Evolving patterns of macrolide and fluoroquinolone resistance in *Mycoplasma genitalium*: an updated systematic review and meta-analysis

Teck-Phui Chua, Lenka A Vodstrcil*, Gerald L Murray, Erica L Plummer, Jørgen S Jensen, Magnus Unemo, Eric P F Chow, Nicola Low, David M Whiley, Emma L Sweeney, Jane S Hocking, Jennifer A Danielewski, Suzanne M Garland, Christopher K Fairley, Lei Zhang, Catriona S Bradshaw†, Dorothy A Machalek†*

Summary

Background Over the past 5 years, since publication of the initial review, studies have provided additional data on macrolide and fluoroquinolone resistance in *Mycoplasma genitalium*, including data from regions previously lacking this information. We aimed to provide contemporary estimates of macrolide and fluoroquinolone resistance in *M genitalium* to inform national, regional, and global treatment guidelines.

Methods This is an update of a previous systematic review and meta-analysis, which was performed up to Jan 7, 2019. In this update, we searched PubMed, Embase, and MEDLINE from Jan 1, 2018, to April 18, 2023, for published studies reporting macrolide, fluoroquinolone, or dual-class (macrolide and fluoroquinolone) resistance in *M genitalium*. Data were combined with the previous meta-analysis to examine resistance prevalence in *M genitalium* samples collected up to and including 2021. Random-effects meta-analyses were used to calculate summary estimates of prevalence. Subgroup analyses by WHO region and four time periods (before 2012 to 2018–21) were performed. This study was registered with PROSPERO, number CRD42021273340.

Findings 166 studies (59 from the previous search period reporting data from *M genitalium* samples collected between 2003 and 2017, and 107 from the updated search period reporting data from *M genitalium* samples collected between 2005 and 2021) were included: 157 reporting macrolide resistance (41 countries; 22 974 samples), 89 reporting fluoroquinolone resistance (35 countries; 14 165 samples), and 74 reporting dual-class resistance (34 countries; 11 070 samples). In 2018–21, the overall prevalence of macrolide, fluoroquinolone, and dual-class resistance were 33·3% (95% CI 27·2–39·7), 13·3% (10·0–17·0), and 6·5% (4·0–9·4), respectively. Over time, there was a slight, although not statistically significant, decline in macrolide resistance in the Western Pacific and the Americas, but there was an increase in macrolide resistance in the European region. Fluoroquinolone resistance was highest in the Western Pacific and increased in the European non-Nordic region. ParC S83I was the most common variant associated with fluoroquinolone resistance, increasing from 0% (95% CI <0·0001–0·30) before 2012 to 7·3% (4·7–10·3) in 2018–21; p_{trend}=0·055.

Interpretation Macrolide and fluoroquinolone resistance in *M genitalium* requires ongoing international surveillance, use of resistance assays for optimal antibiotic stewardship, and novel treatment options.

Funding Australian Research Council.

Introduction

Mycoplasma genitalium is a sexually transmitted bacterium with few effective treatment options. A single-dose of azithromycin, a macrolide, has been widely used as first-line treatment. However, this has resulted in selection of resistance-conferring mutations in the 23S rRNA gene in at least 10% of infections,[1] and is likely to have contributed to the rapid increase in macrolide resistance mutations in *M genitalium* (from 10·0% before 2010 to 51·4% in 2016–17).[2] Coinciding with this increase in resistance was a decline in efficacy of single-dose azithromycin for urogenital *M genitalium*: from 85·3% before 2009 to 67·0% between 2009 and 2015.[3]

Rising macrolide resistance has increased the use of the fluoroquinolone moxifloxacin over the past decade, with a concomitant decrease in moxifloxacin efficacy.[4] The mechanism of resistance to fluoroquinolones is not completely understood, but is known to be associated with specific amino acid changes in the topoisomerase subunit ParC.[5–8] In our earlier systematic review[2] of studies with data collected up to 2017, we reported that 7·7% (95% CI 4·5–11·4) of people harboured specific amino acid changes in ParC associated with moxifloxacin treatment failure (S83I, S83R, D87N, and D87Y), with no change over time. There were, however, few studies available for analysis and those that were available were

Lancet Microbe 2025

Published Online https://doi.org/10.1016/j.lanmic.2024.101047

*Joint first authors
†Joint last authors

Department of Obstetrics, Gynaecology and Newborn Health, University of Melbourne, Melbourne, VIC, Australia (T-P Chua BBMed [Hons], G L Murray PhD, Prof S M Garland MD); **Centre for Women's Infectious Diseases, The Royal Women's Hospital, Melbourne, VIC, Australia** (T-P Chua, G L Murray, E L Plummer PhD, J A Danielewski PhD, Prof S M Garland, D A Machalek PhD); **Molecular Microbiology Research Group, Murdoch Children's Research Institute, Melbourne, VIC, Australia** (T-P Chua, G L Murray, J A Danielewski, Prof S M Garland); **Melbourne Sexual Health Centre, Alfred Health, Melbourne, VIC, Australia** (L A Vodstrcil PhD, E L Plummer, Prof E P F Chow PhD, Prof C K Fairley PhD, Prof L Zhang PhD, Prof C S Bradshaw PhD); **Central Clinical School, Monash University, Melbourne, Victoria, Australia** (L A Vodstrcil, E L Plummer, Prof E P F Chow, Prof C K Fairley, Prof L Zhang, Prof C S Bradshaw); **Research Unit for Reproductive Microbiology, Statens Serum Institut, Copenhagen, Denmark** (J S Jensen MD PhD); **WHO Collaborating Centre for Gonorrhoea and Other STIs, Department of Laboratory Medicine, Faculty of Medicine and Health, Örebro University, Örebro, Sweden** (Prof M Unemo PhD); **Institute for Global Health, University College London, London, UK** (Prof M Unemo); **Centre for Epidemiology and Biostatistics, Melbourne School of Population**

and Global Health, University of Melbourne, Melbourne, VIC, Australia (Prof E P F Chow, Prof J S Hocking PhD, Prof C S Bradshaw); Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland (Prof N Low MD); The University of Queensland Centre for Clinical Research, Faculty of Medicine, The University of Queensland, Brisbane, QLD, Australia (D M Whiley PhD, E L Sweeney PhD); Pathology Queensland Central Laboratory, Brisbane, QLD, Australia (D M Whiley); China–Australia Joint Research Center for Infectious Diseases, School of Public Health, Xi'an Jiaotong University Health Science Center, Xi'an, China (Prof L Zhang); Department of Epidemiology and Biostatistics, School of Public Health, Xi'an Jiaotong University Health Science Center, Xi'an, China (Prof L Zhang); Department of Epidemiology and Biostatistics, College of Public Health, Zhengzhou University, Zhengzhou, China (Prof L Zhang); The Kirby Institute, University of New South Wales, Sydney, NSW, Australia (D A Machalek)

Correspondence to:
Dr Dorothy A Machalek, The Kirby Institute, University of New South Wales, Sydney, NSW, Australia
dmachalek@kirby.unsw.edu.au
or
Prof Catriona S Bradshaw, Melbourne Sexual Health Centre, Alfred Health, Melbourne, VIC, Australia
catriona.bradshaw@monash.edu

See Online for appendix

Research in context

Evidence before this study

Our previous systematic review (published in 2020) included 59 studies from 21 countries, reporting macrolide and fluoroquinolone resistance data in *Mycoplasma genitalium* samples collected between 2003 and 2017. This research revealed that macrolide resistance had increased from 10% before 2010 to 51% in 2016–17. The prevalence of fluoroquinolone resistance and dual-class (macrolide and fluoroquinolone) resistance were 8% and 3%, respectively, in 2016–17. Since our previous systematic review, there has been a substantial increase in publications reporting macrolide and fluoroquinolone resistance in *M genitalium*, including from countries previously lacking resistance data. The only systematic review and meta-analysis of resistance in *M genitalium* that has been published since our earlier review reported resistance in Europe from 25 studies with data up to 2017. The authors found that macrolide resistance prevalence exceeded 50% and fluoroquinolone resistance was 5%, but there has been no update for other WHO regions. We did not identify any systematic review or meta-analysis examining the prevalence and trends of individual ParC and GyrA amino acid changes that drive fluoroquinolone treatment failure.

