

To whom should we prescribe doxy-PEP? A retrospective review of public health surveillance data for bacterial STI diagnoses among gay, bisexual, and other men who have sex with men in Ottawa, Canada

Rates of bacterial STIs, such as chlamydia, gonorrhea, and syphilis have been increasing in Canada and disproportionately affect gbMSM. One new intervention to counter this rise in rates is the provision of doxycycline as post-exposure prophylaxis to gbMSM. In light of ongoing and worsening worldwide antimicrobial resistance for STIs, we thus sought out to answer the question: among gbMSM, who should receive a prescription for doxy-PEP?

Using public health surveillance data from January 2021 to December 2024, from over 21,000 sexually active gbMSM in Ottawa, we saw that 1,819 gbMSM experienced 2,834 positive testing episodes and 3,114 bacterial STI diagnoses. We then calculated the number needed to treat (NNT) to prevent one STI episode under different prescription strategies.

Our analysis showed that only 3% of sexually active gbMSM in Ottawa were diagnosed with a bacterial STI annually, and only one in four experienced reinfection within 12 months. The NNT would therefore be 60 if doxy-PEP was given to all sexually active gbMSM in Ottawa. In other words, 60 gbMSM would need to take doxy-PEP to prevent a single positive test result for a bacterial-STI – or if all gbMSM in Ottawa (21,000) took doxy-PEP, it would prevent 356 bacterial STI's annually. However, if we provided doxy-PEP to gbMSM who had been diagnosed with at least one (1) bacterial-STI within in the last 12 months that would mean that an average of 662 gbMSM would require antibiotics. This NNT dropped to 8, which means we would only need to give 8 gbMSM doxyPEP to prevent 1 bacterial STI diagnosis.

Here is what we found

We therefore concluded that prescribing doxy-PEP to gbMSM with at least one (1) bacterial-STI in the past 12 months is the most efficient and sustainable public health strategy. Universal use would lead to overprescription, and waiting for a second infection misses opportunities for prevention. And finally, our study also emphasizes the importance of proper patient counseling about doxy-PEP's limitations, ongoing testing, and awareness of symptoms to avoid reliance on the drug as a fail-safe.

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ABSTRACT

Introduction Increases in bacterial sexually transmitted infections (bac-STIs), such as gonorrhoea, chlamydia and syphilis, have affected gay, bisexual, and other men who have sex with men (gbMSM). A new strategy to prevent bac-STIs involves giving doxycycline as postexposure prophylaxis (doxy-PEP), and research shows that this intervention can prevent chlamydia and syphilis by 70% and gonorrhoea by 33%–50%. Consequently, the US CDC released guidelines in 2024 recommending doxy-PEP for gbMSM with ≥1 bacterial STI diagnosis in the previous 12 months.

Methods We reviewed public health STI surveillance data between 1 January 2021 and 31 December 2024 for gbMSM in Ottawa, Canada, and analysed the number of infections and episodes of infections per person. We estimated the number of individuals who would need doxy-PEP to prevent a single bac-STI episode.

Results During the study period, 1819 unique gbMSM experienced 2834 positive bac-STI testing episodes (PTE), during which 3114 bac-STIs were diagnosed. Consistently, three-quarters of gbMSM did not have a subsequent infection, whether they were diagnosed with 1 infection, 2 infections or ≥3. Considering the average effectiveness of doxy-PEP in this study population, the average number needed to treat (NNT) if doxy-PEP were prescribed to all gbMSM to prevent a first PTE would have been 60. The NNT among those with their first PTE to prevent a second PTE was 8; among those with their second, the NNT was 7.

Conclusions Based on these data, and in alignment with the CDC guidelines, we conclude that doxy-PEP would likely have the most balanced population-level bac-STI prevention effect if given to gbMSM with ≥1 bac-STI diagnosis within the preceding 12 months. Providing doxy-PEP to all gbMSM would likely result in an overuse of antibiotics, and providing doxy-PEP only after a second PTE would result in fewer infections averted for the same proportion treated.

