



**Australian Government**

**Department of Health**

**COMMUNICABLE  
DISEASES  
INTELLIGENCE**

2018      Volume 42

PII:      S2209-6051(18)00024-6

**Trends in gonorrhoea infection and overseas sexual contacts among females attending a sexual health centre in Melbourne, Australia, 2008-2015**

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**ISSN: 2209-6051 Online**

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This journal is indexed by Index Medicus and Medline.

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# Trends in gonorrhoea infection and overseas sexual contacts among females attending a sexual health centre in Melbourne, Australia, 2008-2015

Jennifer Misson, Eric P.F. Chow, Marcus Y Chen, Tim R.H. Read, Catriona S Bradshaw and Christopher K Fairley

## Abstract

### Introduction

There has been a steady increase in gonorrhoea cases among females in Australian major cities but the reasons remain unclear. The aim of this study was to identify the risk factors associated with gonorrhoea among females attending a sexual health centre in Melbourne.

### Methods

Analysis of retrospective electronic patient records of females aged 16 to 80 years old attending the Melbourne Sexual Health Centre, Australia between 1<sup>st</sup> January 2008 and 20<sup>th</sup> March 2015. East and South-East Asian countries were considered as higher-prevalence countries for gonorrhoea. Logistic regression with a generalised estimating equation was used to identify the risk factors associated with gonorrhoea among females.

### Results

Gonorrhoea positivity by culture among females increased from 0.3% in 2008 to 1.2% in 2015 ( $p_{\text{trend}}=0.004$ ). The rise in positivity was greatest in females reporting sex in a higher-prevalence country (0% to 7.4%,  $p_{\text{trend}}=0.026$ ) but only moderate (0.2% to 0.4%,  $p_{\text{trend}}=0.049$ ) in those reporting sex in Australia and/or in lower-prevalence countries. There was no association between gonorrhoea positivity and age, country of birth, number of male partners, condomless sex, or injecting drug use behaviours in the multivariable analysis. Gonorrhoea positivity by culture was significantly associated with presenting as a contact of gonorrhoea (aOR: 74.79; 95% CI: 44.07-126.93) or having sex with someone from a higher-prevalence country (aOR: 2.46; 95% CI: 1.15-5.25) after adjusting for potential confounding factors.

### Conclusion

There has been a recent four-fold increase in gonorrhoea among females attending a sexual health centre in Melbourne. Females who have sex with a partner from a country with higher-prevalence gonorrhoea (i.e. East and South-East Asian countries) are at higher risk of acquiring gonorrhoea. Public health interventions such as safe sex messages targeting travellers are required.

## Introduction

Gonorrhoea cases in Victoria have increased more than 10-fold over the last 10 years, principally among men who have sex with men (MSM)<sup>1,2</sup>. Historically, the rate of gonorrhoea in heterosexual people in Australian capital cities has been very low and stable<sup>3,4</sup>. The absence of the spread of gonorrhoea among heterosexuals in major Australian cities suggests that the basic reproductive ratio ( $R_0$ ) for gonorrhoea among heterosexuals in Australian cities to date has been less than one. However, since 2014, there has been a steady and worrying increase in gonorrhoea rates among heterosexuals<sup>2</sup>. Gonorrhoea in heterosexuals is important because it causes substantial morbidity in females including pelvic inflammatory disease (PID), infertility, chronic pelvic pain, and ectopic pregnancy<sup>5-7</sup>. Understanding why these increases in gonorrhoea cases have occurred in heterosexual people is important because different causes will need different public health interventions.

To date, the reasons for the increase among Australian heterosexuals remain unclear as the frequency of condomless penile-vaginal sex among heterosexuals has not increased over the last decade<sup>8-11</sup>. It is also possible these rises might be due to large increases in testing after the introduction of duplex nucleic acid amplification tests (NAAT) for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in mid-2000s<sup>3,12</sup> among low-prevalence populations. However, gonorrhoea screening among asymptomatic low-risk heterosexuals may potentially lead to false positives<sup>13</sup>. The rises may also indicate that the basic reproductive ratio for gonorrhoea in heterosexuals is greater than one, and herald the need for more effective prevention programs in heterosexuals. The aim of this study was to identify the risk factors associated with gonorrhoea among females diagnosed by culture at an Australian sexual health centre to determine the most likely explanation for the rise in gonorrhoea cases in females.

