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RESEARCH ARTICLE

REVISED Screening is not associated with reduced incidence of gonorrhoea or chlamydia in men who have sex with men (MSM); an ecological study of 23 European countries [version 2; peer review: 2 approved, 1 approved with reservations]

Chris Kenyon [ID] [1,2]

[1]University of Cape Town, Cape Town, South Africa, 7925, South Africa
[2]Institute of Tropical Medicine, Antwerp, Antwerp, 2000, Belgium

Abstract

Background: Increasing rates of antimicrobial resistance has motivated a reassessment of if intensive screening for gonorrhoea and chlamydia is associated with a reduction in the prevalence of these infections in men who have sex with men (MSM).

Methods: Spearman's correlation was used to evaluate the country-level correlation between the intensity of self-reported sexual transmitted infection (STI) screening in MSM (both anal and urethral screening, taken from a large internet survey of MSM) and the incidence (taken from ECDC surveillance figures) and prevalence (taken from a literature review of studies estimating prevalence in MSM attending STI clinics) of gonorrhoea and chlamydia.

Results: The intensity of both anal and genital screening was found to be positively associated with country level gonorrhoea incidence rates (rho 0.74; p=0.0004; rho=0.73; p=0.0004, respectively) and Ct incidence rates (rho 0.71; p=0.001; rho=0.78; p=0.0001, respectively). No associations were found between anal or genital screening intensity and Ng prevalence in clinic populations (Table 2).

Conclusions: We found no evidence of a negative association between screening intensity and the prevalence of gonorrhoea or chlamydia in MSM. Randomized controlled trials are urgently required to evaluate if the high antimicrobial exposure resulting from intensive screening programmes is justified.

Keywords

Gonorrhoea, chlamydia, MSM, STI screening, PrEP, antimicrobial resistance

Open Peer Review

Reviewer Status ✓ ✓ ?

	Invited Reviewers		
	1	**2**	**3**
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version 1 published 06 Feb 2019	✓ report	✓ report	

1 **Hamish McManus** [ID], The University of New South Wales (UNSW Sydney), Sydney, Australia
   Basil Donovan [ID], The University of New South Wales (UNSW Sydney), Sydney, Australia

2 **Eline L Korenromp** [ID], Avenir Health, Geneva, Switzerland
   Nico Nagelkerke, Independent, Innsbruck, Austria

3 **Mirjam Kretzschmar** [ID], University Medical Center, Utrecht, The Netherlands
   National Institute of Public Health and the Environment (RIVM), Bilthoven, The Netherlands

Any reports and responses or comments on the article can be found at the end of the article.

Corresponding author: Chris Kenyon (chriskenyon0@gmail.com)

Author roles: Kenyon C: Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Software, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing

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> **REVISED** **Amendments from Version 1**
>
> The various edits kindly suggested by the reviewers have been made. In particular we have included the concept of reverse causality in the discussion. We have also added the Callander *et al.*, 2018, and Unemo *et al.* 2017, references as suggested.
>
> **Any further responses from the reviewers can be found at the end of the article**

Introduction

There have been large increases in antimicrobial resistance in a number of sexual transmitted infections (STI) in the recent past. There are serious concerns that both *Neisseria gonorrhoeae* (Ng) and *Mycoplasma genitalium* may become untreatable in the not too distant future[1,2]. For both these bacteria as well as macrolide resistance in *Treponema pallidum,* AMR has frequently first emerged in populations with a combination of high antimicrobial consumption and dense sexual networks[3,4]. HIV pre-exposure prophylaxis (PrEP) cohorts have dense sexual networks and the intense screening STI typically practiced translates into high antimicrobial exposures[5,6]. Three-monthly, 3-site Ng/ *Chlamydia trachomatis* (Ct) screening for example translates into macrolide exposures of around 4400 standard units/1000 population/year, which is many times higher than levels associated with the induction of macrolide resistance in a range of bacteria including *T. pallidum* and Ng[7,8]. These findings have led a number of authors to review the evidence to support Ng/Ct screening in men who have sex with men (MSM) PrEP populations.

