	Missing at random
MEDFASH	Medical Foundation for HIV & Sexual Health
MICE	Multivariable imputation using chained equations
MNAR	Missing not at random
MSM	Men who have sex with men
Natsal	National survey of sexual attitudes and lifestyles (Britain)
NCSP	National Chlamydia Screening Programme
NICE	National Institute for Health and Care Excellence
OR	Odds ratio
PEP	Post exposure prophylaxis
PHE	Public Health England
PID	Pelvic inflammatory disease
PrEP	Pre-exposure prophylaxis
PHOF	Public Health Outcomes Framework
RD	Risk difference
RR	Relative risk
SMS	Short message service
SRE	Sex and relationships education
STI	Sexually transmitted infection
SSA	sub-Saharan Africa
TDA	Theory driven approach

ToC	Theory of change
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organisation

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Chapter 1: STI epidemiology and sexual health services

1.1 Chapter overview

In this chapter, I review the epidemiological data on STIs in England and the United Kingdom (UK), including the risk profiles of key population groups. I present an overview of STI testing services in England, and I introduce internet-accessed STI testing (e-STI testing) as a novel, but emerging, component of service delivery systems. Finally, I review the international evidence base for e-STI testing.

1.2 Introduction

Sexually transmitted infections (STIs) are an important cause of morbidity and mortality worldwide, and a key indicator of sexual ill health. Globally, there are 357 million new infections of curable STIs (chlamydia, gonorrhoea, syphilis, and trichomonas vaginalis) each year (World Health Organisation no date). While global incidence rates of HIV infection are on the decline, prevalence remains significant: UNAIDS estimated 1.8 million new HIV infections in 2016 and that 36.7 million people were living with HIV (Joint United Nations Programme on HIV/AIDS 2017).

Left undiagnosed and untreated, curable STIs such as chlamydia, trichomoniasis, gonorrhoea and syphilis can facilitate the transmission of HIV and can cause sub-fertility, ectopic pregnancy, chronic pelvic pain, neurological and cardiovascular disease, neonatal mortality, and infant morbidities (Holmes KT et al. 2008). Undiagnosed HIV and late diagnosis of HIV lead to diminished health outcomes and reduced life expectancy (Mocroft et al. 2013).

Increasing testing, diagnosis, and treatment of STIs and reducing time to treatment is a global priority to reduce the prevalence of STIs and their associated sequelae (World Health Organisation; United Kingdom Department of Health 2013). In the UK, testing coverage remains sub-optimal. The 3rd National Survey of Sexual Attitudes and Lifestyles (hereon referred to as NATSAL) found that two-thirds of 16-44 year olds who tested positive for chlamydia had not had a chlamydia test in the past 12 months (Sonnenberg et al. 2013). Further, timely diagnosis of HIV is a challenge. In 2016, 41% of adults diagnosed with HIV in the UK were diagnosed late (CD4 count < 350 cells/mm^3) (Public Health England 2017e).

Interventions that increase access among high-risk and hard-to-reach groups are needed to maximise the public health benefits of 'test and treat' strategies for STIs.

1.3 STI epidemiology in England

In 2016, there were 417,584 new STI diagnoses in England, comprised primarily of chlamydia (202,546), followed by anogenital warts (62,721), gonorrhoea (36,244), non-specific genital infection (36,774) and herpes (31,860) (Public Health England 2017d).

Comparable data suggest that between 2003 and 2012, there was a 47% increase in new diagnoses in England, from 305,000 to 448,000 diagnoses (Hughes & Field 2015). This trend has been driven by innovations in diagnostic technologies, improved access to services, combined with an increased incidence of infection among specific populations (Hughes & Field 2015).

Men who have sex with men (MSM), young heterosexuals and black minority ethnic groups continue to be disproportionately affected by STIs. The following sections outline the STI risk profiles of each of these populations.

1.3.1 MSM

In 2016, in England, 49,445 new STI diagnoses were in MSM (Public Health England 2017d). Among male attendees of sexual health clinics, MSM accounted for 64.7% of gonorrhoea and 85.5% of syphilis diagnoses in 2016. Moreover, MSM account for the burden of all syphilis infection (Public Health England 2017b). Of the 5,920 new syphilis diagnoses in England in 2016, 80.9% (4,788) were in MSM (Public Health England 2017d).

There is evidence of increasing incidence of syphilis and gonorrhoea among MSM. Between 2012 and 2015, the overall diagnosis rate per 100,000 attendances rose from 114.7 to 173.1 for syphilis; and from 1,027.2 to 1,348.2 for gonorrhoea (Public Health England 2016b). These increases in diagnoses rates are concentrated in MSM (Public Health England 2016b). Rising incidence of gonorrhoea is of particular concern given the emerging evidence of antimicrobial gonococcal resistance (Public Health England 2016c).

Compared to heterosexual men, MSM are more likely to report higher sexual risk behaviours. A study based on data from Natsal-3 found that MSM were more likely to report higher numbers of lifetime partners and more frequent partner change in the last 12 months, compared to men who exclusively have sex with women (Mercer et al. 2016).

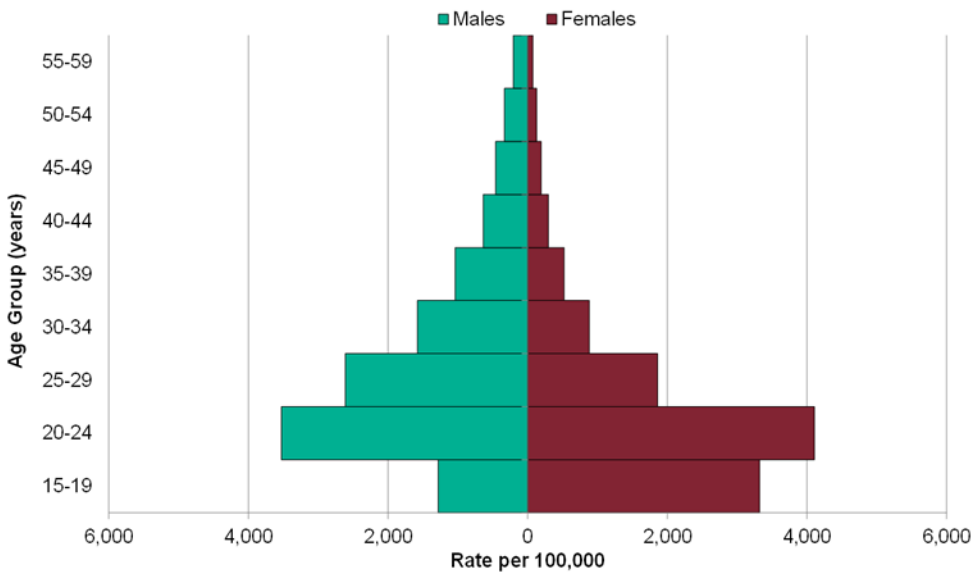
Further, MSM were over 3 times more likely to report condomless sex with two or more partners in the last 12 months compared to heterosexual men (adj OR 3.52, 95% CI 2.13–5.83, p<0.001) (Mercer et al. 2016).

Complex sexual networks that are dense in nature (i.e. higher contact rates) can facilitate rapid STI transmission among MSM (Doherty et al. 2005; Hart & Elford 2010). Unprotected anal intercourse, and particularly receptive unprotected anal intercourse, is associated with an elevated risk of infection compared to other sexual practices (McDaid & Hart 2010). Chemsex (sex under the influence of psychoactive substances), which is more common in London compared to the rest of the UK, is also linked to heightened sexual risk taking among MSM (Pufall et al. 2018; Bourne et al. 2015).

1.3.2 Young adults

Young adults, between 15 and 24 years of age, experience the highest rates of STI diagnoses per 100,000 population compared to all other age group (Figure 1).

Figure 1: Rates of new STI diagnoses by gender and age group, 2016 (Public Health England 2017c, Figure 3)



- Data from specialist and non-specialist SHS (GUMCAD returns)
- ONS Census mid-year 2015 estimates used for denominators
- Data type: service data

As illustrated in figure 1, a much higher proportion of young women aged 15-19 years are diagnosed with STIs compared to young men of the same age. This may be partly explained by sexual mixing patterns (Kraut-Becher & Aral 2006). Young heterosexual women tend to have older sexual partners (Mercer et al. 2009), who in turn have higher risk profiles than

younger men. In Britain, population prevalence estimates for the most common STIs (HPV and chlamydia) are greater in older cohorts of men (20-24 years) compared to younger ones (18-19 years and 16-17 years) (Sonnenberg et al. 2013). Moreover, there is evidence that young women struggle to negotiate safe sex with older partners (Morrison-Beedy, Xia & Passmore 2013).

Among heterosexuals, young people account for the majority of diagnoses in chlamydia, gonorrhoea, genital warts and genital herpes. Among heterosexuals, 62% of chlamydia diagnoses in 2016 were in individuals aged 15-24 years (Public Health England 2017d). The burden of chlamydia infection among young adults is of particular concern and this has prompted the introduction of the National Chlamydia Screening Programme (NCSP) in England. Chlamydia infection is predominantly asymptomatic, and can easily remain undetected and untreated. Population based estimates, based on data from Natsal-3, indicated that among 16-24 year olds, chlamydia prevalence was 3.1% (95% CI 2.2% to 4.3%) in women and 2.3% (1.5% to 3.4%) in men (Sonnenberg et al. 2013). Prevalent chlamydia infection is associated with increasing number of reported sexual partners. However, among those with prevalent chlamydia infection, an estimated 60.4% (95% CI 45.5%–73.7%) of women and 43.3% (95% CI 25.9%–62.5%) of men reported only one sexual partner in the past 12 months (Ibid.).

Undiagnosed and untreated chlamydia is estimated to be responsible for 16% (95% CrI, 6% - 25%) of clinical pelvic inflammatory disease (PID) (Price et al. 2013). Reinfection is also a key concern (Walker et al. 2012; LaMontagne et al. 2007). A study based on NCSP data from 2010 found that among repeat testers (15-24 years), those with a positive baseline test had higher odds of testing positive compared to those with a negative baseline test (Males, adjusted OR 2.57, 95% CI 2.11 to 3.14, $p<0.001$; Females, adjusted OR 1.95, 95% CI 1.76 to 2.16, $p<0.001$) (Woodhall et al. 2013).

Key drivers of young peoples' heightened susceptibility to STIs include more frequent partner change compared to older age groups (Mercer et al. 2013), as well as a lack of knowledge, skills and confidence to negotiate safe sex, including condom use (Marston & King 2006). Young adults also report barriers in accessing sexual health services in the UK (Oliver de Visser & O'Neill 2013; Normansell, Drennan & Oakeshott 2016). Attendance at sexual health services is lower among young men compared to young women. Analyses of Natsal-3 data found that 43.8% (95% CI 41.1–46.5) of women aged 16-24 reported

attending a sexual health clinic in the past 5 years compared to 31.4% (95% CI 28.6–34.4) of men (Sonnenberg et al. 2013). Further, in 2016, chlamydia test coverage among 15-24 year olds was only 12% among men compared to 30% among women (Public Health England 2017d).

The sexual repertoires of young people in Britain are in flux. Evidence from Natsal-3 suggests that a higher proportion of sexually active young people are engaging in anal sex than in previous survey rounds (Lewis et al.). Qualitative research findings indicate that health promotion messaging is not aligned with these changing repertoires (Marston & Lewis 2014).

1.3.3 Black and minority ethnic groups

Black Caribbean and black African minorities have substantially higher rates of STIs, including gonorrhoea, genital warts and trichimoniasis, compared to other ethnic groups in the population (Public Health England 2017d).

A heightened risk of infection among black ethnic minorities is also reported by population based probability studies, though not to the same magnitude as studies based on surveillance data. A study using Natsal-2 data found that compared to white men, black Caribbean and black African men were more than twice as likely to report an STI diagnosis in the last 5 years; and similar associations were reported among women (Fenton et al. 2005).

A subsequent study based on Natsal-3 data, found that a higher proportion of black minority groups reported attending a sexual health clinic in the last 5 years than white British groups. These proportions are as follows: 23.6% of black Caribbean and 19.8% of black African men compared to 11.8% of white British men; and 26.8% of black Caribbean women compared to 12.7% of white British women. However, compared to black African men, a lower proportion of black African women reported clinic attendance (14.6%) (Wayal et al. 2017).

Yet these findings are not an assurance of equity. Such comparisons can mask barriers to care experienced by the dominant referent group (Dixon-Woods et al. 2005); and utilisation of services among black minority groups may still be inadequate relative to need. Indeed, as highlighted later, late diagnoses of HIV among black African heterosexuals is still a concern. Qualitative research has highlighted discriminatory attitudes among health providers

towards minority ethnic groups, which may deter some people from seeking care (Connell, McKevitt & Low 2004).

Research on the determinants of sexual health inequalities by ethnicity is lacking in the UK (Wayal et al. 2017; Jewkes & Dunkle 2017). Analyses of Natsal-2 data has shown that the elevated risk of infection among black minority groups is partially, but not fully, explained by associated socio-economic disparities, such as area level deprivation (Furegato et al. 2016), and individual sexual health behaviours (e.g. higher number of lifetime sexual partners relative to other ethnic groups) (Fenton et al. 2005; Wayal et al. 2017). Additional factors including gender dynamics and sexual mixing patterns specific to particular cultural groups are believed to play a contributory role and warrant further investigation (Jewkes & Dunkle 2017; Wayal et al. 2017; Fenton et al. 2005) .

1.4 HIV in England and the UK

In 2016, an estimated 89,400 (Credible interval (CrI) 87,200 to 94,700) people were living with HIV in England, of whom 10,400 (CrI 8,400 to 15,700) remain undiagnosed (Brown et al. 2017a).

The overall prevalence of HIV in England is 2.2 (Crl 2.1-2.3) per 1,000 population aged 15-74. The burden of infection is concentrated in MSM and black African heterosexuals. Among MSM aged 15-59 years, the estimated prevalence is 77 (Crl 69-86) per 1,000 population; and 23 (CrI 22-25) per 1,000 among black African heterosexual men and 34 (CrI 34-35) per 1,000 among black African heterosexual women (Brown et al. 2017a).

However, new HIV diagnoses in both these populations have declined in recent years. In England, in 2016 there was an overall 18% decline in HIV diagnoses from the previous year (5,152 new diagnoses in 2016 versus 6,278 diagnoses in 2015)(Public Health England 2017e); and this was driven by a sharp fall in diagnoses among MSM (Brown et al. 2017a). This trend was most apparent in five high volume GUM clinics in London (Dean Street, Mortimer Market, Homerton, St Mary's and St Thomas'), where HIV diagnoses in MSM fell by 35% (from 1,034 in 2015 to 672 in 2016) (Brown et al. 2017a). An increased volume of HIV testing, particularly repeat testing, combined with rapid access to treatment is believed to have contributed to a reduction in HIV transmission among MSM. The availability of pre-exposure prophylaxis (PrEP), although still limited in the UK, is also thought to have played a role (Brown et al. 2017b).

The absolute numbers of new diagnoses among black African heterosexual men and women in the UK has dropped from 2,664 in 2007 to 669 in 2016 (Brown et al. 2017a). This is accompanied by a shift in the ethnic distribution of new HIV diagnoses overall. In 2007, 68% of heterosexual adults with a new HIV diagnoses were of black African ethnicity compared to 39% in 2016. Conversely, the proportion attributable to those of white ethnicity has increased (although the absolute number of white heterosexuals diagnosed with HIV has remained fairly constant). This trend can be explained by changing migration patterns, as fewer people from areas of high HIV prevalence, including sub Saharan Africa, have migrated to the UK in recent years (Brown et al. 2017a).

The proportion of diagnoses at a late stage of infection (CD4 count <350 cells/mm3 within 91 days of diagnosis) has declined by 45% since 2007. Yet late diagnoses are still a serious concern. In 2016, 41% of diagnosed adults were diagnosed late in England (Public Health England 2017e). Proportions of late diagnoses were highest among black African heterosexual men (139/215, 65%) and women (165/335, 49%); and lowest among MSM (663/2,096, 32%) (Brown et al. 2017a).

1.5 STI testing services in England

Similar to other industrialised countries, 'test and treat' is a core strategy for the control and management of STIs in England and the rest of the UK. Ensuring rapid access to STI testing services is a central pillar of England's framework for sexual health improvement (United Kingdom Department of Health 2013). Rapid access is defined as those seeking care are attended by a health professional within two working days of contacting a service (British Association for Sexual Health and HIV & Medical Foundation for HIV & Sexual Health 2014). Early diagnosis allows for timely detection and treatment of infection, preventing onward transmission and its associated sequelae.

Further, prompt detection of HIV allows early initiation of antiretroviral therapy (ART). Early initiation optimises clinical outcomes for affected individuals, while supporting prevention efforts by reducing the viral load at the population level (Mocroft et al. 2013). The expansion of HIV testing is also key for widening access to other therapeutic interventions, including PrEP (McDaid et al. 2016).

These secondary prevention measures are complemented by additional prevention initiatives, including sex and relationship education (SRE) in schools, health promotion and

behaviour change campaigns, including access to condoms (Clutterbuck et al. 2012; Public Health England 2015a).

Local authorities in England have a statutory obligation to provide 'open access' STI testing and treatment service (Department of Health 2013). An open access policy permits people to attend any commissioned service regardless of the location of the service or their own area of residence (ibid.). Individuals concerned they may have acquired an infection, or who choose to test regularly, can self-refer into specialist GUM and community based sexual and reproductive health clinics, as well non-specialist primary care facilities (e.g. GP surgeries). Tests are also available in community settings such as universities and sports centres. These employ a range of diagnostic technologies including point of care tests, as well as self-testing and self-sampling testing modalities.

Publicly funded STI testing and treatment services are free at point of use. Particular emphasis is placed on encouraging regular testing among groups most at risk, including young people, MSM and black minority ethnic groups. A summary of recommended testing frequencies by risk group is presented in the table below.

Table 1. Public Health England recommended testing frequencies by risk group

Men who have sex with men	Test for HIV and STIs each year, and every 3 months if having condomless sex with new or casual partners
Young adults who are sexually active (aged 15-24 years)	Screen for chlamydia annually, and on change of sexual partner
Black ethnic minority men and women	Regular STI screen, including HIV, if having condomless sex with new or casual partners

Source: Public Health England (2017d)

As mentioned earlier, an opportunistic screening programme for chlamydia was established in England in 2003 (National Chlamydia Screening Programme - NCSP). The NCSP stipulates that young adults between 15-24 years, who attend sexual health services, primary health care or other community facilities should be offered an annual test for chlamydia or on change of sexual partner (Public Health England 2016a).

National guidelines also recommend the expansion of HIV testing outwith specialist settings in areas of high HIV prevalence, defined as between 2 to 5 prevalent cases per 1,000 population aged 16-59 years (National Institute for Health and Care Excellence 2016). This includes routine testing among adults admitted to hospital who are undergoing blood tests and routine testing of all new patients at GP surgeries. GPs are also advised to offer HIV testing to all patients undergoing blood tests and who have not tested for HIV in the previous 12 months (National Institute for Health and Care Excellence 2016). This strategy reflects efforts to reach high-risk groups who do not attend specialist sexual health services, or who present to services late. Indeed, there is evidence of missed opportunities to diagnose black African patients in London, who had attended primary care facilities prior to their HIV diagnosis in specialist settings (Burns et al. 2008). Geographical targeting also serves to normalise HIV testing in areas most affected by HIV.

Nevertheless, most STI testing (including HIV) continues to take place in specialist GUM clinics, with the exception of chlamydia testing (Public Health England 2017a; Public Health England 2017d). In 2016 more than half (59%) of chlamydia testing among 15-24 year olds took place outwith GUM clinics, including primary care and community settings, yielding approximately 50% of all chlamydia diagnoses among this age group (Public Health England 2017d).

The quality of STI testing provision in the UK is difficult to gauge. The British Association for Sexual Health and HIV (BASHH) and HIV Medical Foundation for AIDS Sexual Health (MEDFASH) published standards for the management of STIs in 2010 (British Association for Sexual Health and HIV & Medical Foundation for HIV & Sexual Health 2014); and a national audit of sexual health services was conducted in the UK in 2011. Participation was voluntary and the audit suffered from low response rates (60% of GUM clinics and 8% of lower level clinics in the UK returned data). Areas of low performance included poor care linkages between non-specialist and GUM clinics; and low proportions of clinic attendees offered HIV tests. A high proportion of GUM clinics (86%), but not lower tier clinics (51%), met the quality standard for providing an appointment within 48 hours (McClean et al. 2012). It should be noted however, that since 2010 the 48 hour access standard is no longer a legal requirement (Foley et al. 2017), leading to concerns that progress achieved on reducing patient delays may be compromised (ibid.).

Since the restructuring of sexual and reproductive health services in England, mandated by the 2012 Health and Social Care Act, there has been increasing concern regarding the fragmentation of services and the ensuing impact on patient care (Public Health England 2017c). Commissioning of sexual, reproductive health and HIV services is divided between Clinical Commissioning Groups (CCGs), Local Authorities and Central Government (NHS England). Sexual health and HIV commissioning responsibilities are summarised as follows:

Table 2. Commissioning roles for sexual, reproductive and HIV services in England

Local Authorities	NHS England	CCGs
STI testing and treatment Chlamydia screening Young people's sexual health services Services in schools Sexual health aspects of psychosexual counselling Sexual health advice, promotion and prevention	STI testing and treatment provided under the GP contract	
HIV testing, prevention, and social care	HIV treatment and care HIV testing when required in other NHS England-commissioned services	HIV testing when required in other CCG commissioned services Community-based HIV clinical nurse specialists

Sources: Adapted from All-Party Parliamentary Group on Sexual and Reproductive Health in the UK (2015) & Robertson et al. (2017)

As a result of these reforms, key services have become decoupled (for example HIV testing is commissioned separately from HIV treatment services); and a lack of collaboration between multiple commissioning entities has led to disjointed care pathways in some regions (Public Health England 2017c; Robertson et al. 2017). Moreover, local authorities are struggling with severe budget cuts against a backdrop of unprecedented demand for STI testing services. Local authority spending on STI testing and treatment services dropped by 3.5% in cash terms between 2014/2015 and 2015/2016 (Robertson et al. 2017, p.30); and a quarter of local authorities in England reduced spending by as much as 20% (Robertson et al. 2017, p.30). Further, in this context of unprecedented change, there are concerns regarding the lack of minimum standards for providers, in addition to confused lines of accountability within commissioning structures (All-Party Parliamentary Group on Sexual and Reproductive Health in the UK 2015).

1.6 STI testing coverage in England

Surveillance data has demonstrated an upward trend in attendances at sexual health services (Hughes & Field 2015), and this finding is echoed in population-based data. Sonnenberg and colleagues (2013) reported that between Natsal-1 and Natsal-3, the proportion of sexually active men attending a sexual health clinic in the previous 5 years rose from 4.4% (95% CI, 3.8-5.0) to 19.6% (95% CI, 18.2-21.2); and among women from 3.4% (95% CI, 2.9-4.0) to 21.4% (95% CI, 20.1-22.7).

England is performing well against the international benchmarks for HIV testing and treatment (90:90:90), set by Joint United Nations Programme on HIV/AIDS (2014). The targets are as follows:

By the year 2020

- 90% of people living with HIV diagnosed;
- 90% of people diagnosed receiving treatment;
- 90% of those on treatment being virally supressed.

In 2016, these targets were met for the first time in London (90%, 97%, 97%), while at a national level, England was behind on testing coverage (88%) but reached the targets for treatment (96% diagnosed receiving treatment and 97% on treatment virally supressed) (Brown et al. 2017a).

Nevertheless, national indicators suggest that STI testing coverage is sub-optimal in England. The Public Health Outcomes Framework (PHOF) monitors two indicators related to STI testing: the chlamydia detection rate among 15-24 year olds and the proportion of adults diagnosed with HIV at a late stage of infection (CD4 count <350 cells/mm3 within 91 days of diagnosis). In 2016, the chlamydia detection rate was 1,882 per 100,000 population (15-24 years) in England, which is well below the target of at least 2,300 per 100,000 population. Only 22% of local authorities in England achieved this national target in the same year (Public Health England 2017d). Furthermore, 41% of adults with an HIV diagnosis were diagnosed late in 2016, which is much higher than the national target of 25% (Public Health England 2017e).

Evidence from national surveys indicates that key population groups are not testing with sufficient frequency. Analysis of Natsal-3 data found that between 2010 and 2012, only 27% (95% CI 19–37) of sexually active MSM in Britain had tested for HIV in the previous 12 months (Sonnenberg et al. 2013), despite national guidelines that recommend annual testing among this group (Table 1). More recent surveys, based on convenience samples, support this finding. Witzel and colleagues analysed a large sample of MSM (n=14,317) recruited as part of the 2014 Gay Men's Sex Survey. They found that 26% had never tested for HIV (Witzel et al. 2016).

The current chlamydia detection rate is an indication of insufficient test coverage among young adults overall. Moreover, recent evidence has demonstrated that coverage continues to be suboptimal even among those at heightened risk of infection. Using data from Natsal-3, Woodhall and colleagues reported that 25.8% of women and 51.2% of men (aged 16-24 years) who reported condomless sex with two or more partners in the previous 12 months, had not tested for chlamydia during the same period (Woodhall et al. 2015). This suggests that screening effects should be intensified to ensure those most at risk of infection are reached (Lewis & White 2018; Woodhall et al. 2015).

Sexually active young adults and MSM are advised to test annually irrespective of sexual risk practices, while it is recommended that black African individuals test regularly if having condomless sex with new or casual partners (Table 1). As discussed earlier, a higher proportion of black African adults, diagnosed with HIV, are diagnosed at a late stage of infection, relative to other risk groups. This is a clear indication that many at risk of

infection in this population subgroup, delay in seeking diagnostic testing for STIs. The following section discusses barriers to care-seeking for STIs.

1.7 Barriers to STI testing

1.7.1 Risk perception

Both national probability and community-based surveys have demonstrated a positive relationship between reported number of sexual partners (a key marker of sexual risk) and attendance at sexual health clinics (Sonnenberg et al. 2013; McDaid et al. 2016; Witzel et al. 2016).

However, low perception of sexual risk inhibits care-seeking for sexual health (Oliver de Visser & O'Neill 2013; Deblonde et al. 2010; Balfe et al. 2010a) , and crucially risk-perception does not always marry with reported sexual behaviours. Clifton and colleagues, using data from Natsal-3, found that among MSM and black African groups who reported unsafe sex in the previous year (condomless sex with a new partner), most perceived themselves to be low risk of HIV: 83.2% (68.6 - 91.9) of MSM and 89.3% (74.5 -96.0) of black African heterosexuals (Clifton et al. 2016). Findings from qualitative studies suggest that while there is high awareness of HIV among these populations in the UK, this has not necessarily translated into a perception of individual risk (Burns et al. 2007).

Similarly, qualitative research with young women in Ireland found a disconnect between sexual risk practices and perceived need for chlamydia testing, as seeking an STI test did not fit with women's social identities as 'responsible moral agents' (Balfe et al. 2010a, p.138).

1.7.2 Stigma

Stigma is understood to be the key barrier to help-seeking for sexual health (Hood & Friedman 2011). Stigma is broadly conceived as a 'spoiled' or 'tainted' identity that symbolises a person's undesirable or risky 'otherness' (Goffman 1963). Sexual practices and illnesses associated with sex carry particular connotations of 'otherness' and social risk. Rhodes and Cusack (2002, p.212) posit that accounts of sexual behaviour are 'inevitably morally charged' particularly if individuals are engaged in high-risk practices that may be judged as irresponsible and derelict of a civil duty to moderate risky behaviour.

Experiences of stigma are influenced and moderated by factors such as age, sexual identity, ethnicity and socio-economic status. Gay and bisexual men have reported specific anxieties

around disclosing their sexual identities to health care providers and this may be more pronounced among younger men (Datta et al. 2018). Young people can be fearful that their sexual practices will be deemed inappropriate for their age, and inconsistent with socially prescribed gender roles (Balfe & Brugha 2009). A key-informant study highlighted a particular concern among black African groups that health professionals may disclose a potential HIV diagnosis to the wider community (Burns et al. 2007).