## Methods

Females aged 16 to 80 years old attending the Melbourne Sexual Health Centre (MSHC) between 1<sup>st</sup> January 2008 and 20<sup>th</sup> March 2015 were included in this analysis. MSHC is the largest public sexual health centre located in Melbourne, Australia. Patients' demographic information, sexual practices, overseas contacts, and history of engaging in sex work are recorded at each visit using a computer assisted self-interview (CASI). Data might also be entered by the clinician in the patient's clinic notes. Self-reported overseas contact refers to sex overseas with someone from overseas or sex in Australia with someone from overseas.

High vaginal or endocervical swabs were collected for gonorrhoea testing. All swabs were taken by clinicians and were directly plated onto gonococcal agar medium for culture during the study period. As per the Australian General Practice guideline<sup>14</sup>, MSHC only tested females for gonorrhoea in presentations with genital symptoms such as vaginal discharge, PID, cervicitis, and/or as the contact of a known gonorrhoea infection and these recommendations did not change over the study period. Gonorrhoea screening of asymptomatic females was not recommended due to low-prevalence of gonorrhoea in the urban population<sup>4,15</sup>. Females who had ever engaged in sex work were excluded from this analysis because the risk of gonorrhoea infection among sex workers was higher than the general female population<sup>16</sup>. Furthermore, screening guidelines in Victoria differ for females who engage in sex work<sup>17</sup>.

Medical records of females who were diagnosed with gonorrhoea were reviewed by a clinician to confirm whether these individuals had overseas sexual partners, and the country where they had sex. Countries were stratified into 'higher-prevalence' or 'lower-prevalence' countries as a proxy for heterosexual contact in the high prevalence country. Higher-prevalence countries included East and South-East Asian countries (Brunei, Cambodia, China, East Timor, Indonesia, Laos, Malaysia, Myanmar, Philippines, Singapore,

Thailand and Vietnam) as these countries had high incidence rate of gonorrhoea among their female population (i.e. more than 100 per 100,000 females)<sup>18</sup>.

Descriptive statistics and frequency distributions were calculated. Gonorrhoea positivity by culture was calculated by the number of positive cases divided by the number of tests conducted in each calendar year. A  $\chi^2$  trend test was used to assess the temporal trend of gonorrhoea positivity. Univariable logistic regression with a generalised estimating equation (GEE) approach was performed to examine the association between gonorrhoea positivity and potential explanatory risk factors such as demographic characteristics (age, country of birth, Aboriginal and Torres Strait Islander status), sexual behaviours (number of partners, condom use, and sex with someone outside Australia or New Zealand), injecting drug use behaviours, and self-reported contact of a known gonorrhoea infection. Risk factors with  $p < 0.10$  in the univariable analyses were included in the multivariable logistic regression. Crude and adjusted odds ratios (OR) and 95% confidence intervals (CIs) were reported.

All statistical analyses were performed using Stata (version 14, Stata Corporation, College Station, TX, US).

This study was approved by the Alfred Hospital Ethics Committee, Melbourne, Australia (No. 445/16).

## Results

There were 97,050 consultations for females at MSHC during the study period. A total of 78,246 consultations were excluded from the analysis for the following reasons: 39,973 (51.1%) consultations in female sex workers; 37,591 (48.0%) consultations were females who did not test for gonorrhoea; 102 (0.1%) consultations for females aged under 16 or above 80 years old; and 580 (7.4%) duplicate records. The remaining 18,804 consultations among 13,843 individual females were included in the analysis. The median age was 26 (interquartile range [IQR] 23-31) years.

The median number of male partners in the last 12 months was 2 (IQR 1-4) and 71.8% of females did not always use condoms with all their male partners in the last 12 months.

Of the 18,804 gonorrhoea tests conducted during the study period, 99 (0.53%; 95% CI 0.43-0.64%) females were tested positive for gonorrhoea by culture. Gonorrhoea positivity by culture increased from 0.30% to 1.21% during the study period ( $p_{\text{trend}} = 0.004$ ) (Figure 1).

In the univariable analysis, as expected, females who reported contact with an individual with gonorrhoea had the highest odds of having gonorrhoea (OR: 79.93; 95% CI: 47.73-133.84). In addition, higher odds of having gonorrhoea were also observed among females who did not use condoms consistently (OR: 2.68; 95% CI: 1.09-6.60); or who had sex with a male from a higher-prevalence country (2.37; 95% CI: 1.16-4.83) (Table 1). Gonorrhoea positivity by culture was not associated with patients' age, Indigenous status, country of birth, number of male partners, or injecting drug use behaviour.