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Doxy-PEP effectively prevents bacterial sexually transmitted infections (bac-STIs).
- ⇒ Doxy-PEP is an appropriate intervention for gay, bisexual, and other men who have sex with men (gbMSM).

WHAT THIS STUDY ADDS

- ⇒ The number needed to treat to achieve prevention outcomes with doxy-PEP based on different target populations of gbMSM.
- ⇒ That giving doxy-PEP to gbMSM with ≥1 bac-STI diagnosis within the preceding 12 months seems most reasonable for balancing antibiotic stewardship and public health STI prevention outcomes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ This study gives empirical evidence regarding subsequent bac-STIs among gbMSM and suggests which gbMSM should be prescribed doxy-PEP.

INTRODUCTION

Internationally, there have been increases in the reported rates of bacterial sexually transmitted infections (bac-STIs), including gonorrhoea, chlamydia and syphilis.¹ Data also suggest that gay, bisexual, and other men who have sex with men (gbMSM) account for a disproportionate number of these infections.¹ While sexual health strategies for bac-STIs among gbMSM have historically included condom use and rescreening every 3–12 months,^{2–3} a new intervention is available. Known as doxycycline postexposure prophylaxis (doxy-PEP), this strategy involves giving a one-time 200 mg oral dose of doxycycline after sexual contact when bac-STI transmission could have occurred.⁴

In June 2024, the US CDC released doxy-PEP guidelines,⁵ which recommended that healthcare providers offer this intervention to gbMSM who had been diagnosed with ≥ 1 bac-STIs in the preceding 12 months. The guideline⁵ detailed that doxy-PEP was to be used after sexual contact (ideally within 24 hours, but up to 72 hours later), and that it could be used up to daily, as needed. The CDC guideline⁵ further specified that clinicians should prescribe as many doses as required until a patient's next clinical follow-up (within 3 months), when another prescription could be given, if warranted.⁵ The CDC's rationale⁵ for endorsing doxy-PEP was twofold: first, if doxy-PEP could be distributed to populations with the greatest bac-STI burden, then it should decrease STI incidence overall; and, second, if doxy-PEP could be given only to those who account for a large proportion of bac-STIs, then fewer people would need to use this intervention for population-level benefits.

In favour of doxy-PEP are findings from randomised controlled trials,^{4–7} which demonstrated that, when gbMSM used doxy-PEP after sexual contact, this intervention prevented syphilis and chlamydia acquisition by at least 70% and gonorrhoea by about 50%. A meta-analysis of randomised controlled studies,⁸ however, found that the preventive effect of doxy-PEP for gonorrhoea might be lower, ranging from 33% to 45%—and that its effect appeared to depend on local rates of gonorrhoea antibiotic resistance⁹ and the site of infection (with potential lessened effectiveness for pharyngeal gonorrhoea infection).¹⁰ Also suggesting a more judicious use of doxy-PEP are medication side effects and the possibility of exacerbating antibiotic resistance.^{4–7} For side effects, doxycycline can cause photosensitivity and gastrointestinal upset (including oesophagitis).¹¹ Regarding the development of antibiotic resistance, while most doxy-PEP studies^{4–7} reported low rates of developed resistance for *Staphylococcus aureus* and no study reported any resistance for MRSA or *Escherichia coli*, other research¹² has found that doxy-PEP use is associated with tetracycline-resistant group A *streptococcus* and *S. aureus*. Other concerns about doxy-PEP relate to healthcare burden³: What volume of patients would be eligible for this intervention, and, if initiated, what might be the public health outcomes?

To understand the potential clinical demand and public health impact of doxy-PEP, we reviewed 4 years of public health bac-STI surveillance data for gbMSM in Ottawa, Canada, and analysed the number of infections and episodes of infections per person. We then estimated the number of individuals who would need treatment (ie, the number needed to treat (NNT)) to prevent a single bac-STI episode. Considering these data, we discuss the potential public health effects of offering doxy-PEP to gbMSM who have been diagnosed with 0, ≥ 1 or ≥ 2 bac-STI diagnoses.