Added value of this study

This systematic review and meta-analysis presents updated estimates of the prevalence of antimicrobial resistance in *M genitalium*. This update includes an additional 107 studies (accounting for 55 245 samples collected between 2005 and 2021) across 41 countries (20 more than last time) spanning four WHO regions (African region, Region of the Americas, European region, and Western Pacific region). 166 studies contributed resistance data to this systematic review and meta-analysis, which provides resistance estimates up to and including 2021. Based on available published data, the global prevalence of macrolide resistance was 33% in 2018–21, a decrease from 42% in 2015–17, although not statistically significant. Globally, the prevalence of dual-class resistance increased to 7% in 2018–21, with the highest levels again reported in the Western Pacific at 29%. There were substantial differences between regions in both estimates and trends. Our results show that the ParC S83I variant is the most dominant fluoroquinolone resistance-associated change overall and has continued to increase, which has important implications for the efficacy of fluoroquinolones.

Implications of all the available evidence

Although there were no further increases in global macrolide and fluoroquinolone resistance levels in the 2018–21 period, our results should be interpreted with caution, as data availability varied among countries, time periods, and specific study populations. The differences between regions in both estimates and trends were probably due to differences in antibiotic availability, antibiotic use, and treatment guidelines, although it is important to note that in some regions, data availability was limited to a few countries. Not unexpectedly, resistance across all antibiotic classes was higher in men than women, because of the high rate of resistance in men who have sex with men. As a sexually transmitted infection with very limited effective antimicrobial options, assays for *M genitalium* that detect resistance markers are becoming increasingly important to guide treatment. Ongoing national, regional, and global surveillance of macrolide and fluoroquinolone resistance in *M genitalium* will be important in informing guidelines to ensure optimal antibiotic stewardship and cure.

limited to specific geographical regions. Recent studies have shown that the DNA gyrase subunit GyrA, particularly amino acid change M95I, plays an additive role in fluoroquinolone treatment failure by increasing the risk of failure when combined with a ParC S83I change.[8,9]

Since the publication of our original systematic review and meta-analysis,[2] an increasing number of publications have provided data on macrolide and fluoroquinolone resistance in *M genitalium*, including data from regions previously lacking this information. Furthermore, growing evidence confirms the role of ParC in fluoroquinolone treatment failure, especially the amino acid change S83I.[8,10] To obtain a more comprehensive picture of antimicrobial resistance in *M genitalium*, we updated our systematic review and meta-analysis to report trends in resistance prevalence in *M genitalium* samples collected up to and including 2021. We also analysed trends of specific ParC and GyrA amino acid changes over time because accumulating evidence suggests the significance of certain ParC and GyrA changes in fluoroquinolone treatment failure.

Methods

Search strategy and selection criteria

We did a systematic review and meta-analysis of published estimates of macrolide and fluoroquinolone resistance in *M genitalium*. This Article is an update of a previously published systematic review and meta-analysis, which covered published studies from inception of the database to Jan 7, 2019.[2] In this update, we searched PubMed, Embase, and MEDLINE from Jan 1, 2018 to April 18, 2023, using the search terms previously described (appendix p 6).[2] We did not search grey literature (ie, conference abstracts, unpublished studies, or reports). Two authors (T-PC and LAV) independently screened abstracts and reviewed full-text articles to determine eligibility. Disagreements were resolved by discussion with DAM and CSB. Studies were eligible for inclusion if they provided the proportions of macrolide or fluoroquinolone resistance, or both, as described in the appendix (p 7). Studies analysing only samples collected at test-of-cure and those with an overall sample size of fewer than ten people who tested positive for *M genitalium* were excluded. If the same dataset was analysed in more than one publication, the publication

with the most comprehensive dataset, or the earliest publication, was included.

Data extraction and analysis

T-PC extracted data using a standardised electronic form, which was checked for transcription errors by LAV; discrepancies were resolved through discussion with DAM and CSB. For fluoroquinolone resistance, data from the previous review were extracted again to incorporate the two additional amino acid changes S83C and S83N (appendix p 7). Variables extracted included author, publication year, study country, study period, setting (eg, sexually transmitted infection [STI] clinic, hospital, or primary care), recruitment method, detection method (ie, the assay used to detect *M genitalium* and each category of resistance mutation), and *M genitalium* prevalence across the study population (when reported). Where available, we extracted information reported by study authors about sex (men or women), age, symptom status, and HIV status for patients positive for *M genitalium*. Within each category of resistance-associated mutations (ie, macrolide, fluoroquinolone, or dual class), the total number of samples successfully tested for resistance markers and frequency of each specific mutation were extracted, as previously described.[2] Data were extracted by year of specimen collection, sex, and male sexual orientation (ie, men who have sex with women and men who have sex with men). In this updated systematic review and meta-analysis, we also extracted the frequency of each of the individual amino acid changes for ParC (S83I, S83R, S83N, S83C, D87N, and D87Y) and GyrA (M95I, D99N, D99Y, and D99G) from included studies in the original and updated systematic review and meta-analysis, where reported (appendix p 7). For brevity, mutations in protein encoding genes will be referred to by the associated amino acid change. Authors were contacted for additional information where required. Methodological assessment of the risks of bias in individual studies was performed by T-PC, according to criteria adapted from published checklists, as previously described (appendix p 8),[2,11,12] with consultation with LAV, DAM, and CSB, as required.

Prevalence of resistance-associated mutations was defined as the sum of samples with at least one key mutation in the 23S rRNA or *parC* genes or both (numerator) divided by the total number of *M genitalium* samples that were successfully sequenced for the corresponding gene (denominator). The following analyses were performed using Stata, version 18.0. We generated summary average estimates using random-effects meta-analysis, with 95% CIs estimated with the score method, after applying the Freeman-Tukey double arcsine transformation.[13] We reported 95% prediction intervals (95% PIs) to assess the amount of heterogeneity between studies and I^2 values as a measure of consistency between studies.[14,15] Subgroup and univariable meta-regression analyses were performed by year of specimen collection (before 2012, 2012–14, 2015–17, and 2018–21), WHO-defined geographical regions, sex (men or women), and male sexual orientation (ie, men who have sex with women and men who have sex with men). The WHO European region was further stratified into Nordic countries and non-Nordic countries, as previously described.[2] We conducted the trend test in meta-regression across all time periods by treating the study period dummy ordered categorical variable (ie, <2012, 2012–14, 2015–17, and 2018–21) as continuous using the metareg command in Stata.[16] The significance of the coefficients indicated differences from the reference category, which was the earliest timepoint (ie, <2012). To test for significance between just two timepoints (2015–17 *vs* 2018–21), we restricted our meta-regression analysis to these periods, using the earlier of the two timepoints as the reference category. We did not investigate publication bias because the current methods are not appropriate for meta-analyses of prevalence data.[15]

This systematic review and meta-analysis is registered with PROSPERO (CRD42021273340) and reported according to the PRISMA 2020 guidelines (appendix pp 4–5).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

166 studies were included in our systematic review and meta-analysis, 59 (36%) of which were part of the previous review[2] and 107 (64%) of which were identified in our updated search (figure 1).[8,9,17–172] The included studies reported data collected between 2003 and 2021 (table 1) from 41 countries (20 countries more than in the previous analysis). 78 (47·0%) studies were from the WHO European region (19 countries), 52 (31·3%) from the Western Pacific (nine countries), 23 (13·9%) from the Americas (six countries), and 12 (7·2%) from the African region (seven countries). No studies were identified from the Eastern Mediterranean or South-East Asian WHO regions. Most of the samples were taken from STI clinic attendees (11 170 [48·6%], 7131 [50·3%], and 5769 [52·1%] for macrolide, fluoroquinolone, and dual-class resistance, respectively; table 1). The absence of random selection was the main source of bias (12 articles [<10%] performed random selection). Assessment of risk of bias for individual studies can be found in the appendix (pp 57–61).