The social significance of infection can drive a fear of a positive diagnosis. HIV carries particular connotations of 'tainted' identity (Goffman 1963), as it is historically associated with the 'unhealthy', 'sexually deviant' and 'contagious' (Crawford 1994, p1347). Denial and avoidance are therefore common coping strategies among individuals with possible exposure to HIV (Lorenc et al. 2011).

Specialist GUM clinics are viewed as socially undesirable spaces by some groups (Scoular, Duncan & Hart 2001) prompting a preference for testing in primary care settings among Irish women (Balfe et al. 2010b) and black Africans in London (Burns et al. 2007). However, young women in London have expressed preference for specialist clinics as primary care facilities are deemed to lack expertise (Normansell, Drennan & Oakeshott 2016); and similar findings have been reported by a discrete choice experiment study with participants with a range of socio-demographic characteristics (Llewellyn et al. 2012).

1.7.3 Convenience and accessibility

Physical inaccessibility, long waiting times and unfriendly staff attitudes are all barriers to attendance (Llewellyn et al. 2012). Lengthy waits are commonly cited in relation to specialist sexual health clinics (Normansell, Drennan & Oakeshott 2016; Llewellyn et al. 2012). Perceived delays in receiving test results also serve to heighten anxieties around STI testing (Lorenc et al. 2011).

1.8 The emergence of e-Sexual health services

1.8.1 Digital health and the patient-centred care agenda in the UK

There is a strong commitment to digital health in the UK (NHS England 2014). Digital technology is viewed as a powerful enabler of the patient centred care agenda (Lupton 2013). In the UK, patient-centred care is framed as part of a normative agenda to increase provider choice and patient involvement through the promotion of equal 'partnerships'

(Mead & Bower 2000) and models of 'shared decision-making' between patients and clinicians (United Kingdom Department of Health 2010; Coulter & Collins 2011).

This is particularly evident in the area of chronic disease, where dedicated 'expert patient' programmes have proliferated, encouraging patients to exercise greater autonomy through the self-management of their condition (United Kingdom Department of Health 2001). This marks a departure from traditional paternalistic models of care in medicine, and the Parsonian framing of the patient as 'passive' and 'dependent' within the context of the clinical encounter (Armstrong 2014).

Demands to reconfigure the power dynamics within the clinical context can be traced to the social movements of the 1960s and 1970s (Rothman 2001). Feminist activists in particular, were instrumental in exposing the limited agency of women to define and realise their own health needs (ibid.). Calls for greater autonomy, information and choice in health have also been increasingly articulated by a burgeoning consumer movement (Kapp 2009; Fox & Ward 2006). This movement espouses a free market model of health care, championing an ideal of 'patient as consumer', equipped with the power of choice and knowledge within a competitive marketplace (Lupton 1997; Fox & Ward 2006) .

Yet there is uncertainty as to how the construct of 'patient autonomy' - a core ideal of the patient-centred paradigm - is both theoretically conceived and empirically practiced. In broad philosophical terms, autonomy encompasses 'a certain idea of persons as self-determining' (Dworkin 1988, p.11); and in the bioethical literature, patient autonomy is commonly considered in relation to the doctrine of informed consent, which safeguards patients' rights to 'be treated as persons, as masters of their own body, as responsible for their decisions, as makers of choices' (Dworkin 1988, p.103).

The limits and boundaries of autonomous action from a bioethical standpoint is subject to much debate. Clinicians may question patients' abilities to understand the complexity of the medical information under discussion, which inevitably limits the potential for self-determination (Kapp 2009). In an era of 'surveillance medicine', whereby the onus is placed on individuals to mitigate and moderate risk behaviours in accordance with biomedical orthodoxy, the concept of patient autonomy creates an interesting paradox (Armstrong 1995; Armstrong 2014). It follows that patients can only be self-determining insofar as they exercise a form of 'regulated autonomy' – one that ensures their choices

and actions are in line with prescribed norms and practices to maximise health (Petersen 1997).

In view of this ambiguity, a more suitable term in this discussion is that of 'patient empowerment'. Patient empowerment is a relational construct which implies a redistribution of power between patients and providers, subject to continual negotiation (Roberts 2001); while patient autonomy is often construed in more atomistic terms (Donchin 1995). Empowerment implies a process of change whereby 'those who have been denied the ability to make choices acquire such an ability' (Kabeer 2002, p.437). Yet it is recognised that individual choices are always constrained and shaped by wider social and structural forces (Ibid.).

1.8.2 The promise of e-STI testing services

There is a normative assumption that e-sexual health services, including STI testing, will enhance patient choice and opportunities for self-management, leading to improved health outcomes (Minichiello et al. 2013).

e-STI testing services may enable users to take control of the testing process, providing more convenient testing pathways. Samples are self-collected, often in the privacy of the user's own home, and in a location and timing of their choosing. Contact with the service provider is maintained 'at a distance' via users' personally controlled devices such as mobile phones and laptops. As in other health domains, this transferral of skills, roles and responsibilities may have significance for the reconfiguration of health care relations.

Indeed, as a 'faceless' provider (Minichiello et al. 2013), the internet may shift the balance of power in favour of the user by limiting opportunities for providers to monitor, influence and ultimately judge patients' sexual risk behaviours. In this way e-STI testing may bypass some aspects of stigma that are associated with face-to-face testing services.

Yet, while e-STI testing services may hold considerable promise for patient empowerment, Lupton warns that the digital revolution in health is situated within 'techno-utopian' discourses which may in fact jar with patients' actual experience (Lupton 2013). She posits that these technologies potentially infringe on patients' power and agency, by permeating patients' private spaces (e.g. their homes) and generating new mechanisms for medical surveillance. The responsibility implied by self-monitoring and management of health conditions may in fact represent an increasing burden for patients (Lupton 2013).

Furthermore, not all patients are at ease with new conceptualisations of patienthood, preferring a more passive role whereby decision-making can be deferred to a trusted professional (Henwood et al. 2003).

1.9 e-STI testing - summary of evidence

Publicly funded or subsidised e-STI testing services are available in a number of international settings, including Sweden, Australia, Canada and the USA. e-STI testing services are not homogenous (Turner et al. 2018). There is considerable variability in the functionality of websites, service components (including remote support), and level of integration with local services. Typically e-STI testing enables users to order a test kit from a virtual service (via a website or app), collect their own samples, post test samples to a laboratory, and be notified of their results by short message service (SMS) text message or telephone (Woodhall et al. 2012; Harding-Esch et al. 2016). Other versions may require users to order their self-sampling kits online, but collect test kits from a face-to-face setting such as a clinic or laboratory.

In the UK, national guidelines recommend e-STI testing to expand routine testing for HIV in areas of high prevalence (National Institute for Health and Care Excellence 2016), as well as opportunistic screening for chlamydia among young adults (Public Health England 2015b). It is envisaged that e-STI testing can complement existing service provision, offering patients more choice. Moreover there is an assumption that e-STI testing can increase utilisation among individuals who do not use face-to-face STI testing services (Public Health England 2015b).

The international evidence base on e-STI testing services is scant. One randomised controlled trial in France has evaluated self-sampling for chlamydia accessed via the internet compared to chlamydia testing in face-to-face settings. It reports an increase in testing uptake (29.2% in the intervention group v 8.7% in the control group, RR 3.37, 95% CI 3.05 – 3.74). However, outcomes were assessed using different measures in the intervention and control groups, and there was low and differential follow up (47% follow up in the intervention group v. 30% follow up in the control group) (Kersaudy-Rahib et al. 2017).

Descriptive studies suggest that e-STI testing can attract high risk groups and yield high STI positivity. In the United States, Ladd and colleagues found that out of 205 rectal samples ordered and returned by women using the 'iwantthekit' website between January 2009 and

February 2011, 18.5% were positive for at least one STI (Ladd et al. 2014). The majority of women in the sample were single (91.2%), young (mean age 25.8 years) and of African-American ethnicity (50.0%). Half had never used condoms for rectal sex (48.7%). A study with male users of the same website found that of 501 STI kits returned by men over the age of 14, between September 2006 and May 2009, 21% tested positive for chlamydia, gonorrhoea or trichomonas vaginalis (Chai et al. 2010). The majority of users were young (median age 24.5 years), single (84%) and a high proportion were of black ethnicity (45%). While these studies are promising, sample sizes have been small and no comparison were made with users of face-to-face pathways.

A recent observational study evaluated an online treatment service or eSexual Health Clinic (eSHC) in London. The eSHC pathway was offered to patients diagnosed with chlamydia in GUM clinics and to patients diagnosed via an e-STI testing service (Checkurself) (Estcourt et al. 2017). The eSHC pathway provided remote access and management of test results, a web-based risk assessment tool, and e-prescription for treatment collection at community pharmacies. In all, among those diagnosed via Checkurself, 89% were treated though a combination of remote and face-to-face care; and this is similar to the proportion of Checkurself users habitually treated in routine settings (~88%). 57% of Checkurself users were treated solely via the eSHC pathway, which included telephone support. These findings suggest that remote treatment pathways are feasible for users of e-STI testing services. However, a randomised study is required to generate conclusive evidence on the public health effectiveness of online treatment services (Estcourt et al. 2017).

Evidence from routine surveillance data in England indicates that chlamydia testing uptake via internet-accessed pathways is much lower than face-to-face testing pathways, but that chlamydia test positivity (the proportion of tests that are positive) is comparable to other settings. In 2016, 8% of chlamydia tests in England among 15-24 year olds were conducted via internet accessed pathways. Internet test positivity was 8.5% which is slightly lower than specialist GUM clinics (11.1%) but higher than GP settings (6.3%) (Public Health England 2017d).

Between November 2015 and October 2017, 44,791 test kits were returned and tested by the national HIV self-sampling website (www.freetesting.hiv). The majority were from MSM (71%). Among this group, 31,734 kits were tested, of which 1.07% (340/31,734) were reactive. Although the service targets black African groups, only 7.25% (3,238/ 44,660) of tested kits were from this population, yielding a reactive rate of 1.76% (57/3,238). Just

under a third (29.9%) of those who returned kits had never tested for HIV previously. The service suffers from inefficiencies as 44.5% of test kits were not returned (Public Health England 2018b).

Qualitative research, conducted with potential users of e-STI testing services suggests that e-STI testing might be acceptable to groups at risk of STIs including MSM and young adults, due to ease, convenience and enhanced privacy (Aicken et al. 2016; Hottes et al. 2012). Privacy, trust and credibility of websites or apps were highlighted as important considerations for service development. However, there is some uncertainty on whether e-STI testing services would be acceptable to marginalised populations. In Scotland, Lorimer and McDaid (2013) found that young men from more deprived areas seemed more disconnected from digital technology and stated a preference for face-to-face services.

Self-sampling diagnostic modalities for STIs not accessed by the internet have demonstrated an increase in testing uptake but they have yet to demonstrate a benefit in terms of cases detected and treated. A Cochrane review of home versus clinic specimen collection for chlamydia and gonorrhoea found inconclusive evidence for an effect on case management, defined as cases tested, diagnosed and treated (pooled risk ratio (RR) 0.88, 95% CI 0.60-1.29) (Fajardo-Bernal et al. 2015). Moreover, home self-sampling yielded a lower proportion of positive tests than clinic sampling (pooled RR for positive test prevalence 0.72, CI 0.61, 0.86). Nevertheless 8 of 10 trials demonstrated an increase in testing uptake, although results were not pooled due to heterogeneity of effect sizes. Many studies had methodological limitations including high attrition (Ibid.).

International guidelines recommend self-testing to expand screening of HIV (World Health Organisation 2016). Self-testing differs from self-sampling testing modalities as it enables a person to take a sample, perform a test and interpret the results without the need for a laboratory (Harding-Esch et al. 2016). A systematic review found that compared to facility-based testing, HIV self-testing increases uptake among hard to reach and high risk populations, including male partners of female clients of ante-natal clinics and MSM (pooled RR 2.12, 1.51 to 2.98). Two studies assessed HIV positivity as a secondary outcome but both trials were two small to draw conclusive findings (Johnson et al. 2017).

There is some limited emerging evidence on linkages to care following unsupervised HIV self-testing in community settings in sub-Saharan Africa (SSA). One observational study in Malawi found that 56% of clients who reported a positive result accessed confirmatory

testing and care, and this level of linkage was deemed acceptable for community based HIV testing in SSA (Choko et al. 2015). A cluster RCT in the same setting found that among adults offered self-testing for HIV, almost 3 times as many participants initiated ART when they were offered home care compared to facility care (RR, 2.94, 95%CI 2.10-4.12; P<0.001). However the proportions initiating ART were low overall, and the study was not powered to assess retention within ART programmes (MacPherson et al. 2014). Further evaluation of linkages to care, including adherence to ART, is required across diverse settings (Sharma et al. 2015).

1.10 Chapter summary

In this chapter, I presented an overview of the distribution of STIs in England and the UK, and I reviewed national STI testing guidelines and current testing coverage among key population groups. I outlined the promise of e-STI testing as a means to bypass the stigma and inconvenience that is associated with face-to-face STI testing services, and its potential to facilitate the normative goals of patient empowerment and patient-centred care. Nevertheless, while promising, I demonstrated the limited evidence base for the effectiveness of e-STI testing. In the following chapter, I introduce the study context and the e-STI testing service – SH:24 - that I evaluated for this thesis.

Chapter 2: SH:24 e-STI testing and results service

2.1 Intervention context

The London boroughs of Lambeth and Southwark are characterised by particularly high levels of sexual ill health relative to the rest of London and the rest of England. This includes high rates of sexually transmitted infections (STIs), early pregnancy and abortion. In 2016, the diagnosis rate for new cases of HIV per 100,000 population (aged 15 years and over) was 105.4 and 44.2 in Lambeth and Southwark respectively, compared to 27.6 per 100,000 population in the London region as a whole. For all other STIs (excluding chlamydia in under 25s) the diagnosis rates were 3,288 and 2,799 per 100,000 population (aged 15-64 years) in Lambeth and Southwark, compared to 1,547 in London and 795 in England (Public Health England).

This epidemiological profile is partly explained by the socio-demographic composition of the boroughs, which includes high proportions of at-risk groups including young people, black and minority ethnic (BME) populations and men who have sex with men (MSM). At the same time, socio-economic factors such as high levels of deprivation are likely to play a contributory role (Lambeth Southwark Lewisham Councils 2014).

In line with the national sexual health framework (United Kingdom Department of Health 2013)(UK Department for Health 2013), preventative and curative sexual health services are currently provided by a range of providers, including genitourinary clinics (GUM), community based sexual and reproductive clinics, general practice (GP) surgeries as well as private providers such as Brook. While face-to-face sexual health services are considered to be high quality, these services are under increasing pressure to meet rising demand in a context of diminishing resources for sexual health (Robertson et al. 2017) .

2.2 SH:24 – an e-STI testing and results service

Sexual Health 24 (SH:24) is a community interest company (CIC), set up in 2013 with funding from Guys and St Thomas' Charity for the purpose of developing and establishing an online sexual health service in Lambeth and Southwark (www.sh24.org.uk). The

overarching aim of the service is to improve sexual health outcomes in the population, while generating efficiency savings (SH:24 2013b).

SH:24 adopts a 'user-led', agile, approach to service development. This is based on build-test-learn philosophy. In the discovery phase a number of product prototypes were developed based on consultation with potential service users in Lambeth and Southwark. Each prototype underwent extensive testing and adaptation to ensure its acceptability with providers and users.

SH:24 completed its first 'minimal viable product' (MvP) in November 2014. MvP1 is an internet-accessed STI testing and results service (e-STI testing). The version that I evaluated offered free postal self-sampling test kits for chlamydia, gonorrhoea, HIV and syphilis. Users who ordered a test kit from SH:24, were required to complete a short order form online. Those reporting STI symptoms were advised via a pop up message to visit their local clinic for immediate treatment. Those reporting complex needs such as depression, drug and alcohol dependency, or exploitative sexual partnerships were telephoned by a clinician and referred to relevant clinical services. Users could continue to use the online service if they wished.

All test kits contained a lancet and collection tube to obtain a blood sample for serological testing for syphilis and HIV. For chlamydia and gonorrhoea, women were sent vaginal swabs and men were sent a container for first catch urine samples. Test kits for MSM also contained swabs to take pharyngeal and rectal samples.

The test kits included pictorial leaflets with guidance on how to collect the specimens. A video demonstrating blood sample collection was available on YouTube and could be accessed via the SH:24 website. Users were encouraged to text or phone the SH:24 team with any questions or concerns. Non-returners were sent reminders via text message and resent test kits if required, as per SH:24's protocols.

Chlamydia, gonorrhoea and syphilis test results were delivered by text message. Participants with reactive results for syphilis or positive results for chlamydia and gonorrhoea were signposted to local clinics for confirmatory testing and treatment as necessary. Reactive results for HIV were communicated by phone by a clinician. The SH:24 website also provided health education information on STIs and safer sex practices.

Since the completion of the first minimal viable product, SH:24 has continued to develop and expand, gradually adding new products and increasing functionality to the website, including telephone support, postal treatment for chlamydia and contraceptive services.

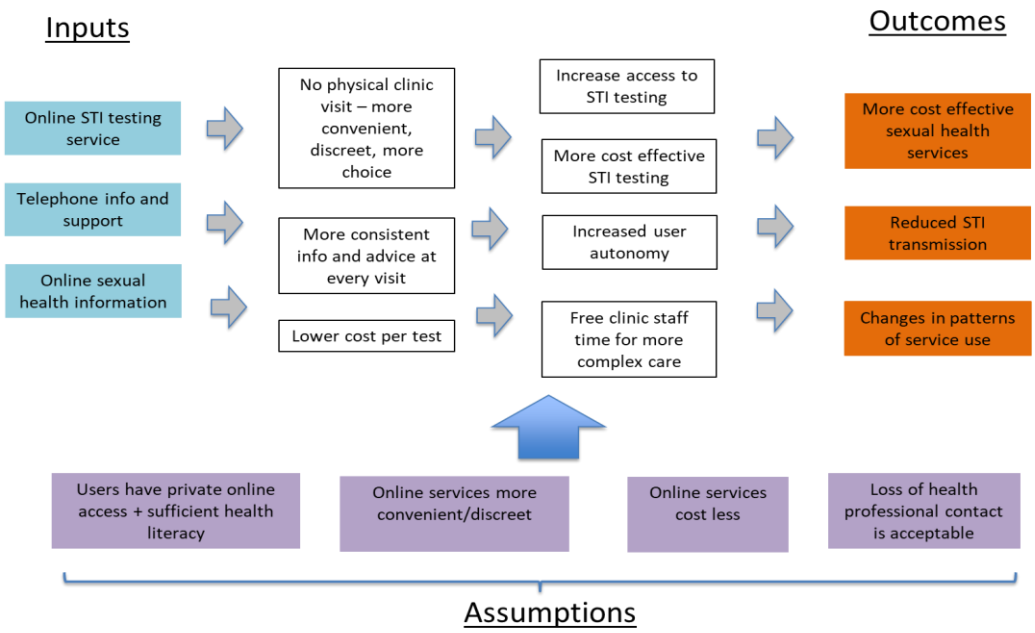
Figure 2: SH:24 user journey (SH:24 2013a)

2.3 SH:24 Evaluation

As an untested intervention, SH:24 has implications for the commissioning of sexual health services not only in London but also nationally. Moreover, given the limited evaluative work in the field of online services for sexual health more generally, the SH:24 evaluation is likely to make an important contribution to the international evidence base.

The theory of change for the e-STI testing component of SH:24, developed by Baraitser and colleagues from Kings College London (Baraitser et al. 2015), draws on the original funding proposal and articulates three anticipated outcomes at the system level. These are: reduced STI transmission, more cost effective sexual health services and changes in patterns of service use.

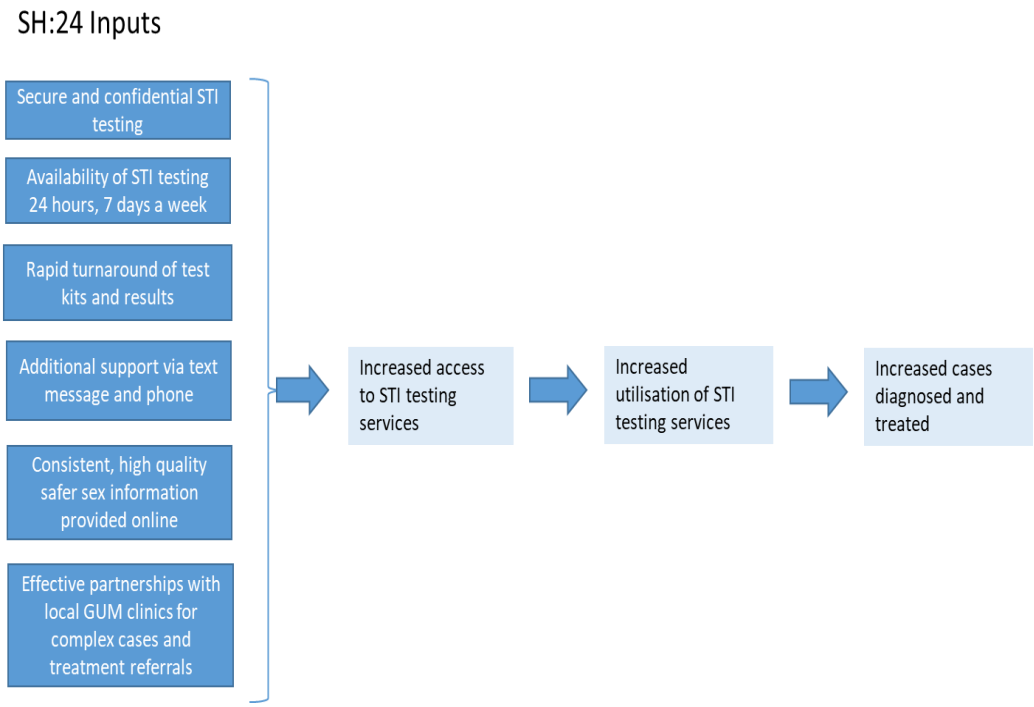
Figure 3. Theory of change for SH:24 (Baraitser et al. 2015, Figure 1)



Increased access to STI testing is deemed to be a key intermediary outcome on the pathway to reducing STI transmission rates in the population. It is hypothesised that the provision of e-STI testing alongside usual face-to-face care will increase uptake of STI testing services, leading to increased diagnoses and treatment of STIs, thus interrupting disease transmission pathways. It is recognised that the contribution of e-STI testing to population health is contingent on the epidemiological profile of the additional users of STI testing services.

Clinical effectiveness of this service is therefore determined by two interrelated outcomes: 1) uptake of STI testing services and 2) diagnoses and treatment of STIs. A simplified logic model outlining this causal pathway is presented in figure 4.

Figure 4. Simplified logic model – SH:24



2.4 Thesis objectives

In line with the objectives of SH:24 outlined in the original funding proposal, my thesis aims to evaluate the clinical effectiveness of SH:24 via a randomised controlled trial (RCT). This is defined as uptake of STI testing, STI diagnoses and STI treatment. National guidelines recommend e-STI testing as a means to increase testing uptake among those who do not attend face-to-face services, and I therefore conduct secondary analyses to determine if SH:24 increases testing uptake among first-time testers.

My specific objectives are as follows:

1) To determine the effect of SH:24 on STI testing uptake, cases diagnosed and treated, when delivered alongside standard care;
2) To determine the effect of SH:24 on STI testing uptake among those who have never previously tested for STIs, when delivered alongside usual care.

The following chapter outlines my theoretical framework for this evaluative work. The SH:24 evaluation adopts a flexible research philosophy to allow for a range of epistemological perspectives. I draw on a critical realist perspective to theorise the causal mechanisms that may underpin the intervention, and in line with this perspective, I consider 'contextual contingencies' that may interact with these causal mechanisms (Fletcher et al. 2016). Further, I use the 'candidacy' framework to conceptualise access to STI testing services (Dixon-Woods et al. 2006). While it was beyond the scope of the thesis to test this model empirically, I utilise the candidacy framework to situate my evaluation findings.

Chapter 3: Theoretical Framework

3.1 Chapter overview

In this chapter, I review theory driven approaches to evaluation, and the challenges of applying these approaches to the evaluation of complex health interventions. I outline the theoretical premise underpinning this thesis, and I apply the 'candidacy' model to theorise how an e–STI testing service (SH:24) may improve access to STI testing in a complex service delivery system.

3.2 Theory driven approaches to evaluation

Theory-driven approaches to programme evaluation have emerged as a response to the so-called 'black-box', method-led, evaluations which historically dominated the field of evaluation science (Scriven 1994). Early investigators, such as Campbell, advocated the co-option of experimental methodologies from the natural sciences to assess the causal effects of large public programmes and policies in the United States (Campbell 1969). Importance was placed on achieving internal validity at the expense of understanding the inner workings of programmes and the underlying processes that trigger social change (Scriven 1994; Shadish, Cook & Leviton 1991; Chen & Rossi 1987).

Prominent critics of this approach, including Cronbach (1980) and later Weiss (1972), Chen and Rossi (1987), Pawson and Tilley (1997), have argued that aggregate measures of effect have limited utility for policy-making if evaluators fail to explain '*why…for whom, and in what circumstances'* (Pawson & Tilley 1997, p.xvi) a programme may work both within and beyond its original social setting. Indeed, after the initial enthusiasm for large-scale experiments, policy makers in the United States became increasingly discontent with an evolving portfolio of evaluative research, characterised by inconclusive and inconsistent findings (Pawson & Tilley 1997). Crucially, outcome-focussed evaluations failed to illuminate whether programme failure could be attributed to poor implementation or poor programme design (Lipsey & Pollard 1989).

To counter this problem, evaluation science took a methodological turn towards 'theory-driven' or 'theory-based' approaches (Shadish, Cook & Leviton 1991; Chen & Rossi 1987; Weiss 1995). This perspective seeks to determine not only whether a programme works, but also to understand 'the transformational relations between treatment and outcomes, as well as contextual factors under which the transformation processes occur' (Chen &

Rossi 1989, p.300). Evaluators may draw on varied sources to develop hypotheses for how social transformation might occur, including formal theories from the social sciences, as well as 'professional logic' arising from stakeholder expertise and perspectives (Weiss 1997b). The resultant overarching 'programme theory' is typically articulated via schematic diagrams such a logic models, which detail the sequential and recursive causal links between programme components, hypothesised intermediary phases, and anticipated outcomes (Rogers 2008; Coryn et al. 2010). These theoretical assumptions can then be subject to empirical testing and exploration (Kazi 2003) .

Theory-driven approaches (TDA) may allow for greater transparency in programme design and evaluation as stakeholders are forced to make explicit their assumptions from the outset, which can then be subject to interrogation and adjustment (Van Belle et al. 2010). Moreover, proponents argue that TDA offers improved 'explanatory power' (Weiss 1997a), providing a conceptual framework within which findings can be situated and interpreted 'beyond the specific operations and idiosyncrasies' of each evaluation setting (Lipsey & Pollard 1989, p.317). TDA therefore attempts to offer some assessment of the external validity of evaluation results in a way that the early method-led evaluations did not (Scriven 1994).

3.3 Theory driven approaches and complex health interventions

3.3.1 The Medical Research Council guidance

In principle, the Medical Research Council in the United Kingdom endorses a theoretical perspective in the development and evaluation of complex health interventions (United Kingdom Medical Research Council 2006). Complex interventions have proliferated in the ambit of public health. This development is indicative of an increasingly broad conceptualisation of population health as determined by the interplay of biological, social and structural factors (Krieger 2001; Cohn et al. 2013).

Defined as 'built up from a number of components, which may act both independently and interdependently' (United Kingdom Medical Research Council 2000, p2), complex interventions inherently pose greater methodological challenges than traditional evaluations of drug interventions. This is due to difficultly in identifying the 'active ingredients' of multi-component interventions and gaining an appreciation for how they may interact (United Kingdom Medical Research Council 2000); and the challenge in understanding how local contextual conditions may shape outcomes via intricate and

lengthy causal pathways (Bonell et al. 2012; United Kingdom Medical Research Council 2006).

The MRC framework underlines the importance of developing a 'theoretical understanding of the likely process of change' at the development stage of an intervention (United Kingdom Medical Research Council 2006, p.9). However it fails to offer guidance on how specific theory-driven approaches can be integrated within the complete cycle of intervention design, implementation and evaluation (De Silva et al. 2014; Anderson 2008). Bonell and colleagues (2012, p.2300) posit that this has resulted in 'an evidence base that is dominated by high quality RCTs of poorly theorised interventions', whose 'effects are poorly understood' thus limiting their potential for replication. Yet this is perhaps not surprising given that the application of theory-driven approaches both within public health and other applied settings such as education and social care is beset with challenges (Weiss 1995). I discuss each of these challenges below.

