

Does screening for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* affect the incidence of these infections in MSM taking HIV-PrEP?

Results from a randomized, multicenter, controlled trial

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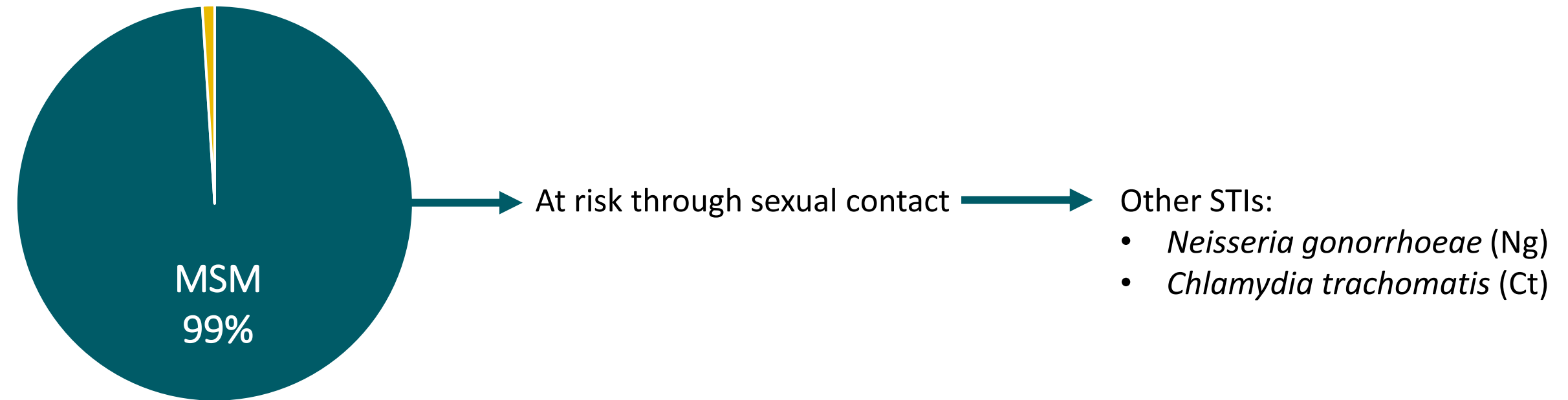
GONOSCREEN STUDY



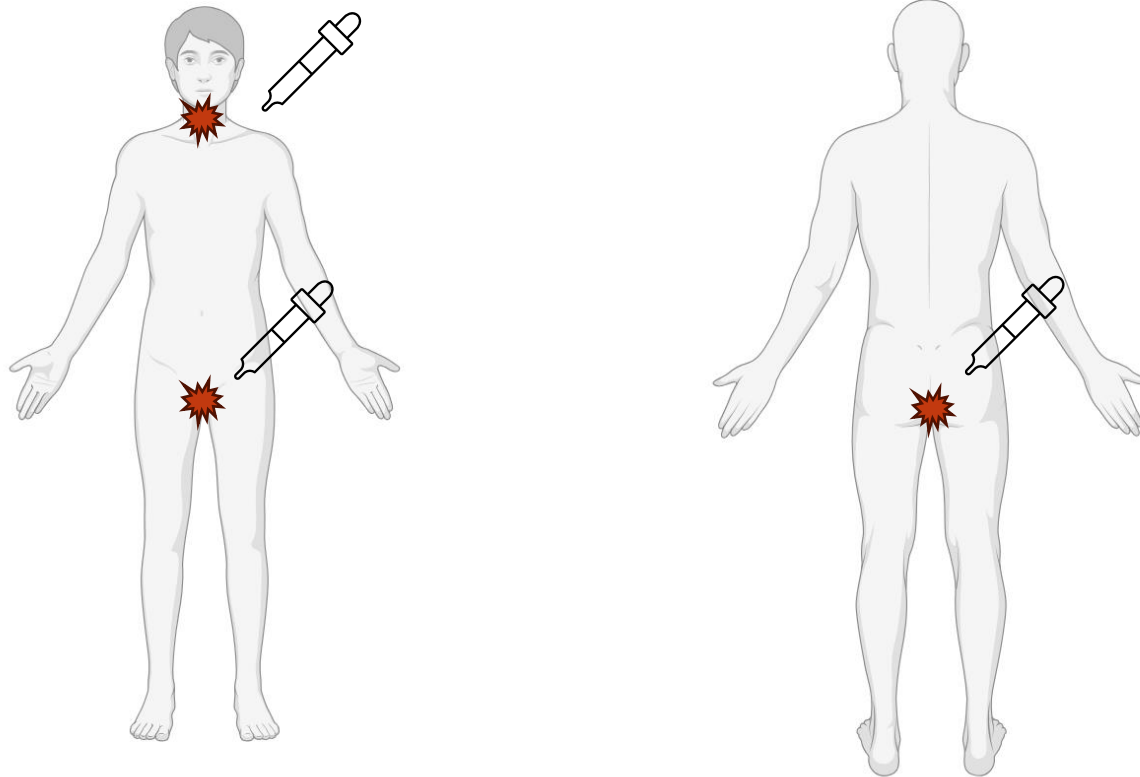
Conflict of interest: none declared

Background

- HIV pre-exposure prophylaxis (PrEP) is a preventive treatment for HIV, given to people at substantial risk for HIV



Background



Majority of Ng/Ct infections in MSM are:

- Extra-genital
- Asymptomatic
- Clear spontaneously

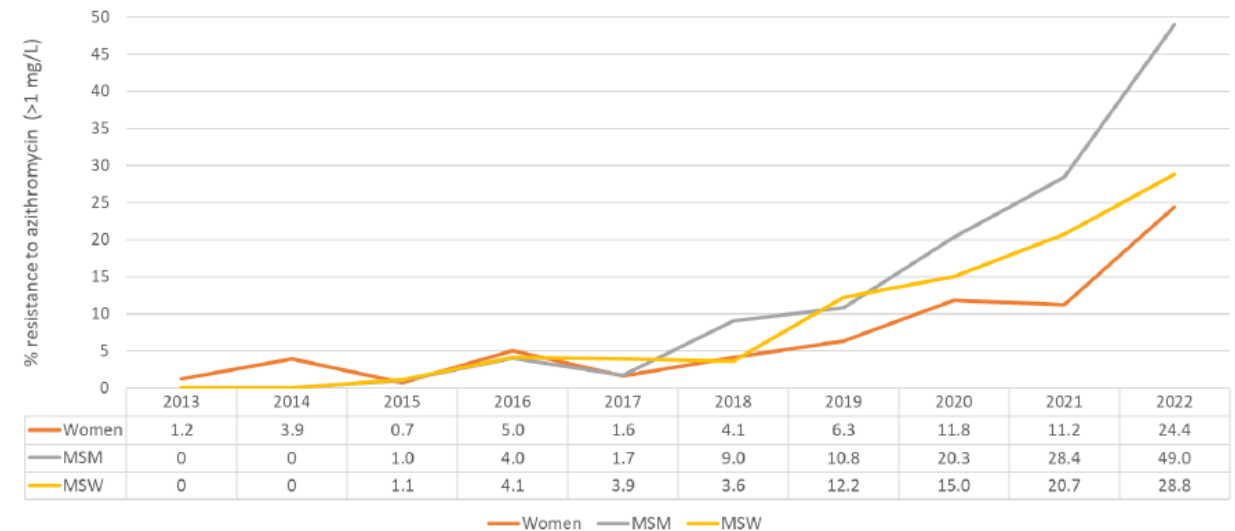
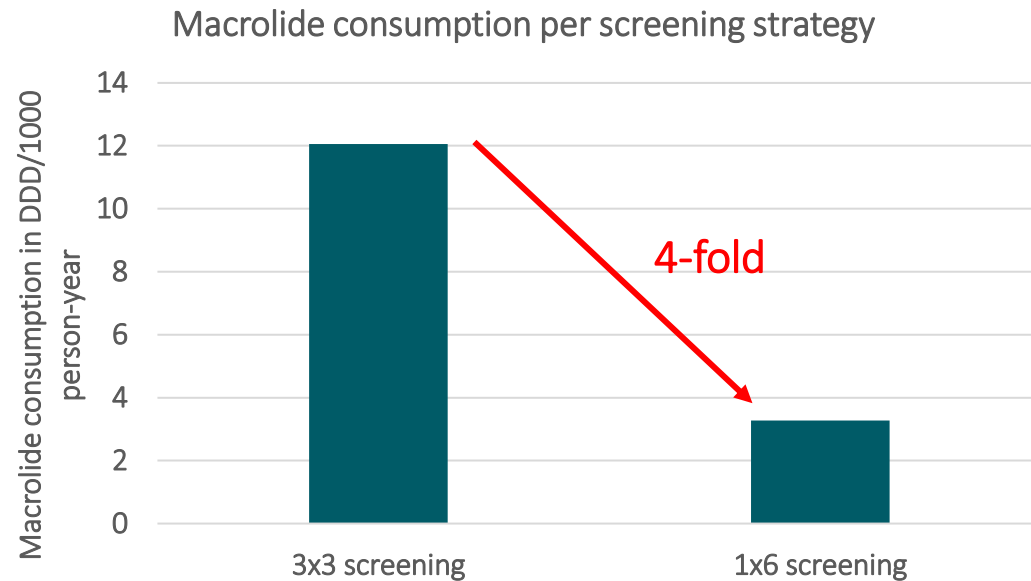
Most PrEP guidelines recommend 3-site, 3-monthly screening for Ng/Ct

The goal of such screening is to reduce transmission/incidence/prevalence, complications (very rare in MSM)

BUT no RCT had been performed to assess if screening for Ng/Ct is effective in reducing the incidence of these infections in MSM taking HIV-PrEP

Background

- AND screening for Ng/Ct leads to high antimicrobial consumption
- Which could in turn lead to the emergence of antimicrobial resistance



The Gonoscreen study

- **Study design:**

- Randomized, multicenter, controlled clinical trial of 3-site (oro-pharyngeal, ano-rectal, urethral), 3-monthly screening for Ng/Ct versus non-screening among MSM taking HIV-PrEP.