For prevalence estimates of macrolide resistance mutations, 157 studies from 41 countries contributed 22 974 samples (14 008 [61·0%] from the updated search) collected between 2003 and 2021 (table 1; appendix pp 72–74). The majority (14 413 samples [62·7%]) were from the European region (3802 [16·5%] from Nordic countries and 10 611 [46·2%] from non-Nordic countries), followed by 5575 (24·3%) from the Western Pacific region, 1451 (6·3%) from the Americas, and 1051 (4·6%) from the African region (table 1). From studies with data collected from 2018 to 2021, the global summary prevalence of macrolide resistance mutations was 33·3% (95% CI 27·2–39·7; 95% PI <0·0001–87·6) with considerable variability between regions

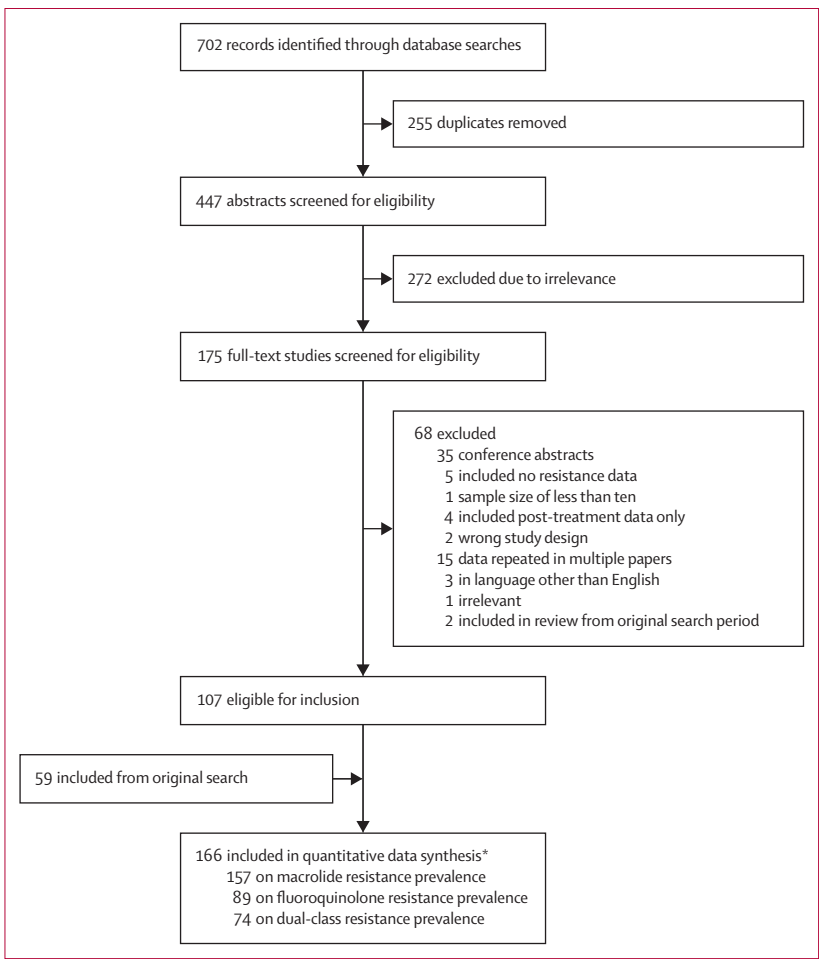

Figure 1: **Study selection**
Prevalence was defined as the proportion of *Mycoplasma genitalium*-positive specimens with single nucleotide polymorphisms in 23S rRNA gene for macrolide resistance and the *parC* gene for mutations associated with fluoroquinolone resistance. *Some studies reported more than one resistance type.

(table 2). From 2018 to 2021, macrolide resistance was highest in Nordic countries (56·8%, 95% CI 47·0–66·3), followed by the Americas (53·0% [95% CI 34·6–71·0; 95% PI 2·5–99·4]), the Western Pacific (46·5% [29·0–64·4; <0·0001–100]), the non-Nordic European countries (43·2% [35·8–50·7; 5·2–86·4]), and the African region (0·13% [<0·0001–2·3; <0·0001–11·1]; appendix p 62). In country-level analyses of data from 2018 to 2021, prevalence ranged from 0·0% to 86·7% (appendix pp 73–74). Macrolide resistance was higher in *M genitalium* samples collected from STI clinics (49·0% [95% CI 42·9–55·1; 95% PI 3·8–95·4]) compared with non-STI clinics or community (25·5% [19·2–32·3; <0·0001–80·0]; table 2).

In analyses of macrolide resistance prevalence over time, the overall prevalence reached a high of 42·4% (95% CI 35·6–49·2; 95% PI <0·0001–97·2) in 2015–17 before a slight, although not statistically significant, decline to 33·3% (27·2–39·7; <0·0001–87·6) in 2018–21 (figure 2A). In the Western Pacific and Americas, prevalence over time peaked in 2015–17 at 59·0% (49·7–67·9; 11·7–98·0) and 63·7% (52·4–74·4; 19·6–97·9), respectively, but this was also not statistically significant (figure 2A). Among Nordic countries and the rest of Europe, macrolide resistance prevalence increased over time from 20·4% (10·7–32·1; <0·0001–71·9) before 2012 to 56·8% (47·0–66·3) in 2018–21 (p_{trend}=0·031) and 4·6% (0·72–10·5; <0·0001–28·4) before 2012 to 43·2% (35·8–50·7; 5·2–86·4) in 2018–21 (p_{trend}<0·0001), respectively (figure 2A). The African region had the lowest prevalence of macrolide resistance mutations and no variation over time (figure 2A). Detailed trends for individual countries with sufficient data are presented in the appendix (appendix pp 63–64).

For prevalence estimates of fluoroquinolone resistance-associated mutations, 89 studies from 35 countries contributed 14 165 samples (10 162 [71·7%] from the updated search) collected between 2005 and 2021 (table 1; appendix pp 72–74). Overall, 8284 samples (58·5%) were from the European region (1020 [7·2%] from Nordic countries and 7116 [50·2%] from non-Nordic countries), 3845 samples (27·1%) from the Western Pacific region, 725 samples (5·1%) from the Americas, and 810 samples (5·7%) from the African region (table 1). The global prevalence of fluoroquinolone resistance-associated mutations was 13·3% (95% CI 10·0–17·0; 95% PI <0·0001–46·3) in 2018–21 (table 2). Prevalence was highest in the Western Pacific region (40·5% [26·6–55·1; 0·70–91·5]), followed by the European non-Nordic countries (12·3% [10·3–14·5; 4·2–23·6]), the Americas (5·5% [2·0–10·3; <0·0001–21·0]), and the African region (5·1% [0·28–13·1; <0·0001–36·6]; appendix p 65). When analysing country-specific data from 2018 to 2021, prevalence ranged from 0·0% to 73·3%, with the lowest estimates generally seen in countries from the Nordic region and the highest in countries from the Western Pacific (appendix pp 73–74). In temporal analyses, the overall prevalence of fluoroquinolone resistance did not change over time (figure 2B), and the largest change was seen in the European non-Nordic region, where prevalence increased from 1·7% (95% CI <0·0001–5·6; 95% PI <0·0001–12·2) before 2012 to 12·3% (10·3–14·5; 4·2–23·6) in 2018–21 (p_{trend}=0·036; figure 2B). There were no changes in prevalence in the Western Pacific or African regions, and there were insufficient data to analyse trends among Nordic countries and the Americas. Detailed trends for individual countries with sufficient data are presented in the appendix (p 66).