3.3.2 What constitutes theory in a theory driven approach?

There is a lack of consensus on what constitutes 'theory' in a theory driven approach and how this theory should be generated (Weiss 1997a; Moore & Evans 2017). In the health literature, there are two dominant frameworks (Blamey & Mackenzie 2007). The first is Theory of Change (ToC), which is a flexible framework that is not wedded to a particular epistemological or ontological perspective (De Silva et al. 2014; Weiss 1997b); the second is the realist (or realistic) approach, which is embedded within a critical realist paradigm (Pawson & Tilley 1997).

Theory of Change can encompass two types of theory. These are implementation theory and programme theory (Weiss 2000) (also referred to by Chen (1989) as 'normative theory' and 'causal theory' respectively). Confusingly, implementation theory is not a theory in any formal sense, i.e. a set of 'general principles that provide explanations for empirical phenomena' (Hammersley 1995, p.56). Instead, it is a *descriptive* and systematic account of the activities and inputs that comprise an intervention. It illustrates the relationship between intervention components and it specifies how planned activities should be executed to achieve desired outcomes. As Weiss (1997b) explains:

> The theoretical assumption it tests is that if the program is conducted as planned, with sufficient quality, intensity, and fidelity to plan, the desired results will be forthcoming. (p.46)

Programme theory, on the other hand, seeks to offer an *explanatory* account of how and why an intervention works (Astbury & Leeuw 2010). Importantly, it articulates the hypothesised mechanisms of change underlying the intervention. Weiss (1997b) forwards:

> An evaluation that attempts to track the theoretical underpinnings of the program has to devise ways to define and measure the psychological, economic, sociological, organisational, or other processes that intervene between exposure to the programme and participant outcomes. (p.48)

Evaluators have drawn upon social-cognitive theories (such as the theory of planned behaviour), and other formal theories from the social sciences, to inform the 'programme theory' component of theory of change evaluations (Weiss 1997b; De Silva et al. 2014). Yet many worked examples still offer pragmatic rather than theoretical insights into change processes (Fletcher et al. 2016; Blamey & Mackenzie 2007). Indeed, theory of change methodologies have evolved with a focus on community development and a commitment to participatory approaches and stakeholder ownership (for example the Aspen Institute Roundtable on Community Change). Emphasis is placed on garnering the perspectives and expertise of local actors (including beneficiaries, programme implementers and community leaders), to determine appropriate outcomes, map causal pathways (including possible unintended effects), and agree required resources (De Silva et al. 2014; Connell & Kubisch 1998).

While important, critics argue that this participatory, community-driven process should not be at the expense of generating 'good theory' (Weiss 1995): one that goes beyond the descriptive elements of an intervention, to conceptualise the underlying mechanisms on which the intervention rests, and how these are shaped by context (Fletcher et al. 2016). To achieve this, evaluators are advised to draw upon theoretical insights from the social sciences (particularly psychology and sociology), research evidence, as well as their own 'logical reasoning' (Weiss 1997b, p.51; Lipsey & Pollard 1989).

The second strand of theory driven approaches in the evaluation of complex health interventions are realist evaluations. First proposed by sociologists Pawson and Tilley (1997), realist evaluations stem from a critical realist philosophy. Critical realism adopts a stratified view of social reality, distinguishing between the realms of the real, the actual and the empirical (Bhaskar 2008). This is in contrast to the 'flat' ontologies of other research philosophies (Sayer 2010, p.12). For example a positivist ontology only pertains to the *empirical* i.e. reality is confined to that which can be observed and experienced.

The stratified ontology forwarded by critical realism is as follows: the *real* pertains to physical or social objects, 'their structures and powers', that exist independently of our experience and understanding of them (Sayer 2010, p.11); the *actual* are the 'patterns of events' that can be triggered by the powers or mechanisms within the real; and the *empirical* refers to the experience of these events (Bhaskar 2008, p.37; Sayer 2010).

As Bonell and colleagues explain (2016):

> …realists believe they can identify objective truths describing the actual realm and can uncover the true causal mechanisms of the real realm based upon data from the empirical realm. (p.2)

Mechanisms, in a realist sense, are therefore 'causal powers' that 'lie behind' an intervention (Pawson & Tilley 1997) – not to be equated with intervention inputs or activities.

> Mechanisms are the agents of change. They describe how the resources embedded in a programme influence the reasoning and ultimately behaviour of programme subjects. (Pawson 2013, p.115)

> Scientific realism holds that mechanisms are not external factors but latent powers and capabilities, which are a function of the interaction between intervention resources and responses of participants. (Van Belle et al. 2016, p.3)

Further, in a realist evaluation, context holds importance beyond the mechanics of intervention delivery. Context is *intrinsic* to the causal process itself. Context *interacts* with mechanisms to generate outcomes, and these processes will vary across social settings (Sayer 2010; Pawson & Tilley 1997). The realist formula underpinning social change is therefore summarised as (Pawson & Tilley 1997, p.xv):

context + mechanism = outcome

Realists prioritise developing and testing 'middle range' theories related to hypothesised context-mechanism-outcome configurations. Put simply, these are 'propositions about how mechanisms are fired in contexts to produce outcomes' (Pawson & Tilley 1997, p.85). Similar to the articulation of programme theory by Weiss (2000), hypotheses can be derived from prior evidence and formal theories from the social sciences, which are then subject to empirical testing and refinement (Kazi 2003).

There is great divergence in the way theory of change and realist approaches are applied in practice (Coryn et al. 2010; Marchal et al. 2012). In the case of complex health interventions, the principles of either approach are often not applied systematically (De Silva et al. 2014; Marchal et al. 2012). Theory of change methodologists appear to have

given greater attention to the development of operational principles rather than to theoretical ones (for example there are a plethora of field manuals giving guidance on conducting ToC in applied settings (Vogel 2012); and this may explain the theory deficit in many evaluations. Realist evaluation, on the other hand, is based on more clearly defined ontological and theoretical propositions. Yet its application is still in a nascent stage in health sciences, and some applied researchers have struggled with the interpretation of the critical realist ontology (Porter 2015; Marchal et al. 2012).

3.3.3 Complexity in complex health interventions

A second, but related challenge, in the application of theoretical-driven approaches is the debate on what is meant by complexity in complex health interventions. Commentators have critiqued the MRC for 'appropriating' complexity science in its guidelines for the evaluation of complex health interventions (Cohn et al. 2013). They argue that an important distinction exists between interventions which are 'complicated' - those comprised of multiple interrelated or interacting components – and interventions (simple or complicated) that are introduced into 'complex systems' (Shiell, Hawe & Gold 2008; Glouberman & Zimmerman 2002).

For complexity theorists, it is preferable to think of complexity as a 'property of a system not an intervention' (Shiell, Hawe & Gold 2008, p.1281). A system may refer to a single entity or combination of entities which often include organisations, schools, communities and service delivery networks (Foster-Fishman Pennie, Nowell & Yang 2007). System boundaries can be fluid, defined by the nature of the problem to be addressed:

> Within the context of systems change, what we refer to as 'the system' is the set of actors, activities and settings that are directly or indirectly perceived to have influence in or be affected by a given problem situation. (Ibid., p. 198)

Complex systems are characterised by behaviours and processes that are dynamic, adaptive and non-linear (Rickles, Hawe & Shiell 2007). Hawe, Shiell & Riley (2009) forward that interventions introduced into these systems are best understood as 'events in systems'. The success of an intervention is contingent not on the discrete workings of its constituent parts, but on how the intervention disrupts, and potentially transforms, pertinent features of the system (Moore & Evans 2017; Hawe, Shiell & Riley 2009). As a consequence, the focus of the evaluation shifts, as Rutter and colleagues explain:

> Instead of asking whether an intervention works to fix a problem, researchers should aim to identify if and how it contributes to reshaping a system in favourable ways. (2017, p.2602)

This thinking challenges evaluators to consider causal processes that might previously have been obscured by more simplistic causal models; and to consider intervention effects at the system level rather than solely at the individual level (Rutter et al. 2017; Shiell, Hawe & Gold 2008).

Indeed, important features of complex systems are their 'emergent properties' (Rickles, Hawe & Shiell 2007) – defined as 'a property of a system that is not reducible to, nor readily predictable from the properties of individual system components' (Halley & Winkler 2008, p.10). Emergent properties pertinent to the production of health might comprise structural characteristics such as community empowerment or social exclusion (Shiell, Hawe & Gold 2008). Moreover, population health is conceived as an emergent property of multiple complex systems. For example Rutter and colleagues (2017, p.2602) cite the changing prevalence of obesity within a population as an, 'emergent property of the food, employment, transport, economic, and other systems that shape the energy intake and expenditure of individuals'.

Critical realists also recognise the emergent properties of natural and social phenomena (Sayer, 2010). Certainly, the realist evaluation framework is well placed to incorporate a complex systems perspective (Fletcher et al. 2016; Byrne 2013). Pawson and Tilley (1997, p.70) conceive interventions to be embedded within dynamic social systems, whose functioning is contingent on the way 'pre-existing structures' within these systems 'enable' or 'disable' the intended mechanism of change. Hence, both frameworks necessitate the foregrounding of context both in the theorisation, and in the applied understanding, of change processes.

While this synergy is conceptually appealing, Cohn and colleagues highlight that the challenge for evaluators interested in complexity is, 'how to go about studying complexity *without* fully unravelling it' (Cohn et al. 2013, p.42). Chen (2016) cautions that excessive complexity – innumerable causal pathways, feedback loops and interactions – runs the risk of rendering evaluation findings uninterpretable. Weiss (2000), while not addressing complexity theorists directly, advises that all theory-driven evaluations focus on a few key theoretical propositions, rather than trying to tackle a programme's theoretical complexity in its entirety. Similarly Hawe (2015), a key proponent of complexity theory in population health, underlines the importance of understanding the core 'functions' of intervention components in generating change, as it is these essential insights that enable the replication of programmes across contexts. As Hawe and colleagues explain (2004):

> Rather than defining the components of the intervention as standard—for example, the information kit, the counselling intervention, the workshops—what should be defined as standard are the steps in the change process that the elements are purporting to facilitate or the key functions that they are meant to have. For example, 'workshops for general practitioners' are better regarded as mechanisms to engage general practitioners in organisational change or train them in a particular skill. (p.1562)
>
> …The issue is to allow the form to be adapted while standardising the process and function. (p.1562)

3.3.4 Epistemological and ontological perspectives in the evaluation of complex health interventions

Finally, applying a theory-driven approach presents challenges due to the contested epistemological and ontological standpoints among the evaluation community. The place of the randomised controlled trial (RCT) in evaluative research is a particular source of contention. While the MRC framework (United Kingdom Medical Research Council 2000) champions RCTs as the most rigorous and valid method for evaluating complex health interventions, this is countered by some evaluation theorists and practitioners on epistemological and methodological grounds.

First, RCTs are assumed to be intrinsically wedded to a positivist epistemology, and therefore incompatible with alternative research philosophies in evaluative research, including critical realism (Van Belle et al. 2016; Pawson & Tilley 1997). Yet as Bonell and colleagues remind us, the RCT is a method used to capture an objective reality (2013), and randomisation a procedure that allows 'minimally biased' comparisons between groups (Bonell et al. 2012, p.2300). The method itself does not preclude researchers applying a number of epistemological and ontological framings to the data, including a critical realist perspective.

> When we do RCTs, we hold the same realist epistemological and ontological assumptions that we hold when we undertake non-randomised evaluations or exploratory qualitative research. Our methods don't determine our assumptions, we as researchers determine our understanding of the data deriving from these methods. (Bonell et al. 2013, p.81)

A second related charge is that RCTs are overly reductionist in their application. Critics question the appropriateness of trials that attempt to 'isolate' the effects of an intervention from the social context within which it is embedded, thus negating the influence of contextual factors on outcomes (Marchal et al. 2013; Cohn et al. 2013; Pawson & Tilley 1997). Bonell, Bennett and Oakley (2003) demonstrate that this reasoning is conceptually flawed. In relation to experimental designs in sexual health, they forward:

> The aim is to see how the intervention interacts with and contributes to the broader picture… rather than pretending this picture does not exist. Experimental evaluations seek to examine the 'added value' that an intervention brings to sexual health outcomes across a population of individuals, rather than seeking to suggest that an intervention 'causes' a sexual health outcome in any one individual. (p.9)

The argument thus follows that RCTs are highly appropriate for evaluations of complex interventions, provided that they are situated within a comprehensive theoretical framework and additional research methods are used to shed light on hypothesised change processes (Bonell, 2012). While RCTs yield an overall aggregate effect of the 'added value' of an intervention embedded within a complex social system, this can be complemented by further statistical analyses. For example, mediation analyses can explore hypothesised causal pathways while moderation analyses may be used to understand how intervention effects are modified by 'contextual contingencies' (Fletcher et al. 2016, p.296). Crucially, qualitative methodologies can facilitate the development of initial theoretical propositions and explore complex change processes with greater depth and flexibility, complementing or indeed challenging findings derived from quantitative data (Oakley et al. 2006; Jamal et al. 2015; United Kingdom Medical Research Council 2015).

Combining and integrating RCT and qualitative evidence, is both theoretically and analytically challenging (Lewin, Glenton & Oxman 2009; United Kingdom Medical Research Council 2015). Some argue that an inherent ontological tension exists in trying to combine evidence generated from apparent positivist and interpretive perspectives (Blackwood, O'Halloran & Porter 2010; Munro & Bloor 2010). Others highlight tensions of a political nature as qualitative social science evidence continues to be devalued within evidence-based public health (Daniels et al. 2016), and therefore the inclusion of qualitative inquiry within multi-disciplinary projects can be somewhat superficial and simplistic (Béhague, Gonçalves & Victora 2008).

Proponents of realist RCTs suggest that a critical realist framework facilitates the combination of RCT evidence and evidence from qualitative inquiry within a cohesive philosophical framing (Blackwood, O'Halloran & Porter 2010; Bonell et al. 2016); and empirical work is underway to further test this proposition (Jamal et al. 2015). It is worth noting however, that Pawson and Tilley (1997), the originators of realist evaluation, take a somewhat instrumental view of qualitative methodologies, positing that the scope of qualitative inquiry should be limited to testing a priori theories with evaluation stakeholders and 'subjects' of social programmes:

> … the researcher's theory is the subject matter of the interview and the interviewee is there to confirm or falsify and, above all, refine that theory. (p.159)

This overlooks the value of capturing emic beliefs, perspectives and experiences within specific contexts and seems to disregard the potential of inductive research strategies to inform formative hypothesis-generation.

3.4 Theoretical premise of thesis

A critical realist perspective provides a useful philosophical and methodological framing for complex health interventions. It is also compatible with key tenets of complex systems theory. While it was beyond the scope of this thesis to conduct a realist evaluation, I draw on concepts from this perspective in developing an explanatory framework for how an e-STI testing service will increase access to STI testing within a complex service delivery system. In subsequent chapters, I situate the evaluation findings within this framework.

To develop this framework, I drew on the *candidacy* model to conceptualise access to STI testing services, alongside research evidence and the initial theory of change for the intervention. I apply a realist understanding of causal mechanisms that may underpin the intervention; and I consider contextual contingencies that may interact with these causal mechanisms. I identify and discuss change processes that may be dynamic, adaptive and recursive.

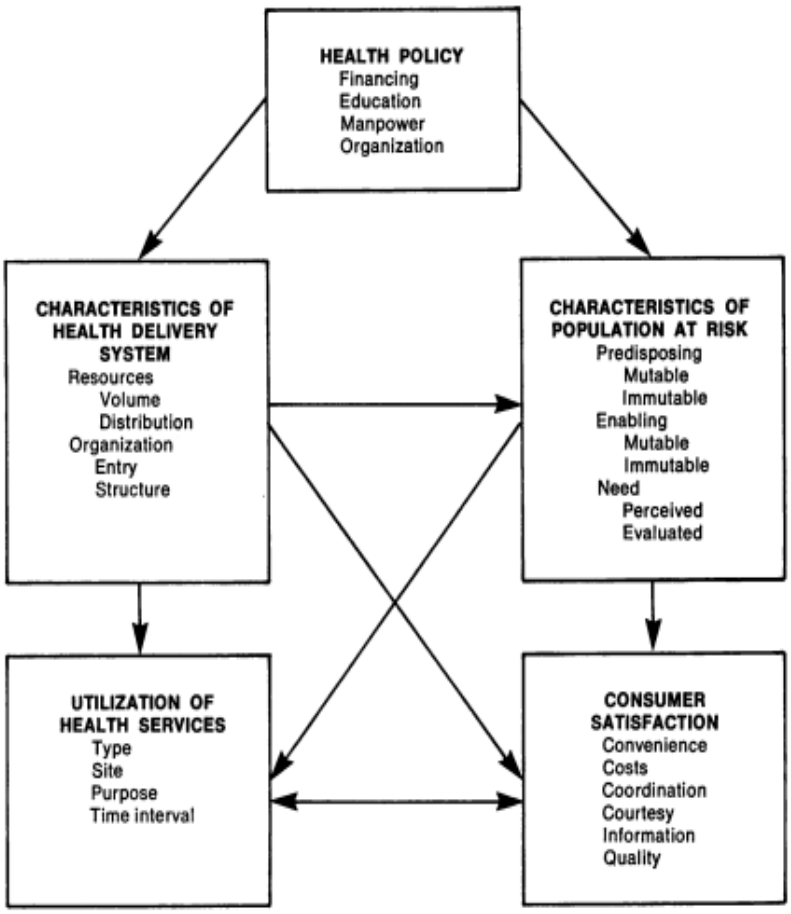
3.5 e-STI testing to improve access to STI testing services – an explanatory framework

3.5.1 Conceptualising access to health

Within health services research, access to health care is conceptualised as a function of the interplay between the needs, preferences and resources of the population on the one hand, and the characteristics of the health system on the other (Penchansky & Thomas 1981b; Aday & Andersen 1974). It follows that a closer alignment between these sets of characteristics will result in desirable outcomes such as improved health status and increased patient satisfaction (Penchansky & Thomas 1981a; Andersen et al. 1983). While it is recognised that access is a multifaceted and complex construct, most frameworks rely on utilisation as a proxy indicator for access (Levesque, Harris & Russell 2013; Goddard & Smith 2001).

Andersen's behavioural model of health services' use – one of the most cited in the health services literature - is commonly used to predict or explain health care utilisation (Andersen 1995; Ricketts & Goldsmith 2005). The model accounts for both supply and demand side determinants underpinning utilisation, including individual socio-demographic characteristics and health seeking beliefs (so called 'predisposing characteristics'). Importantly it also considers the wider social and cultural context in which these beliefs are embedded, as well as the 'enabling resources' at the level of the community and family which can facilitate or hinder health seeking behaviours (Figure 5).

Figure 5. Aday and Andersen's framework for the study of access



Source: (Aday & Andersen 1974, p.212)

Dixon Woods and colleagues (2006) posit that a narrow focus on utilisation – or receipt of health care - obscures the complex interactions between individuals and providers that underpin how people seek out and receive care within formal health systems. Rather than

viewing access solely as a technical fit between supply and demand side factors, they argue that access is best understood through the lens of *candidacy*.

The candidacy lens places emphasis on how the use of health care is a dynamic process of negotiation and social interaction between patients and professionals. Access is not viewed as a single 'event', but rather a continual process, from the initial recognition of candidacy to the subsequent navigation and negotiation of services (Mackenzie et al. 2013). These processes can expose vulnerabilities in health-seeking, which in turn generate barriers to care:

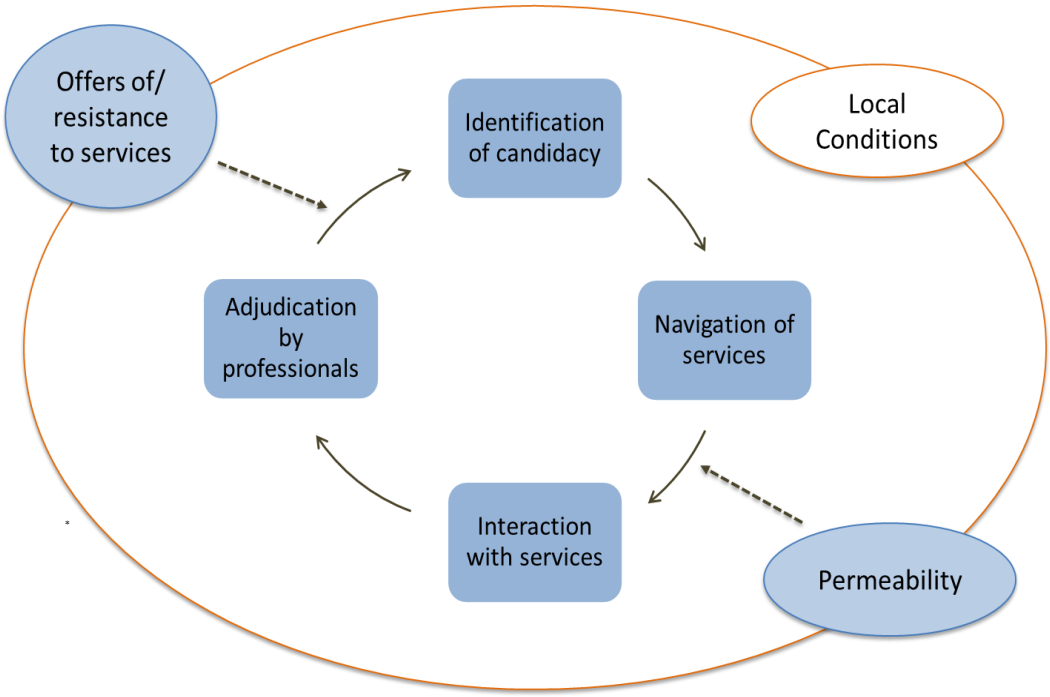
> …. candidacy describes the ways in which people's eligibility for medical attention and intervention is a dynamic and contingent process, constantly being defined and redefined through interactions between individuals and professionals, including how 'cases' are constructed. Accomplishing access to healthcare requires considerable work on the part of users, and the amount, difficulty, and complexity of that work may operate as barriers to receipt of care. (2006:7)

An understanding of candidacy, in conjunction with utilisation evidence, may offer a deeper appreciation of access to health care within complex health systems. In particular, this lens can expose inequities that arise along care-seeking trajectories, which may be obscured by utilisation measures alone (Macdonald et al. 2016; Dixon-Woods et al. 2006).

3.5.2 Applying the candidacy lens to a digital service environment.

Candidacy has been applied to understand health-seeking and use of care in a number of arenas including sexual health (Normansell, Drennan & Oakeshott 2016). Below, I adapt the candidacy model to theorise how an e-STI testing service may increase claims to candidacy in a complex sexual health delivery system. I explain each step of this framework, drawing on seminal publications by Dixon-Woods and colleagues (Dixon-Woods et al. 2005) and more recent work by Macdonald and colleagues (Macdonald et al. 2016) and Mackenzie and colleagues (Mackenzie et al. 2013), as well as the initial theory of change and wider literature. I present propositions for how e-STI testing may prompt increased recognition of candidacy, and enable smoother negotiations of STI testing trajectories, leading to increased utilisation of STI testing services.

Figure 6. The candidacy framework (adapted from Macdonald et al. (2016), Figure 1)



Recognition of candidacy

This is the process through which individuals recognise that they have a legitimate claim to health services. This process is patterned by psychological, social and cultural factors as well as lay health beliefs, including perceived need for care. In the ambit of sexual health, perceived need for care is mediated by individuals' understanding and awareness of past risk behaviour and potential exposure to STIs, particularly in the absence of symptoms. Moreover, perception of risk intersects with social and cultural norms around appropriate help-seeking (Dixon-Woods et al. 2005). As discussed in chapter one, young women may not seek sexual health care in order to safeguard their social identities as 'responsible moral agents' (Balfe et al. 2010a, p138); while young men may perceive help-seeking to be incompatible with traditional masculine traits of strength and invulnerability (Shoveller et al. 2010; Courtenay 2000).

Recognition of candidacy is also influenced by perceptions on the availability, appropriateness, and quality of care, including whether health-seeking behaviour will elicit judgement from health professionals (Dixon-Woods et al. 2005). The theory of change for SH:24 suggested that e-STI testing pathways may bypass the stigma associated with the face-to-face clinical encounter, while offering more choice and convenience. Importantly,

this enhanced choice is mediated by biomedical factors. The primary beneficiaries of e-STI testing are asymptomatic individuals, for whom remote testing is appropriate. Symptomatic users who attempt to order a test kit via SH:24 are signposted to face-to-face facilities for clinical assessment. Nevertheless, the theory of change for SH:24 proposes that these individuals may accrue indirect benefits if asymptomatic patients seeking routine testing, are channelled effectively to online pathways, thus increasing clinic capacity for complex care (Baraitser et al. 2015).

I propose that the offer and availability of e-STI testing will trigger increased recognition of candidacy in the population, as e-STI testing pathways will be perceived to be better aligned with the population's health-seeking preferences. I consider this increased recognition of candidacy to be the principal mechanism that will be triggered by the intervention, which in turn will prompt health-seeking actions. In line with realist approaches to evaluation, the way this mechanism operates is likely to vary across social groups and social contexts.

Formative research with young people in the UK has indicated that remote STI testing pathways may prove acceptable (thereby influencing recognition of candidacy) as they enable young people to avoid the stigma and embarrassment of attending clinical services (Aicken et al. 2016). Qualitative studies in Canada also found that MSM were attracted by the potential anonymity and agency afforded by remote pathways (Hottes et al. 2012). Indeed the avoidance of a face-to-face encounter ensures that patients' social identities remain untainted by possible moral judgements from health care professionals or other members of the public (Datta et al. 2018; Balfe et al. 2010a) .

Yet research with prospective black African users of self-sampling kits for HIV in the UK, found that rather than alleviating stigma, receiving test kits at home could generate embarrassment due to limited privacy (Seguin et al. 2018). This concern is shared by some young people who live with their parents or in shared housing (Lorimer & McDaid 2013). Some black African participants also highlighted that the use of self-sampling kits would require negotiation with their partners (Seguin et al. 2018). Levels of health literacy and competency in the use of new technologies are also likely to influence the acceptability of e-STI testing pathways across all social groups (Baraitser et al. 2015).

The health-seeking actions that are triggered by the introduction of e-STI testing into a complex service delivery system will therefore depend on how e-STI testing is perceived to

alleviate the diverse barriers to care experienced by different socio-demographic groups. Moreover, the translation of these health-seeking actions into concrete health benefits is contingent on how individuals proceed to navigate digital and face-to-face testing pathways.

Navigation and permeability of services

The candidacy model describes discrete phases in the navigation of services (Figure 6). Yet in practice they may overlap (Macdonald et al. 2016). Navigation of services refers to the routes taken from the recognition of candidacy to gaining entry to services. Navigation is contingent on competencies and resources, including knowledge, financial resources (such as transport) and social support (Dixon-Woods et al. 2005).

Permeability of services refers to the ease with which people can use services. 'Porous' services require less qualifications of candidacy, less negotiation and are more culturally aligned with patients' expectations (ibid.).

e-STI testing pathways may be easier to navigate and more 'porous', requiring less time and resources than face-to-face pathways. Crucially, as described in the theory of change, the online pathway avoids the requirement of a physical visit to a health service in order to complete an STI test. Further, the e-STI testing service aims to be user led and to promote user autonomy (Baraitser et al. 2015). e-STI testing may therefore be more culturally aligned to some groups, for example those groups with a preference for self-management.

Interactions with health services

This refers to the work a patient must do to assert their claims to candidacy when interacting with health professionals (Dixon-Woods et al. 2005).

e-STI testing is based on remote interaction with health professionals via text message and telephone, which avoids the traditional social interaction of the clinical encounter. For some users, this 'remote encounter' may be less stigmatising and more empowering, allowing for a smoother negotiation thus contributing to the reconfiguration of patient-provider relations.