- **September 2020 – August 2022**

Study objectives

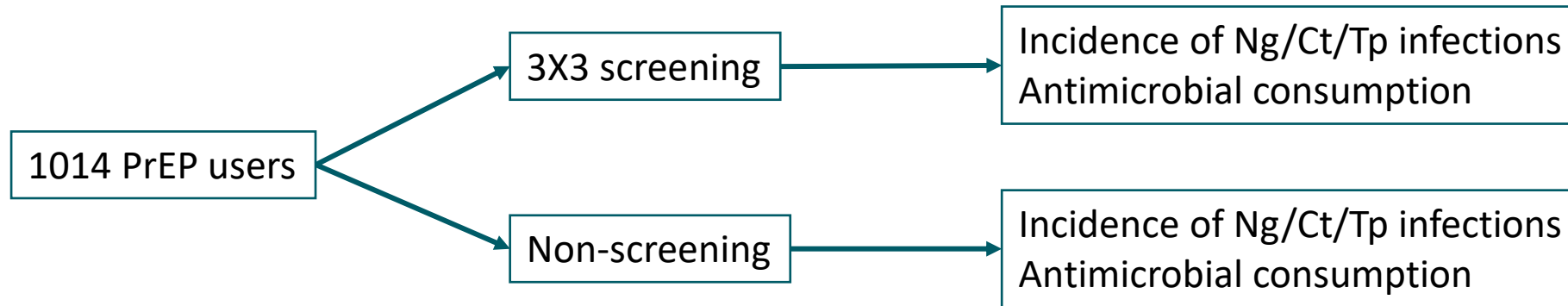
- **Primary objective**

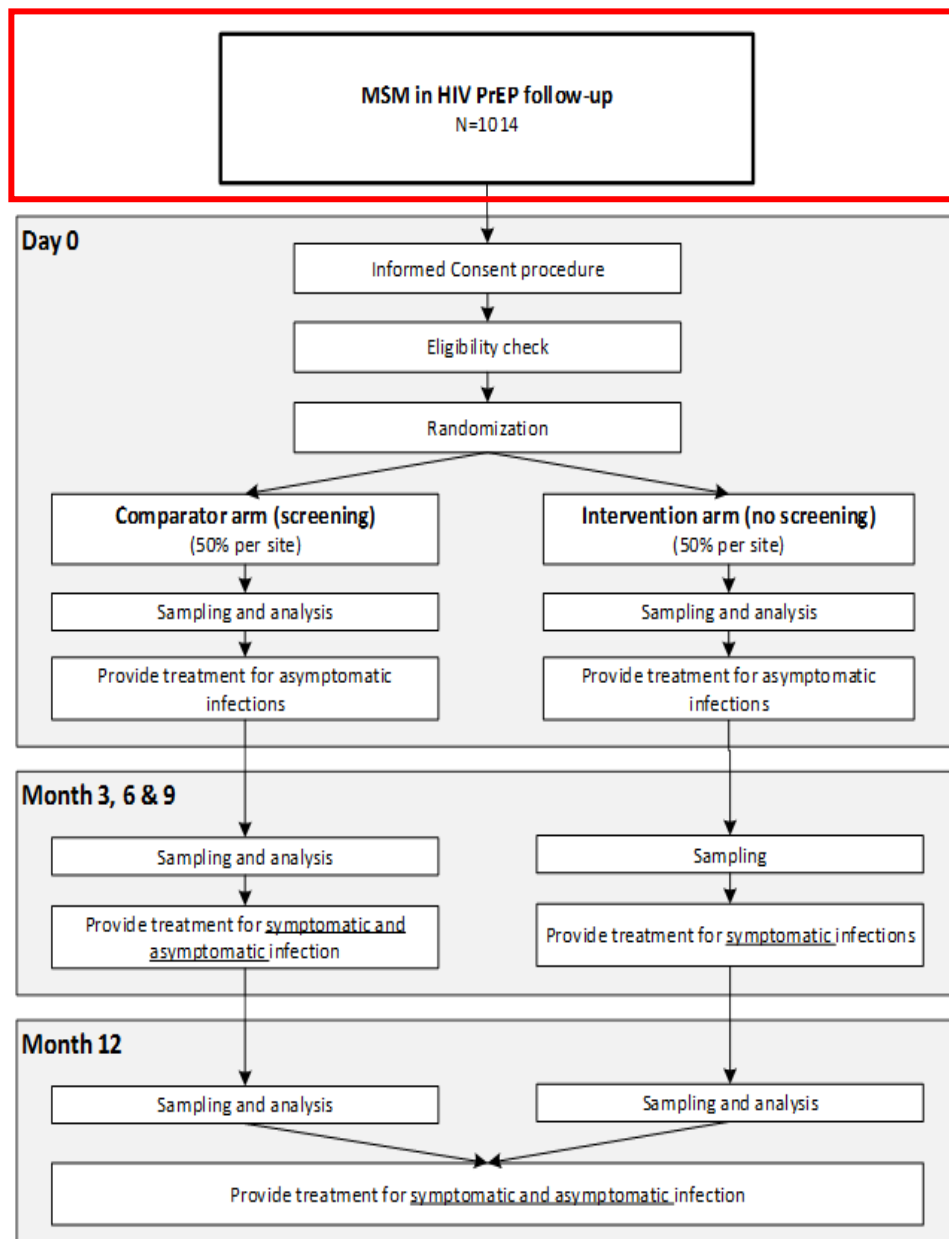
- To assess if **not** screening MSM on HIV-PrEP for Ng/Ct is non-inferior compared to screening in terms of the **incidence rate** of these infections over a 12-month period

- **Secondary objectives**

- To assess if not screening MSM on PrEP for Ng/Ct is non-inferior compared to screening in terms of the **incidence rate** of **symptomatic** Ng/Ct infections
- To assess **antimicrobial exposure** (ceftriaxone/azithromycin/doxycycline) in both arms
- Non-screening arm proven to be non-inferior if the upper limit of the 95% CI of the IRR (non-screening vs screening) lower than 1.25