For dual-class (macrolide and fluoroquinolone) resistance, 74 studies from 34 different countries contributed 11 070 samples (7790 [70·4%] from the updated search) collected between 2005 and 2021 (table 1; appendix pp 72–74). Overall, 7112 samples (64·2%) were from the European region (926 [8·4%] from Nordic countries and 6186 [55·9%] from non-Nordic countries), 2218 samples (20·0%) from the Western Pacific, 575 samples (5·2%) from the Americas, and 740 samples (6·7%) from the African region (table 1). In 2018–21, the global summary prevalence of dual-class resistance was 6·5% (95% CI 4·0–9·4; 95% PI <0·0001–32·4; table 2). The highest prevalence

was seen in the Western Pacific region (29·0% [11·0–51·1; <0·0001–97·3]), followed by the European non-Nordic region (7·3% [5·1–9·8; 0·1–21·6]), the Americas (4·3% [0·92–9·3]), and the African region (0·0% [<0·0001–0·40; <0·0001–0·7]; appendix p 67). In analyses of individual countries, prevalence ranged from 0·0% to 60·2%, with the lowest prevalence in Nordic countries and countries in the African region (<5·0%; appendix pp 73–74). The overall prevalence of dual-class resistance increased before 2012 to 2018–21, which was seen in both the European non-Nordic and the Western Pacific regions (figure 2C). Detailed trends for individual countries with sufficient data are presented in the appendix (p 68).

We also analysed the frequency of individual ParC S83 and D87 changes. 90 studies from 36 countries contributed 14 038 samples. Overall, ParC S83I was the most common variant (6·9% [95% CI 4·5–9·7; 95% PI <0·0001–45·2]); other S83 and D87 changes were less than 1%. In temporal analyses, only the frequency of ParC S83I increased, from 0·0% (<0·0001–0·30; <0·0001–4·5) before 2012 to 7·3% (4·7–10·3; <0·0001–36·1) in 2018–21 (p_{trend}=0·055; figure 3; appendix p 69). Only 42 studies (7971 samples) from 24 countries reported the frequency of individual GyrA amino acid changes. As the frequency of GyrA variants was less than 0·50% overall, there were insufficient data for further analyses.

In analyses stratified by sex, summary prevalence estimates were higher in men than women for all classes of resistance markers: 44·9% (95% CI 39·1–50·8; 95% PI 0·40–96·4) versus 23·9% (19·3–28·8; <0·0001–76·0), respectively, for macrolide resistance (p<0·0001); 14·6% (9·9–20·0; <0·0001–68·8) versus 6·5% (3·9–9·6; <0·0001–36·3), respectively, for fluoroquinolone resistance (p=0·0070); and 7·7% (4·0–12·4; <0·0001–57·0) versus 0·96% (0·11–2·4; <0·0001–13·8), respectively, for dual-class resistance (p=0·0010; figure 4A; appendix p 75). Prevalence was also higher among men who have sex with men than men who have sex with women: 65·2% (95% CI 55·5–74·4; 95% CI 4·0–100·0) versus 36·2% (26·8–46·0; <0·0001–91·0), respectively, for macrolide resistance (p<0·0001); 16·0% (10·7–21·9; <0·0001–55·6) versus 8·9% (4·5–14·2; <0·0001–41·3), respectively, for fluoroquinolone resistance (p=0·050); and 9·9% (5·0–15·7; <0·0001–50·9) versus 2·7% (0·50–5·9; <0·0001–21·7), respectively, for dual-class resistance (p=0·011; figure 4B; appendix p 75). When men who have sex with men were excluded from analysis, men still had a higher prevalence of resistance than women (p=0·018, 0·22, and 0·070 for macrolide, fluoroquinolone, and dual-class resistance, respectively; figure 4C; appendix p 75).

There was high heterogeneity in the estimates between studies, as shown by the large prediction intervals for the overall estimate and in subgroups of studies in different regions and study populations. Stratifying data by year of sample collection, WHO geographical region, sex, sexual orientation, or source of recruitment did not meaningfully reduce this heterogeneity (table 2; appendix pp 62, 65, 67). Other sources of potential heterogeneity (eg, symptoms, HIV status, and age) were not consistently reported and, therefore, we could not account for these in our analysis.

	Macrolide resistance (23S rRNA)	Fluoroquinolone resistance (*parC*)	Dual-class resistance (23S rRNA and *parC*)
Overall	157 (8826/22 974)	89 (2408/14 165)	74 (1085/11 070)
Publication year (range)	2011–23	2010–23	2014–23
Period of sample collection (range)	2003–21	2005–21	2005–21
WHO geographical regions*			
European region†	78 (4838/14 413)	44 (789/8284)	38 (391/7112)
Western Pacific region†	45 (3148/5575)	27 (1510/3845)	19 (655/2218)
Americas region†	23 (765/1451)	12 (65/725)	9 (34/575)
African region†	14 (23/1051)	9 (35/810)	9 (3/740)
Other‡	1 (52/484)	1 (9/501)	1 (2/425)
Period when specimen was collected§			
Before 2012	26 (675/2673)	11 (70/521)	9 (1/440)
2012–14	37 (1262/4238)	20 (456/2261)	17 (40/1703)
2015–17	72 (3033/7253)	35 (588/3566)	29 (153/2442)
2018–21	61 (3630/8385)	44 (1135/7449)	36 (517/5825)
Setting			
Included STI clinics	82 (5258/11 170)	47 (1293/7131)	40 (806/5769)
Non-STI clinics or community¶	57 (2426/7091)	27 (588/3137)	24 (173/2523)
Not reported	18 (1142/4713)	15 (527/3897)	10 (106/2778)
Sex			
Female	99 (2085/8110)	52 (404/4271)	41 (108/3271)
Male	106 (5302/10 720)	64 (1554/7116)	53 (759/5292)
Sexual orientation			
Men who have sex with women	38 (889/2181)	27 (215/1625)	24 (94/1398)
Men who have sex with men	52 (1797/2546)	38 (360/1818)	35 (273/1694)

Data are number of studies (number of *Mycoplasma genitalium*-positive specimens with resistance or number of successfully characterised *M genitalium* positive specimens), unless stated otherwise. Prevalence was defined as the proportion of *M genitalium*-positive specimens with single nucleotide polymorphisms in 23S rRNA gene for macrolide resistance and the *parC* gene for mutations associated with fluoroquinolone resistance. STI=sexually transmitted infection. *None of the studies were from the WHO South-East Asia region. One study[153] included data from the WHO Eastern Mediterranean region (Morocco), which has been included with the African region. †Balkus and colleagues[26] contributed data for countries in the Americas region (USA) and the African region (Kenya), Fernández-Huerta and colleagues[65] contributed data for countries in the European region (Spain) and the Western Pacific region (Australia), Shipitsyna and colleagues[153] contributed data for countries in the European region (Malta), the Americas region (Guatemala and Peru), and the African region (Morocco and South Africa). ‡There were 484, 501, and 425 samples for macrolide, fluoroquinolone, and dual-class resistance, respectively, from French overseas territories (New Caledonia, French Polynesia, French Guyana, La Réunion Island, and Mayotte), which were analysed separately from the European region. §Year of collection was not known for 18 samples. ¶Included seven community-based studies.

Table 1: **Characteristics of the 166 included studies**

Discussion

Based on available published data, the estimated global prevalence of macrolide resistance in *M genitalium* peaked at 42·4% in 2015–17, before decreasing—albeit not statistically significantly—to 33·3% in 2018–21. This non-significant decline following 2017 was also observed in the Western Pacific and the Americas, whereas available data from Europe showed a continued rise in macrolide resistance. Overall fluoroquinolone resistance remained unchanged (14·0% in 2015–17 and 13·3% in 2018–21), although it increased in the European non-Nordic region from 8·1% in 2015–17 to 12·3% in 2018–21. Dual-class resistance prevalence increased slightly from 4·7% in 2015–17 to 6·5% in 2018–21, with the Western Pacific