The US Preventive Task Force, concluded that there is insufficient evidence to advocate for or against screening for Ng in men, including MSM[9]. In a systematic review conducted to inform these guidelines, the authors found no randomised, controlled trials or controlled observational studies that assessed the utility of NG screening in men[10]. In a systematic review of observational studies, we found no evidence that even the most intense Ng/Ct screening such as screening 100% of PrEP cohorts every 3 months was associated with a decline in the prevalence of these infections[11]. Others have argued that this lack of an effect was because the PrEP recipients were having sex with (and being reinfected by) people who were not being screened[12]. This generates the hypothesis that we test in this paper that populations where a high proportion of MSM are screened for Ng/Ct will have a lower prevalence of these infections than populations with less screening. We test this hypothesis in European countries because the intensity of STI screening varies widely here and data for screening and prevalence estimates were available.

Methods
Data sources
STI screening intensity*.* Country level STI screening prevalence were obtained from the European MSM Internet Survey (EMIS), which was an internet-based survey of over 160 000 MSM from 38 countries living in Europe[13]. The survey was conducted between June and August 2010. In the section where

participants were asked about STI testing in the past 12 months, they were asked 3 questions that are relevant to Ng/Ct screening: Did you provide a urine sample for STI screening? Was urethral swab inserted into your penis for STI screening? Was a swab inserted into your anus for STI screening? EMIS combined the results from the first two questions into one variable reporting the proportion of respondents reporting 'urethral STI screening' – via either urine or urethral swab. The third question provided the proportion with 'anal STI screening'. Typically, these urethral and anal samples are tested for Ng/Ct.

Ng/Ct prevalence/incidence*.*
1. National Ng and Ct incidence estimates for men in 2010 were taken from European Centre for Disease Prevention and Control (ECDC) figures[14]. These incidence estimates are based on national surveillance systems. The ECDC does not provide incidence estimates separately for MSM and thus we used the estimates for all men. MSM do however constitute a high proportion of diagnoses in all men[14].

2. Systematic review of Ng/Ct prevalence in MSM Ng/Ct prevalence estimates for MSM were taken from a published literature review of pharyngeal and anorectal Ng and Ct prevalence estimates in MSM (and other populations)[15]. All studies listed in PubMed reporting prevalence of extragenital Ng and Ct in MSM up to 1 December 2015 were included. A total of 53 studies were included from countries around the world. Of these 18 were from 6 European countries (Table 1). For the four European countries with more than one study we selected the study reporting prevalence estimates from 2010 or as soon after this year as possible. All selected studies were prevalence estimates established by Nucleic Acid Amplification Testing of MSM clients attending STI clinics.

Data analysis
In all analyses the correlation between screening intensity and Ng/Ct prevalence/incidence was tested using Spearman's correlation. The statistical analyses were performed in STATA 13.

Results
STI screening
The proportion of respondents in each of the 23 countries reporting anal STI screening varied widely from 6.5 to 70.6% to (median 17.3%, IQR 11.8–47.1; Table 1). Likewise, there were large variations in the proportion reporting genital STI screening (range 37.0 to 94.0%, median 63.6 IQR 50.0–85.0%). There was a strong correlation between the proportions reporting anal and genital STI screening (rho=0.81; p<0.0001).

Incidence of Ng and Ct based on ECDC estimates
For 19 countries with data, the incidence of Ng for men in 2010 ranged between 1.2 and 42.2 cases per 100 000 men per year (median 7.2, IQR 3.6–18.3). There was an even wider distribution in estimated Ct incidence for the 18 countries with data (range 0 to 383.7, median 24.8, IQR 1.3–201).

Table 1. Prevalence of sexual transmitted infection (STI) screening, STI incidence and prevalence in European countries with available data.