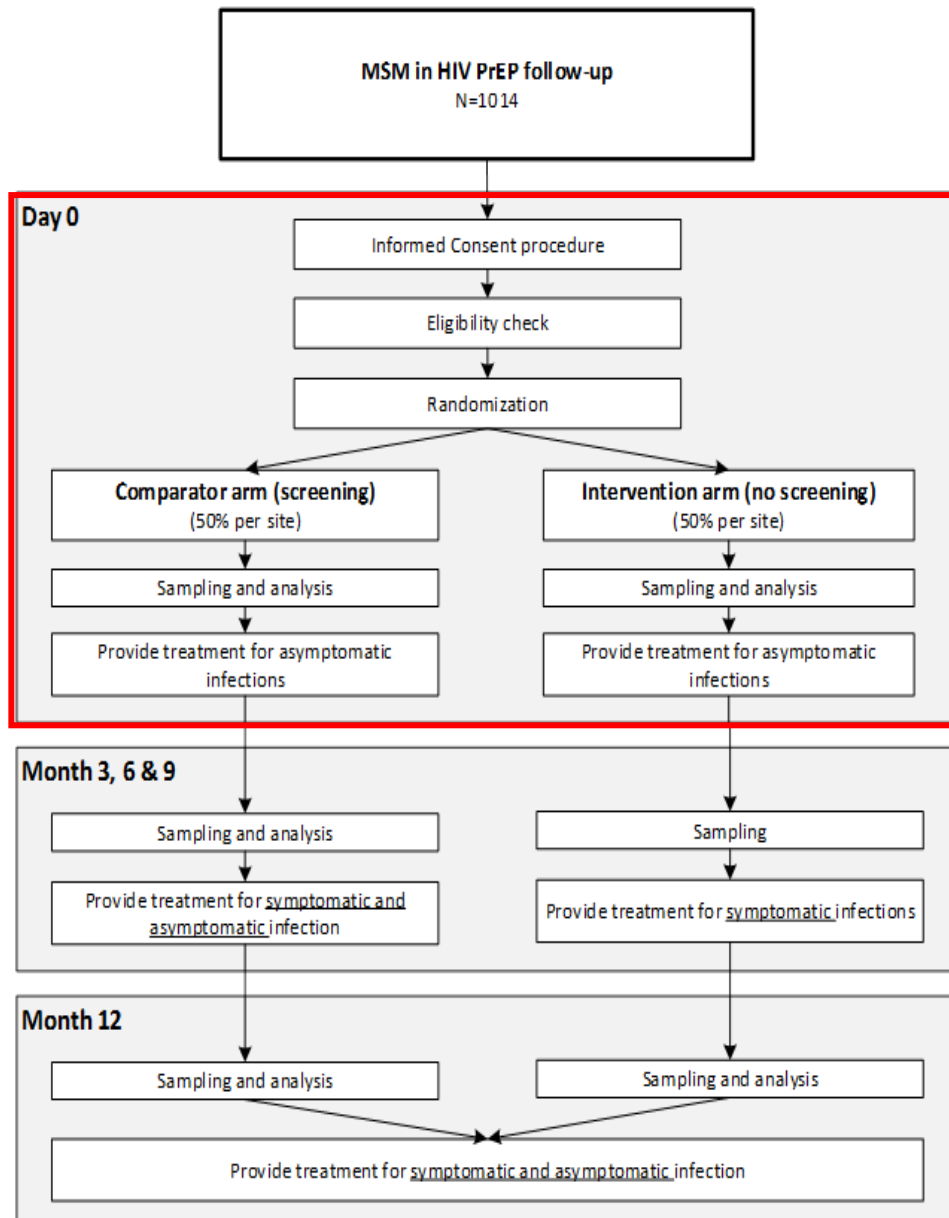


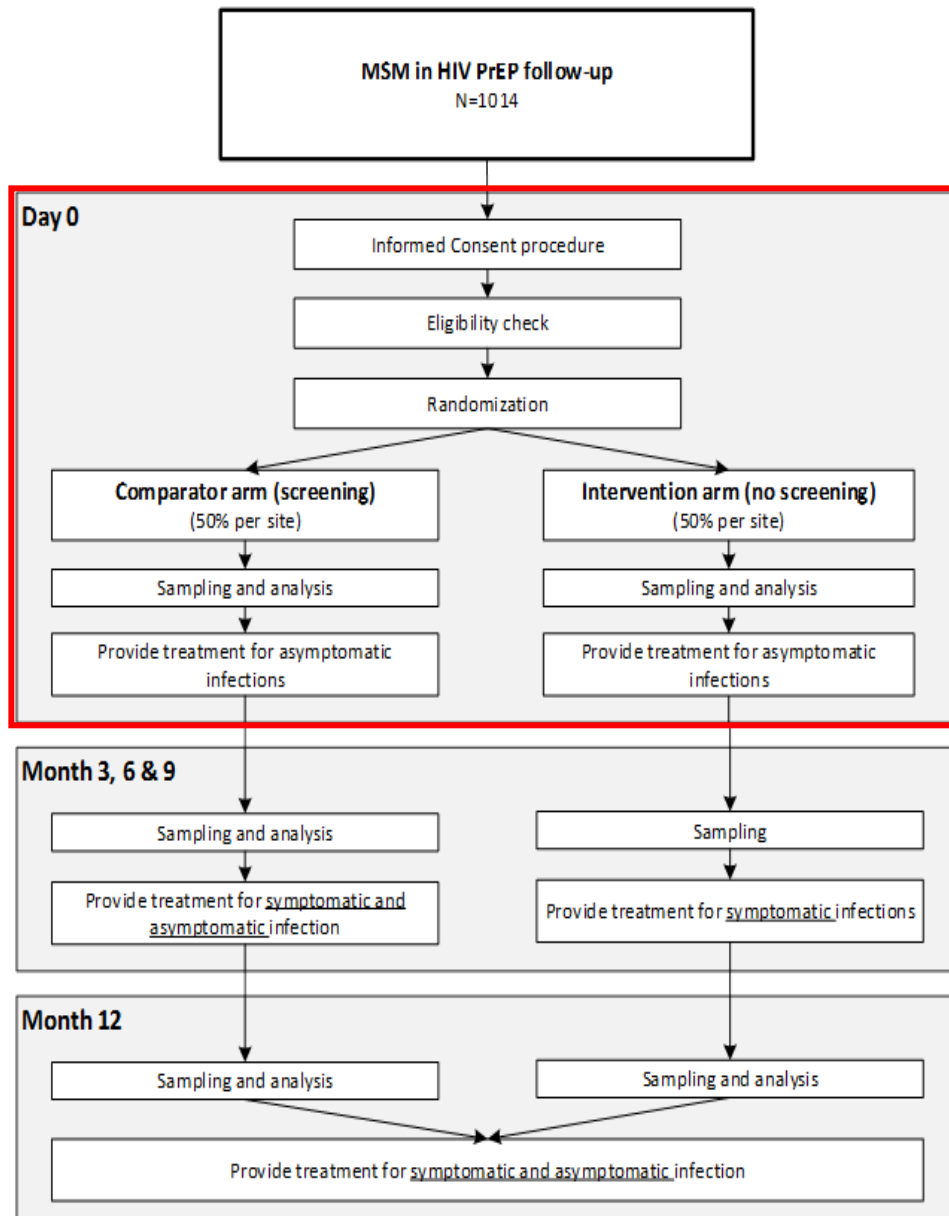
▪ **Inclusion criteria:**

- Able and willing to provide informed consent
- Men (born as males) and transwomen aged 18 or more
- Has had sex with another man in the last 12 months
- Enrolled in Belgian PrEP program
- Willing to comply with the study procedures

▪ **Exclusion criteria:**

- Enrolment in another interventional trial
- Tests HIV-positive at screening
- Symptoms of proctitis or urethritis