METHODS

We undertook this study in Ottawa, Ontario, a Canadian city of just over 1 million residents¹³ during the period included in our analysis. At the time of our analysis, in Ontario, all bac-STIs were reported from the laboratory to the local public health unit, which was mandated to ensure surveillance and case and contact management.¹⁴ For this analysis, we extracted all positive bac-STI testing episodes during which gonorrhoea, chlamydia or syphilis (infectious or unspecified) was confirmed in an Ottawa resident, during 1 January 2021–31 December 2024, from the Ontario Ministry of Health's integrated Public Health Information System; extraction occurred on 12 May 2025. We used demographic and risk factor data collected during routine public health case management to identify gbMSM who were ≥ 18 years of age. We determined, among this subgroup, the number of persons with ≥ 1 PTE within the previous 12 months from their most recent bac-STI diagnosis in a given year during 2022–2024. We considered the number of PTEs and bac-STIs that might be prevented to calculate the NNT to prevent a subsequent PTE using 0, ≥ 1 or ≥ 2 PTEs in a 12-month period as a threshold for prescribing doxy-PEP.

The NNT was calculated as the inverse of the absolute risk reduction (ARR). The ARR was calculated as the difference between the rate of a first (0 threshold), second (≥ 1 threshold) or third (≥ 2 threshold) PTE without intervention and with intervention.

The rate for PTE with intervention was calculated as 1–doxy-PEP efficacy. Because current evidence^{4–8} shows that the efficacy of doxy-PEP varies among bac-STIs, we calculated a weighted efficacy for preventing gonorrhoea, chlamydia or syphilis that accounted for the incidence of each of these infections in our population during the study period (see table 1). Using the CDC's published efficacy of 70% of doxy-PEP for chlamydia and syphilis, and a lower estimate of 33% for gonorrhoea based on published studies,^{4–8} we derived a weighted efficacy for doxy-PEP of 54% in preventing these three infections following a sexual encounter when bac-STI transmission

Table 1 Calculation of a weighted efficacy for doxy-PEP in the prevention of a bac-STI based on surveillance data, Ottawa, 2021–2024

bac-STI	Number of bac-STIs during 2021–2024	Efficacy	Number of bac-STIs averted
Chlamydia	1349	0.70	944
Gonorrhoea	1446	0.33	477
Infectious syphilis	498	0.70	349
Total	3293	0.54*	1770

*Calculated as the proportion of total bac-STIs that would be averted.
bac-STI, bacterial sexually transmitted infection; doxy-PEP, doxycycline as postexposure prophylaxis.

could have occurred. In assuming 33% efficacy against gonorrhoea, even though it might be as high as 50% (per the CDC guidelines)⁵ or 45% (based on meta-analysis)⁸ as low as 0% (for pharyngeal infections in one study),¹⁰ our analyses should give a conservative estimate regarding the potential impact of doxy-PEP. Our estimate of 33% effectiveness for doxy-PEP for gonorrhoea also aligns with the DoxyVAC study, which reported a gonorrhoea resistance rate of 65%—which exceeds the upper end of tetracycline resistance reported in Canada (range of 43.1% in 2020 to 56.4% in 2015)¹⁵ and 48.9% among gbMSM in Canada in 2022.¹⁶

Of note, the conclusions drawn from considering each infection with its respective doxy-PEP efficacy were not different from those drawn from combining the three bac-STIs and using a weighted efficacy. See online supplemental tables 1 to 8 for these analyses.

Lastly, the number of sexually active gbMSM was calculated using the most recent estimate from the 2019 SexNow Survey¹⁷ adjusted for population growth.¹⁸ We used this denominator for two calculations: (1) to determine the overall rate of bac-STI diagnosis among gbMSM in Ottawa and (2) to calculate the NNT for doxy-PEP if it were given to all sexually active gbMSM in Ottawa.