Country	Screening Prevalence in 2010 (%)		STI Incidence in men 2010 (cases/100 000/ year)		STI Prevalence in MSM attending STI clinics (%)						
					N. gonorrhoeae			*C. trachomatis*			Reference
	Urethral	Anal	Ng	Ct	Urethral	Rectal	Pharyngeal	Urethral	Rectal	Pharyngeal	
Bulgaria	39.2	10.0	2.7	.5							
Cyprus	59.9	17.3		.5							
Czech Rep.	67.2	19.6	10.4								
Germany	56.6	20.6			1.9	4.6	5.5	3.4	8	1.5	doi.org/10.1136/sextrans-2012-050929
Denmark	71	40.0	13.2	383.7				2.6	2.6	0	doi.org/10.1136/sti.73.6.493
Estonia	58.4	14.2	6.5	40.5							
Greece	41.4	11.8	4.6	1.4							
Spain	52	15.2					9.5				doi.org/10.1177/0956462413486455
Finland	89	37.9	7.2	201							
Ireland	91	67.2	20.5	104.7	0	4.1	3.3	1.7	6.6	.8	
Lithuania	63.6	13.3	18.3	15.7							
Luxembourg	41.9	9.1	1.2	0							
Latvia	64	14.9	26	33.8							
Malta	85	70.6	20.9	37.5							
Netherlands	87	63.0			3.4	5.5	3.9	4.3	10.1	1.7	doi.org/10.1177/0956462414521165
Norway	84	47.2	15	353.8							
Poland	37	8.9	1.5	2.2							
Portugal	68.9	9.5	1.5								
Romania	45	6.5	4.1	.7							
Sweden	92	59.0	13.3	333.3							
Slovenia	50	29.0	4.1								
Slovakia	60	16.9	3.6								
United Kingdom	94	69.7	42.2		4.7	9	5.2	5.3	6.5	2.2	doi.org/10.1258/ijsa.2012.011378

N. gonorrhoeae - Neisseria gonorrhoeae, C. trachomatis - Chlamydia trachomatis

Prevalence of Ng/Ct in MSM based on STI clinic attendees

There was less variance in the prevalence estimates of Ng and Ct in MSM (Table 1). Rectal Ng0: median 5.5%, IQR 4.6–7; pharyngeal Ng: median 5.4%, IQR 3.9–6.5; urethral Ng: median 1.9%, IQR 1–3.4. Rectal Ct: median 7.3%, IQR 6.5–10.0; pharyngeal Ct: median 1.3, IQR 0.8–1.7; urethral Ct: median 3, IQR 2.5–5.3; Table 1.

Correlation between screening intensity and Ng/Ct incidence/prevalence

The intensity of both anal and genital screening was found to be positively associated with country level Ng incidence rates

(rho 0.74; p=0.0004; rho=0.73; p=0.0004, respectively) and Ct incidence rates (rho 0.71; p=0.001; rho=0.78; p=0.0001, respectively; Figure 1).

No associations were found between anal or genital screening intensity and Ng or Ct prevalence in clinic populations (Table 2).