	Macrolide resistance (23S rRNA; n=157)				Fluoroquinolone resistance (*parC*; n=89)				Dual-class resistance (23S rRNA and *parC*; n=74)			
	Summary prevalence (95% CI; 95% PI)	I^2	Mean difference (95% CI)*	p value	Summary prevalence (95% CI; 95% PI)	I^2	Mean difference (95% CI)*	p value	Summary prevalence (95% CI; 95% PI)	I^2	Mean difference (95% CI)*	p value
Overall	37·3% (32·9 to 41·8; <0·0001 to 90·6)	97·8%	NA	NA	13·3% (9·9 to 17·1; <0·0001 to 60·0)	97·0%	NA	NA	6·5% (4·0 to 9·4; <0·0001 to 45·4)	96·1%	NA	NA
Year of specimen collection												
Before 2012	13·1% (7·8 to 19·2; <0·0001 to 68·1)	91·8%	1 (ref)	NA	7·1% (0·082 to 19·9; <0·0001 to 82·2)	92·1%	1 (ref)	NA	0·0% (0·0 to 0·0; 0·0 to 0·0)	0·0%†	1 (ref)	NA
2012–14	25·7% (18·3 to 33·8; <0·0001 to 85·7)	96·4%	12·3% (1·6 to 22·9)	0·024	15·2% (6·2 to 26·9; <0·0001 to 87·2)	97·5%	9·2% (–5·9 to 24·3)	0·23	0·81% (0·047 to 2·2; <0·0001 to 7·4)	54·1%	2·1% (–8·3 to 12·6)	0·69
2015–17	42·4% (35·6 to 49·2; <0·0001 to 97·2)	96·6%	24·7% (15·2 to 34·2)	<0·0001	14·0% (8·7 to 20·0; <0·0001 to 63·6)	94·4%	4·8% (–9·3 to 18·9)	0·50	4·7% (2·3 to 7·6; <0·0001 to 26·0)	80·3%	6·1% (–4·1 to 16·2)	0·24
2018–21	33·3% (27·2 to 39·7; <0·0001 to 87·6)	96·7%	19·5% (9·8 to 29·2)	<0·0001	13·3% (10·0 to 17·0; <0·0001 to 46·3)	93·5%	3·8% (–9·8 to 17·4)	0·58	6·5% (4·0 to 9·4; <0·0001 to 32·4)	92·1%	8·7% (–1·0 to 18·3)	0·079
WHO regions												
European	38·0% (32·5 to 43·6; 1·6 to 85·7)	97·7%	1 (ref)	NA	8·4% (6·7 to 10·3; 0·70 to 22·0)	84·4%	1 (ref)	NA	4·6% (3·0 to 6·4; <0·0001 to 19·0)	87·8%	1 (ref)	NA
Western Pacific	50·5% (42·2 to 58·8; 4·7 to 95·7)	97·3%	14·2% (5·8 to 22·7)	0·001	35·6% (24·8 to 47·2; <0·0001 to 92·2)	98·1%	28·3% (20·6 to 35·9)	<0·0001	24·3% (11·8 to 39·6; <0·0001 to 92·6)	98·2%	22·5% (14·0 to 30·9)	<0·0001
Americas	52·4% (44·3 to 60·4; 17·0 to 86·5)	87·3%	14·9% (3·2 to 26·5)	0·012	9·1% (4·8 to 14·4; <0·0001 to 29·5)	69·8%	1·1% (–10·9 to 13·0)	0·86	5·6% (2·5 to 9·6; <0·0001 to 18·2)	50·8%	0·92% (–11·8 to 13·6)	0·89
African	1·2% (0·053 to 3·2; <0·0001 to 11·5)	63·3%	–35·2% (–48·0 to –22·3)	<0·0001	2·4% (<0·0001 to 8·0; <0·0001 to 30·9)	83·5%	–3·3% (–15·0 to 8·3)	0·57	0·0% (0·0 to 0·0; 0·0 to 0·0)	7·7%†	–5·3% (–16·7 to 6·2)	0·36
European region												
Europe (excluding Nordic countries)	37·4% (30·9 to 44·1; 0·60 to 87·7)	97·8%	1 (ref)	NA	9·3% (7·7 to 11·1; 1·9 to 20·8)	79·1%	1 (ref)	NA	5·1% (3·4 to 7·2; <0·0001 to 20·0)	87·5%	1 (ref)	NA
Nordic countries	39·8% (29·4 to 50·7; 3·0 to 85·6)	97·5%	0·40% (–12·2 to 13·0)	0·95	2·7 (0·64 to 5·8; <0·0001 to 14·8)	68·3%	–7·7% (–14·4 to –1·0)	0·025	0·96% (0·021 to 2·7; <0·0001 to 7·4)	40·7†	–4·8% (–11·9 to 2·3)	0·18
Source of recruitment												
Included STI clinics	49·0% (42·9 to 55·1; 3·8 to 95·4)	97·5%	1 (ref)	NA	17·1 (11·9 to 23·0; <0·0001 to 67·4)	97·1%	1 (ref)	NA	11·45 (6·6 to 17·1; <0·0001 to 61·5)	97·1%	1 (ref)	NA
Non-STI clinics or community	25·5% (19·2 to 32·3; <0·0001 to 80·0)	97·1%	–19·6% (–28·1 to –11·2)	<0·0001	9·1 (3·3 to 16·7; <0·0001 to 66·6)	97·1%	–5·78% (–15·6 to 4·1)	0·25	2·9% (0·67 to 6·3; <0·0001 to 28·3)	90·5%	–7·99% (–17·4 to 1·4)	0·095

Prevalence was defined as the proportion of *M genitalium*-positive specimens with single nucleotide polymorphisms in 23S rRNA gene for macrolide resistance and the *parC* gene for mutations associated with fluoroquinolone resistance. NA=not applicable. PI=prediction interval. *Regression coefficient multiplied by 100. †Non-significant I^2 value. All other I^2 values were significant (<0·032).

Table 2: **Prevalence of macrolide, fluoroquinolone, and dual-class resistance in *Mycoplasma genitalium*, in subgroup and meta-regression analyses**