RESULTS

During 1 January 2021–31 December 2024, in Ottawa, Canada, 1,819 unique gbMSM experienced 2834 PTEs, during which 3114 bac-STIs were diagnosed (table 2). Among the annual average 21 274 gbMSM during 2022–2024, an average of 663 gbMSM (3.1%, range, 2.9%–3.3%) were diagnosed with ≥1 bac-STI each year.

To determine the impact of doxy-PEP on subsequent infection rates, we compared observed reinfection rates among gbMSM who had a PTE in 2021, 2022 and 2023 with expected rates had doxy-PEP been used. An annual average of 3.1% (range, 2.9%–3.3%) of gbMSM had a

single PTE during 2022–2024 (table 3). Furthermore, an average of 24.5% (range, 23.2%–26.5%) with one PTE had a second PTE, and 25.5% (range, 19.3%–30.3%) with two PTEs had a third. Considering the proportion of individuals with diagnoses during 2022–2024 with a previous PTE and the expected effectiveness of doxy-cycline in this study population, the average NNT for doxy-PEP prescribed to all gbMSM to prevent a first PTE would have been 60 (range, 56–63). That is, 60 gbMSM would have needed to take doxy-PEP to avert a single PTE. To prevent a second PTE among those after a first PTE, the NNT was 8 (range, 7–8); to prevent a third PTE among those with their second PTE, the NNT was 7 (range, 6–10). Notably, while the absolute number of PTEs changed year over year during the study period, the frequency of subsequent PTEs was relatively constant at one-quarter.

To estimate the potential public health impact of doxy-PEP on the total number of bac-STIs, we determined the average annual percent of PTEs and bac-STIs averted had doxy-PEP been prescribed and used (tables 4 and 5). If doxy-PEP were prescribed to all gbMSM, 54% (based on the weighted efficacy of doxy-PEP—see methods calculations above) of subsequent PTEs and bac-STIs would have been averted. If doxy-PEP were prescribed following all first-time PTEs, 26% of PTEs and 15% of bac-STIs would have been averted; if not prescribed until the second PTE, 10% of PTEs and 4% of bac-STIs would have been averted. See online supplemental tables 9 and 10 for calculations.

DISCUSSION

In the context of increasing bac-STI rates internationally^{1–3} and the emergence of a new bac-STI intervention known as doxy-PEP,⁵ we used public health surveillance data from Ottawa, Canada to analyse bac-STI diagnosis episodes among gbMSM between 2021 and 2024.

Table 2 Unique gbMSM, positive bacterial STI (bac-STI) testing episodes (PTE) and chlamydia, gonorrhoea and syphilis bac-STI diagnoses in Ottawa during 2021–2024, by year

	# of gbMSM*	# of gbMSM with ≥1 PTE	% of gbMSM with ≥1 PTE	Total # of PTEs	# of chlamydia diagnoses	# of gonorrhoea diagnoses	# of syphilis diagnoses	Total # of diagnoses
2021	20 497	385	1.9	448	231	169	87	487
2022	20 884	614	2.9	747	388	368	74	830
2023	21 290	711	3.3	863	399	449	98	946
2024	21 650	663	3.1	776	331	460	60	851
Sum, 2021–2024	N/A	1819†		2834	1349	1446	319	3114
Average, 2022–2024	21 274	663	3.1	795	373	426	77	876

*Based on population growth following 2019 estimate for Sex Now.

†Individuals are counted in each calendar year in which they experience a PTE but only once in the total sum.

bac-STI, bacterial sexually transmitted infection; gbMSM, gay, bisexual, and men who have sex with men; N/A, not available.