Discussion

The prevalence of Ng and Ct has been increasing in MSM populations in a number of countries[16,17]. Intensified screening in MSM would be one way to reduce the incidence and
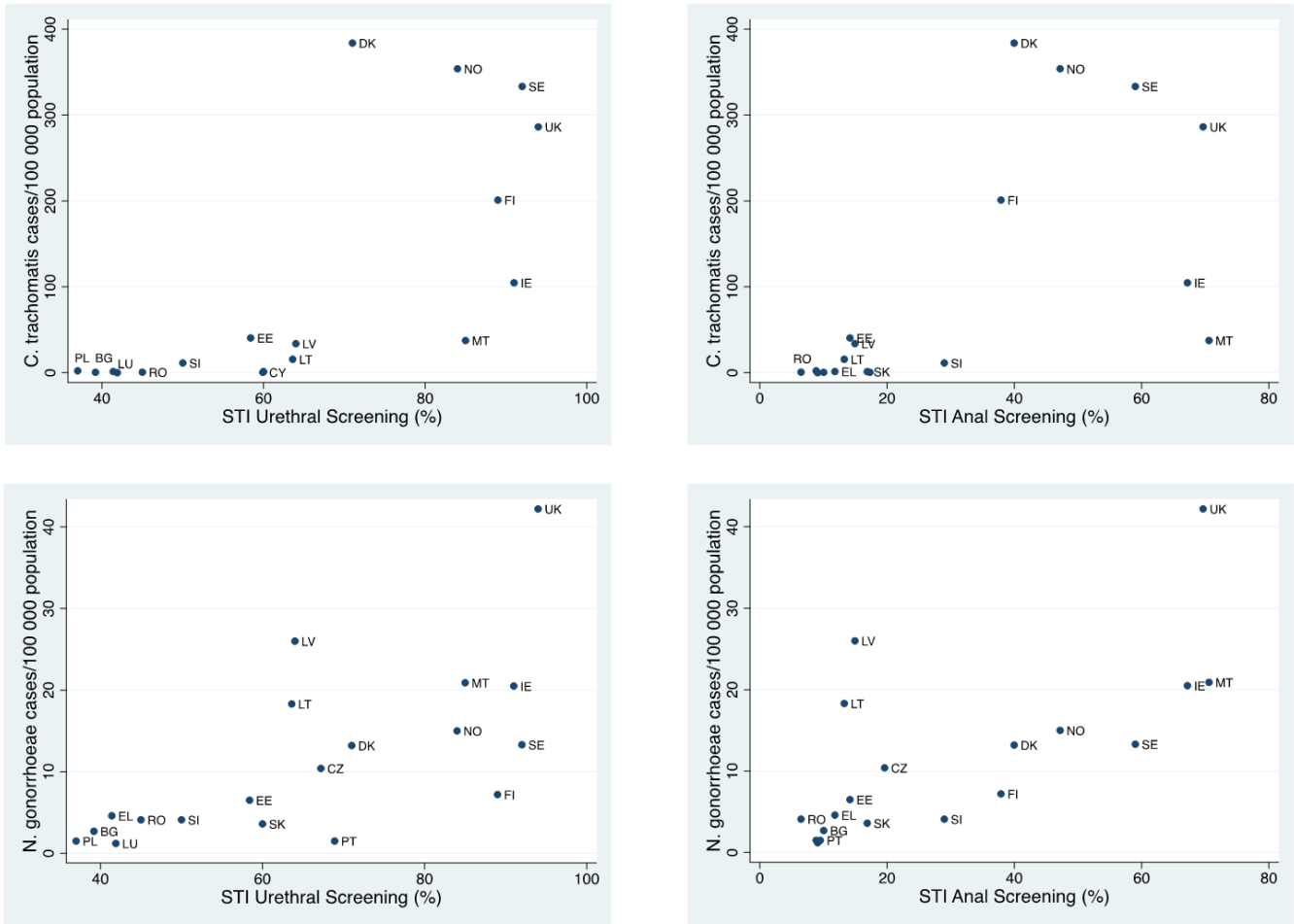
Figure 1. Scatter plots of country-level association between self-reported anal and urethral sexual transmitted infection (STI) screening intensity in men who have sex with men (MSM) and incidence of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in men in European countries in 2010. Country designations: AT, Austria; BE, Belgium; CZ, Czech Republic; DE, Germany; DK, Denmark; EL, Greece; ES, Spain; FI, Finland; FR, France; HR, Croatia; HU, Hungary; IE, Ireland; IT, Italy; LU, Luxembourg; LV, Latvia; NL, the Netherlands; PT, Portugal; SE, Sweden; SI, Slovenia; SK, Slovakia; UK, United Kingdom.