In the multivariable analysis, the adjusted odds of having gonorrhoea among females who had sex with a male from a higher-prevalence country was 2.46 (95% CI: 1.15-5.25) times higher than among females who did not have sex with someone outside Australia or New Zealand (Table 1). Females who reported contact with an individual with gonorrhoea remained the strongest risk factor for gonorrhoea (aOR: 74.79; 95% CI: 44.07-126.93) after adjusting for other confounding factors. However, gonorrhoea positivity by culture was not associated with females who had sex with someone from lower-prevalence countries. In addition, condomless sex was no longer a risk factor for gonorrhoea in the multivariable analysis after adjusting potential confounding factors including sex with someone outside Australia or New Zealand.

Figure 2 shows that the proportion of all females attending MSHC who had sex with someone outside Australia or New Zealand increased significantly from 27.7% (653/2,360) to 40.1%

Table 1. Factors associated with gonorrhoea positivity by culture among females attending the Melbourne Sexual Health Centre, 2008-2015.

Characteristics	Number of gonorrhoea tests in females, N	Tested positive for gonorrhoea, n (%)	Odds ratio (95% CI) <sup>Δ</sup>	P-value	Adjusted odds ratio (95% CI) <sup>Δ</sup>	P-value
Year	18,804	99 (0.53%)	1.15 (1.04-1.26)	0.005	1.12 (1.01-1.23)	0.027
<b>Age<sup>ε</sup></b>						
≤26	9,524	55 (0.58%)	1	Ref		
>26	9,280	44 (0.47%)	0.82 (0.55-1.22)	0.327		
<b>Indigenous status<sup>Δ</sup></b>						
Indigenous	121	1 (0.83%)	1	Ref		
Non-Indigenous	16,336	78 (0.48%)	0.58 (0.08-4.19)	0.585		
Unknown	2,347	20 (0.85%)	1.03 (0.14-7.80)	0.975		
<b>Country of birth</b>						
Australia	7,830	32 (0.41%)	1	Ref		
Overseas	9,887	61 (0.62%)	1.51 (0.98-2.32)	0.061		
Unknown	1,087	6 (0.55%)	1.35 (0.56-3.25)	0.502		
<b>Number of male partners in the last 12 months<sup>φ</sup></b>						
≤2	8,336	39 (0.47%)	1	Ref		
>2	8,279	50 (0.60%)	1.28 (0.84-1.95)	0.243		
Declined to report	2,189	10 (0.46%)	0.91 (0.44-1.86)	0.793		
<b>Condom use in the last 12 months</b>						
Always / no sex	2,236	5 (0.22%)	1	Ref	1	Ref

Characteristics	Number of gonorrhoea tests in females, N	Tested positive for gonorrhoea, n (%)	Odds ratio (95% CI) <sup>Δ</sup>	P-value	Adjusted odds ratio (95% CI) <sup>Δ</sup>	P-value
<i>Not always</i>	13,506	81 (0.60%)	2.68 (1.09-6.60)	0.032	2.29 (0.92-5.70)	0.076
<i>Declined to report</i>	3,062	13 (0.42%)	1.81 (0.64-5.12)	0.260	2.19 (0.65-7.35)	0.207
<b>Injecting drug use</b>						
<i>Never</i>	16,105	88 (0.55%)	1	Ref		
<i>Ever</i>	361	1 (0.28%)	0.50 (0.07-3.66)	0.496		
<i>Declined to report</i>	2,338	10 (0.43%)	0.74 (0.38-1.44)	0.374		
<b>Contact of infection</b>						
<i>No</i>	18,706	75 (0.40%)	1	Ref	1	Ref
<i>Yes</i>	98	24 (24.49%)	79.93 (47.73-133.84)	<0.001	74.79 (44.07-126.93)	<0.001
<b>Sex with someone outside Australia/ New Zealand</b>						
<i>No</i>	10,076	54 (0.54%)	1	Ref	1	Ref
<i>Yes, with a male from a higher-prevalence country<sup>Ⓟ</sup></i>	710	9 (1.27%)	2.37 (1.16-4.83)	0.017	2.46 (1.15-5.25)	0.020
<i>Yes, with a male from a lower-prevalence country</i>	4,779	26 (0.54%)	1.01 (0.63-1.62)	0.954	1.06 (0.65-1.72)	0.828
<i>Yes, with a male from an unknown country</i>	702	0 (0%)	N/A			
<i>Declined to report</i>	2,537	10 (0.39%)	0.71 (0.36-1.41)	0.327	0.69 (0.25-1.87)	0.465

<sup>Ⓟ</sup>Age was categorised into two groups using the median of age as the cut-off value.