Table 3 Number and percentage of gbMSM with ≥ 1 PTEs in a 12-month period, with corresponding NNT, Ottawa, 2022–2024, by year

Year	# of PTEs / individual	# of individuals with given # of PTEs	% of individuals with given # of PTEs who have their first or another PTE	% of individuals with given # of PTEs who would have their first or another PTE were doxy-PEP used	NNT to have prevented another PTE
2022	0	20884	2.9	1.4	63
	1	468	23.8	11.0	8
	2	106	27.4	12.7	7
	3	40			
2023	0	21290	3.3	1.5	56
	1	546	23.20	10.70	8
	2	115	30.30	14.00	6
	3	50			
2024	0	21650	3.10	1.40	61
	1	487	26.50	12.30	7
	2	142	19.30	8.90	10
	3	34			
2022–24 average	0	21274	3.10	1.40	60
	1	500	24.50	11.30	8
	2	121	25.50	11.80	7
	3	41			

The calculation of PTEs averted takes average efficacy of doxy-PEP into account.

bac-STIs, bacterial sexually transmitted infections; doxy-PEP, doxycycline as postexposure prophylaxis; gbMSM, gay, bisexual, and men who have sex with men; NNT, number needed to treat; PTE, positive bac-STIs testing episodes.

Our goal was to determine the possible public health outcomes of prescribing doxy-PEP to gbMSM with 0, 1 or ≥ 2 bac-STI diagnoses. With such data, we sought to answer the question, ‘among gbMSM, to whom should we prescribe doxy-PEP?’.

Based on our data, in Ottawa, only approximately 3% of all gbMSM were diagnosed with a bac-STI during 2021–2024. In offering doxy-PEP to all sexually active gbMSM in Ottawa, the NNT would, therefore, have been approximately 60, which is much higher than for gbMSM with ≥ 1 PTE in the previous 12 months (NNT=8). Consistent with the CDC guidelines,⁵ we found that providing

doxy-PEP to gbMSM with ≥ 1 bac-STI diagnosis in the preceding 12 months appeared to strike the best balance between public health bac-STI prevention impact and antibiotic stewardship, in that it would result in a reasonable population-level outcome with a lower NNT.

To explain further, while providing doxy-PEP to all gbMSM in Ottawa regardless of a previous bac-STI diagnosis could have prevented up to a weighted estimate of 54% of the incident bac-STIs we observed, it would have required an NNT of 60 (or, stated differently, the provision of doxycycline to over 21 000 gbMSM to prevent an average of 356 bac-STIs per year). By comparison,

Table 4 Potential public health impact on PTEs of offering doxy-PEP to individuals with 0, 1 or 2 previous PTEs, annual average, Ottawa

# of PTEs/individual in a 12-month period ending with the individual's most recent PTE	Average # of individuals with number of PTEs including the individual's most recent PTE	Average total # of PTEs in the following 12 months	Average # of PTEs averted in the following 12 months if given doxy-PEP after a given PTE	% of PTEs in the following 12 months averted if given doxy-PEP
1 PTE	500	663	356	54%
2 PTEs	121	325	175	26%
3+PTEs	41	124	67	10%

doxy-PEP, doxycycline as postexposure prophylaxis; PTEs, positive bac-STIs testing episodes.

Table 5 Potential public health impact on bac-STIs of offering doxy-PEP to individuals with 0, 1 or 2 previous PTEs, annual average, Ottawa

# of PTEs/individual in a 12-month period ending with the individual's most recent PTE	Average # of bac-STIs diagnosed in a 12-month period ending with their last diagnosis in individuals who had a given # of PTEs	Average total # of bac-STIs diagnosed	Average # of bac-STIs averted in the following 12 months if given doxy-PEP after a given PTE	% of bac-STIs in the following 12 months averted if given doxy-PEP
1 PTE	632	876	471	54%
2 PTEs	176	244	131	15%
3+PTEs	68	68	37	4%

bac-STIs, bacterial sexually transmitted infections; doxy-PEP, doxycycline as postexposure prophylaxis; PTE, positive bac-STIs testing episodes.