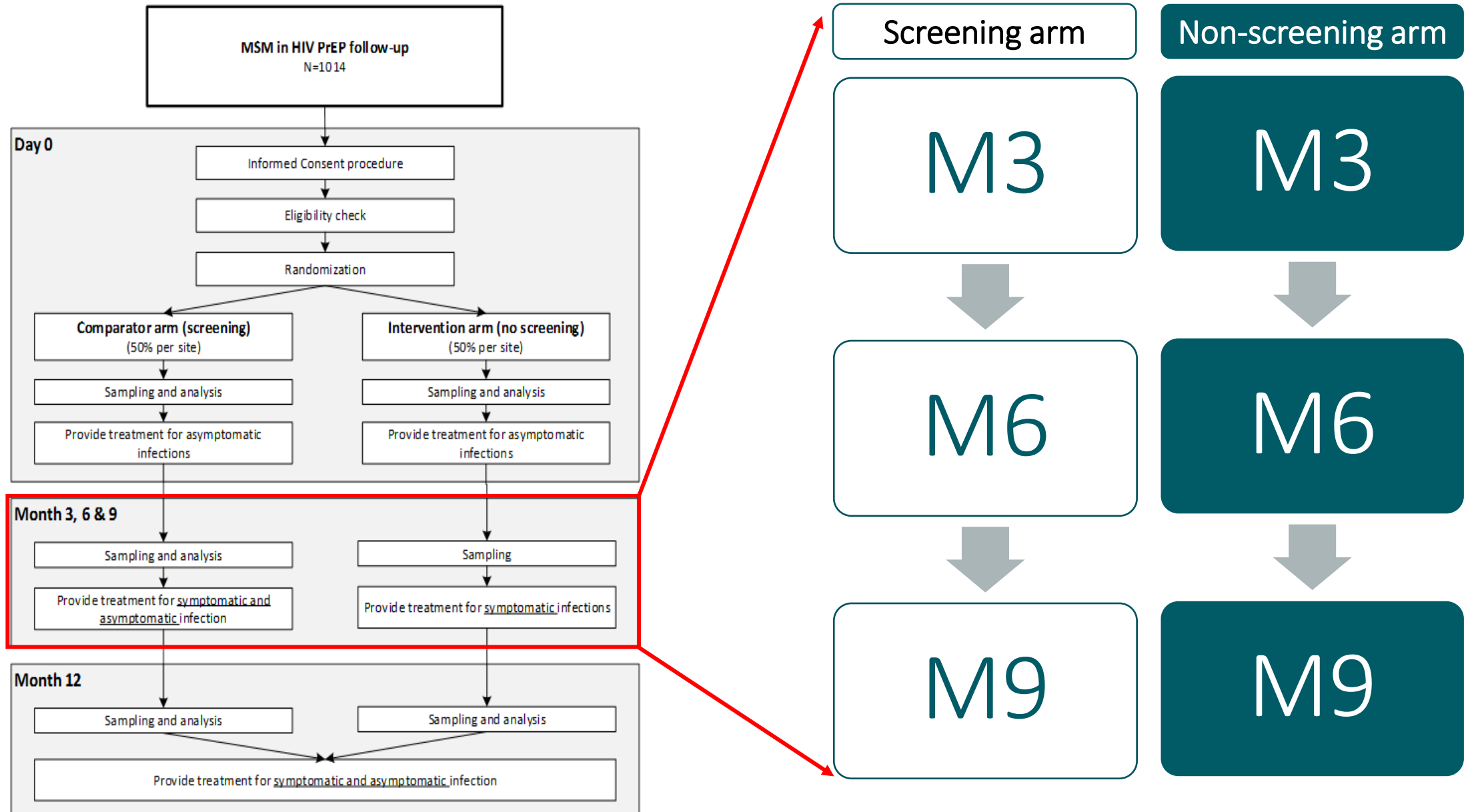


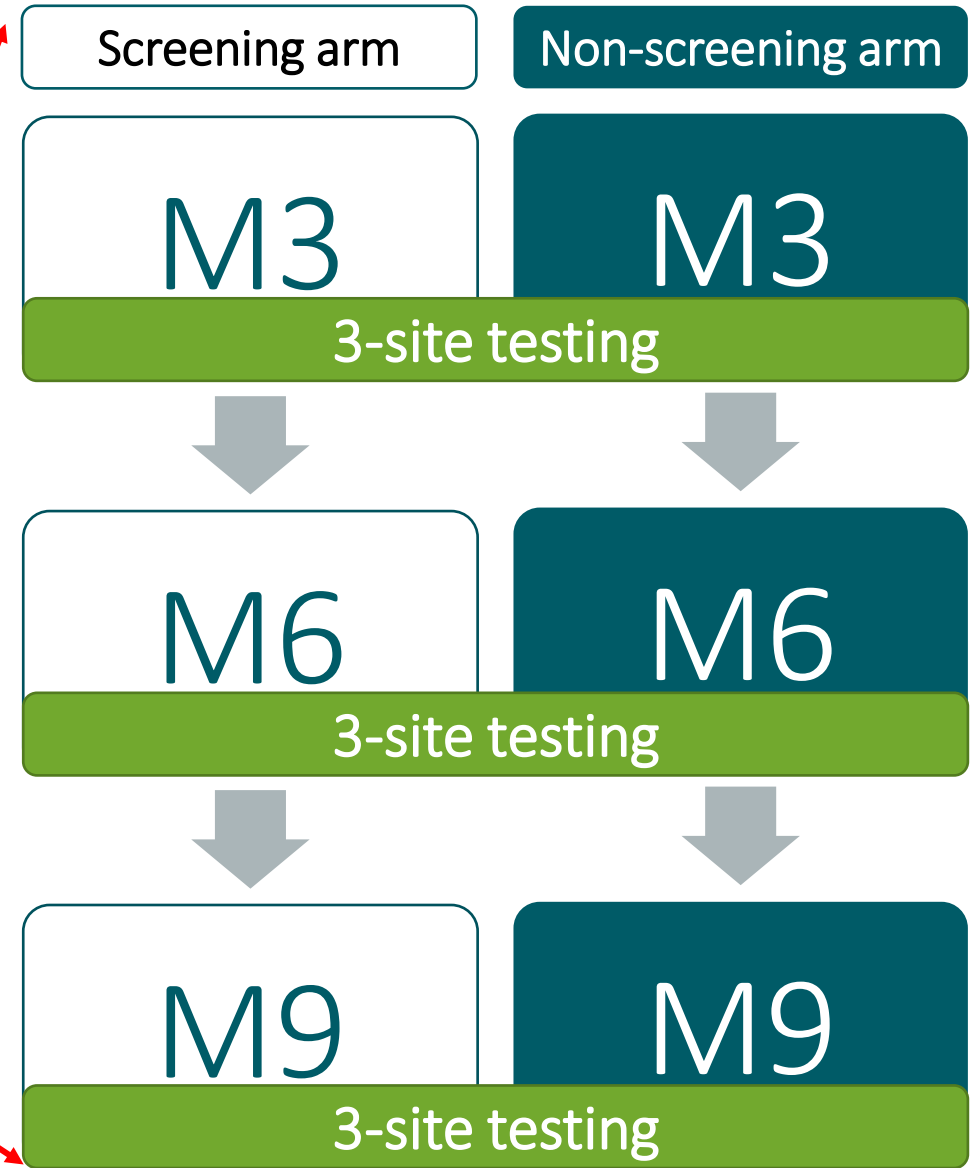
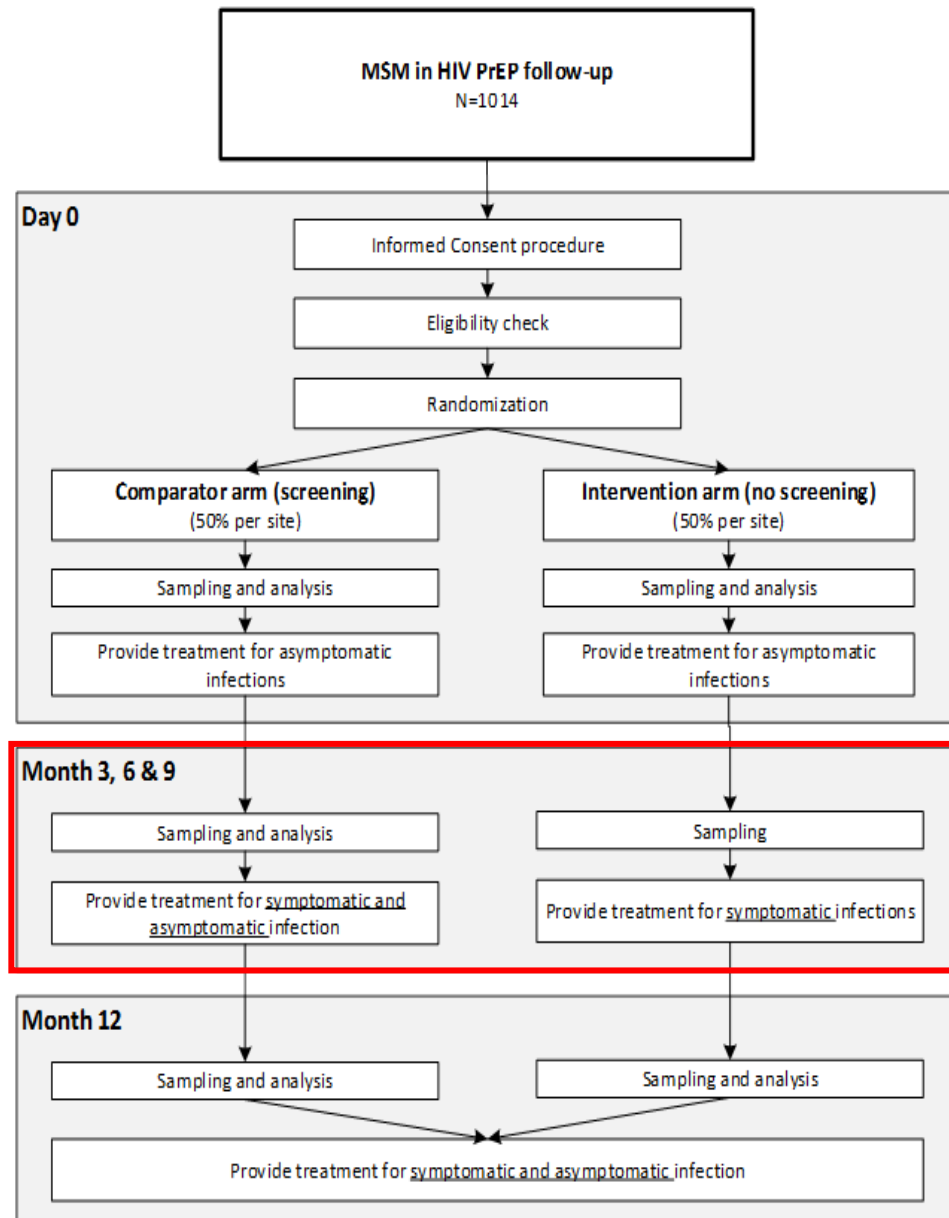
3-site testing for Ct and Ng (PCR)