Adjudications and resistance

Adjudications are the judgements made by professionals on the continued candidacy of individuals including follow up and referrals. These adjudications may be subsequently refused and resisted by patients (Dixon-Woods et al. 2005).

e-STI testing pathways are designed to be user-led with individuals directing the candidacy process. However, e-STI testing modalities are often integrated with face-to-face care, which may introduce opportunities for professional adjudication. As discussed in chapter 2, SH:24's care pathways involve two principal referrals points. Firstly, users with complex needs and symptoms are referred to clinic during the initial screening process, and secondly at the time of the evaluation, users who completed an STI test via SH:24 were referred to clinic at the point of diagnosis. These adjudications may have implications for the continued candidacy of users, and could be subject to resistance.

Operating conditions and the local production of candidacy

These are the influences on future service use including availability of local resources as well as the emergent relationships between professionals and patients. This shapes the future recognition of candidacy and the ability of individuals to claim their candidacy. Both professional and lay interpretations of candidacy are contingent on broader social, cultural and political factors, which are also in flux and subject to change (Dixon-Woods et al. 2006).

The change processes prompted by the introduction of e-STI testing within a complex service delivery system are likely to be dynamic and adaptive. It is envisaged that e-STI testing will facilitate patient empowerment and lead to a reconfiguration of patient-provider relations. This is likely to impact on how individuals negotiate their future candidacy not only within digital service environments but across the entire sexual health delivery system.

3.5.3 Contextual contingencies

There are a number of potential contextual factors that may modify the implementation of the intervention and the way intervention mechanisms operate.

1) Given that health seeking preferences are patterned by demographic and psychosocial factors (Mackian, Bedri & Lovel 2004), the way in which intervention components trigger increased recognition of candidacy is likely to vary across individuals and groups

of individuals. Candidacy is also highly contingent on perceived need for care and the interpretation of symptoms (Dixon-Woods et al. 2005). Recognition of candidacy for STI testing and preferences for health services is likely to be mediated by perception of risk and concerns related to recent sexual activity.

2) The successful navigation of online services, including interactions with health providers, will rely on the competencies and resources within the population. As discussed in chapter 1, digital services confer new roles and responsibilities onto patients. The theory of change suggested the varying competencies in a digital service environment could be symbolised by two contrasting user identities (Baraitser et al. 2015).

   First, it envisaged an informed and 'active' user, in line with consumer-oriented health identities (Lupton 1997; Fox & Ward 2006). This user is characterised by high levels of health literacy, confidence and skills to manage their own health needs and to negotiate their preferred health care pathways within an online service environment.

   Second, they described a user characterised by potential vulnerabilities on account of their (young) age, heightened risk to STIs, social status and lower levels of health literacy. It was suggested that these so called 'vulnerable' users would be less comfortable with this emerging consumer driven construct of patienthood, particularly the potential burden implied by the conferral of responsibility from providers to users. Importantly, there was concern that existing inequities may become exacerbated, as such users may struggle to use an online service independently and may require additional support (and potentially vigilance) from health professionals (Baraitser et al. 2015).

3) SH:24 aimed to provide seamless care pathways that integrate both online and face-to-face services. The 'porosity' of online pathways will depend on the integration of clinical and online services. Users with complex needs and symptoms who begin their testing journey online will be referred to clinic services, while those diagnosed via online pathways will be referred into clinic for treatment. Much will depend on whether this integration is deemed acceptable by users and health professionals alike. Moreover it is likely that the integration of digital and clinic-based care pathways will be influenced by local commissioning policies and procedures.

3.6 Chapter summary

In this chapter, I discussed the merits and challenges of theory-driven approaches to evaluation. I posited that a critical realist perspective provides a useful philosophical and methodological framing for the evaluation of complex health interventions. I adopted a critical realist conceptualisation of causal mechanisms to theorise possible change processes triggered by the intervention; and I drew on the 'candidacy' lens to conceptualise these change processes in relation to access and utilisation of STI testing services. In line with realist evaluative approaches, I outlined a number of contextual contingencies that may modify the effect of the intervention. The following chapter outlines the study design and methods for this evaluation.

Chapter 4: RCT Methods and Implementation

RESEARCH PAPER COVER SHEET

PLEASE NOTE THAT A COVER SHEET MUST BE COMPLETED FOR EACH RESEARCH PAPER INCLUDED IN A THESIS.

SECTION A – Student Details

Student	Emma Wilson
Principal Supervisor	Dr. Caroline Free
Thesis Title	Evaluation of an internet-accessed STI testing (e-STI testing) and results service in two London boroughs

SECTION B – Paper already published

Where was the work published?	Journal of Medical Internet Research Wilson, E., Free, C., Morris, T.P., Kenward, M.G., Syred, J. & Baraitser, P. (2016) Can Internet-Based Sexual Health Services Increase Diagnoses of Sexually Transmitted Infections (STI)? Protocol for a Randomized Evaluation of an Internet-Based STI Testing and Results Service. *JMIR Res Protoc*, **5** (1)**,** e9. Wilson, E., Free, C., Morris, P.T., Syred, J. & Baraitser, P. (2016) Addendum to: Can Internet-Based Sexual Health Services Increase Diagnoses of Sexually Transmitted Infections (STI)? Protocol for a Randomized Evaluation of an Internet-Based STI Testing and Results Service. *JMIR Res Protoc*, **5** (3)**,** e141.		
When was the work published?	15.01.2016		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	**Yes**	Was the work subject to academic peer review?	**Yes**

**If yes, please attach evidence of retention*

*Please see scanned publication with evidence of copyright retention in Appendix 1.

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I was first-author on this paper. I was reponsible for designing the evaluation, with advice from my two supervisors (Dr. Caroline Free and Dr. Paula Baraitser) and Dr. Tim Morris, who advised on the statistical methods. This chapter is an extended version of the published trial protocol. I drafted the protocol and my co-authors commented on the manuscript.

[redacted]

Student Signature: _____ **Date:** 24.05.2018

[redacted]

Supervisor Signature: _____ **Date:** 24.05.2018

4.1 Chapter overview

In this chapter, I outline the rationale and design of the randomised controlled trial that was used to evaluate the intervention. I discuss the development of the recruitment strategy and how this was employed, in addition to the study follow up procedures.

4.2 Study design

The aim of the primary study was to assess the additional benefit of providing e-STI testing and treatment service alongside standard care in a pragmatic setting. We implemented a parallel group, individual, randomised controlled trial (RCT) in the London boroughs of Lambeth and Southwark. Participants were randomly allocated to:

1) the SH:24 website which offered free self-sampling postal STI kits for chlamydia, gonorrhoea, syphilis and HIV, results via SMS text messaging (reactive results for HIV delivered by phone), and direct referrals into clinics for treatment;
2) or to a bespoke sexual health information website with signposting to local clinic-based sexual health services in Lambeth and Southwark.

Participants were free to use any other services or interventions during the trial.

4.2.1 Eligibility

The trial aimed to evaluate SH:24 among a population with an unmet need for STI testing. One way of defining unmet need is on the basis of sexual risk behaviours. For example not having tested for STIs in the last 12 months and having at least one episode of condomless sex in the same period. However, these criteria might stigmatise potential participants, particularly during face-to-face recruitment. The trial was therefore designed to target a key population group at risk of STIs, namely young sexually active adults.

The inclusion criteria were as follows: aged 16-30 years, sexually active (at least one partner in the last 12 months), being resident in the London boroughs of Lambeth and Southwark, a willingness to take an STI test and access to the internet (owner of a smart phone or able to access laptop, tablet, personal computer in their own home).

Particular efforts were made to ensure the sample population included young MSM and black minority ethnic groups, in view of the elevated risk profiles of these socio-demographic groups.

Participants were excluded if they were unable to read in English. It is possible that this criterion excluded vulnerable populations with a need for STI testing. However, at the time, the e-STI service under evaluation operated its website in English only. Participants who were unable to give informed consent, such as people with severe learning difficulties were also excluded on ethical grounds.

4.2.2 Intervention and control

Participants in the intervention group were sent a text message with the URL of SH:24 (www.sh24.org.uk). SH:24 offered free postal self-sampling test kits for chlamydia, gonorrhoea, HIV and syphilis. Participants who ordered a test kit from SH:24, were required to complete a short order form, online. Those reporting STI symptoms were advised via a pop up message to visit their local clinic for immediate treatment. Those reporting complex needs such as depression, drug and alcohol dependency, or exploitative sexual partnerships were telephoned by a clinician and referred to relevant clinical services. All participants could continue to use the online service if they wished.

All test kits contained a lancet and collection tube to obtain a blood sample for serological testing for syphilis and HIV. For chlamydia and gonorrhoea, women were sent vaginal swabs and men were sent a container for first catch urine samples. Test kits for MSM also contained swabs to take pharyngeal and rectal samples.

The tests kits included pictorial leaflets with guidance on how to collect the specimens. A video demonstrating blood sample collection was available on YouTube and could be accessed via the SH:24 website. Participants were encouraged to text or phone the SH:24 team with any questions or concerns. Non-returners were sent reminders via text message and resent test kits if required, as per SH:24's protocols.

Chlamydia, gonorrhoea and syphilis test results were delivered by text message. Participants with reactive results for syphilis or positive results for chlamydia and gonorrhoea were signposted to local clinics for confirmatory testing and treatment as necessary. Reactive results for HIV were communicated by phone by a clinician. The SH:24 website also provided health education information on sexually transmitted infections and safer sex practices.

Participants in the control arm were sent the uniform resource locator (URL) of a bespoke website with the contact details, websites and location (google map image) of sexual health

clinics in Lambeth and Southwark. These clinics provided usual care via walk-in services. Some clinics also offered an appointment service for those with symptoms or complex needs. All participants were free to use any other sexual health services or interventions during the trial period.

4.2.3 Risk of contamination

Contamination, whereby some individuals allocated to the control arm receive the intervention, and vice versa, can lead to underestimation or overestimation of effect estimates. Small levels of contamination are acceptable and can be offset by recruiting more participants to the study (Torgerson 2001).

At the design phase of this study, the possibility of contamination was considered as it was plausible that individuals allocated to the intervention could share the SH:24 URL with those allocated to the control. It was not a concern if control participants shared the control URL, as intervention participants were free to use any other service if they wished. To reduce the risk of contamination, an alternative design based on cluster randomisation was mooted. For example, randomising entire boroughs might have allowed for greater control over the intervention, as access to the website could be restricted to people with eligible postcodes, and trial participants from different boroughs might be less likely to interact with each other. However SH:24 was funded to deliver e-STI testing in the boroughs of Lambeth and Southwark only, and hence a cluster RCT was not feasible. Further, a cluster RCT would have required a much larger sample size and budget. Ensuring sufficient comparability between boroughs with respect to the underlying STI epidemiology of the population, and the characteristics of 'usual' face-to-face care might also have proved challenging.

To minimise the risk of contamination between groups the following sentence was included in the intervention text message, 'Please do not share this link with anyone'. During recruitment, SH:24 monitored the proportion of the control arm who accessed the SH:24 website, by cross checking control participants' mobile phone numbers with the SH:24 database.

4.2.4 Changes to the control conditions

Recruitment began in November 2014. Initially the SH:24 website and service was available only to trial participants. However, in order to comply with their funding agreement, SH:24 launched the service to the general public in Lambeth and Southwark in March 2015. They

opted for a soft launch, without the use of large scale advertising. Nevertheless the launch of the service changed the composition of usual care, as the SH:24 website was promoted in face-to-face clinical settings. This was considered in the analyses by assessing if the effect of the intervention on our co-primary outcomes was modified by the launch of SH:24 (see section 5.3.3).

4.2.5 Laboratory processing and diagnostic testing platforms

The intervention provided postal self-sampling test kits for gonorrhoea, HIV, syphilis and chlamydia which were processed by The Doctors Laboratory (TDL). Chlamydia and gonorrhoea are detected by BD Viper Platform/ BD Assay. Positive Gonorrhoea results were confirmed using Cepheid GeneXpert (Dual Target).

HIV I and II/p24Ag were detected by Roche Platform/ Roche Assay and Syphilis IgG/IgM by Abbott Architect/Abbott Assay.

Reactive results for HIV and syphilis required a confirmatory assay performed in clinic settings. Any unconfirmed reactive results in the intervention were counted as negative test results.

4.2.6 Primary outcomes

The co-primary outcomes were self-reported diagnosis of an STI at 6 weeks, confirmed by patient health records, and self-reported completion of an STI test at 6 weeks, confirmed by patient health records. Completion of an STI test was defined as samples processed by the laboratory and results delivered to SH:24 or to clinic.

4.2.7 Secondary outcomes

Secondary outcomes were the proportion of participants prescribed treatment for an STI, time from randomisation to completion of an STI test, and time from randomisation to treatment of an STI.

4.2.8 Process outcomes

Process outcomes were the proportion of STI tests that were positive in each group, median time from diagnosis to treatment in each group, the proportion of participants who completed an STI test in each group by service type, the proportion of participants diagnosed in each group by service type, and, in the intervention group only, the

proportion who agreed that the intervention was acceptable and the proportion who adhered to an appropriate e-STI testing pathway.

All pathways were considered appropriate unless participants completed a test via SH:24, received a negative result, and then retested for the same STI in a face-to-face setting within 6 weeks.

In addition to the pre-specified process outcomes, the proportion of participants who tested positive for an STI among those who completed a test at 6 weeks, with 95% confidence intervals are reported.

4.2.9 Sample size

The study was powered for the first co-primary outcome measure which is the proportion of participants diagnosed with at least one STI in each arm. Two factors determined the number of participants needed for this trial: the estimated proportion of participants with an STI and the size of the treatment effect.

These estimates were based on the following data:

In 2014, the Greenwich sexual health service demonstrated a 50% return rate among users who order test kits online (personal communication Dr David Pinson, Health Improvement Principal, Royal Borough of Greenwich). Eligibility for this study was restricted to people who were willing to take an STI test. However, not all of those allocated to the intervention group were likely to order a test kit. It was estimated that 30% would not complete this first step. Among the 70% who ordered a kit, it was assumed that 50% would return the kit for analysis, based on the Greenwich data. Following these assumptions, 35% of the intervention group were likely to complete an STI test.

There were no available data which would give us an estimate of the likely numbers that will get tested in the control group. However, it was assumed that far fewer people (10%) were likely to seek a test in clinic-based settings.

Chlamydia is the most commonly diagnosed STI of the four STIs of interest in this study both at the national level (England) and at the local authority level (Lambeth and Southwark) (Public Health England 2017d; Public Health England). The prevalence estimates are based on the proportion of positive chlamydia tests among 15-24 year olds in general practice settings in Lambeth and Southwark, which was 6% in 2012 (Public Health England).

The estimated losses to follow up on were based on previous eHealth studies in the United Kingdom which have achieved 90% follow up (Free et al. 2011).

A sample size of 3000 would lead to 90% power (two-sided alpha=5%) to detect a relative risk of 3.5, (2.1% risk of diagnosis in the intervention group vs 0.6% risk of diagnosis in the control group), allowing for 10% losses to follow up. This equates to 10% of the control group being tested, with a 6% probability of infection as in general practice settings and 35% of the intervention tested with a 6% probability of infection as in general practice settings.

With regard to the co-primary outcome measure, a trial with 3000 participants we would have 99% power (two-sided alpha=5%) to detect an absolute difference of 25% between the proportion of participants who complete a test in the intervention group versus the proportion who complete a test in the control group (35% versus 10%).

4.2.10 Ethical approval

Ethics approval was granted by the National Research Ethics Service Committee London-Camberwell St Giles (ref 14/LO/1477). The trial is registered with Current Controlled Trials, number ISRCTN13354298.

4.3 Statistical analyses

Randomisation was based on a minimisation algorithm to balance key prognostic covariates. Minimisation introduces correlation between treatment groups and this requires an adjusted analysis (Kahan & Morris 2012). Ignoring minimisation factors leads to the incorrect estimation of the standard error for the treatment effect, which is biased upwards in an unadjusted analysis (Kahan & Morris 2012) . Accounting for correlation between groups therefore ensures no loss of power, confidence intervals of the correct width and correct type 1 error rates (Kahan et al. 2014).

The adjusted analyses were based on a propensity score approach. Propensity score methods are commonly used to adjust for confounding in the estimation of causal effects using observational data (Austin 2011). In individually randomised controlled trials, where confounding is not an issue, propensity score methods, and specifically inverse probability treatment weighting (IPTW), can be used to adjust for chance imbalances of prognostic co-variates between treatment arms (Williamson, Forbes & White 2014). In the case of balanced randomisation such as minimisation, IPTW can adjust for the balancing variables,

thus breaking the dependency in the data between treatment groups. In both cases, adjustment of baseline prognostic factors using IPTW increases the precision of effect estimates (ibid.).

The outcome models used an inverse probability of treatment estimator, to estimate the average treatment effects (ATE) on the co-primary outcomes. In these models the ATE is expressed as the weighted risk difference between the intervention group and the control group. Weighted risk ratio estimates and their confidence intervals were obtained via the delta method of transformation. I report the p-values from the treatment effects model, which correspond to the null hypothesis of the risk difference parameter.

The propensity score for treatment allocation was estimated from all minimisation factors (gender, age, sexual orientation and number of sexual partners in the last 12 months) in addition to ethnicity, as this is also a predictor of the co-primary outcomes (Fenton et al.).

4.3.1 Handling of missing data

Differential losses to follow up were anticipated, as outcome data at the SH:24 service were captured on a single database, whereas in the clinic arm, participants had the choice of a number of clinics, which required searches of patient records at multiple sites (see section 5.7). It was hypothesised that participants in the clinic arm might choose to use clinics outside of the study area (Lambeth and Southwark), which would prove more challenging for data collection.

Losses to follow up, irrespective of whether they are differential or not, can lead to biased estimates if appropriate methods are not used to handle missing data (Bell et al. 2013). Missing data also reduces power and efficiency. We accounted for missing data using multiple imputation techniques assuming data were Missing at Random (MAR). Under this assumption, the distribution of the outcome for both missing and non-missing groups is conditional on observed data, and independent of the unobserved data (Carpenter & Kenward 2008, p.12).

Imputation was based on Multivariate Imputation by Chained Equations (MICE). The two co-primary outcomes (testing and diagnoses) and the secondary outcome (treatment) were imputed using three conditional models. Self-reported outcomes were included as these are auxiliary variables that provide partial information for missing groups.

Each model included randomised group as a covariate and was weighted by the inverse of the estimated propensity score (for compatibility with the model for analysis). In addition, the two models to impute STI testing and STI diagnosis conditioned on self-reported testing, self-reported diagnoses and self-reported treatment, which were also incomplete. The model to impute treatment conditioned on self-reported testing and self-reported treatment only, due to collinearity with other variables, which led to non-convergence. Each incomplete variable conditioned on other incomplete variables. Each imputed dataset was produced with 10 cycles. One hundred imputed datasets were generated for each missing outcome. Multiple imputation inference proceeded via Rubin's rules (Rubin 1987).

For the publication of the RCT results, Dr. Tim Morris (TM) performed a sensitivity analysis to explore departures from MAR. Under this assumption, the distribution of outcome is assumed to be different between those with missing data and those with the outcome observed, after adjusting for observed covariates.

TM multiply imputed missing outcome data, using inverse probability weighting on the estimated propensity score and with allocated group and self-reported testing, diagnoses and treatment as covariates. The odds of STI diagnosis and the odds of a completed STI test for missing participants were varied to be ¼, ½, 1, 2 and then 4 times larger than the MAR analyses. This was done factorially for the two randomised arms, giving a total of 25 analyses (including the principal analysis assuming MAR).

4.3.2 Missing covariates

All baseline characteristics were fully observed, except for sexual orientation as participants could opt out of this question. A missing category was therefore used (coded 99 in Stata).

4.3.3 Subgroup analyses

To explore heterogeneity of the intervention effect on the co-primary outcomes, interaction tests at a 5% level of significance were carried out to assess whether effectiveness varied by the following baseline characteristics: gender (male, female); ethnicity (White, Black/ African/ Caribbean/ Black British, Asian/Asian British/ All other groups); sexual orientation (msm, all other groups); age group (16-19 years, 20-24 years, 25-30 years); number of sexual partners (1, 2+); and index of multiple deprivation (IMD) rank (linear). We also tested possible heterogeneity of effect that may have resulted as a result of SH:24's launch to the general public (see section 4.2.4.). Effectiveness was compared prior to SH:24's launch and post launch.

These analyses were conducted in the complete cases under a MAR assumption using a log binomial model. They were not weighted by the inverse of the estimated propensity score, as specified in the analysis plan, due to non-convergence of the models. Given that the study was not powered to test for interactions, these analyses were designed to be exploratory and the statistical significance of the interaction tests have been interpreted with caution.

4.3.4 Time to event analyses

Survival analysis was used to estimate the restricted mean survival time (RMST) from randomisation to completion of an STI test and prescription of treatment for each group. The Royston Palmar semi-parametric method was used to estimate the restricted mean survival time. The RMST is an appropriate measure even when the proportional hazard assumption is in doubt (Royston & Parmar 2011). As with other analyses, the RMST accounted for covariates by weighting on the inverse of the estimated propensity score. The mean survival time was set to t* = 6 weeks (42 days) for time-to-test and t* = 3 months (84 days) for time-to-treatment.

4.4 Recruitment

4.4.1 Overview

I led the design and implementation of the recruitment strategy for the trial. Assisted by colleagues from Kings College London, and a small team of research assistants, I approached community networks, organizations, and institutions such as further education colleges, universities, patient groups, sexual health advocacy groups, sports centres, entertainment and leisure venues and major employers to recruit participants. We also utilized social media sites popular among our study population. These included Facebook, Twitter, and dating applications for gay and bisexual men such as Scruff and Grindr.

4.4.2 Informed consent

After potential participants were assessed for their eligibility, they were provided with detailed verbal and written information about the study, and given the opportunity to ask any questions. If the participant agreed to participate, we asked them to provide consent via the trial website (e.g. using a mobile phone or tablet) or via paper-based forms. If potential participants wanted more time to consider their involvement, we gave them the contact details of the study coordinator so that they could talk through any queries or doubts.

Potential participants were also able to access the study website independently, for example via social media sites.

4.4.3 Developing the 'offer' of the RCT

Prior to recruitment, I conducted informal focus group discussions with local residents of Lambeth and Southwark and the Sex Positive group at Brook Young People. The aim of this formative research was twofold: 1) to understand what might motivate young people to enrol in the study; and 2) to determine how to communicate the objectives of the trial in a non-technical way.

The main learning from this research was as follows:

- The enrolment process should be quick and straightforward. Ideally, participants should be able to enrol on their smart phones and the baseline questionnaire should be short;
- Participants should be offered a financial incentive for taking part and young peoples' time should be respected;
- The potential benefits of the study for young people should be emphasised. These include opportunities to shape local sexual health service provision and to screen for STIs thereby taking care of one's health.

Based on this feedback, I developed some simple messages to facilitate the promotion of the trial in community settings. These are as follows:

"Help us improve sexual health services, get tested, get £10 for your time"

"Thinking about a sexual health check? Get tested, get £10"

These messages were then included in the promotional materials (Figure 7)

Figure 7. Promotional leaflet and web banner

In order to avoid performance bias, we did not advertise that we were evaluating an e-STI testing service. Instead we informed potential participants that the purpose of the study was to evaluate sexual health services in Lambeth and Southwark more broadly. We explained that there are many types of sexual health services available in the boroughs, and if they chose to take part, they would be invited to use one type of service. This approach was approved by our ethics committee.

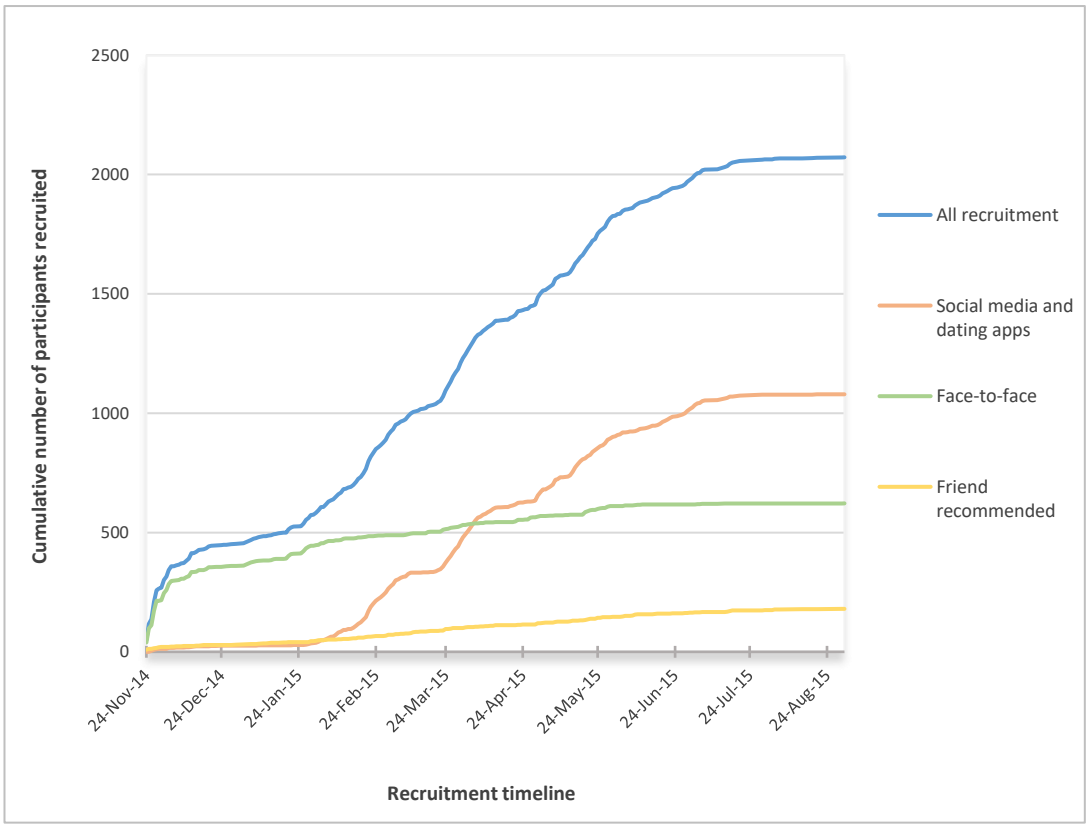
4.4.4 Face-to-face recruitment

RCTs of sexual health interventions have successfully recruited students in universities in the UK (Ivaz et al. 2006). Initially I contacted four universities in South London (Goldsmiths, Kings College London, Southbank University and London College of Arts), where I proposed entering lecture halls at the beginning or end of lectures to give a brief 5 minute overview of the study and give students the opportunity to enrol. I also approached two further education colleges – Lewisham Southwark College (LeSoCo) and Lambeth College – with a view to giving more in-depth educational talks on sexual health to sensitise students on the benefits of STI testing.

I felt that these strategies would give the study team exposure to high volumes of young people, who may reside in South London. In principal, these institutions were highly supportive of the study and granted approval for the team to be on campuses. However, access to classrooms and lecture halls had to be negotiated with individual teachers and lecturers, which was extremely time-consuming.

I therefore revised our approach. Rather than targeting students in classrooms and lecture halls, we held regular stalls in student unions, halls of residences, major thoroughfares (e.g. outside large lecture halls), bars and eating venues. I also worked closely with student societies (such as KCL Sexpression society) during events such as HIV testing week. This proved highly effective and we succeeded in recruiting 269 participants during this first week of recruitment (Figure 8).

Figure 8. Recruitment timeline by main method of recruitment



4.4.5 Online recruitment

Social media platforms offer an alternative avenue to promote sexual health studies. The Sexunzipped trial recruited primarily via Facebook advertising in the UK (Bailey et al. 2013), while 44% of participants in the 2014 English Gay Men's sex survey (2014) were recruited via dating apps, such as Grindr (Hickson et al. 2016).

Together with a systems developer, I designed an enrolment system that allowed participants to self-enrol remotely via the trial website. Initially there was a concern that advertising the trial on social media might result in high levels of contamination (for example if intervention participants chose to share the intervention URL via twitter or

Facebook). However, it proved difficult to sustain the intensity of face-to-face recruitment and as figure 8 demonstrates, face-to-face recruitment began to taper off in February 2015. We therefore took the decision to try online recruitment in February 2015. Jonathan Syred from KCL ran a series of successful campaigns via Facebook, twitter and the MSM dating app, Grindr, recruiting a total of 1,079 participants.