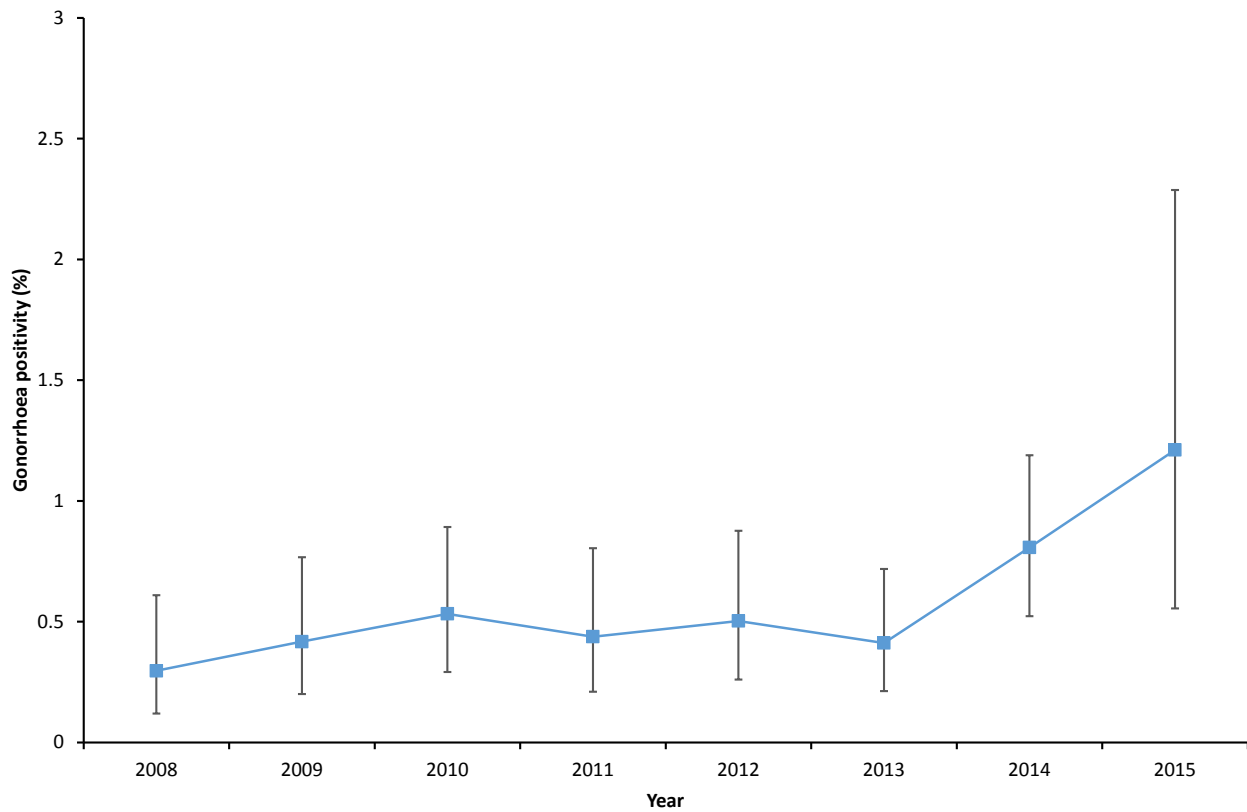
<sup>Ⓛ</sup>Indigenous people were defined as Aboriginal and Torres Strait Islander people.

<sup>Ⓢ</sup>Number of partners was categorised into two groups using the median number of partners as the cut-off value.

<sup>Δ</sup>Effect estimates derived from a generalized estimating equation logistic regression model.

<sup>Ⓢ</sup>Higher-prevalence countries include Brunei, Cambodia, China, East Timor, Indonesia, Laos, Malaysia, Myanmar, Philippines, Singapore, Thailand and Vietnam.