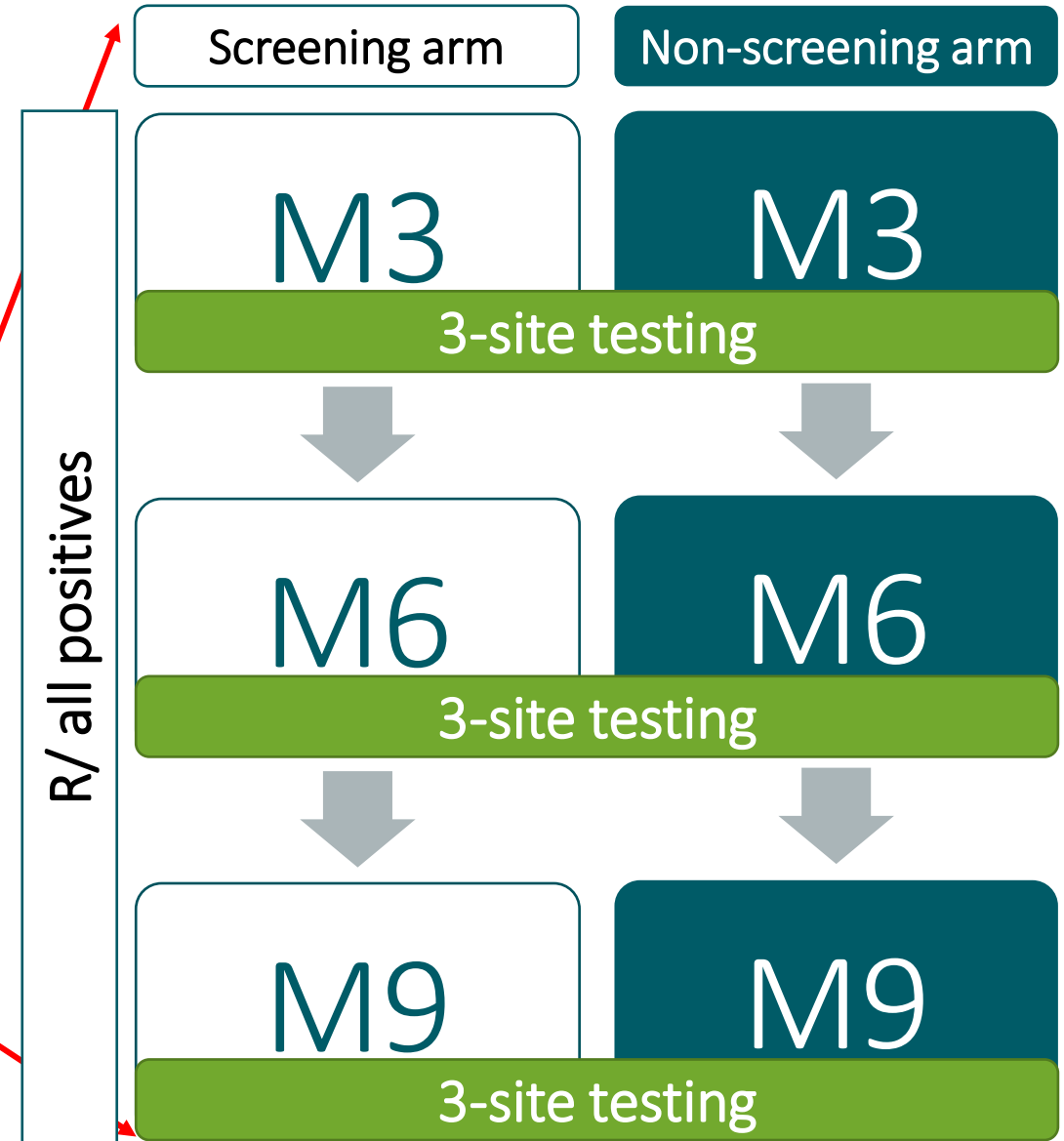
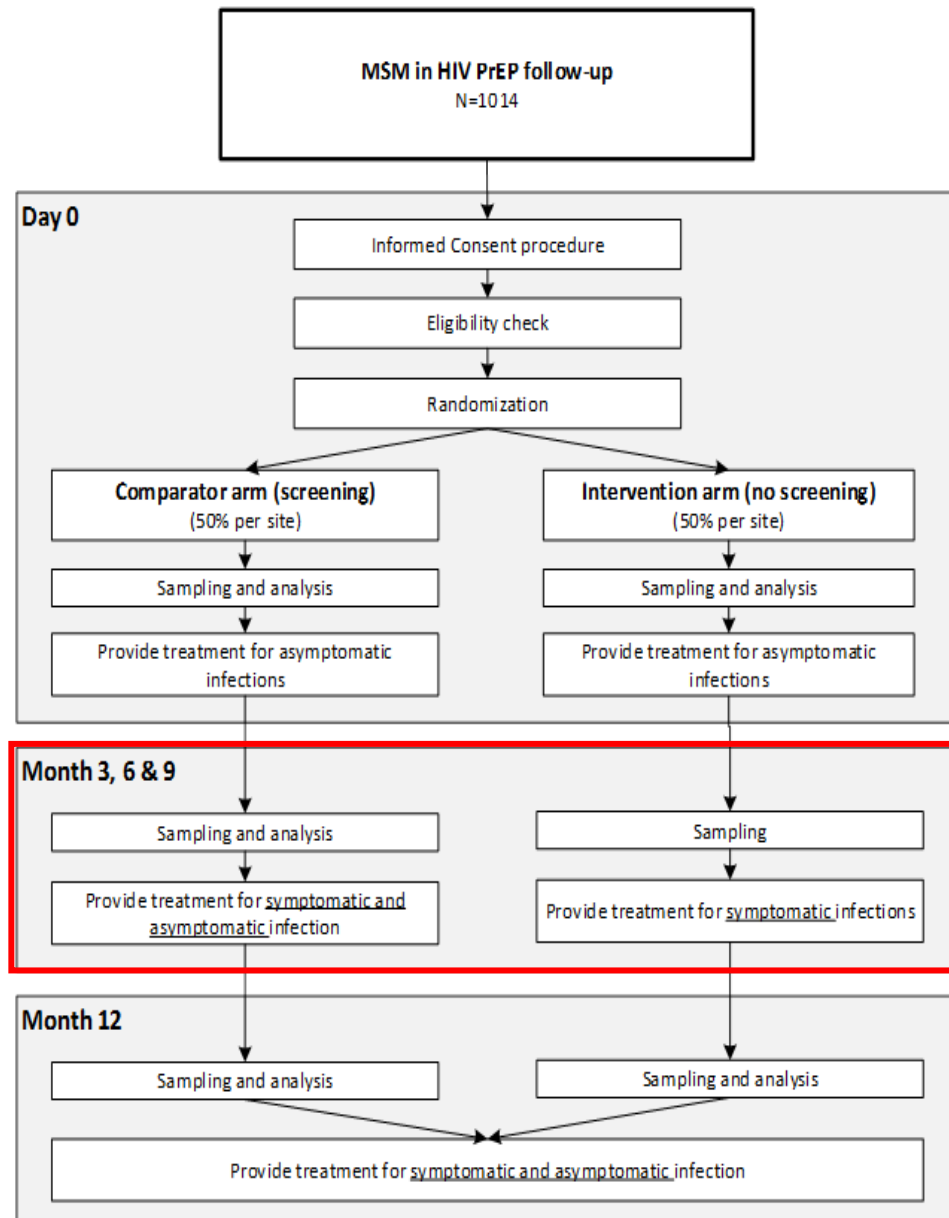
- oro-pharyngeal swab
 - ano-rectal swab
 - urine sample
- => pooled sample

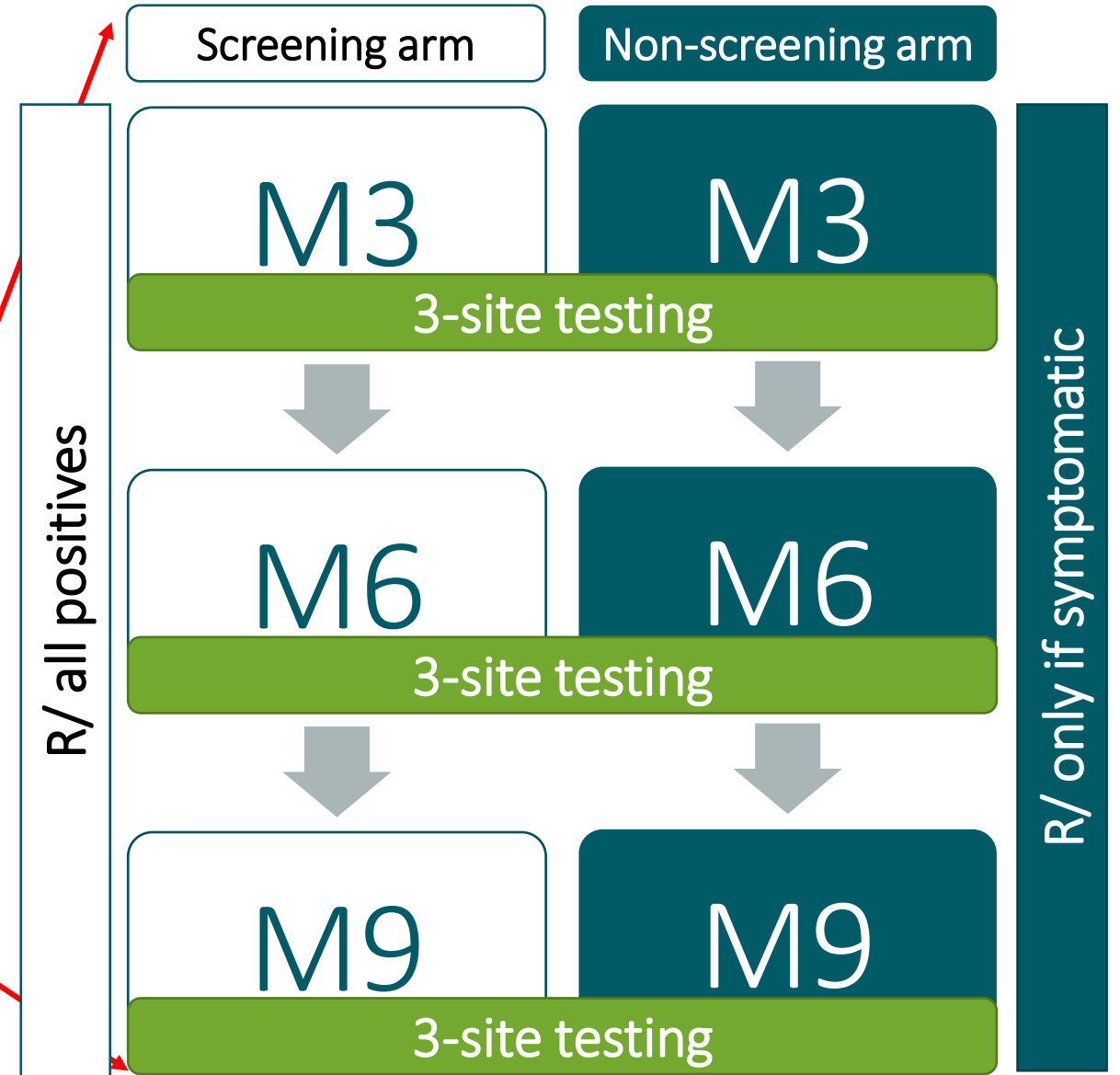
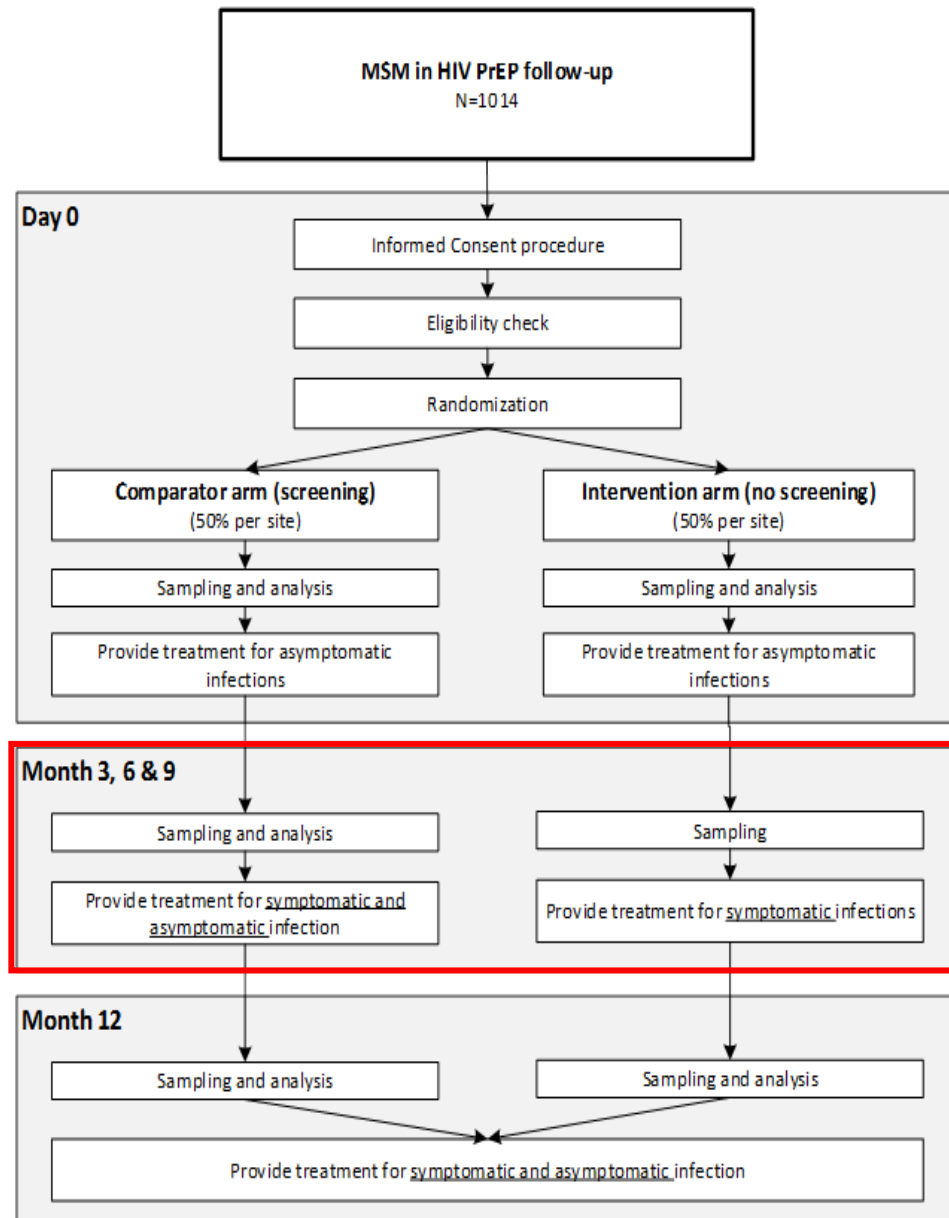
R/ all positives