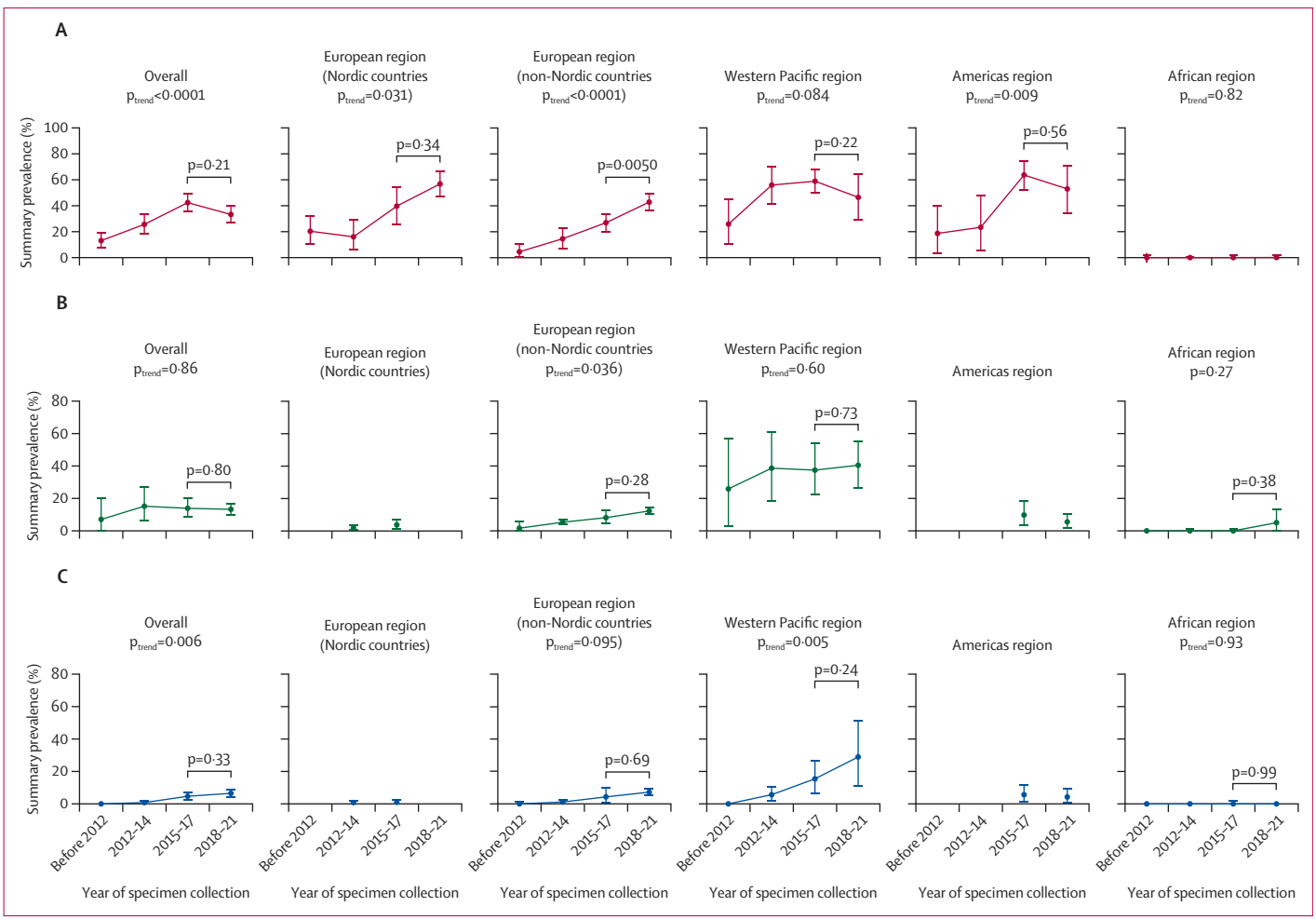

Figure 2: **Prevalence of macrolide (A), fluoroquinolone (B), and dual-class (C) resistance in *Mycoplasma genitalium*, by year of specimen collection and WHO geographical region**
Prevalence was defined as the proportion of *M genitalium*-positive specimens with single nucleotide polymorphisms in 23S rRNA gene for macrolide resistance and the *parC* gene for mutations associated with fluoroquinolone resistance. Error bars represent 95% CIs. A trend test in meta-regression across all time periods was performed by treating year of specimen collection as a continuous ordered categorical variable and the first time period as the reference category (ie, before 2012). p_{trends} could not be presented for fluoroquinolone resistance and dual-class resistance for the European Nordic and Americas regions due to limited data. Meta-regression was also restricted to the last two timepoints (2015–17 and 2018–21).

showing the highest levels (29·0% in 2018–21). The ParC S83I amino acid change was the most frequent ParC S83/D87 variant and increased in prevalence from 0·0% before 2012 to 7·3% in 2018–21. Men who have sex with men had higher prevalence of all classes of resistance in *M genitalium* compared with women and men who have sex with women.

The apparent stabilisation of macrolide resistance in some regions might be due to several factors. For instance, in the 2018–21 period, some WHO regions, such as the Americas, included the first published data from populations with very low levels of macrolide resistance (eg, female sex workers in Ecuador and women attending for STI screening in Guatemala).[90,153,172] This situation is contrasted to Canada and the USA where macrolide resistance levels are higher, with a 2023 surveillance study from the USA observing a prevalence of 59% in their study population.[173] In the Western Pacific, where macrolide resistance was estimated at 46·5% in 2018–21, the observed stabilisation is likely to have been influenced by Australian data, which contributed

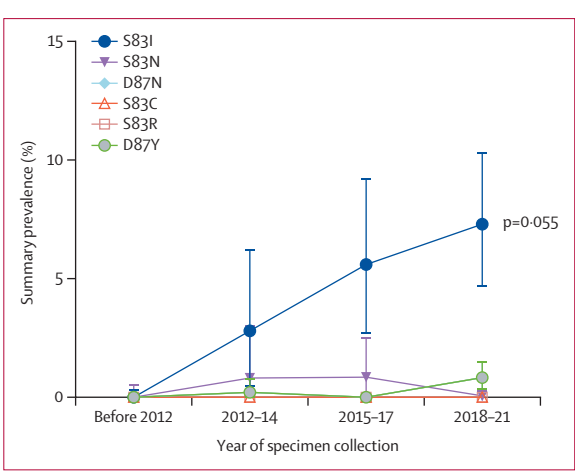

Figure 3: **Prevalence of changes at S83 and D87 of ParC, by year of specimen collection**
Meta-regression p values for linear differences in the average prevalence between the subgroups for S83I is shown. All other p values ranged from 0·39 to 1·0.

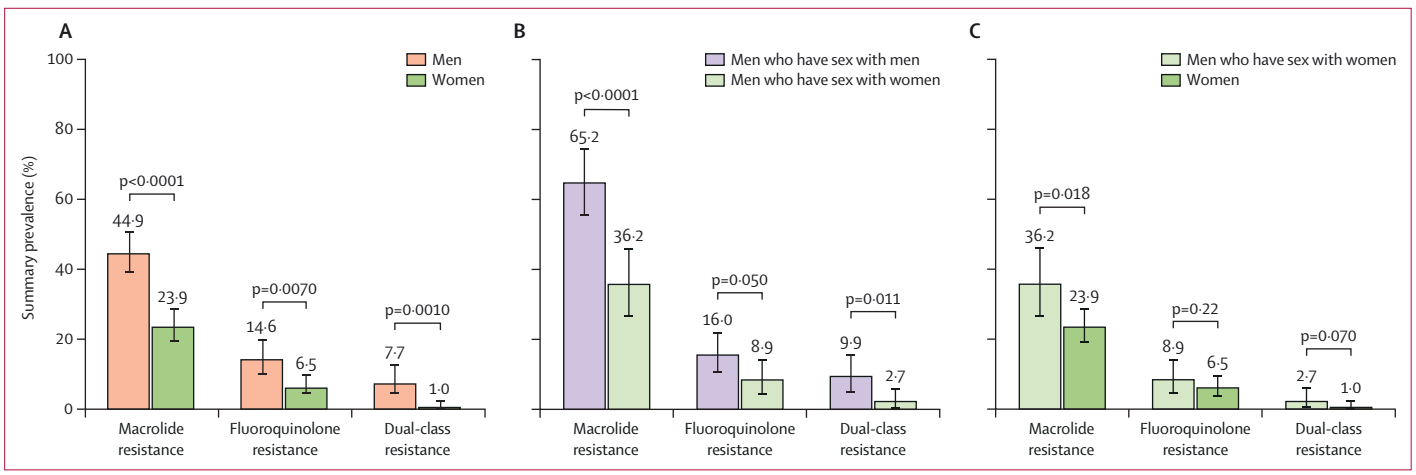

Figure 4: **Prevalence of macrolide, fluoroquinolone, and dual-class resistance in *Mycoplasma genitalium*, by sex (A), sexual orientation (B), and between men who have sex with women and women (C)**
Prevalence was defined as the proportion of *Mycoplasma genitalium*-positive specimens with single nucleotide polymorphisms in 23S rRNA gene for macrolide resistance and the *parC* gene for mutations associated with fluoroquinolone resistance. Error bars represent 95% CIs. p values for meta-analysis subgroup effects are shown.

57% of the data in that region for that period. The apparent stabilisation of macrolide resistance in Australia from 2018 to 2021 might be linked to two recent national guideline changes made in 2017: first, recommending doxycycline over single-dose azithromycin for STI syndromes and rectal chlamydia infections[174] and second, introducing resistance-guided therapy for managing *M genitalium*.[175]

Conversely, there were ongoing increases in macrolide resistance in Europe (20·4% before 2012 to 56·8% in 2018–21 in Nordic countries [p_{trend}=0·031], and 4·6% before 2012 to 43·2% in 2018–21 in non-Nordic countries [p_{trend}<0·0001]; figure 2). Of note, in Sweden, where doxycycline is prescribed as first-line treatment for non-gonococcal urethritis (NGU) and chlamydial infections, lower macrolide resistance levels were reported (20% in 2015–17) compared with other Nordic and European countries, although the most recent prevalence estimate, published after our search date, was 31% in 2018.[176] Most European guidelines now recommend doxycycline for syndromic treatment of NGU or an extended dose of azithromycin if the patient has a macrolide-susceptible *M genitalium* infection.[177,178] Hence, a decrease in resistance prevalence, as seen in other regions, might become evident in the near future. Another potential contributing factor to the increase in macrolide resistance in the European region in 2018–21 was the inclusion of studies for which the majority of samples were from men who have sex with men, who have a higher prevalence of resistant infections.[33,140,144]