Figure 9. Example of Twitter advertisement

4.4.6 Other forms of recruitment

I contacted key organisations working on sexual health in Lambeth and Southwark to promote the trial via their youth engagement work. These included Brook Young People, Southwark Council and Healthwatch. Together with a research assistant, I attended relevant events (such as health fayres or discussion groups) and accompanied health promoters during their visits to colleges and housing estates.

A key concern during recruitment was the low numbers of participants from BME groups. In July 2015 I contacted two health promoters from SHAKA services - a sexual health organisation working with BME communities in South London. They promoted the study, together with the study coordinator, as part of their outreach activities in barber shops, hairdressers and community markets.

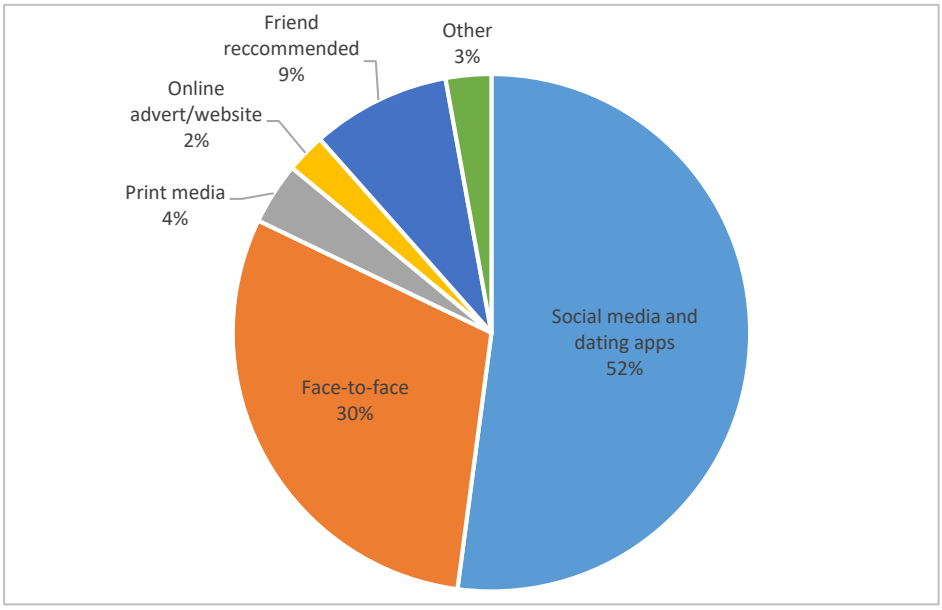
Forging relationships with these organisations was time-intensive and did not yield high numbers of participants. Much of the outreach work conducted by these groups was not well coordinated and did not engage significant numbers of young people. Nevertheless, these partnerships enabled participation (albeit in very low numbers) by individuals from more marginalised communities, who were not reached by face-to-face and online strategies.

Other methods used to promote the trial included leafleting large housing estates, advertising via online media targeting MSM such as QX and Boys. However, while increasing the visibility of the trial, these methods did not yield many enrolments.

4.4.7 Recruitment of key population groups

The proportion of participants from non-white ethnic backgrounds was highest among those recruited in university or further education colleges (Figure 11). The proportion of black or black British groups was lowest among those recruited via MSM dating apps.

Figure 10. Participants recruited by method of recruitment (n=2,072)



Those recruited in face-to-face settings (university or college) had a lower sexual risk profile with respect to the number of sexual partners in the last 12 months, compared to those who were recruited remotely (via social media or dating apps). It is plausible that those with a higher number of sexual partners may have felt less comfortable engaging with the study team in public spaces, for fear of being judged. As expected, those recruited via MSM dating apps had more frequent partner change in the previous 12 months compared to those recruited by other methods.

Figure 11. Recruitment by source and by ethnic group

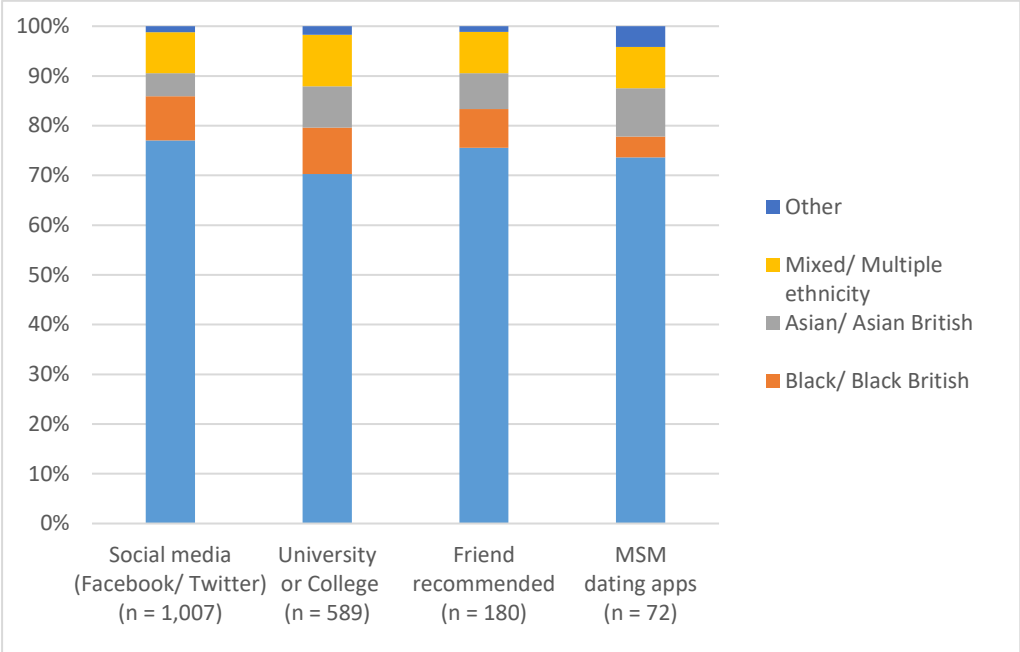
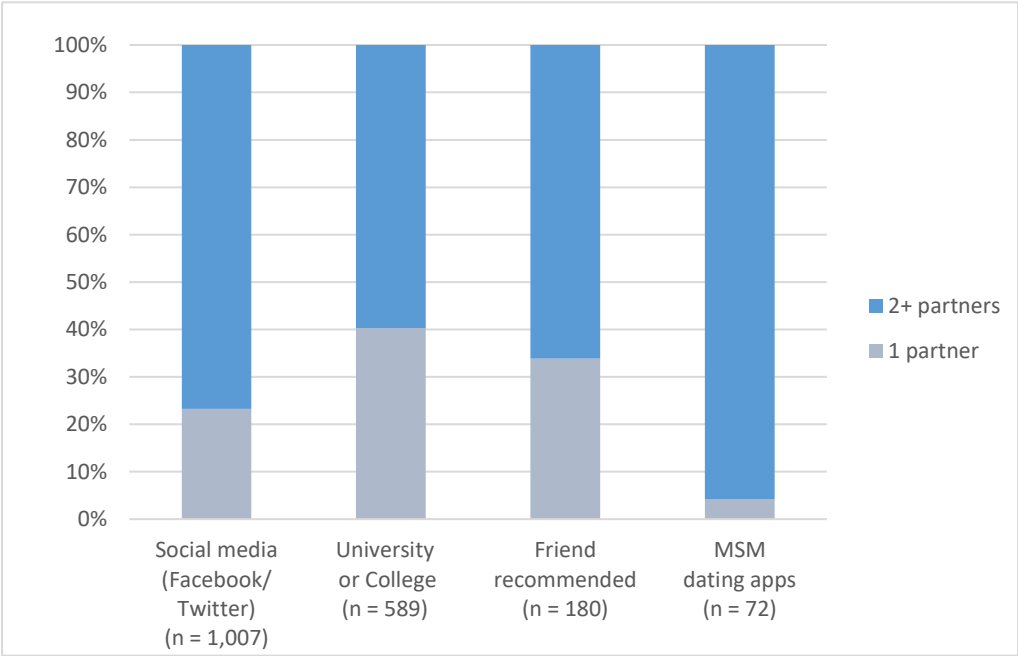


Figure 12. Main modes of recruitment, by number of sexual partners in last 12 months



4.4.8 Lessons learned

- Reaching black and minority ethnic groups proved challenging. A high proportion of students at further education colleges are from BME backgrounds. For example approximately 60% of LeSoCo students identify as BME (Lewisham Southwark College no date). However, we were unable to gain access to the classrooms in these colleges, and unlike the universities, there was limited social infrastructure (such as student societies), which could facilitate engagement outside of the classroom. On reflection, we required greater buy-in from senior management at these colleges. With more time and resources, it also might have been feasible to develop an effective outreach strategy to reach BME communities in the boroughs.

- Advertising via social media platforms is efficient as advertisements can target populations with specific socio-demographic characteristics and by geographical location (determined by users IP addresses). In face-to-face settings, particularly in universities, we encountered large numbers of young adults who were not eligible as they did not reside in Lambeth and Southwark.

  Nevertheless there were inefficiencies later in the online enrolment pathway. There was a very high drop off rate after participants 'clicked through' to the study welcome page. During the 9 months of recruitment (24/11/2014 – 31/08/2015) 34,124 new users[1] landed on the study welcome page, but only 8,330 (24.4%) clicked through to the study information sheet. The transition from highly optimised platforms such as Facebook to the study website, which was far less user friendly (particularly on a mobile phone), may have acted as a strong deterrent. Although it is also plausible that potential participants may have been deterred by the requirements of the study.

- Engagement with non-governmental organisations and other community groups in Lambeth and Southwark did not yield many enrolments. We found it difficult to explain the study objectives, and there was some confusion as to why we could not reveal that we were evaluating an online service (see section 4.5.3). We found that outreach activities and sexual health promotion were not well-coordinated in the boroughs, which is of concern considering the high rates of infection.

[1] Data include participants recruited in face-to-face settings who enrolled via tablets or mobile phones

4.5 Data collection - self reported

4.5.1 Baseline data

At enrolment, participants were asked to enter their baseline data directly onto the trial website or to complete a paper-based form (Appendix 4). We collected the following information:

- Contact details: first name, surname, main mobile number, email address, primary postal address.
- Demographic data: date of birth, gender, ethnicity, sexual orientation.
- Sexual health behaviours: last STI test, service used at last STI test, number of sexual partners in the last 12 months

Other markers of sexual risk were considered, such as condomless sex in the last 12 months, as well as additional socio-demographic data, such as participants' education level. However we decided against a lengthy baseline questionnaire in order to keep the enrolment procedures to a minimum.

I matched participants' postcodes to the national index of multiple deprivation (IMD). IMD is a relative measure deprivation that ranks every small area in England from 1 (most deprived area) to 32,844 (least deprived area)(Department for Communities and Local Government). As an area level measure of deprivation, IMD can not be used to draw conclusions about deprivation at the individual level. Nevertheless, studies have found IMD to be useful marker of inequity with respect to the availability of services, given that services are often commissioned on an area level basis (Sonnenberg et al. 2013).

4.5.2 Follow up instrument

The follow up instruments (Appendix 5) asked participants if they used a service to test for STIs, which type of service they used and to state their results and any treatment prescribed. If they used a service, they were asked to assess the acceptability of the service. If they stated that they did not use a service, they were asked the reasons for declining the invitation to test.

It was beyond the scope of this project to develop a validated scale to assess service acceptability in the context of e-STI testing. We therefore selected four individual questions from a patient satisfaction questionnaire validated for use in GUM clinics (Weston et al.

2010). We modified the questions to ensure they were relevant to an online service. These questions do not have any psychometric properties.

> ***Did you feel that your personal information was kept confidential by this service?***
> A. Yes (2), B. Yes to some extent (1) C. No (0)
>
> ***Did you have trust in the clinical expertise of this service?***
> A. Yes (2), B. Yes to some extent (1) C. No (0)
>
> ***Would you use this service again if you needed to?***
> A. Yes definitely (2) B. Yes, probably (1) C. No (0)
>
> ***Would you recommend this service to a friend?***
> *Yes definitely (2) B. Yes, probably (1) C. No (0)*

Acceptability was constructed as a binary variable. A score of 8 was coded as 1 (acceptable); a score <8 was coded as 0 (not acceptable).

The follow up forms were piloted among clinic users to gauge their understanding of the questions and their acceptability of the questionnaire, prior to commencing follow up.

4.5.3 Follow up procedures

I used evidence based methods to ensure high response rates (Edwards et al. 2002). These include providing incentives to all participants, contacting respondents prior to sending questionnaires and contacting non-responders using phone call, texting, email.

At 6 weeks from randomisation all participants were sent a hard copy of the follow up form together with a £5 cash incentive. Within 5 days of posting the form, I sent a text message to remind participants that on receipt of the completed questionnaire they would receive a further £5.

The text message also included a link to a web -based version of the follow up form. Participants were sent a further two text message reminders.

4.5.4 Discrepant and incomplete data

EW, together with two research assistants, telephoned participants who returned discrepant data. For example, a number of participants stated that they did not get an STI test but completed the section on acceptability, suggesting that they did in fact get a test.

In addition, if participants stated that they tested, but there was no record found in any of the services in Lambeth and Southwark, we called them to ask if they had used a different

type of sexual health service (for example a GP service or GUM clinic outside of Lambeth and Southwark).

4.5.5 Non responders

Between November 2015 and January 2016, we contacted all non-responders via text message, email and phone.

4.5.6 Data collection - objective

I collected objective outcome data between October 2015 and June 2016. Data managers at Kings College Hospital NHS Foundation Trust and Guy's and St. Thomas' NHS Foundation Trust searched the patient record databases for all randomised participants. I also searched the SH:24 orders database for all randomised participants.

If a participant reported using a different service (e.g. a GP surgery or other sexual health service in London or the UK), I contacted the service to verify if the participant attended the service between the date of randomisation and the date when follow up was collected (as per the date logged in the follow up database). If the participant attended the service within this time period, we requested data on STI tests completed, STI test results and treatment prescribed.

Given that GUM and secondary sexual health services in the UK are anonymous and not linked to patients' NHS numbers, I used the following identifiers to locate participants' health records:

Table 3. Identifiers used in patient record checks

Service	Identifier
Walk-in GUM clinics & SH:24	– Mobile phone number **AND** Gender (and/or) – Name **AND** Date of birth
GP surgeries	– Name **AND** Date of birth

4.6 Assessment of primary endpoints

The co-primary outcome measures are:

- Self-reported diagnosis of at least one STI at 6 weeks (42 days), confirmed by patient health records.

- Self-reported completion of at least one STI at 6 weeks (42 days), confirmed by patient health records.

I defined 'Completion' of an STI test as samples returned, processed by the laboratory, and results uploaded onto the information management systems of the clinic or intervention.

Most participants tested for more than one infection. If one test result was received within 42 days of randomisation, I counted all tests and diagnoses linked to that index clinical attendance or index internet test order. If a participant used a service on the same day as randomisation, I assumed they were randomised first.

The data received from GUM settings were coded according to the coding framework for Sexual Health and HIV Activity Property Types. These are as follows:

Table 4. Public Health England SHHAPT codes for testing services – summary of definitions (Public Health England)

HIV only	HIV antibody test	**P1A**
	HIV test offered & refused	**P1B**
	HIV test not appropriate	**P1C**
STI	Chlamydia only	**T1**
	Chlamydia & gonorrhoea	**T2**
	Chlamydia, gonorrhoea & syphilis	**T3**
	Chlamydia, gonorrhoea, syphilis & HIV	**T4**
	HSV (herpes simplex virus)	**T5**
	Hepatitis A / B / C	**T6**
	Syphilis & HIV	**T7**
	Self-sampling (no HCW consultation)	**T8**
	STI tests not required	**T9**
	Rapid testing (same day results)	**T10**
	Microscopy	**TS**
	3 site testing	**TT**

I counted all codes related to laboratory based STI testing. These included P1A, T1, T2, T3, T4, T5, T6, T7. Other activity, such as clinical examination for the presence of STIs (e.g. genital warts) were not counted.

I counted all new diagnoses arising from laboratory testing for STIs and not those arising from clinical examination or microscopy. I discounted existing diagnoses for STIs (e.g. previously diagnosed HIV infection).

I counted STI treatment where a person was treated and received a positive laboratory test for STI. Treatment could be provided presumptively as long as it was accompanied by positive laboratory test result.

4.6.1 Verification of self-reported data

If a participant reported completing an STI test in any named service between the date of randomisation and the date of follow up, a data search was subsequently conducted in the named service for that corresponding time period.

Some participants in the control arm reported completing an STI test in a sexual health clinic but did not provide the name of the clinic. Their data were considered to be objectively verified if an attendance record for STI testing or clinical examination for STI was retrieved from the services in Lambeth and Southwark, between the date of randomisation and the date of follow up. Given that the clinic arm was invited to test in the sexual health clinics in Lambeth and Southwark, it is reasonable to assume that this is the clinical experience that they were referring to. Attendances for STI testing and clinical examinations for STI were counted, but not other non-STI services such as contraception, vaccinations, and cervical cytology.

If a participant did not submit a 6 week outcome questionnaire but they completed an STI test via SH:24 or one of the sexual health clinics in Lambeth and Southwark within 42 days of randomisation, they were counted as having tested.

If a participant reported that they were prescribed treatment for a sexually transmitted infection in a named service, but a record could not be found in that service, then they were counted as not prescribed treatment.

If a participant reported data by more than one mode (e.g. via the web-based form and via hard copy questionnaire) the first data received were the data used for analysis. The only exceptions to this rule were:

- If a participant submitted incomplete data via the web-based data collection portal and subsequently submitted complete data on the same day, the latest data collected will be the data used for analysis.
- If a participant has been contacted to verify their answers (e.g. to ask for the name of the service used or to clarify discrepant data), the latest data collected were used for analysis. This included participants who originally indicated that they tested but subsequently changed their answer.

4.7 Chapter summary

In this chapter, I discussed the study methods and procedures for the RCT. In addition, I outlined the recruitment strategy, and lessons learned from the employment of this strategy. In the following chapter, I present the main results from the RCT.

Chapter 5: Main Trial Results

RESEARCH PAPER COVER SHEET

PLEASE NOTE THAT A COVER SHEET MUST BE COMPLETED FOR EACH RESEARCH PAPER INCLUDED IN A THESIS.

SECTION A – Student Details

Student	Emma K. Wilson
Principal Supervisor	Dr. Caroline Free
Thesis Title	Evaluation of an internet-accessed STI testing (e-STI testing) and results service in two London boroughs

SECTION B – Paper already published

Where was the work published?	PLOS Medicine Wilson, E., Free, C., Morris, T.P., Syred, J., Ahamed, I., Menon-Johansson, A.S., Palmer, M.J., Barnard, S., Rezel, E. & Baraitser, P. (2017) Internet-accessed sexually transmitted infection (e-STI) testing and results service: A randomised, single-blind, controlled trial. *PLOS Medicine*, **14** (12)**,** e1002479.		
When was the work published?	27.12.2017		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	**Yes**	Was the work subject to academic peer review?	**Yes**

**If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.*

Please see evidence of retention in Appendix 1.

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I was first-author on this paper. I was responsible for designing and leading the implementation of the evaluation, with advice from my two supervisors (Dr. Caroline Free and Dr. Paula Baraitser). Dr. Tim Morris conducted the statistical analyses for the published trial paper. I drafted the manuscript and my co-authors commented on drafts. The following chapter (chapter 5) is an extended version of the published trial report. I conducted the analyses presented in the thesis with advice from Dr. Clémence Leyrat who is on my PhD advisory committee.

Student Signature: [redacted] **Date:** 24.05.2018

Supervisor Signature: [redacted] **Date:** 24.05.2018

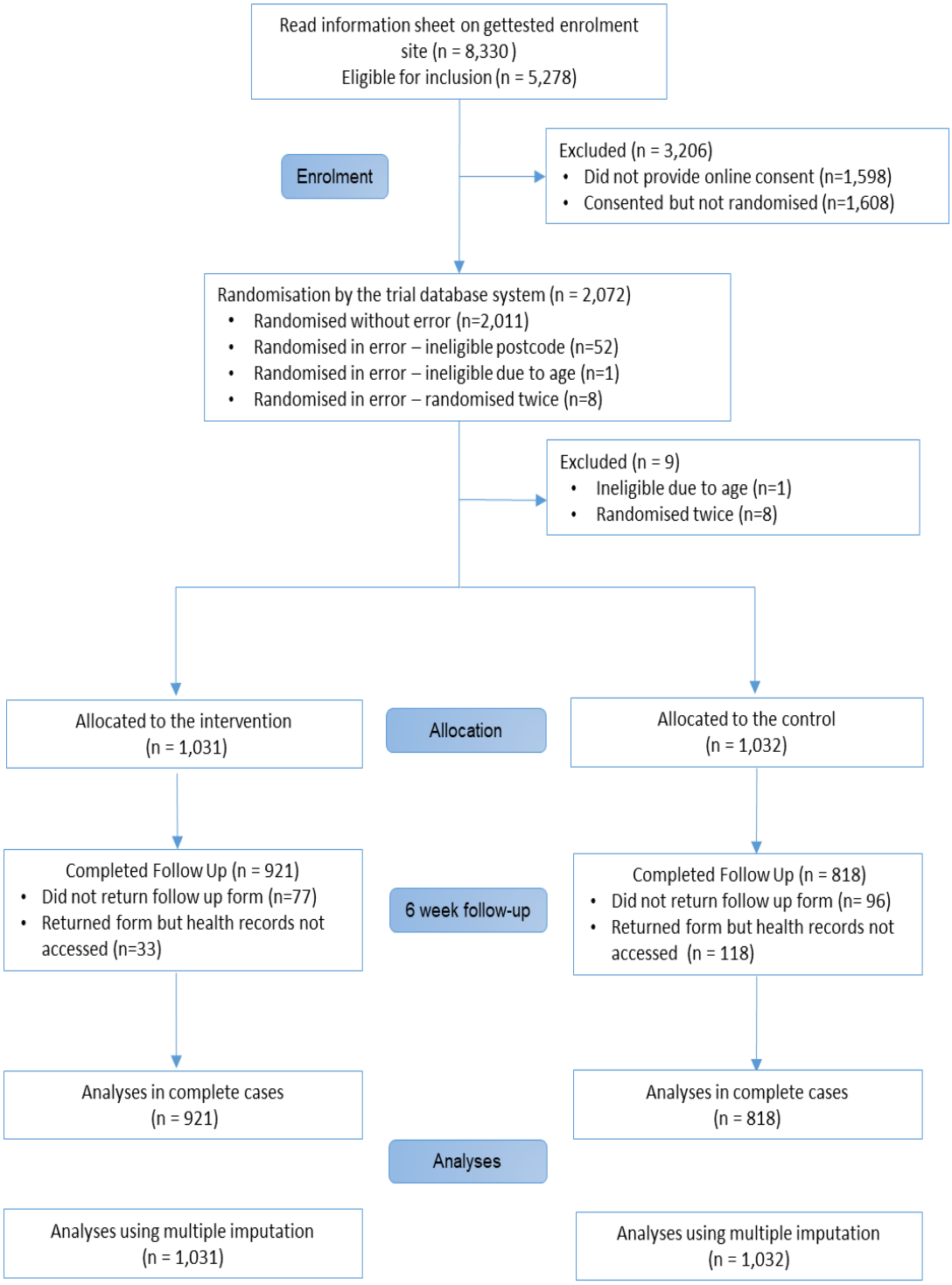
5.1 Chapter overview

This chapter is an extended version of the published trial report (Wilson et al. 2017). I replicated the original analyses that were conducted by the trial statistician and therefore some results may differ slightly from the main publication.

5.2 Baseline characteristics

2,072 participants were randomly assigned to the SH:24 online testing and results service or to the control group (Figure 13). We excluded 8 participants who were randomised twice and 1 participant who was randomised and did not meet the age criterion (Figure 13). We were unable recruit to target and therefore we lacked power for the co-primary outcome of STI diagnoses.

Figure 13. CONSORT flow diagram



Baseline characteristics are presented in Table 5.

Table 5. Baseline characteristics of participants

	Intervention group (n=1031)	Control group (n=1032)
Sex		
Female	604 (58.6)	609 (59.0)
Male	424 (41.1)	422 (40.9)
Transgender	3 (<1)	1 (<1)
Mean age (years)	23 (3.5)	23 (3.6)
Age group (years)		
16-19	206 (20.0)	220 (21.3)
20-24	440 (42.7)	432 (41.9)
25-30	385 (37.3)	380 (36.8)
Sexual Orientation		
Men who have sex with men	129 (12.5)	133 (12.9)
Other	890 (86.3)	888 (86.0)
Refused	12 (1.2)	11 (1.1)
Partners		
1	302 (29.3)	304 (29.5)
2+	729 (70.7)	728 (70.5)
Ethnic Group		
White/ White British	779 (75.6)	749 (72.6)
Black/ Black British	81 (7.9)	110 (10.7)
Asian/ Asian British	70 (6.8)	57 (5.5)
Mixed/ Multiple ethnicity	89 (8.6)	99 (9.6)
Other	12 (1.2)	17 (1.6)
Last STI test (months)		
0-3	144 (14.0)	155 (15.0)
3-6	161 (15.6)	140 (13.6)
6-12	181 (17.6)	165 (16.0)
12+	301 (29.2)	288 (27.9)
Never	244 (23.7)	284 (27.5)
Place of last STI test		
Sexual health clinic	521 (50.5)	494 (47.9)
GP	121 (11.7)	115 (11.1)
Hospital	51 (4.9)	43 (4.2)
Pharmacy	7 (0.7)	11 (1.1)
Internet STI test	32 (3.1)	28 (2.7)
Other	55 (5.3)	55 (5.3)
N/A	244 (23.7)	286 (27.7)

Data are n (%) or mean (SD)

Primary outcome data, prior to multiple imputation, were available for 921 (89%) participants in the intervention group and 818 (79%) in the control group (Figure 13).

The proportions of participants in each arm who reported completing a test at 6 weeks, and who were confirmed to have tested via patient record checks, are provided in figure 14 and figure 15. Record checks in clinics, SH:24 and GP surgeries were completed by 17 June 2016.

5.3 Primary analyses

The primary analyses were based on multiply imputed datasets. 1,031 in the intervention arm and 1,032 in the control arm were included in the analyses. At 6 weeks, 48.4% of the intervention group had completed an STI test compared to 24.6% in the control group (RR 1.97, 95% confidence interval 1.74 to 2.22, P<0.0001; Table 6). 2.3% of the intervention *v* 1.2% in the control had been diagnosed with an STI (RR 2.14, 95% confidence interval 1.08 to 4.25, P=0.052[2]; Table 6).

There were similar results for the complete case analysis. In the main trial analyses, the results were similar to all the scenarios that we investigated under the assumption that our missing outcome data are Missing Not at Random (MNAR). These are reported in the published trial report (Wilson et al. 2017) and in the appendices (Appendix 6).

The effect on the proportion of participants treated was 1.7% in the intervention *v* 1.0% in the control (RR 1.85, 95% confidence interval 0.85 to 4.01, P=0.18; Table 6).

In the complete cases, time-to-test, estimated by the restricted mean survival time, was shorter in the intervention arm compared to the control arm (28.8 days vs 36.5 days; P<0.0001, Table 7); no differences were observed for time-to- treatment (83.2 days vs 83.5 days; P=0.51, Table 7).

[2] The p-value relates to the risk difference and these are coherent. The risk ratio is estimated from parameters of the same model but its confidence intervals are computed using a delta method transformation of the standard errors. As the proportions are close to zero, the transformation is highly nonlinear which gives confidence intervals for the risk ratio that are inconsistent with the p-value for the risk difference.