Table 2. Spearman's correlation between prevalence of sexual transmitted infection (STI) screening (anal and urethral) and prevalence of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* (pharyngeal, rectal and urethral). All P-values were greater than 0.1.

STI prevalence	Anal testing	Urethral testing
N. gonorrhoeae		
Pharyngeal	-0.70	-0.70
Rectal	0.40	0.40
Urethral	0.40	0.40
C. trachomatis		
Pharyngeal	0.50	0.50
Rectal	-0.20	-0.20
Urethral	0.30	0.30

prevalence of these infections. In this analysis, we did not find evidence of a negative correlation between the intensity of STI screening in MSM and the incidence/prevalence of Ng/Ct. Instead, we found evidence of a positive association between the intensity of screening in MSM and the estimated incidence rate for men. This positive association may be explained by the fact the incidence estimates are influenced by the intensity of screening – countries with more intensive screening programmes would be expected to diagnose more asymptomatic Ng and Ct infections which lead to higher incidence estimates. This could also be considered a form of reverse causation: the higher prevalence of Ng/Ct is the cause rather than the effect of more intensive screening.

To deal with this bias and the fact that the ECDC Ng/Ct incidence estimates do not provide incidence estimates for MSM, we also evaluated the association between screening intensity and Ng/Ct prevalence in MSM attending STI clinics. Here

we found no evidence of an association between screening intensity and prevalence.

These findings are open to a number of interpretations. Firstly, screening intensity may be negatively associated with Ng/Ct rates but we missed this association due to methodological issues. Our estimates of screening intensity were based on a single cross-sectional source. Although EMIS had a large sample size and the accuracy of its prevalence estimates for other variables has been validated in other studies[13,18], these screening estimates may be inaccurate and may have changed over time. As noted above, the STI incidence estimates were for all men and were likely strongly influenced by practices such as screening intensity, access to health care and accuracy of national case reporting. The STI prevalence estimates in MSM were all taken from men attending STI clinics and thus are likely higher than general populations of MSM. The study design of each of the 6 studies contributing Ng and CT prevalence estimates differed somewhat further limiting the extent to which correlations could be assessed between screening intensity and prevalence across these studies. We could find no comparable data on the prevalence of Ng or Ct in general MSM populations.

Alternatively, screening intensity as measured may not be associated with reduced Ng/Ct rates in MSM. Randomized controlled trials of the efficacy of screening for Ct in women on the prevalence of Ct have produced equivocal results[19–22]. Although no RCTs have been conducted in MSM, a systematic review of observational studies revealed that Ng/Ct screening, even when conducted at 3-sites every 3-months, was not associated with reductions in the prevalence of Ng or Ct[11]. If we consider Ng, numerous aspects of the way it circulates in contemporaneous populations of MSM may explain why screening has little or no effect on prevalence. Symptomatic disease is thought to typically occur soon (2–21 days) after infection and if symptoms do not develop the infection (particularly in the pharynx and rectum) tends to persist in a low abundance, low infectious state for up to 6 months[23]. Highly exposed individuals develop a type-specific immunity, but this immunity is largely ineffective in low exposure individuals[23,24]. As a result, the vast majority of Ng infections are asymptomatic and self-limiting in

MSM PrEP populations[23,25]. Similar considerations apply to Ct. In the case of Ct there is however better evidence that treatment of Ct results in "arrested immunity" and thereby paradoxically increases the probability of reinfection[26,27]. If screening results in 'arrested immunity' it may paradoxically increase Ng/Ct prevalence/symptomatic disease. The sexual networks of PrEP recipients are very dense (up to a mean of 18 partners per 3 months[28]) and this is responsible for generating the high prevalences of Ng and Ct[5]. Removing individuals piecemeal from this network for screening and treating has no effect on the underlying determinant of high prevalence. As a result, the probability of reinfection and prevalence remaining high.