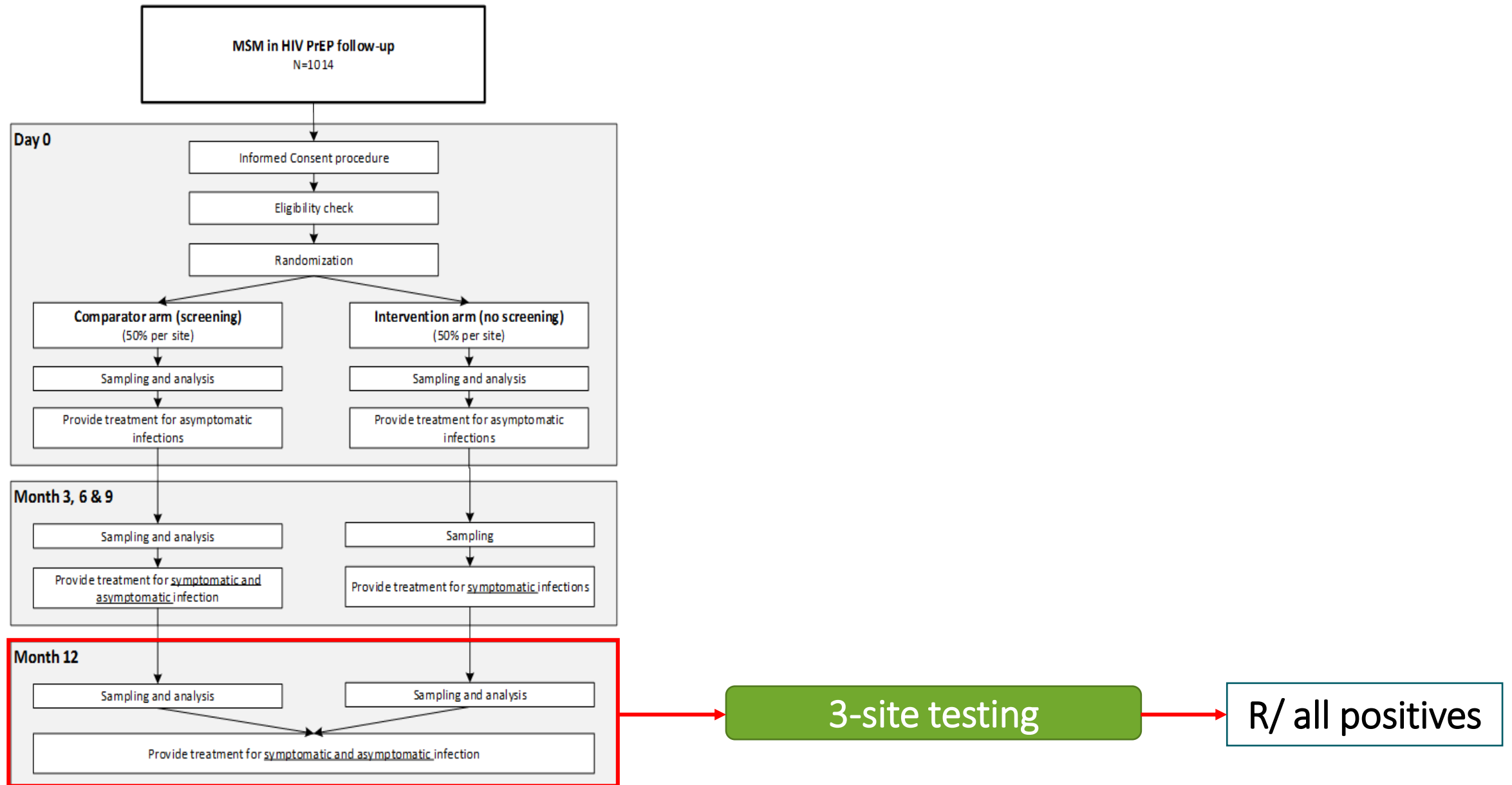










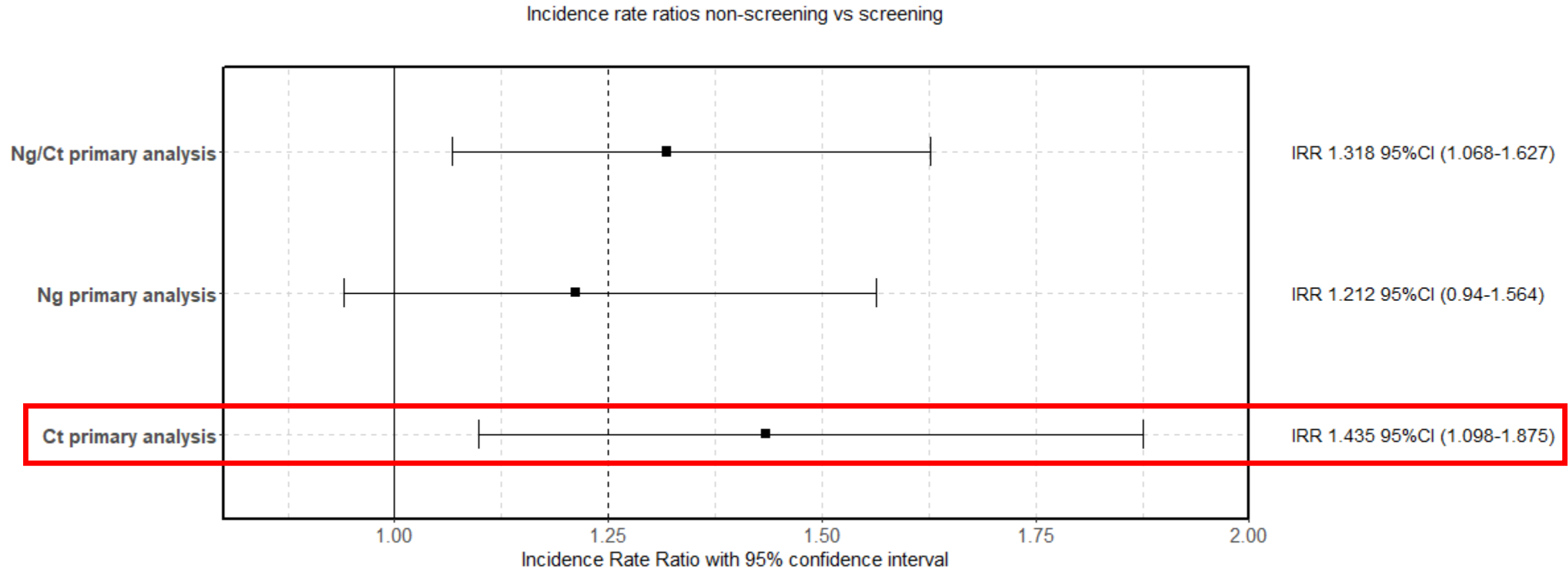


Baseline characteristics

	3 x 3 Screening (N=506) n (%) / Median (IQR)	Non-screening (N=508) n (%) / Median (IQR)	Total population (N=1014) n (%) / Median (IQR)
Age	39 (33 - 47)	39 (32.5 - 48)	39 (33 - 47)
Sex: Man	506 (100%)	505 (99.4%)	1011 (99.7%)
Sex: Transwoman	0 (0%)	3 (0.6%)	3 (0.3%)
Number of sex partners (past 3 months)	4 (2 - 8)	4 (2 - 8)	4 (2 - 8)
Number of unprotected sex partners (past 3 months)	2 (1 - 5)	2 (1 - 5)	2 (1 - 5)
Any antibiotic (past 6 months)	192 (37.9%)	173 (34.1%)	365 (36.0%)
Cephalosporins	67 (13.2%)	77 (15.2%)	144 (14.2%)
Macrolides	81 (16.0%)	94 (18.5%)	175 (17.3%)
Penicillins	63 (12.5%)	47 (9.3%)	110 (10.8%)
Quinolones	11 (2.2%)	5 (1.0%)	16 (1.6%)
Tetracyclines	57 (11.3%)	54 (10.6%)	111 (10.9%)