The highest burden of fluoroquinolone resistance was in the Western Pacific (40·5% in 2018–21). Australia reported a two-times increase (15·6% in 2015–17 to 34·5% in 2018–21) and in Japan, a five-times increase in resistance was observed (12·2% before 2012 to 64·9% in 2015–17). These patterns are probably related to the concurrent high prevalence of macrolide resistance, resulting in higher consumption of fluoroquinolones. Based on available data, dual-class resistance was also high in this region (29·0% in 2018–21) compared with other regions, where prevalence was less than 7·3%. While lower than the Western Pacific, the European non-Nordic region had increases in fluoroquinolone resistance from 1·7% before 2012 to 12·3% in 2018–21, which is double the 5% estimate reported in a meta-analysis of *M genitalium* resistance in Europe before 2018.[179] Dual-class resistance also rose in this region, from 0·0% before 2012 to 7·3% in 2018–21. Given the increase in macrolide resistance in the European region, efforts need to be made to prevent the otherwise inevitable rapid rises in fluoroquinolone and dual-class resistance. The scarcity of effective antibiotics for the treatment of dual class-resistant *M genitalium* highlights the importance of restricting fluoroquinolone use where possible, and emphasises the need for exploring non-quinolone treatment regimens for *M genitalium*, whether through new antibiotics,[180] repurposing existing ones like minocycline,[181–186] or combination therapies.[185,187–189]

Compared with our earlier systematic review, this update includes more data from low-income and middle-income countries (LMICs), including Burkina Faso, Côte d'Ivoire, Ecuador, Guatemala, Kenya, Mali, Papua New Guinea, Peru, the Solomon Islands, and Togo,[49,83,89,90,146,153,172] although this represented a small proportion (10%) of all samples. Of the available data, macrolide and fluoroquinolone resistance were generally low in these regions, probably due to the limited availability and use of antibiotics in many LMICs.[190] However, the implementation of mass drug administration of azithromycin to control and eliminate certain infectious diseases, such as trachoma in some LMICs, might exert considerable pressure on the selection of macrolide resistance. It will be important to monitor the impact of these programmes on resistance through surveillance. An additional influence on the macrolide resistance estimates in LMICs is the number of recent studies

performed in populations with low risk of resistance, such as pregnant women.[119,121,128,146] Since our search, additional data from Brazil, Taiwan, India, Madagascar, and Viet Nam have been made available, but more data from LMICs are needed.[191–195]

To our knowledge, we reported for the first time trends in specific ParC S83 and D87 amino acid changes in *M genitalium*. The ParC S83I amino acid change was the most common and increased over time from 0·0% before 2012 to 7·3% in 2018–21. Published data show that this alteration is the dominant mutation driving fluoroquinolone treatment failure in countries like Australia,[8,9,189] and this increase, although not statistically significant, suggests that it might carry a lower fitness burden compared with other ParC changes. Published studies have also shown that a concurrent GyrA M95I amino acid change doubles the risk of fluoroquinolone failure compared with the ParC S83I change alone.[6–10,189] Unfortunately, there were insufficient published data to analyse trends in GyrA amino acid changes over time, but based on data from the Western Pacific, GyrA changes are commonly observed with a ParC change.[8,9]

When stratifying resistance by sex, the prevalence of all resistance mutations was higher among men than women, and men who have sex with men had a higher prevalence of resistance compared with men who have sex with women. The differences in resistance between men and women is probably due to the high prevalence of resistance in men who have sex with men. Overall, men who have sex with men have higher levels of antibiotic use compared with the general population, which has been attributed to higher rates of STI screening, detection and treatment, and high-density sexual networks, facilitating rapid spread of resistant infections, making *M genitalium* infections within this group increasingly challenging to cure.[196–198]

The study has several limitations. First, the overall summary estimates should be interpreted with caution and not be construed as representative of the entire region or country, since data availability differed among countries, time periods, and specific study populations. As discussed, regional and time-trend estimates might be skewed, as certain countries contributed data only at specific time-points, and some countries had data only from sub-populations with differing risks. Aside from one study from Morocco, studies from the WHO Eastern Mediterranean and South-East Asia regions were lacking from our search results. More data from these regions are required to understand the global burden of antibiotic-resistant *M genitalium*. Second, most studies were conducted in sexual health clinics, limiting the generalisability of our findings beyond high-risk groups. Third, we did not analyse the impact of the COVID-19 pandemic on sampling or study results. The progression and impact of the pandemic varied in speed and magnitude across different countries. This would have impacted health-seeking behaviour and testing practices. Fourth, we have included four S83 and two D87 ParC amino acid changes although the role of some of these ParC amino acid changes in fluoroquinolone treatment failure has not yet been confirmed. Finally, there was substantial heterogeneity, which was most likely due to real differences in prevalence due to time period, geographical location, source of recruitment, and populations sampled, as seen in most prevalence meta-analyses.[14] To better understand risk factors associated with *M genitalium* resistance, studies should consistently report data stratified by variables such as symptom, HIV status, and age, where feasible.

Although additional global and regional data are now available to provide more accurate estimates of trends, data incorporating additional countries and populations are required to provide a comprehensive understanding of contemporary antibiotic resistance in *M genitalium*. Pilot surveillance studies in the UK, the USA, and Australia have recently provided such data.[69,173,199] However, antibiotic resistance data are also routinely generated by resistance assays that are now recommended by most international guidelines to optimise antibiotic use and cure for *M genitalium*. This provides an important opportunity for countries to collate these routine data and generate sustainable surveillance for antimicrobial resistance in *M genitalium*. As quinolone resistance assays become increasingly relevant to clinical care, these data will also be more frequently available within services. Existing gonococcal surveillance systems can also be leveraged for *M genitalium* surveillance, ideally using standardised collection and testing protocols, to maximise comparability across countries and to inform regional specific guidelines. *M genitalium* is the first STI where treatment limiting antimicrobial resistance is increasingly impacting on cure. Strategies to improve antibiotic misuse and overuse including routine use of resistance assays and avoidance of asymptomatic screening are needed to curb further rises.

Contributors

DAM, T-PC, LAV, JSJ, MU, NL, and CSB designed the study, which was conceived by DAM and CSB. T-PC and LAV performed the systematic search. T-PC and LAV extracted the data. T-PC synthesised the data with assistance from DAM, CSB, LAV, and NL. T-PC, LAV, CSB, and DAM drafted the Article, with assistance from GLM, ELP, JSJ, MU, EPFC, NL, DMW, ELS, JSH, JAD, SMG, CKF, and LZ. T-PC, LAV, DAM, and CSB had access to and verified the data, and were responsible for the decision to submit the manuscript.

Declaration of interests

T-PC received travel funding from the Henry and Rachel Ackman Travelling Scholarship (University of Melbourne), Rowden A E White Scholarship (University of Melbourne), and an Educational Grant (Sexual Health Society of Victoria) for presentation of preliminary results at the STI & HIV 2023 World Congress. LAV receives personal fees from the journal *Sexually Transmitted Infections* as an editorial fellow. ELP reports grants from the Jack Brockhoff Foundation for unrelated projects. JSJ reports personal fees from LeoPharma and Hologic; grants and non-financial support from Hologic, Freya, and Nabriva; and is on the board of Hologic, Nabriva, and Abbott Rapid Diagnostics. SMG reports personal fees from Merck. EPFC reports personal fees from Abbott Rapid Diagnostics and MSD. NL is on the board of Sefunda. DMW reports grants from SpeeDx for unrelated research. ELS reports personal fees from SpeeDx for unrelated research. CSB receives personal fees from Abbott Rapid Diagnostics.

Data sharing

Data used in this study are available upon request to the corresponding authors.