providing doxy-PEP only to gbMSM in Ottawa with ≥ 2 bac-STI diagnoses in the preceding 12 months would likely have prevented only 4% of incident infections, but with a much lower NNT of only 8 (and the provision of antibiotics to only an average of only 162 gbMSM per year). For a very similar NNT, providing doxy-PEP to gbMSM in Ottawa with ≥ 1 bac-STI diagnosis in the preceding 12 months would have potentially prevented 15% of incident bac-STIs in gbMSM annually (or approximately 616 infections per 100 000 sexually active Ottawa gbMSM population¹⁷ and 12 infections per 100 000 Ottawa population). Strategically providing doxy-PEP to gbMSM with ≥ 1 bac-STI diagnosis in the preceding 12 months would also have only required antibiotic use by an average of 662 gbMSM (in a city of >1 million residents and an estimated 21 000 gbMSM), or 4 times the number of men who would use antibiotics if the threshold of ≥ 2 bac-STI diagnoses to prescribe doxy-PEP.

We thus believe, when taken as a whole, that our data support the conclusion that, to best balance antibiotic stewardship and public health preventive outcomes, doxy-PEP should be prescribed to gbMSM with ≥ 1 bac-STI diagnosis within the preceding 12 months. We also believe our findings suggest that consideration could be given to an even more restricted use of doxy-PEP (ie, to having a higher threshold for the number of previous bac-STI diagnoses needed before prescribing doxy-PEP). However, this point comes with the caveat that, while such an approach would decrease antibiotic use, it would also diminish the potential public health impact that doxy-PEP could have on ongoing bac-STI transmission.

To the best of our knowledge, our calculations regarding the potential population-level impact of doxy-PEP are one of the first based on public health STI surveillance data, rather than on cohort data or modelled estimates. We feel that such analyses of real-world data are useful because they can inform decision-making about which gbMSM could use doxy-PEP to achieve the best prevention outcomes while minimising the harms of antibiotic overuse. Our data show that making doxy-PEP universally available to gbMSM who have not had any bac-STI diagnoses within the preceding 12-month period would likely result in a mass, non-judicious overuse of antibiotics. In

the context of worsening gonorrhoea resistance,^{15 16} such an approach seems unwise.

Our results also signal that, to maximise the benefits of doxy-PEP, it is important that clinicians give patients clear instructions on three points. The first is that doxy-PEP is not 100% effective,⁴⁻⁷ and that its impact for gonorrhoea (and perhaps pharyngeal gonorrhoea even more so) may be low to nonexistent. For doxy-PEP to achieve any of the potential public health benefits we identified herein, it is essential that patients and clinicians are not overconfident in its effectiveness. The second point for counselling is about how patients should proceed if they develop symptoms that are suggestive of a bac-STI or if one of their sexual partners develops STI-like symptoms or is diagnosed with a bac-STI.¹⁹ In such cases, clinicians should instruct patients to seek healthcare services to have an examination and/or possibly be treated empirically as a contact of someone who was diagnosed with a bac-STI, irrespective of doxy-PEP use.¹⁹ This approach could placate the concern that, without adequate assessment and treatment, people could have a false sense of security related to the benefits of doxy-PEP, which—when it fails—could lead to increased bac-STI transmission. This would be especially true for asymptomatic infections and for all gonorrhoea infections, for which this intervention has the least effect. The third point for patient counselling is that healthcare providers need to reinforce the need for routine testing every 3 months⁵—and that testing should not be deferred based on doxy-PEP use. Doxy-PEP will fail and many bac-STIs are asymptomatic, especially at extragenital sites. In such cases, retesting every 3 months would result in quick, routine access to testing and treatment, were doxy-PEP to have failed. If persons defer testing, the result again could be an inadvertent increase in ongoing bac-STI transmission. In other words, overconfidence in doxy-PEP could undo its potential to yield benefits.