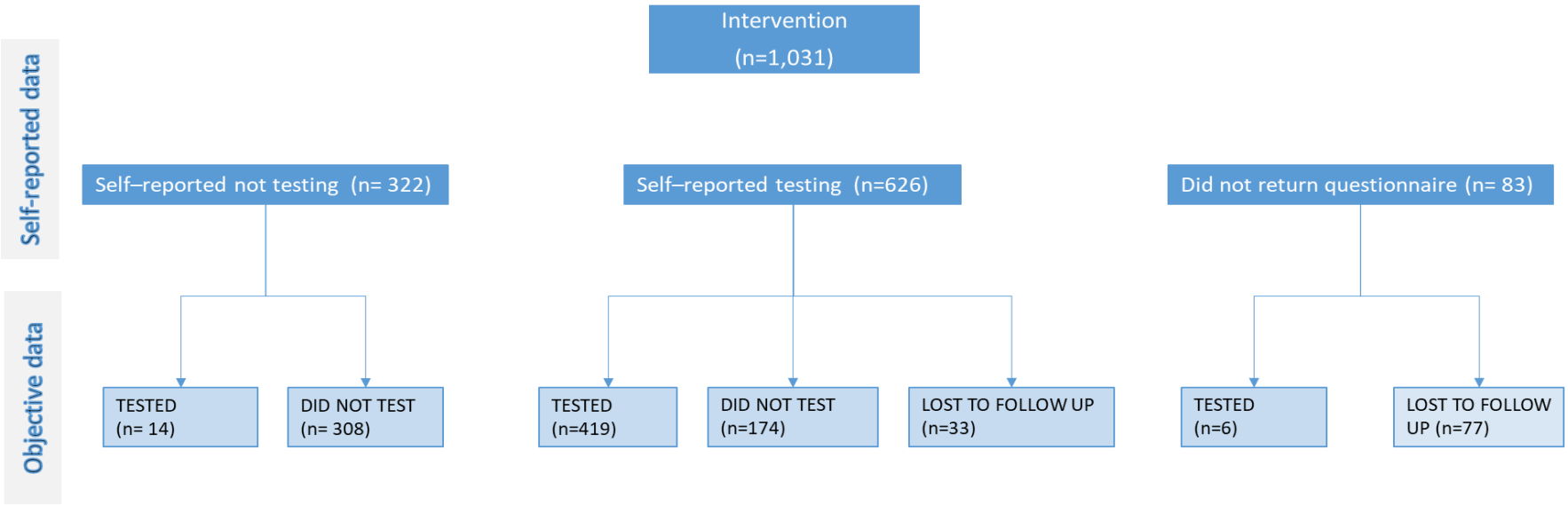
Table 6. Primary and secondary outcomes

		Intervention n=1,031	Control n=1,032	Risk difference (95% CI)	Relative risk (95% CI)	P value
Primary outcomes						
Diagnosis of STI at 6 weeks	**Weighted MICE**	**2.3%**	**1.2%**	**1.3% (0.0, 2.6)**	**2.14 (1.08, 4.25)**	**0.052***
	Weighted Complete cases	*2.1% (19/921)*	*1.0% (8/818)*	1.3% (0.1,2.4)	2.35 (0.45, 4.24)	0.031*
Completion of STI test at 6 weeks	**Weighted MICE**	**48.4%**	**24.6%**	**23.7% (19.4, 28.1)**	**1.97 (1.74, 2.22)**	**<0.0001**
	Weighted Complete cases	*47.7% (439/921)*	*21.1% (173/818)*	26.2% (22.0-30.4)	2.24 (1.91-2.57)	<0.0001
Secondary outcomes						
STI cases treated	**Weighted MICE**	**1.7%**	**1.0%**	**0.8% (–0.4, 2.0)**	**1.85 (0.85, 4.01)**	**0.18**
	Weighted Complete cases	*1.2% (11/913)*	*0.9% (7/817)*	0.5% (-0.5,1.4)	1.59 (0.11,3.07)	0.322

MICE: Multiple Imputation by Chained Equations (number of imputations =100). All estimates (including proportions) are derived from multiply imputed data sets.

*The p-value relates to the risk difference and these are coherent. The risk ratio is estimated from parameters of the same model but its confidence intervals are computed using a delta method transformation of the standard errors. As the proportions are close to zero, the transformation is highly nonlinear which gives confidence intervals for the risk ratios that are inconsistent with the p-values for the risk difference.

Figure 14. Self-reported data verified via patient record checks (intervention group).

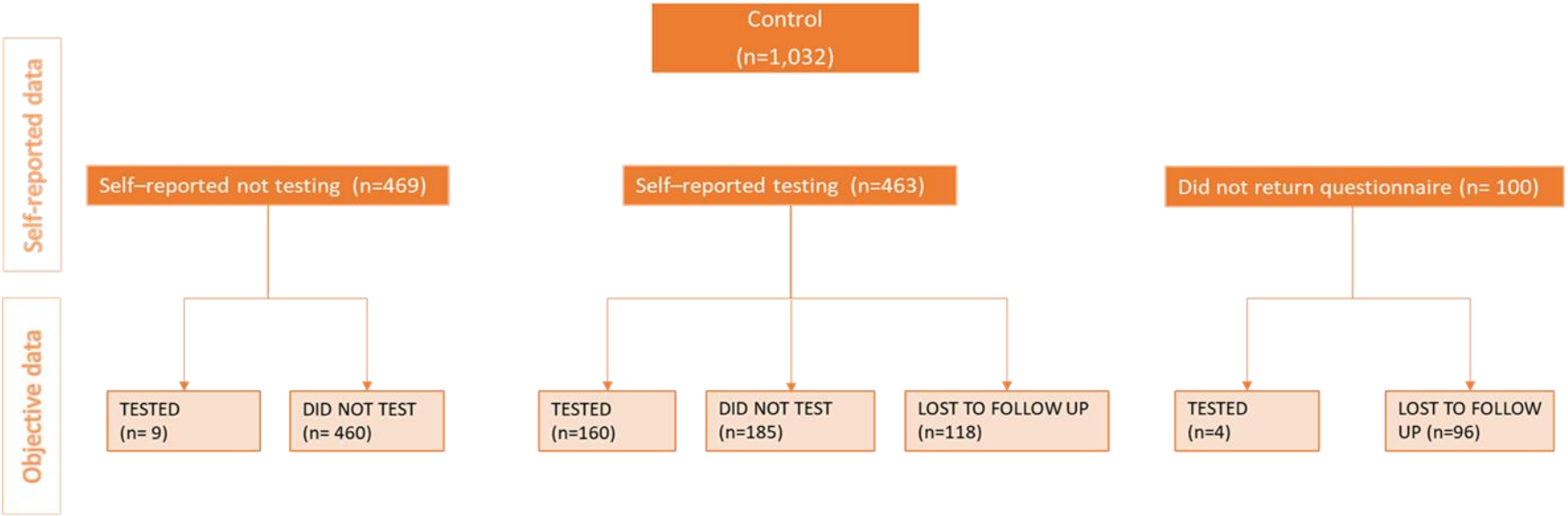


Summary:
In the intervention arm, 626 participants reported completing an STI test at 6 weeks. 419 of 626 were confirmed to have tested. 174 of 626 were confirmed to have not tested as there was no record of a completed STI test in clinics in Lambeth and Southwark, SH:24 or the service where they reported taking a test (within 6 weeks of randomisation).

33 of 626 were lost to follow up. Among these 33 participants, 27 were lost to follow up as there was no record of an STI test in clinics in Lambeth and Southwark or SH24, and they did not name an alternative service where they were tested. The remaining 6 participants were lost to follow up as they named an alternative service but the service did not provide us with data.

14 participants reported not testing, but they were confirmed to have completed an STI test in clinics in Lambeth and Southwark or SH:24.
6 participants did not return a follow up form but they were confirmed to have completed an STI test in clinics in Lambeth and Southwark or SH:24.

Figure 15. Self-reported data verified via patient record checks (control group).



Summary:
In the control arm, 463 participants reported completing an STI test at 6 weeks. 160 of 463 were confirmed to have tested. 185 of 463 were confirmed to have not tested as there was no record of a completed STI test in clinics in Lambeth and Southwark, SH:24 or the service where they reported taking a test (within 6 weeks of randomisation).

118 of 463 were lost to follow up. Among these 118 participants, 100 were lost to follow up as there was no record of an STI test in clinics in Lambeth and Southwark or SH24, and they did not name an alternative service where they were tested. The remaining 18 participants were lost to follow up as they named an alternative service but the service did not provide us with data.

9 participants reported not testing, but they were confirmed to have completed an STI test in clinics in Lambeth and Southwark or SH:24.
4 participants did not return a follow up form but they were confirmed to have completed an STI test in clinics in Lambeth and Southwark or SH:24.

Table 7. Secondary outcomes (time to event)

	Intervention RMST (SE)	Control RMST (SE)	**RMST difference (95% CI)**	P value
Secondary Outcomes				
Time to test (t*= 42 days)	28.8 (0.5)	36.5 (0.4)	**7.7 days (6.4, 8.9)**	<0.0001
Time to treatment (t*= 84 days)	83.2 (0.3)	83.5 (0.2)	**0.3 days (–0.6, 1.2)**	0.51

RMST: Restricted Mean Survival Time. Estimates derived from complete cases.

Kaplan Meier plots for time-to-test and time-to-treatment are presented below (Figure 16, Figure 17). The survival curves for time-to-test indicate that the effect of the intervention on STI testing is time dependent.

Figure 16. Kaplan Meier Plot. Time-to-test.

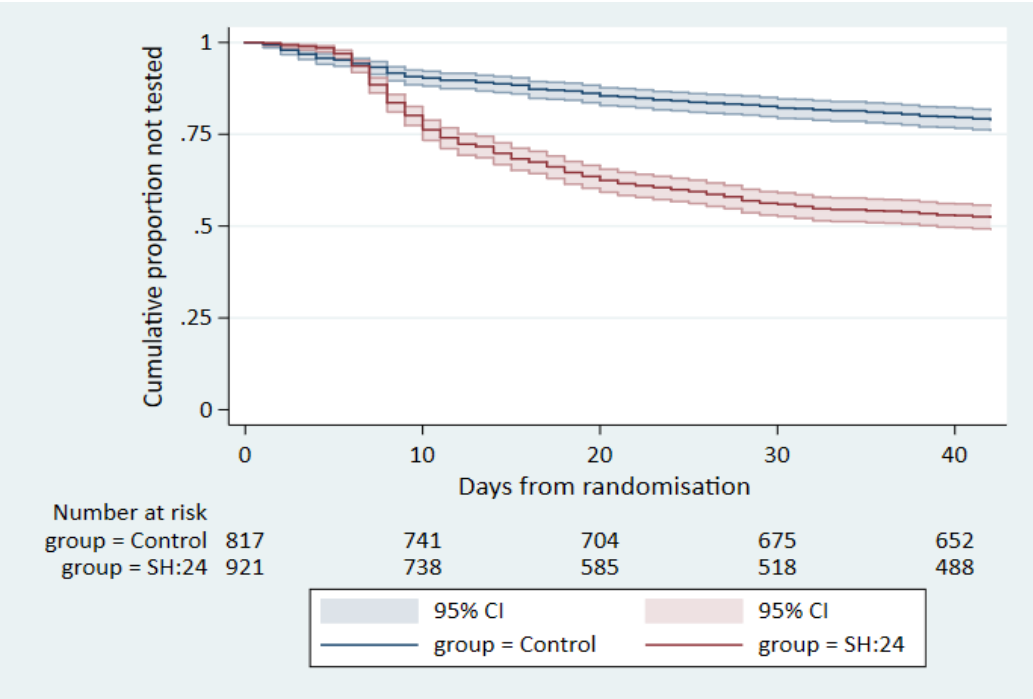
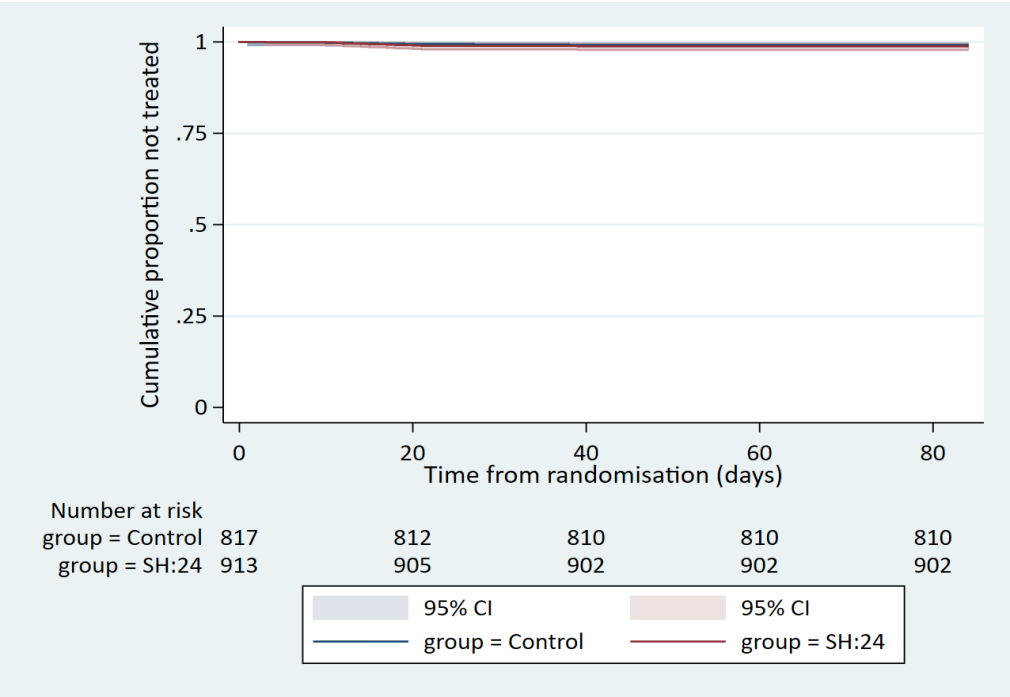


Figure 17. Kaplan-Meier Plot. Time-to-treatment



There is evidence that the effect of intervention on STI testing may be modified by gender. There is no evidence of heterogeneity for any of the other pre-specified subgroup analyses, conducted in the complete cases (Figure 18, Figure 19). Given that there was a lack of power for the analyses of STI diagnoses, the subgroup analyses for this outcome are even more underpowered.

Figure 18. Effect of the intervention on STI testing, by subgroup

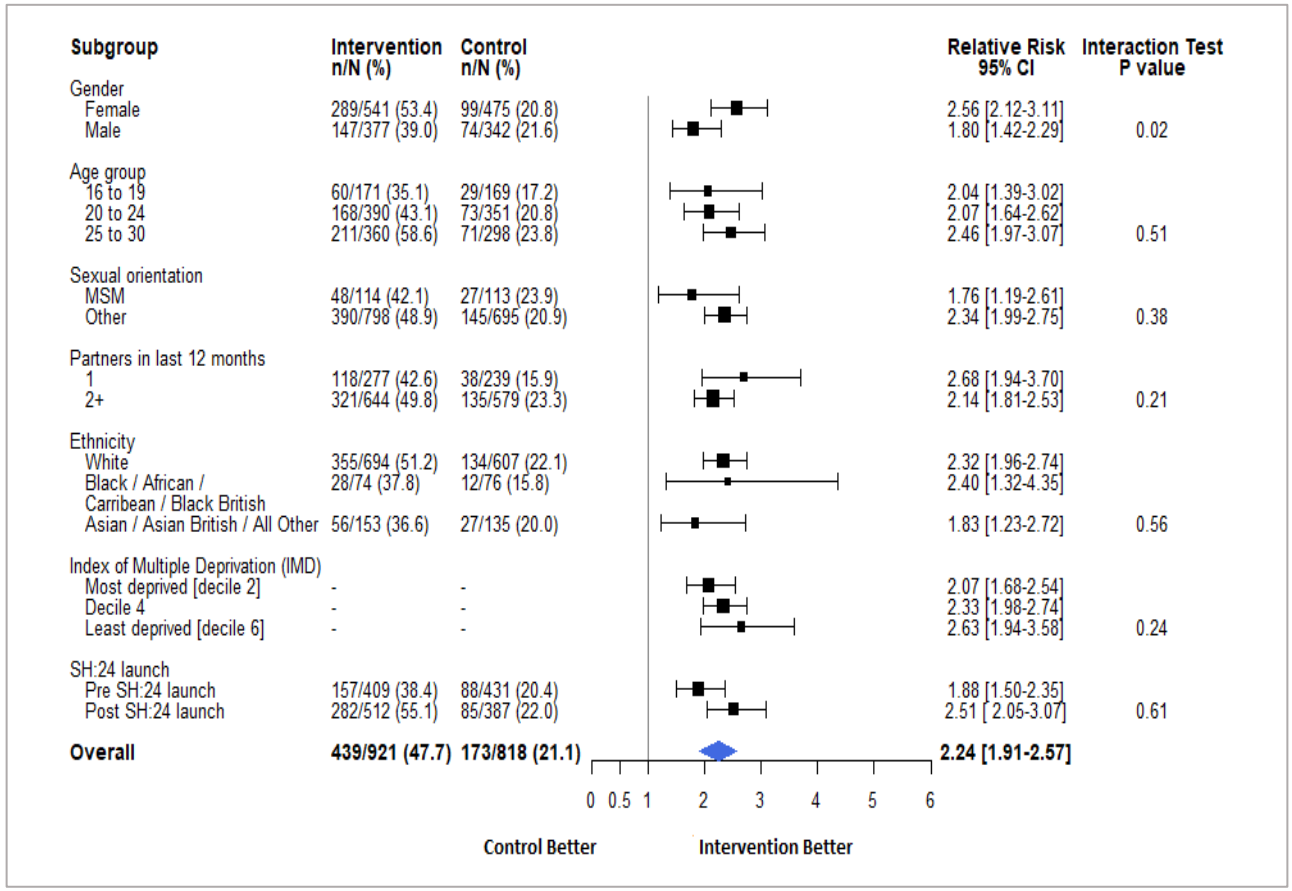
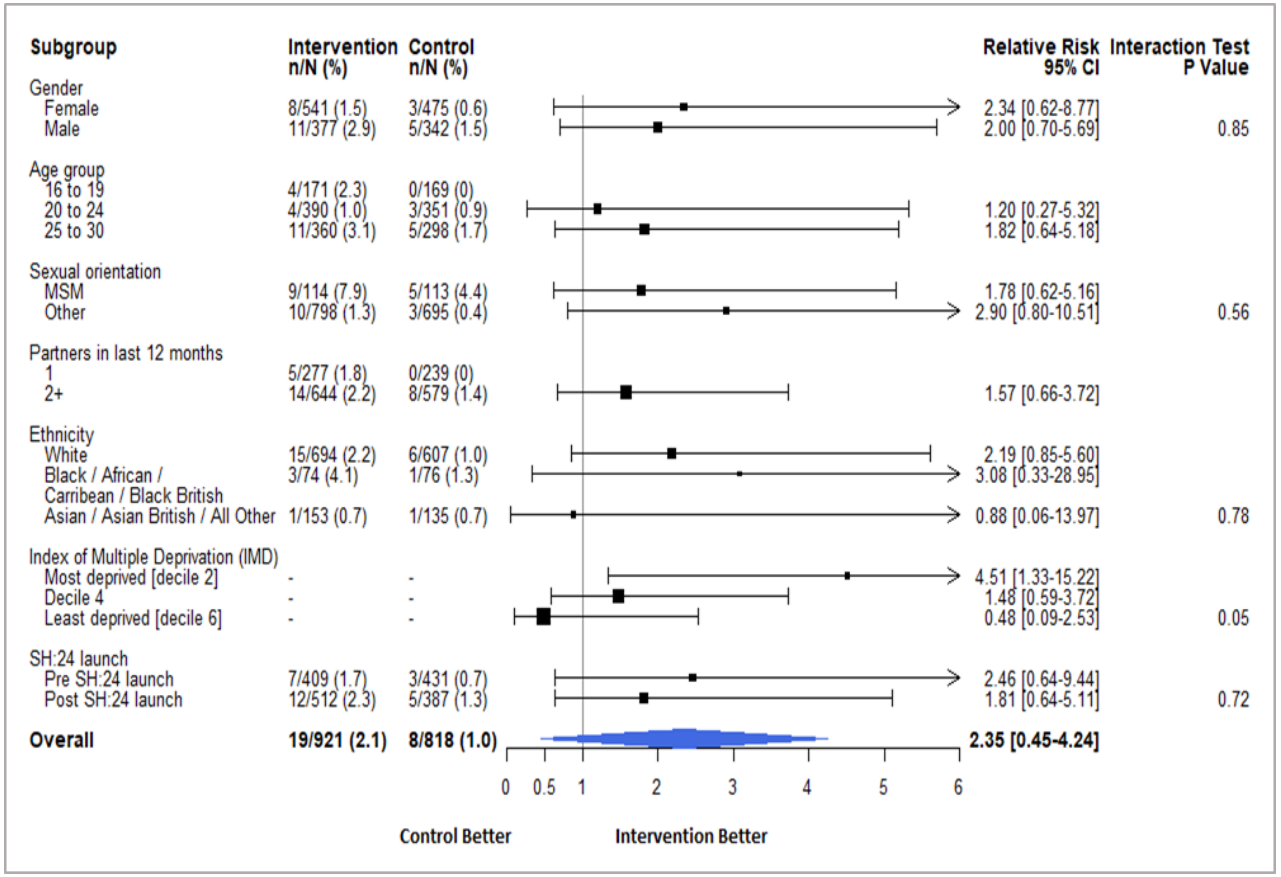


Figure 19. Effect of the intervention on STI diagnoses, by subgroup



5.3.1 Process outcomes

Among participants who completed an STI test at 6 weeks, 4.3% (19/439; 95% CI 2.8-6.7) tested positive for an STI in the intervention group and 4.6% (8/173; 95% CI 2.3-9.0) of participants tested positive for an STI in the control group. The median time from diagnosis to treatment among those with complete treatment data was 2 days in the intervention group and 4 days in the control group (Table 8). Four of the 18 cases treated received treatment prior to a laboratory confirmed diagnosis, and are not included in these summary statistics. The excluded cases were evenly distributed between groups.

Table 8. Process outcomes

	Intervention	Control
Adherence to appropriate testing pathways at 6 weeks	99.2% (0.4)	-
Self - reported acceptability of intervention at 6 weeks	71.1% (2.6)	-
Median time from diagnosis to subsequent treatment (days) among those with complete treatment data (n=9 in the intervention; n=5 in the control)	2 days (1 - 5)	4 days (1-7)

Data are % (SE) and median (IQR)

76% (294/ 388) of the intervention group who tested via SH:24, provided acceptability data. Of these, 71% (209/294) found the intervention to be acceptable (Table 8).

88% (388/439) of participants in the intervention group who completed an STI test at 6 weeks, tested via SH:24 (Table 9). 19 participants in the intervention arm were diagnosed with an STI. Of these, 12 were diagnosed via SH:24 and 7 were diagnosed in a sexual health clinic (Table 9).

Table 9. Proportion of participants who completed an STI test and proportion of participants diagnosed with an STI, by service type

	STI test completion		STI diagnoses	
	Intervention	Control	Intervention	Control
Sexual health clinic in Lambeth and Southwark	41 (9%)	145 (84%)	3 (16%)	4 (50%)
Other sexual health clinic	9 (2%)	15 (9%)	4 (21%)	3 (38%)
GP	1 (<1%)	2 (1%)	0 (0%)	0 (0%)
SH:24	388 (88%)	11 (6%)	12 (63%)	1 (13%)
Total	*439 (100%)*	173 (100%)	*19 (100%)*	*8 (100%)*

Data are n (%). Percentages do not add up to 100% due to rounding.

In the intervention group, 2.8% (12/432) of chlamydia tests were positive, 1.4% (6/433) of gonorrhoea tests were positive, 0.8% (3/363) of syphilis tests were positive. In the control group, 2.4% (4/169) of chlamydia tests were positive, 3% (5/169) of gonorrhoea tests were positive. None of the 137 (0/137) syphilis tests in the control arm were positive.

365 participants tested for HIV in the intervention group and 140 in the control group. There were no confirmed HIV diagnoses. One participant tested for hepatitis B in the intervention group and 11 in the control group. There were no hepatitis B diagnoses in either group.

Among participants who were diagnosed, most (24/27) were diagnosed with a single STI and three with more than one STI.

5.4 Discussion

5.4.1 Statement of principal findings

When STI testing is promoted, offering e-STI testing alongside usual care significantly increases uptake of STI testing. The intervention increased STI testing in all groups including those at high risk for STIs. Higher proportion of participants in the intervention arm tested for all infections, including HIV and syphilis, compared to the control arm.

There was a lack of power for the analyses of STI diagnoses and STI cases treated, but the estimates are in the expected direction. The intervention reduced time-to-test but not time-to-treatment.

5.4.2 Strength and weaknesses

This study has several strengths. Randomisation was via an independent remote computer based randomisation system to ensure study staff had no prior knowledge of the treatment allocation. We collected objective outcomes even for those participants who tested outside of Lambeth and Southwark or via a different pathway (e.g. at the GP). Laboratory staff and researchers carrying out the analyses were blinded to the allocation. Baseline prognostic factors were well balanced between groups and our co-primary outcomes were known for 84% of participants. In trials where it is not possible to blind participants, allocation to the control group could reduce motivation to carry out the desired behaviour. To mitigate potential performance bias, participants were informed at the time of recruitment that they would be invited via text message to use one type of sexual health service without stating the options. All analyses were intention to treat as far as possible, as 9 participants were excluded from the analyses.

The trial included high-risk groups including MSM (262/2,063; 13%), 16-24 year olds (1,298/ 2,063; 63%) and individuals reporting two or more sexual partners in the last year (1,457/2,063; 71%). We enrolled individuals who reported limited prior contact with conventional STI testing services. A quarter of the study population had never tested for STIs prior to the trial (528/2,063) (Table 5). 17% of MSM (45/262) and 21% of 16-24 year olds (277/1,298) had not tested within the last 12 months, despite national guidelines which recommend annual STI testing among these groups (British HIV Association, British Association of Sexual Health and HIV & British Infection Society; Public Health England)

The trial has a number of limitations. We fell short of the recruitment target of 3,000 participants and it was not possible to extend the recruitment period due to a pre-existing plan to promote SH:24 widely across the study area. As a result, the study lacked power to detect differences in STI diagnoses and STI cases treated.

As with other online enrolment systems (Bailey et al. 2013), a high number of potential participants started, but did not complete, the enrolment process (Figure 13). 1,608 potential participants consented to the study but were not randomised. The reasons for this are unknown. It is plausible that interested individuals who were channelled from highly optimised social media platforms, such as twitter and Facebook, were put off by the enrolment website which was less user friendly. It is also possible that the requirement to submit baseline data was deemed cumbersome. We do not know if there were systematic

differences between those who continued to randomisation and those who dropped out. In order to minimise potential selection bias and reduce inefficiencies in the enrolment process, it will be important for future studies to monitor online enrolment procedures carefully to ensure that a higher proportion of consented participants are randomised. This point is particularly salient given that we were underpowered for our analyses of the co-primary outcome of STI diagnoses.

It is likely that those who enrolled in the study had a greater interest in STI testing than those who declined. Testing uptake in the control and intervention arms in all trials may be higher than in the general population. This could result in a smaller risk difference if the intervention were to be implemented in the general population. 26% of our study population identified as BME at baseline. This is lower than the proportion of individuals in Lambeth and Southwark identifying as BME (44% and 48% respectively (Southwark Council; Lambeth Council May, 2015)), which may limit the generalisability of the results.

While there is some reporting bias in the self-reported data (Figure 14, Figure 15), the potential to bias the co-primary endpoints is limited, as these were objectively verified via participants' health records.

Only one scenario would result in any misclassification of the co-primary endpoints: if a participant tested at a service outside of Lambeth and Southwark, but told the study team they did not test. This scenario is judged to be fairly extreme, as it is reasonable to assume that participants were more likely to over-report than under-report the outcome of interest (STI testing), as this is the socially desirable behaviour in this context.

There was potential for contamination as the URL for SH:24 was promoted in Lambeth and Southwark when the service was launched in March 2015. However, only 11 control group participants used SH: 24 in the trial and any contamination would have biased our results towards the null. In the subgroup analyses there was no evidence of heterogeneity as a result of SH:24's change in availability.

At enrolment, participants were informed that the £10 incentive was for completing follow up, but some participants later reported that they thought it was for completing an STI test. Given that all participants were told about the £10 incentive, and sent money at follow up, the impact of this incentivisation should be non-differential and would not explain the statistically significant results.

Although the laboratory tests used by services are highly sensitive and specific, some misclassification is possible. This misclassification could have biased our STI diagnoses results towards the null. Eight people were randomised twice and therefore excluded from the analyses. It is possible other people were randomised twice but only if they used a false name and date of birth. All services were motivated to record STI testing data in line with national surveillance requirements. If some services were more accurate than others, this might result in differential misclassification and bias.