Mathematical models of Ng and Ct transmission in European countries like Belgium have thus found that the sexual network of MSM was so dense that current levels of Ng screening were having little to no effects on Ng prevalence[29]. In contrast, a modelling study from the United States found that 6-monthly screening of an expanded number of PrEP recipients could avert 40% of Ng and Ct infections[30]. This study did not however model pharyngeal transmission of Ng (which plays a major role in transmission) and did not model the impact of immunity or Ng's ability to adapt to antibiotic pressure. These omissions may explain the discrepancy between its prediction, and our and the earlier systematic review of observational studies[11].

Based on the findings of this study and those reviewed here we conclude that we can still not exclude the possibility that intense screening (at least 3-site, 3-monthly) may have a small to moderate influence on Ng/Ct prevalence in MSM. Randomized controlled trials are urgently required to test this hypothesis. In the interim, given the mounting evidence that Ng/Ct screening does not have a large effect on prevalence but does result in high levels of antimicrobial exposure, consideration should be given to reducing the intensity or stopping Ng/Ct screening in MSM in a phased and controlled manner that allows a detailed evaluation of the risks and benefits of screening.

Data availability
Underlying data
All data underlying the results are available as part of the article and no additional source data are required.

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Open Peer Review

Current Peer Review Status: ✔ ✔ ?

Version 2

Reviewer Report 20 September 2019

? **Mirjam Kretzschmar** iD

[1] Julius Center for Health Sciences and Primary Care, University Medical Center, Utrecht, The Netherlands
[2] Centre for Infectious Disease Control, National Institute of Public Health and the Environment (RIVM), Bilthoven, The Netherlands

In this paper the author uses a combination of data sources to study the relationship of testing and treatment for gonorrhoea and chlamydia infections and the incidence and prevalence of these infections in MSM populations. The main finding is that screening rates and incidence are positively correlated. It is an interesting idea to analyse these ecological relationships, however, as the author also acknowledges, there are many caveats for the interpretation of the results. Ecological analyses are always fraught with difficulties, as there is no information on individual level on the relationship between variables. In the data sets used in this paper the difficulties are magnified by a number of properties of the data sets used, which are not sufficiently discussed in the paper.

Firstly, the EMIS data set: To understand the quality of the data about STI screening rates, one would need to know how representative EMIS respondents were for the general MSM population. How were EMIS respondents recruited, how does their sexual risk behaviour compare to other MSM study populations? Were there differences between countries participating in the EMIS survey in recruitment and representativeness?

Secondly, the ECDC surveillance data set: ECDC collects data from national surveillance systems of member states in their TESSy data base. The quality and completeness of national surveillance systems is very variable between countries, and depends strongly on health care systems in the countries. In addition, given that a large proportion of all chlamydia infections and a good proportion of gonorrhoea infections are asymptomatic, reporting of these infections in surveillance systems will always reflect mainly the health seeking behaviour of the population and quality of reporting, more than the incidence of an infection. Estimating incidence from these data is difficult if not impossible, and in my opinion these data cannot be interpreted as incidence. It is therefore very plausible that numbers of notified cases increase with screening rates, which is reflected in the positive correlations, but this does not give any information about possible impact of screening on incidence. ECDC has also published a review on the

impact of screening on chlamydia prevalence in Europe, which may be worthwhile mentioning in this context (ECDC 2014).

Thirdly, prevalence of STI in MSM who attend STI clinics: Again, it is difficult to say what these estimates mean for the prevalence in the general MSM population, as men attending STI clinics are a selected group with in general higher risk of acquiring STIs than average. What proportion of men attend STI clinics also depends on the health care system of a country and possible stigmatization of MSM in the society. It is striking that prevalence estimates are available mainly for North-Western European countries, which may be similar in their health care systems, and not for other European regions. How does the population of STI clinic patients compare with the participants of the EMIS survey in terms of sexual behaviour and health care uptake?