Limitations

Our results must be interpreted considering certain limitations. First, our data are based on laboratory diagnosed infections, which might undercount the true number of bac-STIs as it would exclude those that were

not diagnosed and those that were treated empirically without testing. In addition, infections might go undiagnosed because individuals deny or ignore possible symptoms, infections are asymptomatic, or there are barriers to accessing testing.²⁰ Also potentially undermining our counts of true bac-STI numbers is that some bac-STIs diagnosed outside our jurisdiction might not have been reported to our public health unit. Second, risk factors are missing in a subset of cases, meaning positive results from gbMSM may not have been included in this analysis. Undercounting bac-STIs would prevent the identification of some initial and subsequent PTEs, which would have affected our estimated NNTs. Third, we did not stratify our analysis by the anatomical site of infection. Averting repeat oral chlamydia infections is likely less significant than averting syphilis or rectal gonorrhoea—both of which have worse sequelae and correspond with an increased risk of HIV acquisition.¹⁴ Future analyses might further refine the criteria for doxy-PEP, including searching to determine if there are subpopulations with better NNTs (eg, HIV-positive gbMSM or gbMSM who use PrEP or who have recurrent rectal chlamydia infections). Third, our estimates regarding averted infections rely on the assumption of complete uptake. Knowing that less than 100% of persons will use (or will correctly use) doxy-PEP,^{4 6 7} it is likely that the real-world impact of doxy-PEP will be less than what we have calculated. Lastly, our results would likely vary based on local rates of antibiotic resistance for gonorrhoea. As resistance increases, the potential impact and NNTs we calculated would worsen. Similar changes in NNT would arise if the distributions of infections differed from what we have in Ottawa, Canada.

CONCLUSIONS

In the context of rising bac-STI rates, there is interest in the effects of doxy-PEP by gbMSM after a sexual contact during which bac-STI transmission could have occurred. Trial data suggest that, among gbMSM, doxy-PEP corresponded with 70% reductions in chlamydia and syphilis acquisition and 33%–50% reductions in gonorrhoea acquisition. In June 2024, the US CDC consequentially released guidelines for doxy-PEP prescription, suggesting—based on the doxy-PEP trial protocols—that this intervention be given to gbMSM who have had ≥ 1 bac-STI diagnosis within the preceding 12 months. To add further understanding about the threshold of bac-STI diagnoses and the potential impact of doxy-PEP, we reviewed bac-STI diagnoses and subsequent infections within 12 months of a first bac-STI diagnosis among gbMSM in Ottawa, Canada from 1 January 2021 to 31 December 2024. We found that about three-quarters of these men who had a single PTE did not have a subsequent infection within 12 months, and the same proportion of gbMSM with a second PTE did not have a third. There was thus no specific threshold of previous diagnoses above one that seemed to yield the best outcome

for limited antibiotic use and enhanced public health benefit.

Based on these data, and in alignment with the June 2024 CDC guidelines, we conclude that doxy-PEP would likely have the most balanced population-level bac-STI prevention effect if given to gbMSM with ≥ 1 bac-STI diagnosis within the preceding 12 months. Providing doxy-PEP to all gbMSM would likely result in an overuse of antibiotics, and providing doxy-PEP only after a second PTE would result in fewer infections averted for the same proportion treated. Our findings thus support a somewhat limited use of doxy-PEP (1) to prevent antibiotic resistance and (2) to maximise its potential impact at the individual and population levels.

Despite this recommendation, we still recognise that doxy-PEP could result in more onward transmission if gbMSM and/or clinicians overestimate the effectiveness of this intervention. Because of this possibility, we believe our findings also highlight that doxy-PEP needs to be explained to patients with its caveats: it will fail, and people still need to seek testing if they are bac-STI contacts or if they have STI-like symptoms. On the whole, though, we feel that clinicians and public health officials should consider providing doxy-PEP to gbMSM who have ongoing risk factors for bac-STI acquisition and who have been diagnosed with ≥ 1 bac-STI within the preceding 12 months. Perhaps with a judicious use of this intervention, we can begin to curb the increasing rates and diagnosis numbers of bac-STIs and do so without worsening antibiotic resistance among both bac-STIs and other bystander organisms.

Contributors POB: conception, analysis, drafting, editing, final submission; DSF: analysis, writing, editing, final submission. LO: conception, drafting, editing, final submission. POB accepts full responsibility for the finished work and/or the conduct of the study, had access to the data and controlled the decision to publish.

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