Although there were high response rates for our co-primary outcomes, these rates were differential as there was higher follow up in the intervention group than in the control group. This can result in biased estimates under a complete case approach (Bell et al. 2013). To deal with missing outcome data, the primary analyses used multivariate imputation techniques under the assumption that data are MAR. This approach is well-established and it is more valid and efficient than other approaches to deal with missing data (Carpenter & Kenward 2008). It is reassuring that the results of all sensitivity analyses reported in the main trial paper (Wilson et al. 2017; Appendix 6) are similar to these results for the primary analyses

5.4.3 Strengths and weaknesses in relation to other studies.

To my knowledge, this is the first trial of an e-STI testing service, which offers testing for four STIs (chlamydia, gonorrhoea, HIV and syphilis). Descriptive studies from the United States suggest services that offer internet-based testing for chlamydia, gonorrhoea and trichomoniasis, can attract at-risk populations (young and black and minority ethnic groups) and yield high STI positivity (Chai et al. 2010; Ladd et al. 2014). One randomised controlled trial in France has evaluated self-sampling for chlamydia accessed via the internet compared to chlamydia testing in face-to-face settings. It reports an increase in testing uptake (29.2% in the intervention group v 8.7% in the control group, RR 3.37, 95% CI 3.05 – 3.74). However, outcomes were assessed using different measures in the intervention and control groups, and there was low and differential follow up (47% follow up in the intervention group v. 30% follow up in the control group) (Kersaudy-Rahib et al. 2017).

Our findings for STI testing are similar to increases in testing reported in trials of self-sampling and self-testing interventions that are not accessed via the internet (Fajardo-Bernal et al. 2015; World Health Organisation 2016).

5.4.4 Meaning and mechanisms

In chapter 3, I applied the candidacy lens to theorise how SH:24 may increase access and utilisation of STI testing in a complex service delivery system. Rather than viewing 'access' as a single event, the candidacy lens conceptualises the use of health care as a dynamic process of social interaction between patients and professionals (Mackenzie et al. 2013; Dixon-Woods et al. 2005). Drawing on the initial theory of change and wider literature, I presented propositions for how SH:24 may prompt increased recognition of candidacy, and enable smoother negotiations of STI testing trajectories, leading to increased utilisation of STI testing services. While the study results are consistent with this conceptualisation, the RCT findings are unable to shed light on the precise change processes underlying the intervention, and further research is warranted.

The similar effect of e-STI testing on testing uptake among different population groups is of public health importance as it suggests a potential to increase testing among groups with diverse risk profiles including those most at risk for STIs. Yet the way in which the intervention triggered increased recognition of candidacy among diverse socio-demographic groups, and their subsequent navigation of e-STI testing pathways, is unlikely to have been uniform. Investigation of possible variation in the negotiation of e-STI testing pathways may potentially illuminate inequalities that are obscured by the positive effects observed in this study.

Seven of the 19 participants diagnosed in the intervention arm were diagnosed in a sexual health clinic. Those in the intervention arm who opted to test in clinic were at greater risk of an STI diagnosis, compared to those who opted to test via SH:24 (14%, (7/50) v 3.1%, (12/388)). It is not known if those who opted to test in clinic were prompted to do so by the SH:24 website (as they reported symptoms) or if they chose to test in clinic independently. This highlights the continued importance of face-to-face services and is consistent with the theory of change, which proposes that e- STI testing offers patients more choice.

National guidelines in the UK recommend increasing testing among key population groups, and in areas of high HIV prevalence, in order to detect asymptomatic infection and normalise testing practices (Public Health England 2015b; National Institute for Health and Care Excellence 2016). The results for STI testing uptake suggest that e-STI testing could play a role in achieving these public health objectives. STI testing uptake and STI diagnoses are important intermediary outcomes on the pathway to increasing cases treated, cured and

managed in community settings. However, the study provides limited evidence on these latter outcomes.

e-STI testing is currently being implemented in the UK as one measure to meet increasing demand for STI testing against a backdrop of severe budget cuts (Robertson et al. 2017; Cleary & O'Sullivan 2017). Publication of the cost-effectiveness evaluation of the intervention is pending and may provide additional insights on the contribution of e-STI testing. A larger trial is required to assess outcomes later in the cascade of STI care including STI diagnoses, cases treated and cured.

The effect size for STI cases treated was lower than our estimate for STI diagnoses, as it was not possible to confirm if all those diagnosed were treated. At the time of the trial, SH:24 required those diagnosed with an infection to attend clinics in person for treatment. Attendance at clinic for treatment was confirmed for 11 of 19 diagnosed in the intervention group and 7 of 8 people diagnosed in the control group.

Some participants may have obtained treatment outside the study area. Five participants in the intervention arm reported (via the self-completed questionnaire or via telephone follow up) that they were treated (Table 10).

Table 10. Self-reported attendance for treatment, among participants with missing treatment outcomes

Reported place of treatment	Intervention	Control
Sexual Health Clinic	3	-
Pharmacy	1	-
Online Pharmacy (Med Express)	1	-
Not Stated	3	1
Total	*8*	*1*

However, these self-reported accounts could not be verified as not all named the precise service where they were treated; while others reported receiving treatment in a private service and the study ethical approval did not extend to these services.

The intervention did not reduce time-to-treatment. It is plausible that whilst the intervention removed the barrier of having to attend a service for testing, the subsequent requirement to attend services for treatment may have deterred some participants. This supports the processual framing of health service utilisation central to the candidacy model, as users with a positive or reactive result were required to negotiate and renegotiate both digital and face-

to-face environments in their care-seeking for STIs. Additional inputs are required so that increases in STI testing and STI diagnoses translate into similar increases in cases treated. This is likely to ensure that the potential public health benefits of e-STI testing can be fully realised.

5.5 Conclusions

We trialled SH:24 in a community setting and in two boroughs well–served by face-to-face clinical services. Providing e- STI testing in contexts where supply is more limited, or targeting particular high risk groups might strengthen the contribution of e- STI testing to the control and management of STIs.

e-STI testing models could be adapted for countries with sufficient laboratory facilities. Established distribution channels for health products may be suitable for sending and receiving test kits, where postal services are limited. Future iterations of e-STI testing could include a wider range of services such as self-testing for HIV. Self-testing differs from the self-sampling modality evaluated by this study. Self-testing enables individuals to take a sample, perform a test and interpret the results by themselves, without the need of a laboratory (Harding-Esch et al. 2016).

Delivering e-STI testing and results services to scale is technically feasible as demonstrated by SH:24, which currently delivers 42,000 tests per year in six regions in the UK. The long-term public health benefits of e-STI services will depend on testing, diagnosis and treatment rates when implemented. These outcomes should be subject to ongoing monitoring and evaluation.

Chapter 6: Secondary Analyses. Effect of e-STI testing among never testers.

SECTION A – Student Details

Student	Emma Wilson
Principal Supervisor	Dr. Caroline Free
Thesis Title	Evaluation of an internet-accessed STI testing (e-STI testing) and results service in two London boroughs

**If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work*

SECTION B – Paper already published

SECTION C – Prepared for publication – but not yet published

Where is the work intended to be published?	Sexually Transmitted Infections
Please list the paper's authors in the intended authorship order:	Wilson. E; Leyrat. C., Baraitser. P, Free C.
Stage of publication	**Not yet submitted**

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SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I am first-author on this paper. I developed the hypotheses for these secondary analyses, undertook the analyses and drafted the manuscript, with advice from my two supervisors (Dr. Caroline Free and Dr. Paula Baraitser) and Dr. Clémence Leyrat who is on my PhD Advisory Committee

Student Signature: [redacted] **Date:** 24.05.2018

Supervisor Signature: [redacted] **Date:** 24.05.2018

6.1 Chapter overview

In the previous chapter, I presented results for the main trial analyses. In this current chapter, I present the results and implications of a secondary analysis, which examines the effect of the intervention on STI testing on a subsample of participants who reported having never tested for STIs at baseline.

6.2 Background

As discussed in chapter 1, STI testing coverage in suboptimal in England. Both psychosocial and contextual factors inhibit access to face-to-face sexual health services (Oliver de Visser & O'Neill 2013; Deblonde et al. 2010). Self-sampling accessed via the internet (e-STI testing) may overcome some of these barriers, by enabling users to bypass the stigma, embarrassment and inconvenience associated with face-to-face STI testing (Minichiello et al. 2013; Hottes et al. 2012; Baraitser et al. 2015; Lorimer & McDaid 2013).

Public Health England recommends e-STI testing to expand access to opportunistic screening for chlamydia and HIV, particularly for at-risk groups not reached by conventional services (National Institute for Health and Care Excellence 2016; Public Health England 2015b). Yet the evidence on the effectiveness of e-STI testing services to increase testing uptake among those who have never tested for STIs is extremely limited.

One large observational study among MSM in Canada found that those who reported barriers in accessing testing services had higher odds of intending to use an e-STI service compared to those who did not report barriers [OR 1.65 95% CI 1.40-1.96] (Gilbert et al. 2013). In the UK, descriptive data suggest that the national HIV e-testing service (test.hiv), which targets MSM and black African heterosexuals, can reach those who have never previously tested among these populations. Between November 2015 and October 2017, 29.9% of the 44,660 returned kits were from first-time users who had never previously tested (Public Health England 2018a) . However, it is not known how this compares to the proportion of first-time testers who attend face-to-face services, as testing history is not routinely collected in these settings.

In the previous chapters, I discussed the results of a large randomised controlled trial in an inner city area of London which demonstrated that e-STI testing increases uptake of testing at 6 weeks when offered alongside usual care in community settings (48.4% v 24.6%, relative risk 1.97, 95% confidence interval 1.74 to 2.22, $p<0.001$)(Wilson et al. 2017). The

trial sample included participants with a range of socio-demographic and behavioural characteristics, as well as testing profiles. For these secondary analyses, I examine the effect of offering e-STI testing on testing uptake at 6 weeks and time-to-test among trial participants who reported never having tested for an STI at baseline.

6.3 Methods

6.3.1 Study population

I analysed a subsample of the main trial sample (n=528), who reported never having had an STI test at baseline.

6.3.2 Outcomes

The outcomes are: 1) the proportion of participants who tested for any STI at 6 weeks from randomisation, 2) time from randomisation to completion of an STI test in each arm.

The process outcomes are the proportion who tested positive for any STI among participants who completed a test within 6 weeks; the proportion of participants who completed an STI test, by service type; the proportion who consider the intervention to be acceptable (intervention group only).

In addition to these outcomes, I assess the proportion of participants who tested for HIV at 6 weeks from randomisation and the proportion of participants who tested for chlamydia or gonorrhoea at 6 weeks from randomisation.

6.3.3 Sample size

The published trial results are as follows: 50.0% of the intervention group completed an STI test compared to 26.6% in the control group, RR 1.87, P<0.0001 (Wilson et al. 2017). I hypothesised that in this subpopulation, far fewer participants would complete an STI test in each arm, but that the relative effect of e-STI testing on testing uptake would be similar. A sample size of 420 would lead to 90% power (two-side alpha=5%) to detect a relative risk of 1.87. This equates to 28% of the intervention group completing a test compared to 15% in the control group.

6.3.4 Statistical methods

We adopted a similar statistical approach to the main trial analyses to ensure comparability. Randomisation was based on a minimisation algorithm to balance key prognostic covariates. This required an adjusted analysis.

Our analysis model used an inverse probability of treatment estimator, to estimate the average treatment effects (ATE). Covariates included all minimisation factors (gender, age, sexual orientation and number of sexual partners in the last 12 months) in addition to ethnicity, as this is also a predictor of the outcome. The ATE was used to obtain the value of the weighted risk difference. I obtained estimates for the weighted risk ratio and its confidence intervals via the delta method of transformation.

To account for missing outcome data (STI testing), I used multivariate imputation by chained equations assuming data are Missing at Random (MAR). In our imputation models, I conditioned on self-reported testing and diagnoses, which were also incomplete. I included randomised group as a covariate. This was weighted by the inverse of the propensity score to ensure compatibility with our model for analysis. I generated 100 imputed datasets and inference proceeded via Rubin's rules (Rubin 1987).

6.3.5 Missing covariates

All baseline characteristics were fully observed, except for sexuality as participants could opt out of this question. A missing category was therefore used.

6.3.6 Sensitivity analyses

For the main trial, TM conducted a sensitivity analysis to explore departures from MAR for our co-primary outcomes. The results were similar to our estimates under MAR for all the scenarios we investigated (Wilson et al. 2017). For the purposes of these secondary analyses, we consider our assumption that data are MAR to be valid.

6.3.7 Subgroup analyses

To explore heterogeneity of the intervention effect on our outcome, I tested for interaction at a 5% level of significance to assess whether effectiveness varied by the following baseline characteristics: gender (male, female); ethnicity (Black/ Black British, White/ White British, Other); age (16-19; 20-24, 25-30 years); number of sexual partners in the last 12 months (1, 2+), sexuality msm, other); index of multiple deprivation (linear) and recruitment source (face-to-face; online). These analyses were conducted in the complete cases under a MAR assumption using a log binomial model.

6.3.8 Time to event analyses

I used survival analysis to estimate the restricted mean survival time from randomisation to completion of an STI test for each group. This is an appropriate measure even when the

proportional hazard assumption is in doubt (Royston & Parmar 2011). In the main trial analyses, the Kaplan Meier plots for our co-primary outcome (uptake of STI testing) suggested that the effect of the intervention was time-dependent. In these secondary analyses, the mean survival times were set to t* = 6 weeks (42 days), t*= 2 weeks (14 days), and t*= one week (7 days) to investigate possible time-dependency of the intervention among this sub-sample.

I obtained ethical approval for these secondary analyses from the London School of Hygiene and Tropical Medicine Ethics Committee (Ref: 14414).

6.4 Results

Outcome data (STI testing) were available for 87% (213/244) of the intervention group and 79% (224/284) of the control group.

This subsample of first-time testers includes key prevention groups for STIs: 80% (420/528) are young adults aged between 16-24 years and 7% (35/528) are MSM. In addition over half (56%, 294/528) reported having at least two sexual partners in the last 12 months.

Baseline characteristics are presented in Table 11.

Table 11. Baseline characteristics of participants – secondary analyses

	Intervention Group (n=244)	Control Group (n=284)
Sex		
Female	130 (53.3%)	142 (50.0%)
Male	113 (46.3%)	141 (49.6%)
Transgender	1 (<1%)	1 (<1%)
Mean (age)	21.3 (3.5)	21.3 (3.6)
Age group (years)		
16-19 years	96 (39.3%)	118 (41.5%)
20-24 years	96 (39.3%)	110 (38.7%)
25-30 years	52 (21.3%)	56 (19.7%)
Sexual Orientation		
MSM	14 (5.7%)	21 (7.4%)
Other	224 (91.8%)	258 (90.8%)
Refused	6 (2.5%)	5 (1.8%)
Partners in last 12 months		
1	111 (45.5%)	123 (43.3%)
2 or more	133 (54.5%)	161 (56.7%)
Ethnic Group		
White/ White British	176 (72.1%)	194 (68.3%)
Black/ Black British	18 (7.4%)	25 (8.8%)
Asian/ Asian British	33 (13.5%)	34 (12.0%)
Mixed/ Multiple ethnicity	14 (5.7%)	26 (9.2%)
Other	3 (1.2%)	5 (1.8%)

At 6 weeks, 45.3% of the intervention completed at least one STI test, compared to 24.1% of the control group (RR 1.88, 95% CI 1.47-2.40, p<0.001) (Table 12). For HIV testing alone, 40.6% of the intervention completed an HIV test compared to 21.7% in the control group (RR 1.87, 95% CI 1.44 -2.44, p<0.001). For chlamydia and gonorrhoea testing combined, 44.3% completed a test in the intervention compared to 24.1% in the control (RR 1.84, 95% CI 1.44-2.36, p<0.001).

Table 12. Effect of SH:24 on testing uptake (MICE) – secondary analyses

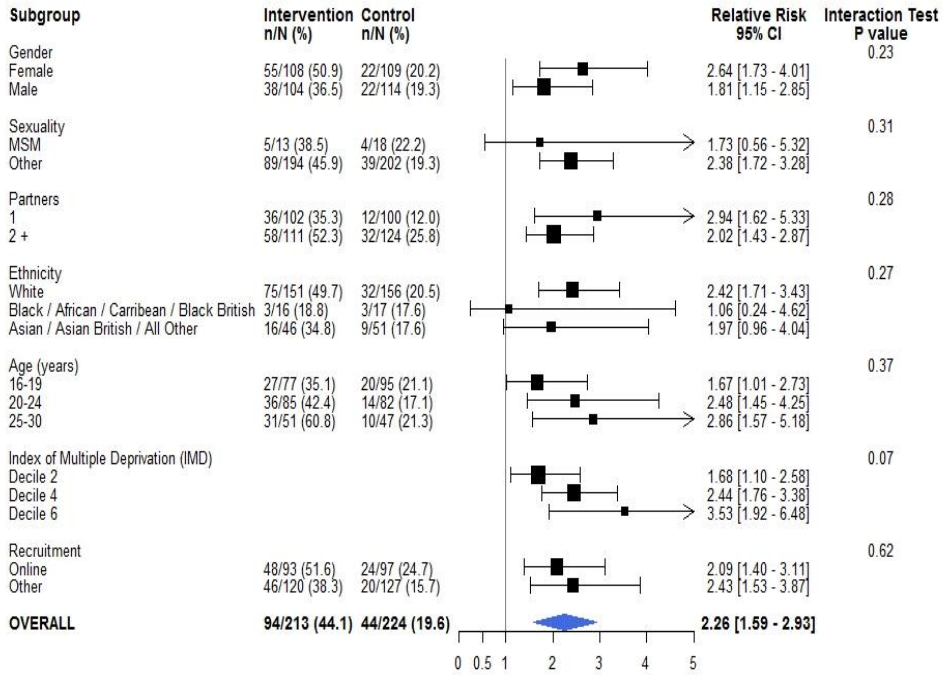
	Intervention	Control	Risk difference (95% CI)	Relative risk (95% CI)	P value
Uptake of testing (any STI)	45.3%	24.1%	21.2% (12.5, 29.8)	1.88 (1.47, 2.40)	<0.001
Uptake of HIV testing	40.6%	21.7%	18.9% (10.3, 27.4)	1.87 (1.44, 2.44)	<0.001
Uptake of chlamydia and gonorrhoea testing	44.3%	24.1%	20.2% (11.7, 28.8)	1.84 (1.44, 2.36)	<0.001

Similar results were observed for the analyses in the complete cases (Appendix 7). In the complete cases, the intervention reduced time to test for any STI at 42 days, but not at 7 and 14 days (Table 13).

Table 13. Time to test (any STI) – secondary analyses

	Intervention RMST (SE)	Control RMST (SE)	RMST difference (95% CI)	P value
Time to test (t*= 42 days)	29.0 (1.1)	36.3 (0.8)	7.3 days (4.6 to 10.0)	<0.001
Time to test (t*= 14 days)	12.2 (0.2)	12.9 (0.2)	0.7 days (0.1, 1.2)	0.21
Time to test (t*= 7 days)	6.8 (0.04)	6.71 (0.07)	-0.1 days (-0.25, 0.06)	0.22

Figure 20. Effect of the intervention on STI testing uptake, by subgroup – secondary analyses



There was no evidence of heterogeneity for the subgroup analyses (Figure 20).

6.4.1 Process outcomes

Among those who completed a test, 4.3% (4/94) of the intervention arm tested positive for an STI, compared to 2.3% (1/44) in the control. 89% (84/94) of those who tested in the intervention arm, tested via SH:24 (Table 14).

Table 14. Service used for testing, by arm

	Intervention	Control
Sexual health clinic in Lambeth and Southwark	9 (10%)	39 (89%)
Other sexual health clinic	1 (1%)	1 (2%)
GP	0 (0%)	1 (2%)
SH:24	84 (89%)	3 (7%)
Total who completed a test	*94 (100%)*	*44 (100%)*

6.5 Discussion

6.5.1 Statement of principal findings

When promoted in community settings and delivered alongside usual care, e-STI testing increases testing uptake among those who had not previously attended STI testing services. Similar estimates were observed when I examined the effects on uptake of chlamydia and gonorrhoea testing, and uptake of HIV testing separately. The intervention reduced time-to-test. There was no evidence of heterogeneity for any of our subgroup analyses.

6.5.2 Strengths and weaknesses

The strengths of the main trial have been discussed in chapters four and five. Briefly, an independent remote computer based randomisation system was used, and laboratory and outcome assessors were blinded to allocation. Due to the nature of the intervention it was not possible to blind participants. To mitigate any performance bias, participants were informed at recruitment that they would be invited via text message to use one type of sexual health service without stating the options.

The main outcome (uptake of any STI test) was known for 83% of participants in this subsample. In the main trial, a minimisation algorithm was used to balance key prognostic factors. In this study I analysed a sub-sample from the main trial sample, and therefore not all baseline characteristics were balanced (Table 11). I accounted for this in the analyses, by adjusting for baseline covariates (ethnicity, age, gender, sexuality and number of sexual partners in the last 12 months) via inverse probability of treatment weighting. All analyses were intention to treat.

6.5.3 Limitations

Our study has several limitations. It was not possible to assess the effect on outcomes later in the cascade of care such as STI diagnoses and STI cases treated due to the size of the sample. Nevertheless undiagnosed infections were detected in this subpopulation. Of those who tested, 4.3% (4/94) in the intervention arm and 2.3% (1/44) in the control arm were diagnosed with an STI. Four participants were diagnosed with chlamydia and one with gonorrhoea. This underlines the importance of public health strategies to reach populations who do not access services.

We were underpowered for our subgroup analyses, which were exploratory in nature. Further research may be warranted to confirm no heterogeneity of effect among these subgroups of never testers.

All services in this trial were required to record STI testing data. However if some services were more accurate than others, this could result in differential misclassification and bias. Secondary analyses of RCT data are recommended to generate additional insights beyond the primary research question, and to take full advantage of the potential richness of trial datasets (Ebrahim et al. 2016; National Institute for Health Research no date). In line with best practice, secondary hypotheses were specified and ethical approval was obtained prior to conducting these analyses. We also ensured that we had sufficient power to detect an effect of the intervention on STI testing in this subpopulation.

6.5.4 Meaning and mechanisms

To my knowledge, this is the first study to assess the effectiveness of an e-sexual health service among a subpopulation who had never tested for STIs. The intervention increased testing uptake for all STIs, including HIV. National guidelines recommend HIV testing in routine settings such as GPs and hospitals in areas of high prevalence (2 - 5 prevalent cases per 1,000 population, aged 15-59 years). Yet provider adherence to these guidelines can be variable (Elmahdi et al. 2014). Limited resources and expertise, combined with a reluctance to offer testing to patients perceived to be low risk may explain this variability (Burns et al. 2007). Our findings would suggest that e-STI testing is a viable option for expanding and normalising HIV testing outside of specialist care, when combined with a health promotion message to encourage testing.

The provision of chlamydia testing is widely available in non-specialist settings. In 2016, 32% of chlamydia screening in England was conducted by GPs or by secondary level sexual and reproductive health clinics (Public Health England 2017d). The results for testing uptake for chlamydia and gonorrhoea, suggest that e-STI testing can reach young people who do not access these conventional screening services. The number of chlamydia cases (n=4) were too few to assess care pathways for those diagnosed by online and clinic services in this study. Results from a preliminary observational evaluation of an eSexual health clinic - offering web-based results and risk management, and remote treatment for chlamydia via pharmacy collection - suggests that online treatment pathways are feasible for users of e-STI testing services (Estcourt et al. 2017).

The overall effect estimate for STI testing (relative risk) is comparable in magnitude to the effect size from our main trial analyses and this was expected. The proportions who completed a test are also comparable, but this was not anticipated. It was assumed that this subpopulation would be more reluctant to accept the offer of a test. Our recruitment strategy may offer insights into how STI testing can be promoted to first time testers in community settings. Moreover, the subgroup analyses indicate that the intervention is effective irrespective of mode of recruitment (face-to-face or online).

The effect of the intervention is time-dependent. There was a reduction in time-to-test at time horizons of 42 days but not at 14 and 7 days. While most participants in the intervention arm ordered the kits almost immediately after randomisation (median time <1 day), they delayed in returning the kits to the laboratory to be processed (median time from kit order to kit return = 9 days). SH:24 sent reminder text messages at 2 weeks to all non-returners. Future iterations of e-STI testing services could reduce delays on the care pathway, by sending earlier and more frequent reminders.

The barriers to seeking sexual health care are multifaceted and operate at individual, structural and societal levels (Deblonde et al. 2010; Oliver de Visser & O'Neill 2013). Over half (~55%) of the intervention group did not complete a test, which suggests that e-health services do not circumvent all obstacles associated with face-to-face care. Indeed, psychological barriers such a fear of a positive diagnosis are likely to persist. Further research is needed to understand the precise mechanism of change among this subpopulation and why some non-attenders of face-to-face services declined the offer to test via an alternative testing pathway. Moreover, both the recognition of candidacy and the subsequent navigation of clinical pathways may vary between populations with and without a prior history of STI testing.

6.5.5 Conclusions

Sexual health services in the UK are currently being reconfigured to include e-STI testing with a view to saving costs for routine asymptomatic testing and increasing access among hard-to-reach groups. This study has demonstrated that e-STI testing can increase testing uptake and reduce time-to-test among those who have never tested, when delivered alongside usual care.

The findings lend weight to national policies in the UK, which promote e-STI testing as a measure to expand access to opportunistic testing for HIV and chlamydia. e-STI testing

services can be delivered to scale as demonstrated by SH:24 and national programmes such as test.hiv (HIV) and freetest.me (chlamydia).

e-STI testing requires ongoing monitoring and evaluation. Larger studies are needed to assess outcomes later in the cascade of care such as STI diagnoses, cases treated and adherence to antiretroviral therapy for those diagnosed with HIV.

6.6 Chapter summary

I discussed the results of the main trial analyses in chapter 5 and in this chapter, I presented a secondary analysis, which examined the effect of STI testing on a subsample of participants who had not tested for STIs prior to their enrolment in the study. In the following chapter, I present my discussion for the whole thesis. I situate the findings from both the primary and secondary analyses within my theoretical framework and I outline the implications for public health policy in the UK. I end the chapter by outlining an agenda for further research in this area.

Chapter 7: Discussion

7.1 Summary of findings

When e-STI testing is promoted in community settings and delivered alongside usual care, it almost doubles uptake of STI testing. The intervention increased STI testing in all groups including those at high risk for STIs. The trial lacked power for the analyses of STI diagnoses and STI cases treated, but these estimates were of the expected magnitude and in the expected direction. The effect of the intervention was time-dependent. The intervention reduced time-to-test but not time-to-treatment.

Secondary analyses of the RCT data examined the effect of the intervention among a subsample of trial participants who reported never testing for STIs at baseline. The intervention increased uptake of testing among this subsample. Similar estimates were observed for both uptake of chlamydia and gonorrhoea testing, and uptake of HIV testing. The intervention reduced time-to-test. As in the main trial analyses, no heterogeneity was observed in the subgroup analyses.

7.2 Meaning and mechanisms

The main trial results are consistent with the causal pathway stipulated in the original funding proposal and the theory of change, which proposed that introducing e-STI testing within a complex service delivery system would increase access to, and subsequently utilisation of, STI testing services. It was hypothesised that this would result in an increased proportion of STI cases diagnosed and treated in the population. Whilst the results are consistent with this hypothesis, the precise effects remain uncertain.

Increased access to STI testing is a key intermediary outcome on this hypothesised causal pathway. I utilised the candidacy lens to understand the construct of 'access' within a sexual health service delivery system. Rather than viewing access as a one-off event, the candidacy framework emphasises the processual nature of health service utilisation - one that is underpinned by continual interaction and negotiation between patients (or users) and health professionals. Arguably this processual framing of access is particularly applicable in this current context, given that clinical care pathways traverse both online and face-to-face environments. This necessitates that users negotiate and renegotiate both environments in their care-seeking for STIs.

In my theoretical framework, I drew on a critical realist perspective to theorise how SH:24 would lead to changes in STI testing behaviours. In line with the stratified ontology of critical realism (Bhaskar 2008), causal mechanisms are conceived as 'latent powers and capabilities' rather than tangible intervention inputs or activities. These latent powers are considered 'a function of the interaction between intervention resources and responses of participants' (Van Belle et al. 2016, p.3).