Primary analysis



Unresolved infections bias in the non-screening arm

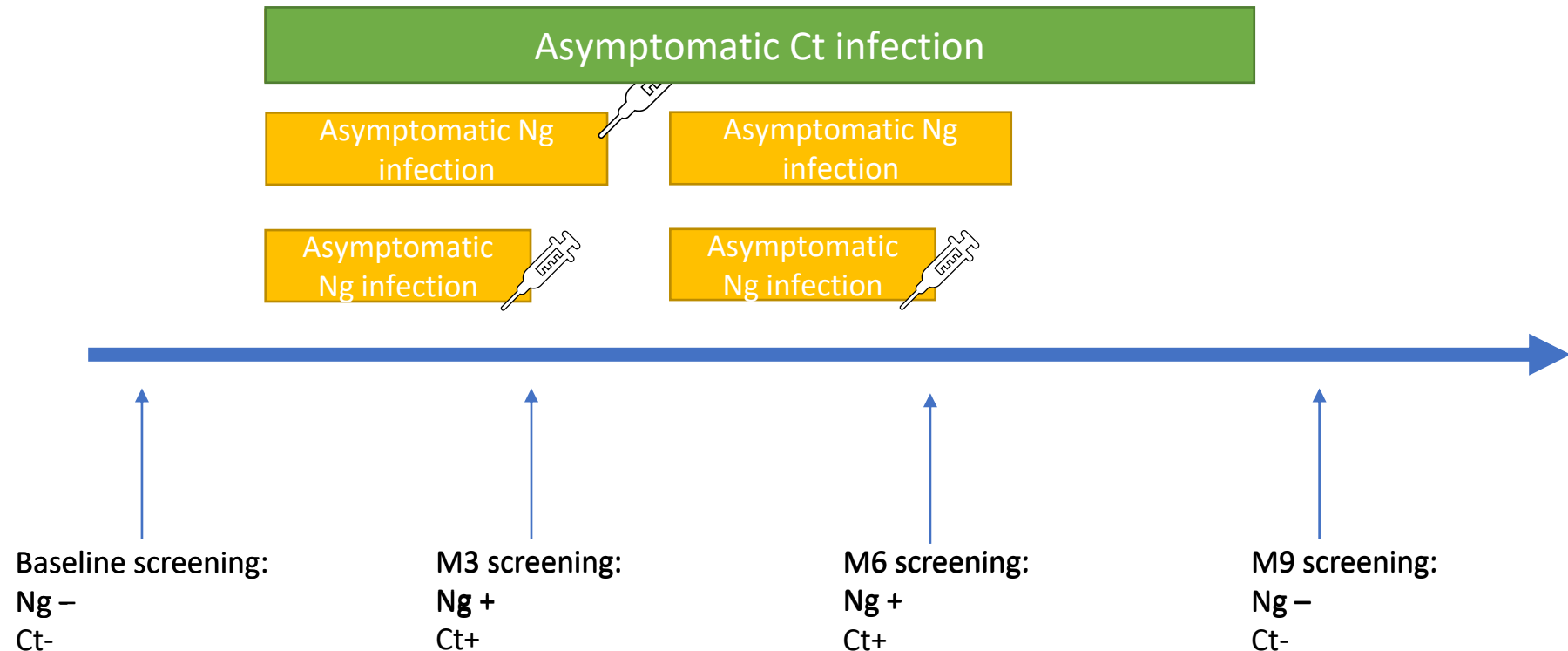
Primary analysis = 2 infections

Sensitivity analysis = 1 infection ... unless evidence of the use of an effective antibiotic against the pathogen