Figure 1. Annual gonorrhoea positivity by culture among females attending the Melbourne Sexual Health Centre, 2008-2015. Note. Gonorrhoea positivity in 2015 was calculated between January and March 2015 only.



(298/743) over the study period ( $p_{\text{trend}} < 0.001$ ). Furthermore, the gonorrhoea positivity by culture among females who had sex with a male from a higher-prevalence country increased dramatically from 0% (0/102) in 2008 to 7.4% (2/27) in 2015 ( $p_{\text{trend}} = 0.026$ ). In addition, the gonorrhoea positivity by culture among females who had sex with someone from lower-prevalence countries increased gradually from 0.19% (1/535) in 2008 to 0.42% (1/240) in 2015 ( $p_{\text{trend}} = 0.049$ ) but the positivity remained low over the study period.

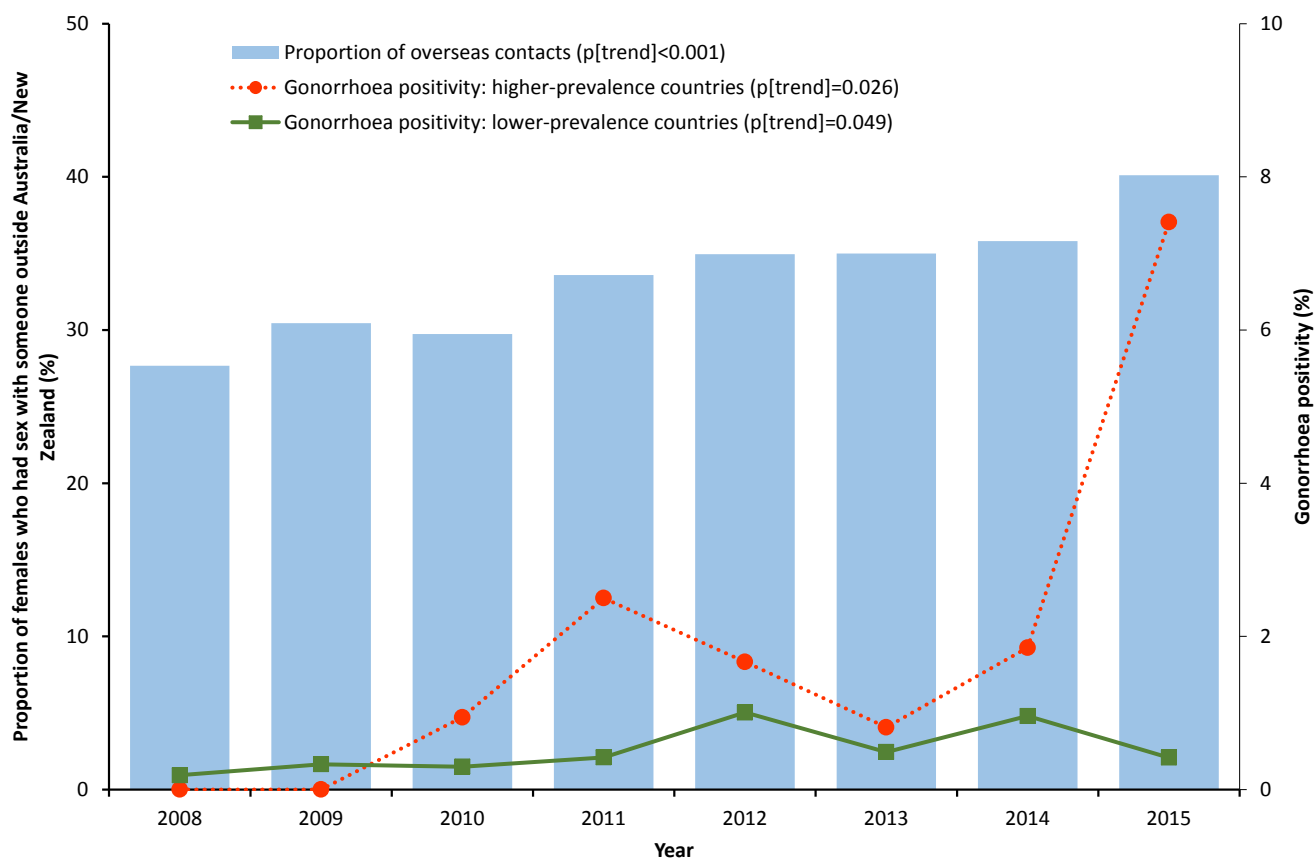
## Discussion

The proportion of positive gonococcal cultures increased four-fold in women attending a clinic in Melbourne between 2008 and 2015. The absence of sexual behavioural risk factors for gonorrhoea such as high number of sexual partners and condomless sex, suggests another cause for the increase. During the study period time, notifications of gonorrhoea in MSM increased