This ecological analysis could be improved and would be more interesting, if it would include a more in-depth comparison of the study populations and a more extensive analysis of how data were collected and their possible biases.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Mathematical modelling of infectious diseases

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Version 1

Reviewer Report 03 September 2019

https://doi.org/10.5256/f1000research.19637.r53339

✔   **Eline L Korenromp** iD
Avenir Health, Geneva, Switzerland
Nico Nagelkerke
Independent, Innsbruck, Austria

General Comments:
This is a useful study, well designed, analyzed, and written, ending in a well-reasoned call for improving the evidence base for gonorrhea and chlamydia screening programs.

The discussion adds particular value, comparing and contrasting findings from empirical studies with predictions by modelling studies. This part could possibly be structured better (e.g. I found it confusing to see reference 11 discussed twice on page 6). The authors might add a general statement about the value of mathematical models to answer complex epidemiological questions such as this. For example "*This illustrates that mathematical models to assess health interventions may be wrong for reasons that are not always obvious, and underlines the importance of empirical evidence*".

The specific comments below may serve to improve readability and interpretation.

Methods:
Page 3, right column, top: '*A total of 53 studies were included of which 18 were from 6 European countries*'. I suppose the remaining 35 studies were from other European countries, or also non-European? Perhaps just drop 'European' from this sentence, so to avoid this confusion.

While, according to reference 14, a large proportion of Gc/Ct diagnoses takes places in MSM, it is unlikely that this reflects actual incidence, especially with regard to Ct which is highly prevalent, often asymptomatically, in the heterosexual population (e.g. in adolescent girls). This may be worth mentioning (in Introduction or Discussion) – to put the importance of MSM in the overall epidemic in context.

Results:
Page 4: 'No associations were found between anal or genital screening intensity and Ng prevalence in clinic populations'. You found the same for CT, right? Please add that.

Discussion:
Page 4: The authors offer as a possible explanation for the observed positive (and not, the hoped negative) association that screening makes people susceptible to reinfection. To me a more basic explanation in this ecological analysis based on cross-sectional data, is screening programs are likely targeted to regions and populations with high prevalence. Reverse causality: the high prevalence is likely the cause rather than the effect of the screening program being there.

Page 5: '*To deal with this bias … we also evaluated the association in MSM attending STI clinics*': Not clear, the association between what and what? You mean, between national screening intensity and prevalence in MSM attending STI clinics? Please rephrase, and refer back to Table 2 here.

Page 5: '*As noted above, the STI incidence estimates were for all men and were likely strongly influenced by practices such as screening intensity*'. A more general limitation of these incidence estimates based on national surveillance data is that NG and Ct incidence is hardly measurable, and case notifications are no good indication of underlying incidence of these infections, which are most often asymptomatic and not presenting to clinics. Besides variations in screening intensity, variations across countries in health care access and population awareness of STIs contribute to varying case notification rates, which do not reflect true variations in underlying incidence, and so may bias (or at least dilute the power) of the ecological analysis.

Page 6: '… *limiting the extent to which comparisons can be made between prevalence estimates'*: Please consider to rephrase as *'… limiting the extent to which correlations could be assessed between screening intensity and prevalence across these studies'*

Page 6: About the systematic review of observational studies, quoted as reference 11, could you summarize how this differs from your current study, in methodology, scope, populations covered and/or other aspect?

Page 6: *'These omissions may explain the discrepancy between its finding and that of the systematic review of…'* This sentence may be clearer if written as: *'… between its prediction, and our and the earlier systematic review of observational studies'*.