In considering the possible causal mechanisms underpinning SH:24, I proposed that both the awareness and availability of the intervention would trigger increased recognition of candidacy. Recognition of candidacy is the process through which individuals identify that they have a legitimate claim to health services, prompting health-seeking actions. I posited that this increased recognition of candidacy would occur, as e-STI testing pathways would be perceived to be better aligned with the population's health-seeking preferences. Given that these preferences are patterned by demographic and psychosocial factors, the way in which intervention components triggered recognition of candidacy is likely to have varied across individuals and groups of individuals.

Almost a quarter of the control arm in the main trial analyses, accepted the offer to complete an STI test. This suggests that additional mechanisms were at play in this context. The health promotion message which accompanied the offer to enrol in the trial may have influenced perceived need for STI testing among participants in both groups (and hence their identification of candidacy). The cash incentive may also have triggered a response in both arms. Understanding the role of health promotion in decisions to seek an STI test is of public health importance, particularly among those who reported never testing for STIs prior to the study. However, it may also be the case, that for some participants, their decision to test and their subsequent choice of service, were influenced by mechanisms that are not associated with the study nor the intervention.

It was beyond the scope of the thesis to test and explore the causal processes underlying the intervention. Nevertheless my conceptual model provides an explanatory framework within which to situate the evaluation findings. In line with realist evaluative approaches, I outlined several contextual contingencies that may influence the effectiveness of the intervention, and the way intervention mechanisms may operate. In the following section, I discuss each of these contingencies in light of the evaluation findings.

7.3 Contextual contingencies

SH:24 aims to provide seamless pathways between online and face-to-face services. I proposed that the navigation of online pathways was contingent on the integration of these two service environments, and whether care pathways would be acceptable to participants. The main trial findings suggest that in some cases, adjudications on the continued candidacy of participants were resisted. A higher proportion of those diagnosed in the intervention arm declined the treatment pathway that was offered at the point of diagnosis, compared to the control arm. Whilst it is not known if these participants sought treatment elsewhere, participants' resistance to these referral pathways may indicate that these care options were not aligned with their health-seeking preferences.

Macdonald and colleagues (Macdonald et al. 2016) describe the point of diagnosis as a 'critical juncture' in the navigation of services. They distinguish between negotiations of candidacy pre and post diagnosis, as they found that post-diagnostic negotiation is greatly influenced by the social significance of the illness in question. The stigma attached to STI diagnoses may introduce new barriers in the continued navigation of services. In the trial, these barriers may have been compounded by the requirement to obtain treatment in face-to-face settings, which necessitated the negotiation of a new service environment. These findings suggested that additional inputs may be required to ensure that a higher proportion of cases diagnosed via e-STI testing are subsequently treated.

The service delivery system for sexual health in Lambeth and Southwark has changed substantially since completing the trial. Due to local authority cuts in sexual health funding, three sexual health clinics in Lambeth and Southwark were closed in 2017; and STI testing in existing services is subject to new restrictions and protocols. Individuals who attend GUM clinics are triaged and those without symptoms are supported by a health worker to use SH:24 (Turner et al. 2018). At the same time, SH:24 has been forced to implement a daily cap on the number of orders in Lambeth and Southwark, in order to ensure they do not surpass their commissioning agreement.

This presents a new and challenging funding and service environment. The RCT findings showed that when delivered alongside usual care, e-STI testing increased uptake of testing, and this increased utilisation may incur a modest public health benefit, with respect to cases diagnosed and treated. Yet it is possible that changing local conditions could threaten the potential benefits of e-STI testing. Those seeking STI testing in clinic settings

need to do more to demonstrate their qualification for candidacy (i.e. demonstrate STI symptoms). In the trial, 50 participants allocated to the intervention, declined the offer to test in SH:24 and chose to use a clinic service, yielding 11 of the 19 diagnoses in the intervention arm. This suggests that choice, and ease of navigation between face-to-face and online care pathways, may have contributed to the effects observed. Given the new qualifications to service use, it is unclear whether in this new funding environment, the potential benefits of e-STI testing will be fully realised.

7.4 Policy implications

The findings lend weight to national policies in the UK, which promote e-STI testing as a measure to expand access to HIV testing. It is particularly encouraging that the intervention increased uptake of HIV testing among those who had never previously tested. Nationally, provider adherence to guidelines for routine HIV testing outwith of specialist settings is variable (Elmahdi et al. 2014). Our findings suggest that e-STI testing is a viable option for expanding and normalising HIV testing outside of GUM settings, in areas of high HIV prevalence.

The similar effect observed for uptake of chlamydia testing among never testers, suggests that e-STI testing can reach young people who have yet to be screened for chlamydia in face-to-face services. e-STI testing is recommended by the National Chlamydia Screening Programme to expand access to opportunistic screening. However in routine settings, uptake of this testing modality is low, relative to GP and other specialist services - only 8% of all chlamydia tests were carried out via internet-accessed pathways in 2016.

The findings may have implications for the way e-STI testing is promoted to increase chlamydia screening. In the trial, intervention participants were made aware of the SH:24 service via text message. In routine settings, young people may lack awareness of STI testing modalities on offer. Further, SH:24 is based on a user-led design and it is subject to continuous testing and optimisation. Commissioned e-STI testing services may vary in quality, not only in terms of specific service components, but also with respect to the design and functionality of the websites.

e-STI testing is increasingly viewed by sexual health commissioners as one measure to meet increasing demand for STI testing in a context of severe budget cuts (Robertson et al. 2017). SH:24 was trialled in a community setting and in two boroughs that were well–served by face-to-face clinical services. Providing e- STI testing in contexts where supply is more

limited, or targeting particular high risk groups might strengthen the contribution of e- STI testing to the control and management of STIs. In the trial, STI positivity in the intervention arm was lower than in routine GP and clinic settings in Lambeth and Southwark. Observational studies have also found that users of SH:24 continue have lower STI positivity than GUM patients (Turner et al. 2018). An observational study has examined the cost-effectiveness of SH:24, and will account for this lower positivity. Publication of this study is pending and may provide additional insights on the contribution of e-STI testing.

e-STI testing does not circumvent all barriers to STI testing. Almost 56% (119/213) of participants allocated to the intervention, who had never previously tested, did not accept the offer the test in an e-STI testing service; of whom 83% (99/119) were aged 16-24 years of age and 45% (53/119) had changed partners in the last year. Exploration of persistent barriers to STI testing is warranted.

Since implementing the trial, pathways to care are increasingly adjudicated by health professionals, who have been assigned new gate-keeping roles in this current funding environment. The adjudication of candidacy to specific care pathways appears to be based on a biomedical model (i.e. presence of symptoms), rather than patients' own assessment of need. This development may compromise opportunities for patient empowerment and patient-centred care within sexual health. Moreover, national standards for STI testing precede these current funding challenges (British Association for Sexual Health and HIV & Medical Foundation for HIV & Sexual Health 2014). It may be important to question whether new gate-keeping roles, and restrictions on patient choice, serve to undermine quality standards.

7.5 Limitations and challenges

It was not feasible to continue recruiting beyond August 2015 as SH:24 began to expand their marketing strategy in line with their funding agreement, and the risk of contamination was too high. Furthermore, once launched, SH:24 was keen to increase the functionality of the website and adapt the service, in line with their test-build-learn philosophy. We therefore did not recruit to target and we were underpowered for the analyses of STI diagnoses and cases treated.

The effectiveness of interventions in research contexts may differ from their effectiveness when implemented in routine settings. It is probable that trial participants were more motivated to complete an STI test than individuals in routine settings. While we succeeded

in recruiting participants with a range of socio-demographic characteristics and testing histories, we struggled to recruit high numbers of participants from non-white ethnic backgrounds. No heterogeneity was observed for the effect of SH:24 on testing uptake across the ethnicity subgroup. However, the trial was not specifically powered for these analyses, and therefore these findings are not conclusive. Observational data has shown that a lower proportion of SH:24 users are from minority black ethnic backgrounds compared to attendees of GUM clinics (Barnard et al. 2018; Turner et al. 2018). Given the rapid and extensive changes to the commissioning and service delivery environment, it will be important to monitor utilisation patterns across different subgroups, and to understand persistent and changing barriers to care.

The precise mechanism or mechanisms triggered by SH:24 in this complex service delivery system remain unexplored. As a result, the 'core functions' of the intervention (Hawe 2015), which may facilitate replication in different social settings, are not known. Nevertheless my explanatory framework for the intervention can provide a platform for future research. I discuss directions for future research below in section 7.7.

7.6 Reflections

There is some debate on the benefits of minimisation as a method of allocation in RCTs (Scott et al. 2002; Proschan, Brittain & Kammerman 2011; Berger 2011). Minimisation can ensure that treatment arms are balanced with respect to known prognostic factors and can be advantageous in small trials (Altman & Bland 2005). However, in larger trials, simple randomisation may be preferable followed by adjustment for chance imbalances. Unmeasured characteristics are more likely to be balanced via simple randomisation than via minimisation; and the benefits of minimisation can be negated given that an adjusted analysis is required to account for correlation in data between treatment groups (Morris 2012).

Clinical trials often fail to recruit ethnically diverse samples and this study was no exception. If I were to repeat the trial and this PhD, I would spend more time fostering relationships with further education colleges in Lambeth and Southwark, as a high proportion of students at these institutions are from BME backgrounds.

With more time and resources, I would have designed and implemented a mixed method study for this PhD. This would include formative work to develop hypotheses on how the offer and availability of e-STI testing triggers increased recognition of candidacy and how

this process might vary among according to individuals' socio-demographic characteristics, risk profiles, and STI testing histories. I would then have tested these propositions empirically via qualitative investigation with trial participants. Such investigation may have illuminated the causal mechanisms of the intervention, adding richness to the RCT findings while also facilitating replication of the intervention to other social settings.

7.7 Future research

A larger trial is required to understand the effects of e-STI testing on outcomes later in the cascade of care including STI cases diagnosed, treated, cured and managed in community settings. There were no HIV diagnoses in the trial. Further research is needed to establish if those diagnosed with HIV via e-STI testing pathways seek timely treatment.

It has been beyond the scope of this thesis to generate additional data to investigate the causal processes underlying the intervention. Further research is required to understand how candidacy is recognised and negotiated in a digital service environment by different risk groups and in varied contexts. This should include formative qualitative investigation to develop hypotheses that can be tested empirically. Arguably however, there is a need to explore candidacy with respect to both *online* and *face-to-face* entry points to STI care pathways, particularly in light of recent funding cuts. In the study context of Lambeth and Southwark, individuals who are asymptomatic and who attend face-to-face clinical services for STI testing, are now triaged in clinic and channelled towards SH:24. The impact of these new protocols on the ability of patients to assert their claims to candidacy, and the ensuing implications for equity in sexual health care, warrant investigation.

A recent observational study found that between July and September 2016, almost a third of attendees of the Camberwell sexual health centre in South London who were triaged and signposted to SH:24 did not complete a test and it is not known if they sought care elsewhere (Turner et al. 2018). As highlighted in the original theory of change, a key concern is to understand what opportunities may be lost by shifting patterns of service use, and the reduction of face-to-face interaction with health professionals (Baraitser et al. 2015).

Longitudinal research can generate insights into the dynamic and adaptive features of the STI testing service delivery system. The introduction e-STI testing may lead to changes in patient-provider relations across the entire system, as the clinical encounter for STI testing is transferred into a digital space, characterised by remote interaction between patients

and professionals. Moreover, as STI testing becomes a habitual activity, and one that increasingly takes place in domestic rather than clinical spaces, this may in turn may have implications for the social significance of STI testing.

This thesis examined the effect of a specific model of e-STI testing that provided postal self-sampling test kits for chlamydia, gonorrhoea, HIV, and syphilis, results delivered via text message or telephone, and web-based safer sex health information. Other models of e-STI testing are being piloted both in the UK and internationally, and are subject to evaluative work (Spielberg et al. 2014; Estcourt et al. 2017). These investigations may generate additional insights on the contribution of e-STI testing to population health. e-STI testing services should be subject to ongoing monitoring and evaluation, particularly as services develop and adapt.

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Appendices

Appendix 1. **Evidence of copyright retention**

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RESEARCH ARTICLE

Internet-accessed sexually transmitted infection (e-STI) testing and results service: A randomised, single-blind, controlled trial

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Abstract

Background

Internet-accessed sexually transmitted infection testing (e-STI testing) is increasingly available as an alternative to testing in clinics. Typically this testing modality enables users to order a test kit from a virtual service (via a website or app), collect their own samples, return test samples to a laboratory, and be notified of their results by short message service (SMS) or telephone. e-STI testing is assumed to increase access to testing in comparison with face-to-face services, but the evidence is unclear. We conducted a randomised controlled trial to assess the effectiveness of an e-STI testing and results service (chlamydia, gonorrhoea, HIV, and syphilis) on STI testing uptake and STI cases diagnosed.

Methods and findings

The study took place in the London boroughs of Lambeth and Southwark. Between 24 November 2014 and 31 August 2015, we recruited 2,072 participants, aged 16–30 years, who were resident in these boroughs, had at least 1 sexual partner in the last 12 months, stated willingness to take an STI test, and had access to the internet. Those unable to provide consent and unable to read English were excluded. Participants were randomly allocated to receive 1 text message with the web link of an e-STI testing and results service (intervention group) or to receive 1 text message with the web link of a bespoke website listing the locations, contact details, and websites of 7 local sexual health clinics (control group). Participants were free to use any other services or interventions during the study period. The primary outcomes were self-reported STI testing at 6 weeks, verified by patient record checks, and self-reported STI diagnosis at 6 weeks, verified by patient record checks. Secondary outcomes were the proportion of participants prescribed treatment for

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Abbreviations

HIV: human immunodeficiency virus
ITT: intention-to-treat
MAR: missing at random
MSM: men who have sex with men
NCSP: National Chlamydia Screening Programme
OR: odds ratio
RMST: restricted-mean survival time
SMS: short message service
STI: sexually transmitted infection
TDL: The Doctors Laboratory

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Appendix 2. **Ethical Approval**

NHS
Health Research Authority

NRES Committee London - Camberwell St Giles
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Telephone: 0117 3421391

09 September 2014

]Dr Paula Baraitser
Weston Education Centre, Kings College London
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Denmark Hill
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Dear Dr Baraitser

Study title:	**Can internet-based sexual health services increase diagnoses of sexually transmitted infections compared to face-to-face services? Evaluation of an internet-based sexual health service in Lambeth and Southwark.**
REC reference:	**14/LO/1477**
IRAS project ID:	**159386**

Thank you for your letter of 1st September 2014, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information was considered in correspondence by a Sub-Committee of the REC on 9th September 2014 A list of the Sub-Committee members is attached.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Assistant, Miss Elizabeth Hearn, nrescommittee.london-camberwellstgiles@nhs.net.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

The Committee has not yet completed any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. We will write to you again as soon as an SSA application(s) has been reviewed. In the meantime no study procedures should be initiated at non-NHS sites.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Copies of advertisement materials for research participants [Study web advert]	v3	01 September 2014
Copies of advertisement materials for research participants [Study poster advert]	v3	01 September 2014
Covering letter on headed paper [Cover letter]	1	29 July 2014
Interview schedules or topic guides for participants [Follow Up questionnaire]	v5	01 September 2014
Interview schedules or topic guides for participants [Baseline questionnaire]	v5	01 September 2014
IRAS Checklist XML [Checklist_29072014]		29 July 2014
Letters of invitation to participant [Follow up letter]	v4	01 September 2014
Participant consent form [MvP1 consent]	v4	01 September 2014
Participant information sheet (PIS) [MvP1 PIS]	v6	01 September 2014
REC Application Form [REC_Form_29072014]		29 July 2014
Referee's report or other scientific critique report [Evaluation Steering Group Approval]	v1	23 July 2014
Research protocol or project proposal [Research protocol]	v5	24 July 2014
Summary CV for Chief Investigator (CI) [CI CV July 2014]	v1	22 July 2014
Summary CV for student [Student CV July 2014]	v1	22 July 2014
Summary CV for supervisor (student research) [Supervisor CV July 2014]	v1	22 July 2014

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at
http://www.hra.nhs.uk/hra-training/

14/LO/1477	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

[redacted]

Mr John Richardson
Chair

Email:nrescommittee.london-camberwellstgiles@nhs.net

Enclosures: *List of names and professions of members who were present at the meeting and those who submitted written comments* "After ethical review – guidance for researchers"

Copy to: *The Research Office*
Dr. Zoe Harris, King's College Hospital NHS Foundation Trust

NRES Committee London - Camberwell St Giles

Attendance at Sub-Committee of the REC meeting on 09 September 2014

Committee Members:

Name	*Profession*	*Present*
Ms Sally Gordon Boyd	Medical Ethicist	Yes
Mr John Richardson (Chair)	Retired Director of COREC; Ecumenical Officer for Churches Together in South London	Yes

Also in attendance:

Name	*Position (or reason for attending)*
Miss Elizabeth Hearn	REC Assistant

Appendix 3. **Participant Consent Form**

King's College Hospital NHS
NHS Foundation Trust

KING'S College LONDON

Participant Identification Number for this trial:

CONSENT FORM

Title of Project: Evaluation of sexual health services in Lambeth and Southwark.

Principal Investigator: Dr Paula Baraitser
Please read the following 6 statements carefully and tick all boxes

1. I confirm that I have read and understood the information sheet [version 9, 17.02.15] for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary (my choice) and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that all information I provide will remain confidential in accordance with the Data Protection Act of 1998 and will only be used for the purposes of the study. Only the research team directly involved with the study will have access to this information. ☐
4. I understand that relevant sections of data collected during the study, may be looked at by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
5. I agree to the sexual health services participating in the study to provide the research team with details of any tests for sexually transmitted infections (STIs) and treatment undertaken during my involvement in the study. ☐
6. I agree to take part in the above study. ☐

The following two statements are **optional**. Please tick yes or no. If you answer no, you can still take part in the study.

7. I agree to the sexual health services participating in this study providing the research team with details of my use of sexual health services for a period of five years. Yes ☐ No ☐
8. I agree to the research team contacting me periodically to verify my contact details for a period of five years Yes ☐ No ☐

Name of participant	Signature	Date
Name of person taking consent	Signature	Date

If you need more information to help you decide, please contact:

Emma Wilson (Study Coordinator)
Email: emma.wilson@lshtm.ac.uk, **Tel:** 07425083297

MvP1 Consent v5 17.02.15

Appendix 4. **Baseline questionnaire**

MvP1 Baseline v7 09.12.14

(None of the information you give to us will be shared with anyone outside our team)

Your contact details **Participant ID**

1. First name
2. Surname

We will be contacting you again 6 weeks from now

3. Main mobile phone number
4. Main email address

Main postal address:

5. House or flat number — House or flat number
6. Address line 1 — Address line 1
7. Address line 2 — Address line 2
8. City — City
9. County — County
10. Postcode — Postcode

Sexual health

11. When was the last time you had a test for a sexually transmitted infection (STI)?

In the last 3 months	3-6 months	6 -12 months	More than 1 year ago	Never

12. Where did you take your last STI test?

Sexual Health Clinic	GP	Hospital	Pharmacy	Ordered test on internet

Other (Please specify)	I have never been tested

13. How many people have you had sex with in the last 12 months?

1	2	3	4	5	6	7	8	9	10+

Please Turn Over

About you

14. Date of birth:

DD	MM	YYYY

15. Gender:

Female	Male	Transgender

16. Are you:

Heterosexual (straight)	
Gay or Lesbian	
Bisexual	
Prefer not to say	

17. Choose one option that best describes your ethnic group or background (please tick)

White	
English/ Welsh/ Scottish/ Northern Irish/ British	
Irish	
Gypsy traveller or Irish traveller	
Any other white background	
Mixed/ Multiple ethnic group	
White and Black Caribbean	
White and Black African	
White and Asian	
Any other Mixed/ Multiple Ethnic Background	
Asian/ Asian British	
Indian	
Pakistani	
Bangladeshi	
Chinese	
Any other Asian background	
Black/ African/ Caribbean/ Black British	
African	
Caribbean	
Any other Black/ African/ Caribbean background	
Other ethnic group	
Arab	
Any other ethnic group	

Appendix 5. **Follow up form**

Follow up questionnaire MvP1 v7b SH24 10.02.15

Evaluation of sexual health services in Lambeth and Southwark

Participant ID ☐

SECTION ONE: Testing and treatment for Sexually Transmitted Infections (STIs)

1.1. Have you taken any STI tests, either at home or in a health care setting (e.g. clinic, GP surgery, pharmacy) since signing up to the study?

Yes ○
No ○ ⇨ ***go to section 3***

1.2. Where did you get your STI tests?

Sexual Health Clinic ○
GP surgery ○
Pharmacy ○
Ordered on the internet from SH:24 ○
Other [please specify] ○ _____

1.3. Which of the following tests have you taken since signing up to the study?

	Yes	No	
Chlamydia [urine/swab]	○	○	
Gonorrhoea [urine/ swab]	○	○	
Syphilis [blood]	○	○	
HIV [blood]	○	○	
Other [please specify]	○	○	_____

1.4. What were the results of the tests you took?

	Positive	Negative	Don't know
Chlamydia	○	○	○
Gonorrhoea	○	○	○
Syphilis	○	○	○
HIV	○	○	○

⇨ ***IF** all your results were negative, please go straight to **Section 2***

1.5. If you tested positive for chlamydia, gonorrhoea or syphilis, did you get treatment?

	Yes	No
Chlamydia	○	○
Gonorrhoea	○	○
Syphilis	○	○

Please turn over

1.6. Where did you get treated?

- Sexual Health Clinic ○
- GP surgery ○
- Pharmacy ○
- Other [please specify] ○ _____

SECTION TWO: Your experience of STI testing

2.1 Please think back to the first STI test that you took after signing up to the study, did you obtain this test from:

- Internet based service ○ (SH:24 or other)
- Face-to-face service ○ (e.g. clinic, GP, pharmacy)

2.2 Thinking about this service please rank the following statements:

2.2.1 *Did you feel that your personal information was kept confidential by this service?*

- ○ Yes
- ○ Yes to some extent
- ○ No

2.2.2 *Did you have trust in the clinical expertise of this service?*

- ○ Yes
- ○ Yes to some extent
- ○ No

2.2.3 *On a scale of 1 to 10, with 10 being the most positive, how would you rate the service?*

○	○	○	○	○	○	○	○	○	○
1	2	3	4	5	6	7	8	9	10

Negative ***Positive***

2.2.4 *Would you use this service again if you needed to?*

- ○ Yes, definitely
- ○ Yes, probably
- ○ No

2.2.5 *Would you recommend this service to a friend?*

- ○ Yes, definitely
- ○ Yes, probably
- ○ No

Please continue to Section 3

SECTION THREE: Your experience of using SH:24

3.1 Did you order a test from the SH:24 online service?

- ○ Yes ⇨ *go to question 3.3*
- ○ No

3.2 If No, why did you choose NOT to get a test [please tick all that apply]?

- No time ○
- Felt at low risk of sexually transmitted infections (STIs) ○
- Recently been tested ○
- Worried about the test results ○
- Did not want to provide sexual health information online ○
- Did not feel that my personal information would be kept confidential ○
- Did not trust the clinical expertise of this service ○
- Not enough privacy at home ○
- Difficulty accessing the internet ○
- Did not like the look and feel of the website ○
- It was not clear to me how to order a test online ○
- Would prefer to go to the clinic to get tested ○
- Did not want to use an internet testing service ○
- Other [please specify] _____ ○

⇨ *go to question 3.5*

3.3 Did you return the test kit in the post to SH:24?

- ○ Yes ⇨ *go to question 3.5*
- ○ No

3.4 If NO, why did you NOT return the test kit [please tick all that apply]?

- No time ○
- No longer wanted a test ○
- Did not want to take the samples myself ○
- Had difficulty taking the vaginal/urine/ rectal samples ○
- Had difficulty taking the blood sample ○
- Did not understand the instructions ○
- Not enough privacy at home ○
- Other [please specify] _____ ○

3.5 Did you feel you needed help to use the SH24 website?

- ○ Yes
- ○ No ⇨ *go to question 3.7*

Please turn over

3.6 If YES, what aspects of the service did you feel required extra support? [please tick all that apply]

- Making the decision to take an STI test ○
- Ordering a test online ○
- Taking the urine sample ○
- Taking vaginal/ rectal/ throat swabs ○
- Taking the blood sample ○
- Returning the test kits ○
- Understanding the text messages ○
- Other [please specify] _____ ○

3.7 Did you want to speak to a health care provider when you used the SH:24 website?

○ Yes
○ No ⇨ *go to question 3.9*

3.8 If YES, how would you like to communicate with a health care provider when using the SH:24 website? [please tick your most preferred option]

- Phone call ○
- SMS Text message ○
- Web Chat ○
- Email ○
- Other [please specify] _____ ○

3.9 In your opinion, how could we improve the experience of getting a test from an online sexual health service?

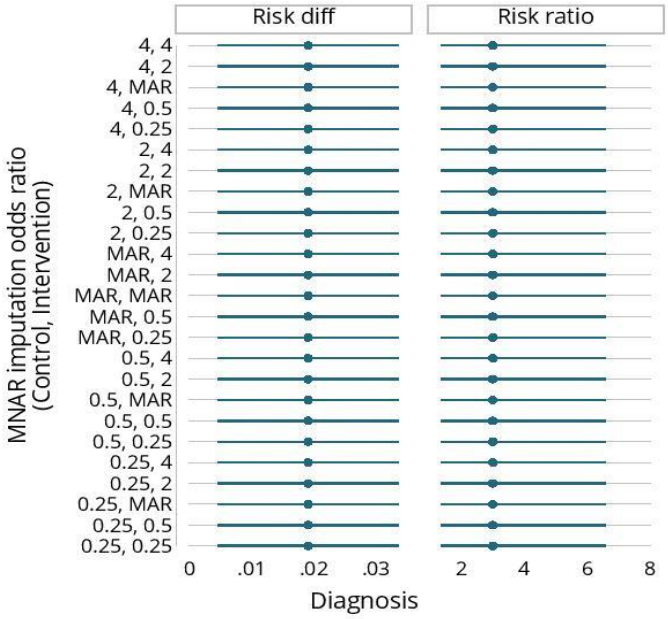
SECTION FOUR: Future studies

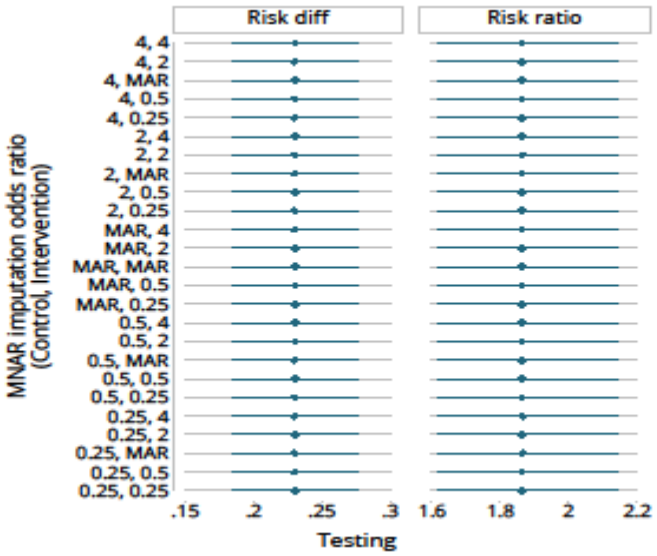
4.1 Can we contact you about participating in future studies with us?

○ Yes
○ No

Thank you very much for your feedback

Appendix 6. **Main trial - sensitivity analyses**





Appendix 7. **Complete case analyses – never testers**

Weighted complete case analyses – never testers

	Intervention	Control	Risk difference (95% CI)	Relative risk (95% CI)	P value
Any STI test	44.1% (94/213)	19.6% (44/224)	24.9% (16.7, 33.0)	2.26 (1.59, 2.93)	<0.0001
HIV	39.4% (84/213)	17.9% (40/224)	21.9% (13.9,29.9)	2.22 (1.51,2.92)	<0.0001
Chlamydia and Gonorrhoea	43.2% (92/213)	19.6% (44/224)	24.0% (15.9,32.1)	2.22(1.56, 2.88)	<0.0001