substantially and it is plausible that transmission to females via bisexual males could explain the increase in gonorrhoea positivity in women without any alteration in the women's sexual behaviour. However, we found that having sex with someone from a country with a high prevalence of gonorrhoea was a significant risk factor, particularly since 2014. This finding has implications for public health messages that might be directed specifically to travellers at risk.

This study has several limitations. Firstly, this study was conducted at a single urban sexual health service in Melbourne, Australia. Our population would be biased towards females with genital symptoms and contacts of infection, and thus our findings may not be generalizable to females across the wider Victorian or Australian population. If the risk factors for gonorrhoea were different in females outside these groups then our results would not be generalizable. Secondly, we did not record or ask

Figure 2. Annual proportion of overseas contacts and gonorrhoea positivity by culture among females who had overseas contacts stratified by higher- and lower-prevalence countries, 2008-2015.



females routinely about sex with a bisexual man. This is a difficult risk factor to identify and it is likely most females would not know the answer to this question even if it was routinely asked. We are not aware of other studies that have asked women with gonorrhoea about this risk. Thirdly, patients were only asked to report one country when they report overseas contacts via the computer assisted self-interview. Patients with more than one overseas contact may not report to their clinicians about all relevant countries, and even if they did, there is only the option of reporting a single country (i.e. a single data field) in the medical files. It is a common practice at MSHC for clinicians to report the country where the patients perceive to be higher risk. Finally, we were unable to examine the gonorrhoea positivity by culture after March 2015 because our centre changed the method of gonorrhoea diagnosis from culture to NAAT in March 2015. NAAT has a higher sensitivity and lower specificity than culture for gonorrhoea detection and thus

it is not appropriate to calculate the positivity rate from two different methods<sup>19, 20</sup>. However, by using culture throughout the study period we ensured all positive samples were true positives given the high specificity of culture.

Our findings suggest that gonorrhoea positivity is significantly associated with females who had sex with someone from a country with higher-prevalence of gonorrhoea. A meta-analysis has concluded that overseas sexual contact is highly associated with individuals who expect or plan to have sex during travels<sup>21</sup>. According to the Australian Bureau of Statistics, the number of short-term resident departures almost doubled from 5.8 million in 2008 to 9.5 million in 2015<sup>22</sup>. We showed that the proportion of females who reported sex with someone from overseas also increased over the same period at MSHC. There is no evidence suggesting gonorrhoea positivity is associated with females who had sex with someone from Australia, New Zealand or

lower-prevalence countries. Further studies on genotyping the strain of *Neisseria gonorrhoeae* would be useful to examine whether there is a spread of gonorrhoea from these countries to Australia.

The four-fold rise in notifications in females in Australia is similar to the rise in gonorrhoea that has been reported among the MSM population in Australia<sup>3,19</sup>. It is possible that bisexual males acting as a potential bridge of STI transmission to females<sup>23</sup> but in the absence of data on this elusive risk factor we could not examine this association. This is because male partners are unlikely to disclose sex with men to their female partners nor was this systematically sought by clinicians. Currently, there are no published data estimating either the proportion of females who know whether their male partners are bisexual or the proportion of bisexual males who disclose their sexual orientation to their female partners.

We could not identify the number of male partners as a risk factor for gonorrhoea, suggesting that possibly only a few very specific men put women at risk of gonorrhoea. These men may be bisexual or heterosexual males who have had sex with someone from higher-prevalence countries. Both groups of men represent a small fraction of all male partners. Further research is required to examine the association between gonorrhoea positivity and heterosexual males who have sex overseas and bisexual males.

To our best knowledge, there is only one public health campaign in Australia promoting safe sex for travellers (<http://www.whereversexhappens.com/sexandtravel.php>)<sup>24</sup> and this campaign is mainly focused on MSM and HIV. It would be useful for clinicians to discuss safe sex issues with the patients who plan to travel, particularly to those higher-prevalence countries.

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