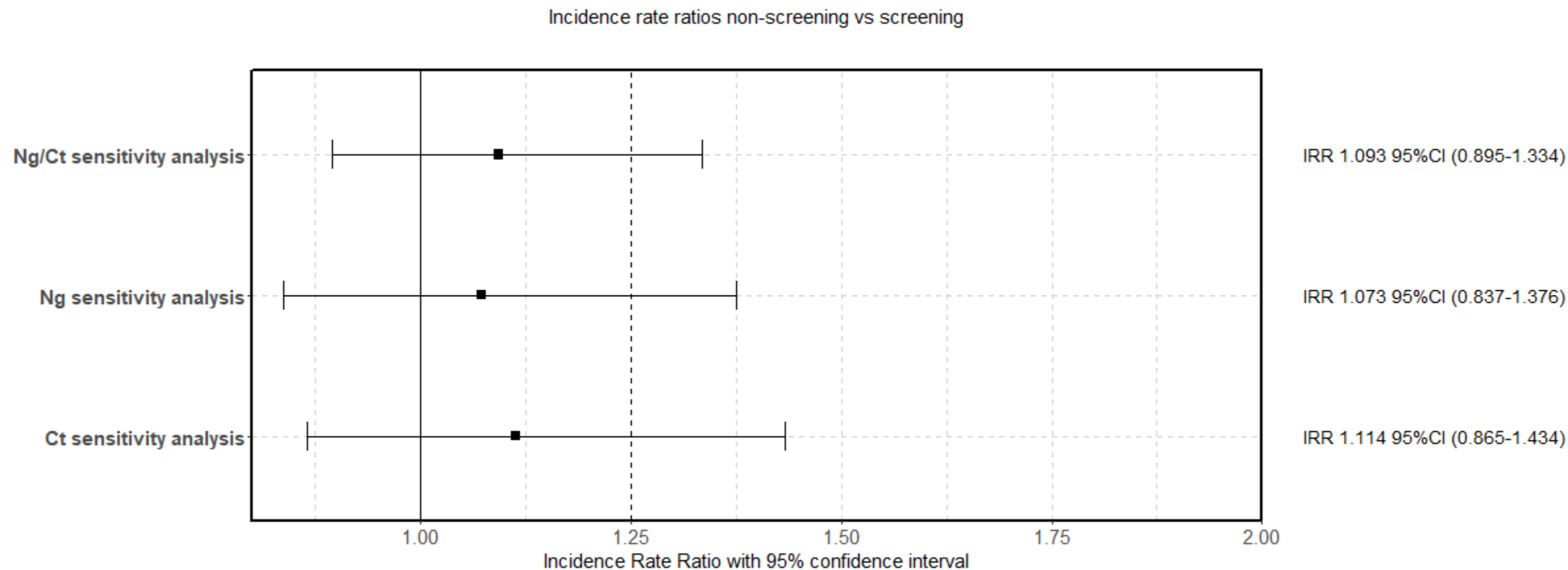
Non-screening arm

Non-screening arm

Screening arm

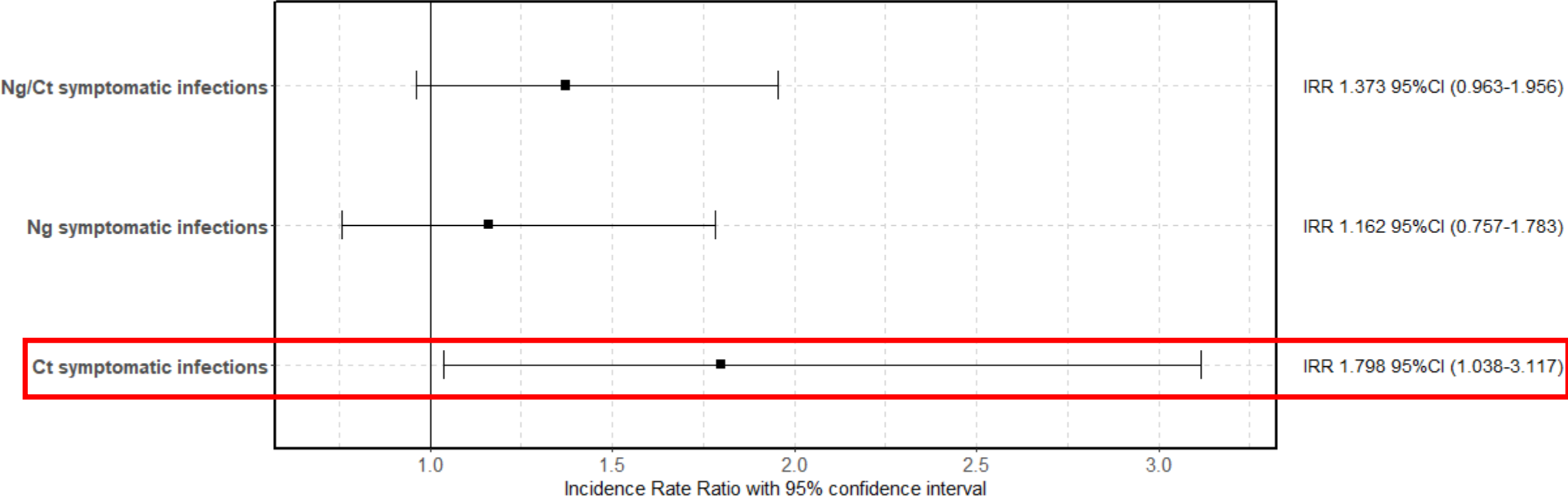


Sensitivity analysis



Symptomatic infections

Incidence rate ratios non-screening vs screening

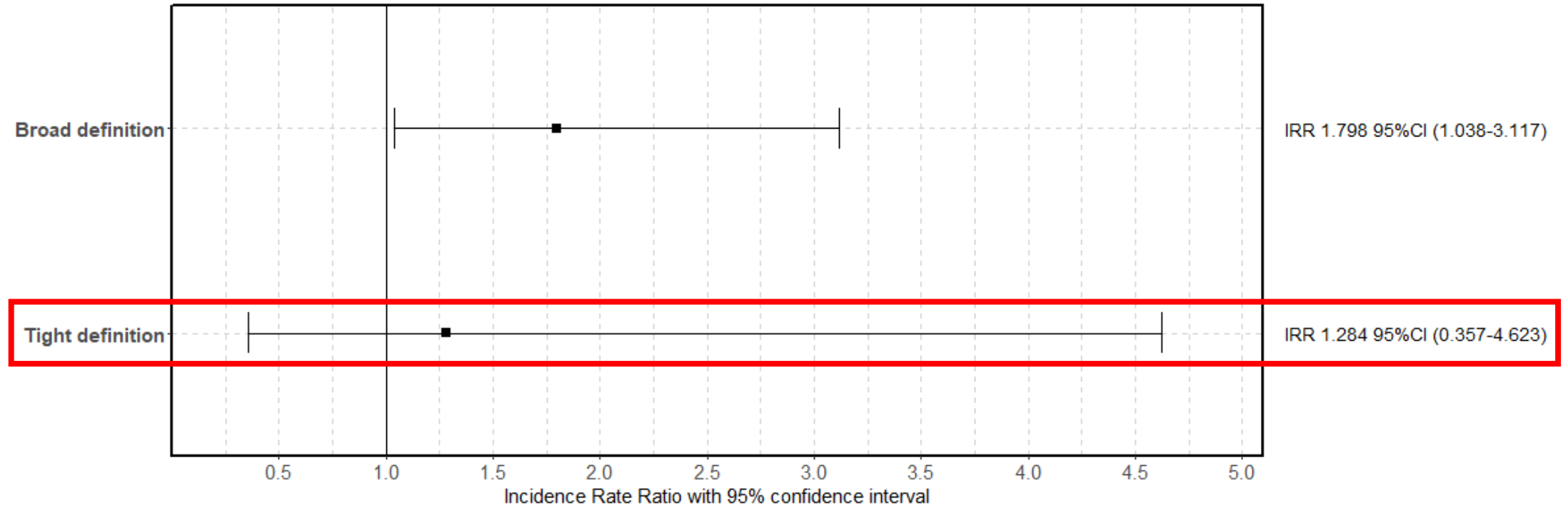


Symptomatic Ct infections

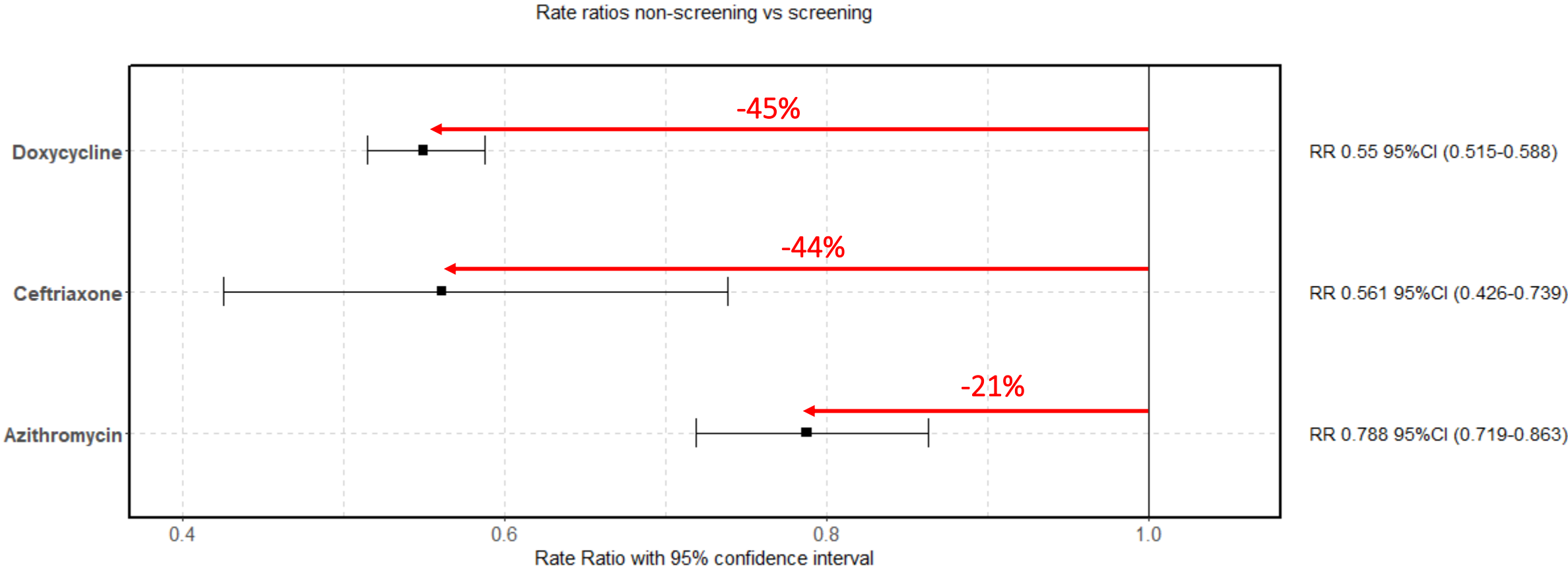
- **Broad** definition of symptoms: e.g., pharyngitis and genital ulcer
- Repeat analysis with **tighter** definition of symptoms:
 - Urethritis
 - Epididymitis
 - Proctitis



Incidence rate ratios non-screening vs screening



Antimicrobial consumption



Conclusion

- Non-screening for Ng/Ct in MSM taking HIV-PrEP is associated with a higher incidence of Ct infections but not Ng infections
- When controlling for the untreated infection bias in the non-screening arm, no difference was found between arms
- Screening for Ng/Ct leads to a substantial increase in antimicrobial consumption
- Based on our findings, the benefits of screening for Ng/Ct in PrEP cohorts do not seem to outweigh the harms



Gonoscreen study: impact

- Results published in *The Lancet HIV*
- Results presented at the 2023 STI&HIV world congress in Chicago
- Several international contacts regarding 'the Belgian approach'
- **The results of the Gonoscreen study, combined with other evidence, informed the 2024 Belgian PrEP guidance, which do not recommend systematic screening for Ng/Ct in MSM using PrEP**



Effect of screening for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* on incidence of these infections in men who have sex with men and transgender women taking HIV pre-exposure prophylaxis (the Gonoscreen study): results from a randomised, multicentre, controlled trial

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Summary

Background Guidelines recommend screening for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* at three anatomical sites (urethra, anus, and pharynx) every 3 months (3×3) in men who have sex with men (MSM) and transgender women taking HIV pre-exposure prophylaxis (PrEP). We present the first randomised controlled trial to compare the effect of screening versus non-screening for *N gonorrhoeae* and *C trachomatis* on the incidence of these infections in MSM and transgender women taking PrEP.

Methods A multicentre, randomised, controlled trial of 3×3 screening for *N gonorrhoeae* and *C trachomatis* versus non-screening was done among MSM and transgender women taking PrEP in five HIV reference centers in Belgium. Participants attended the PrEP clinics quarterly for 12 months. *N gonorrhoeae* and *C trachomatis* was tested at each visit in both arms, but results were not provided to the non-screening arm, if asymptomatic. The primary outcome was incidence rate of *N gonorrhoeae* and *C trachomatis* infections in each arm, assessed in the per-protocol population. Non-inferiority of the non-screening arm was proven if the upper limit of the 95% CI of the incidence rate ratio (IRR) was lower than 1.25. This trial is registered with ClinicalTrials.gov, NCT04269434, and is completed.

Findings Between Sept 21, 2020, and June 4, 2021, 506 participants were randomly assigned to the 3×3 screening arm and 508 to the non-screening arm. The overall incidence rate of *N gonorrhoeae* and *C trachomatis* was 0.155 cases per 100 person-days (95% CI 0.128–0.186) in the 3×3 screening arm and 0.205 (95% CI 0.171–0.246) in the non-screening arm. The incidence rate was significantly higher in the non-screening arm (IRR 1.318, 95% CI 1.068–1.627). Participants in the non-screening arm had a higher incidence of *C trachomatis* infections and symptomatic *C trachomatis* infections. There were no significant differences in *N gonorrhoeae* infections. Participants in the non-screening arm consumed significantly fewer antimicrobial drugs. No serious adverse events were reported.

Interpretation We failed to show that non-screening for *N gonorrhoeae* and *C trachomatis* is non-inferior to 3×3 screening in MSM and transgender women taking PrEP in Belgium. However, screening was associated with higher antibiotic consumption and had no effect on the incidence of *N gonorrhoeae*. Further research is needed to assess the benefits and harms of *N gonorrhoeae* and *C trachomatis* screening in this population.

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Introduction

International guidelines stipulate that screening programmes should only be introduced once they have met a set of criteria: the benefits should outweigh the harms, screening should be cost-effective, and there should be scientific evidence of screening programme effectiveness.¹ No randomised controlled trial (RCT) has evaluated the efficacy of screening for *Neisseria gonorrhoeae* or *Chlamydia trachomatis* in men who have sex with men (MSM) and transgender women.² Two large cluster RCTs have evaluated the effect of screening for

C trachomatis in general populations.^{3,4} Both found no significant effect of screening on the prevalence of *C trachomatis*. No RCTs have evaluated the efficacy of screening for *N gonorrhoeae*.⁵

Ecological analyses have found that countries where MSM are more intensively screened for *N gonorrhoeae* and *C trachomatis* do not have lower incidence and prevalence of asymptomatic or symptomatic *N gonorrhoeae* and *C trachomatis* infection than countries that screen less.⁶ One study that used self-reported data from two surveys in 2010 and 2017

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