Conclusion:
The first concluding sentence is a perhaps optimistic twist to a negative finding, which may surprise some readers (such as me). It does serve as a good introduction to the authors' call for randomized trials to test the impact of screening in MSM. For readability, the authors may consider to a few word changes: *'Based on the findings of this study and those reviewed we conclude that we can **STILL** not exclude...'.*

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 19 March 2019

✓

Hamish McManus (iD)
The Kirby Institute, The University of New South Wales (UNSW Sydney), Sydney, Australia
Basil Donovan (iD)
The Kirby Institute, The University of New South Wales (UNSW Sydney), Sydney, Australia

This is a well written study aimed to measure correlation between country-level sexually transmissible infection (STI) screening intensity in MSM, and country-level incidence of *Neisseria gonorrhoeae* (NG) and *Chlamydia trachomatis* (CT) in MSM in European countries. The study sought to address a hypothesised association between risk of reinfection by unscreened cases and the intensity of screening in those populations. This hypothesis is consistent with no prior studies having detected negative correlation between screening and prevalence of STIs. While the study is ultimately unable to draw conclusions on the association between screening intensity and prevalence, its importance lies in potentially motivating discussion and further examination of this topic. One of the most important points it illustrates is that findings based on cross-sectional data such as these are open to a number of interpretations, and hence motivate more thorough analyses using longitudinal data.

In part the reason for the fairly limited conclusions and presentation of a range of interpretations of the findings lies with limitations of the ecological source data. For example, the source data used for incidence estimation should be interpreted cautiously. The ECDC estimates cited are, precisely, national-level notification rates for the general male population rather than incidence rates for the respective MSM population. This is problematic for several reason. Firstly, the association between increased screening intensity and notification rates has been established by previous studies and estimates of incidence based directly on notification rates need to be adjusted accordingly to reflect this.[1,2] And, secondly, it is not made clear what effect the use of general male population ECDC estimates rather than MSM specific estimates has on results. Although authors suggest that the ECDC estimates are strongly weighted by MSM, this statement is not supported. While MSM are disproportionately represented in NG/CT notifications, it is still probable that the strength of correlation between screening in this population and general incidence rates could be reduced substantially given that MSM comprise a very low (<7%) proportion of the male population.

In part to address these limitations ("To deal with this bias and the fact that the ECDC NG/CT incidence estimates do not provide incidence estimates for MSM" [P5]), the correlation between screening and prevalence estimates in MSM from STI clinics was also evaluated. However, this analysis is relatively limited, and we are not sure that it addresses these concerns successfully. Specifically, the prevalence results do not improve the interpretability of the incidence results. Also, they are based on complete results from only 4 countries (2 of which are not included in the incidence comparison) which is likely to limit the levels of correlation capable of being determined.

To overcome the limitations of this ecological study, the author concludes that randomised controlled

trials are urgently required. However, as this would require abandoning STI screening for some of the participants, such a trial would be ethically dubious and contrary to current clinical guidelines. Alternatively, longitudinal administrative data can be subject to retrospective cohort analysis. Using this technique, we were able to determine a true national increase in the incidence of NG in MSM but, after controlling for test frequency, this could be explained by increasing partner numbers and condomless anal sex.[3]

However, the statistical analyses in Kenyon's study are appropriate and robust. More complex methods may have been inappropriate for the broad ecological source data used. Appropriately, the conclusions drawn are careful and, in that regard, supported by the results. This study should proceed to being indexed for the reason that it motivates discussion and should motivate more rigorous research into these growing epidemics.

References

1. European Centre for Disease Prevention and Control: Sexually transmitted infections in Europe 1990–2010. *ECDC*. 2012. Publisher Full Text | Reference Source

2. Chen MY, Fairley CK, Donovan B: Nowhere near the point of diminishing returns: correlations between chlamydia testing and notification rates in New South Wales.*Aust N Z J Public Health*. 2005; **29** (3): 249-53 PubMed Abstract

3. Callander D, Guy R, Fairley CK, McManus H, Prestage G, Chow EPF, Chen M, Connor CCO, Grulich AE, Bourne C, Hellard M, Stoové M, Donovan B: Gonorrhoea gone wild: rising incidence of gonorrhoea and associated risk factors among gay and bisexual men attending Australian sexual health clinics.*Sex Health*. 2018. PubMed Abstract | Publisher Full Text

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Yes

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Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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