Acknowledgments

This work was supported by an Australian Research Council (ARC) Industrial Transformation Research Hub Grant (IH190100021 to GLM, CSB, and DMW), Australian National Health and Medical Research Council (NHMRC) Leadership Investigator Grants (GNT1172900, APP1197951, and GNT1173361 to CKF, SMG, and CSB, respectively), an Australian NHMRC Emerging Leadership Investigator Grant (GNT1172873 to EPFC), an NHMRC Senior Research Fellowship Grant (GNT2025960 to JSH), an Australian Government Research Training Program Scholarship (to T-PC), and a Henry and Rachel Ackman Travelling Scholarship (to T-PC). We acknowledge Yusha Tao and Hannah Shilling, who contributed to the original Article. We also thank the following authors for providing additional information or stratified data, or both: Helene Zondag, Joyce Braam, Vita Jongen, Inna Edelstein, Irith De Baetselier, Belén Rivaya, Sabine Pereyre, Cécile Laurier Nadalié, Béatrice Berçot, Cécile Bébéar, Mahlape Precious Mahlangu, Ivva Philipova, Patrick Blanco, Peng Junping, Roger Dumke, Claire Broad, Tariq Sadiq, Rachel Pitt, Nigel Field, Laura Chambers, Liesbeth Martens, Michaela Day, Gwen Wood, Laura Bachmann, Emily Learner, Bob Kirkcaldy, Remco Peters, Etienne Muller, Max Chernesky, Luis Dario Piñeiro Vazquez, Nidhi Parmar, Jo-Anne Dillon, Helen Fifer, Irene Stafford, Evelyn Toh, Dave Nelson, Stephen Jordan, Miguel Fernández-Huerta, Vanessa Allen, Dionne Gesink, Judith Lucena Nemirosky, Núria Prim, Ferran Sánchez-Reus, William Geisler, Xiao Li, Jodie Dionne, Trevor Anderson, and Karolina Gullsby.

References

1 Read TRH, Fairley CK, Murray GL, et al. Outcomes of resistance-guided sequential treatment of *Mycoplasma genitalium* infections: a prospective evaluation. *Clin Infect Dis* 2019; **68:** 554–60.

2 Machalek DA, Tao Y, Shilling H, et al. Prevalence of mutations associated with resistance to macrolides and fluoroquinolones in *Mycoplasma genitalium*: a systematic review and meta-analysis. *Lancet Infect Dis* 2020; **20:** 1302–14.

3 Lau A, Bradshaw CS, Lewis D, et al. The efficacy of azithromycin for the treatment of genital *Mycoplasma genitalium*: a systematic review and meta-analysis. *Clin Infect Dis* 2015; **61:** 1389–99.

4 Li Y, Le WJ, Li S, Cao YP, Su XH. Meta-analysis of the efficacy of moxifloxacin in treating *Mycoplasma genitalium* infection. *Int J STD AIDS* 2017; **28:** 1106–14.

5 Deguchi T, Maeda S, Tamaki M, et al. Analysis of the *gyrA* and *parC* genes of *Mycoplasma genitalium* detected in first-pass urine of men with non-gonococcal urethritis before and after fluoroquinolone treatment. *J Antimicrob Chemother* 2001; **48:** 742–44.

6 Couldwell DL, Tagg KA, Jeoffreys NJ, Gilbert GL. Failure of moxifloxacin treatment in *Mycoplasma genitalium* infections due to macrolide and fluoroquinolone resistance. *Int J STD AIDS* 2013; **24:** 822–28.

7 Murray GL, Bradshaw CS, Bissessor M, et al. Increasing macrolide and fluoroquinolone resistance in *Mycoplasma genitalium*. *Emerg Infect Dis* 2017; **23:** 809–12.

8 Murray GL, Bodiyabadu K, Danielewski J, et al. Moxifloxacin and sitafloxacin treatment failure in *Mycoplasma genitalium* infection: association with *parC* mutation G248T (S83I) and concurrent *gyrA* mutations. *J Infect Dis* 2020; **221:** 1017–24.

9 Murray GL, Plummer EL, Bodiyabadu K, et al. *gyrA* mutations in *Mycoplasma genitalium* and their contribution to moxifloxacin failure: time for the next generation of resistance-guided therapy. *Clin Infect Dis* 2023; **76:** 2187–95.

10 Murray GL, Bodiyabadu K, Vodstrcil LA, et al. *parC* variants in *Mycoplasma genitalium*: trends over time and association with moxifloxacin failure. *Antimicrob Agents Chemother* 2022; **66:** e0027822.

11 Hoy D, Brooks P, Woolf A, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. *J Clin Epidemiol* 2012; **65:** 934–39.

12 Baumann L, Cina M, Egli-Gany D, et al. Prevalence of *Mycoplasma genitalium* in different population groups: systematic review andmeta-analysis. *Sex Transm Infect* 2018; **94:** 255–62.

13 Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. *Arch Public Health* 2014; **72:** 39.

14 Migliavaca CB, Stein C, Colpani V, et al. Meta-analysis of prevalence: I^2 statistic and how to deal with heterogeneity. *Res Synth Methods* 2022; **13:** 363–67.

15 Barker TH, Migliavaca CB, Stein C, et al. Conducting proportional meta-analysis in different types of systematic reviews: a guide for synthesisers of evidence. *BMC Med Res Methodol* 2021; **21:** 189.

16 Harbord RM, Higgins JPT. Meta-regression in Stata. *Stata J* 2008; **8:** 493–519.

17 Adelantado Lacasa M, Beristain X. Prevalence of *Mycoplasma genitalium* infection and antibiotic resistance in Navarra (North Spain). *Sex Transm Infect* 2019; **95:** 549.

18 Allan-Blitz LT, Mokany E, Campeau S, Wee R, Shannon C, Klausner JD. Prevalence of *Mycoplasma genitalium* and azithromycin-resistant infections among remnant clinical specimens, Los Angeles. *Sex Transm Dis* 2018; **45:** 632–35.

19 Anagrius C, Loré B, Jensen JS. Treatment of *Mycoplasma genitalium*. Observations from a Swedish STD clinic. *PLoS One* 2013; **8:** e61481.

20 Anderson T, Coughlan E, Werno A. *Mycoplasma genitalium* macrolide and fluoroquinolone resistance detection and clinical implications in a selected cohort in New Zealand. *J Clin Microbiol* 2017; **55:** 3242–48.

21 Ando N, Mizushima D, Takano M, et al. High prevalence of circulating dual-class resistant *Mycoplasma genitalium* in asymptomatic MSM in Tokyo, Japan. *JAC Antimicrob Resist* 2021; **3:** dlab091.

22 Angela A, Raffaele DP, Federica R, Adriana M, Luigi S, Luigi R. Multi-year prevalence and macrolide resistance of *Mycoplasma genitalium* in clinical samples from a southern Italian hospital. *Eur J Clin Microbiol Infect Dis* 2021; **40:** 893–95.

23 Trueba Argamasilla AA, Martínez Jordán J, Moreno-Docón A. Azithromycin and moxifloxacin resistance-associated mutations in *Mycoplasma genitalium*, in the Region of Murcia, by a commercial PCR assay. *Enferm Infecc Microbiol Clin* 2023; **41:** 198–99.

24 Asenjo A, Kusters JG, Severs TT, Alós JI. *Mycoplasma genitalium* in Spain: prevalence of genital infection and frequency of resistance to macrolides. *Enferm Infecc Microbiol Clin* 2018; **36:** 169–71.

25 Bachmann LH, Kirkcaldy RD, Geisler WM, et al. Prevalence of *Mycoplasma genitalium* infection, antimicrobial resistance mutations, and symptom resolution following treatment of urethritis. *Clin Infect Dis* 2020; **71:** e624–32.

26 Balkus JE, Manhart LE, Jensen JS, et al. *Mycoplasma genitalium* infection in Kenyan and US women. *Sex Transm Dis* 2018; **45:** 514–21.

27 Barberá MJ, Fernández-Huerta M, Jensen JS, Caballero E, Andreu A. *Mycoplasma genitalium* macrolide and fluoroquinolone resistance: prevalence and risk factors among a 2013-2014 cohort of patients in Barcelona, Spain. *Sex Transm Dis* 2017; **44:** 457–62.

28 Basu I, Roberts SA, Bower JE, Henderson G, Reid M. High macrolide resistance in *Mycoplasma genitalium* strains causing infection in Auckland, New Zealand. *J Clin Microbiol* 2017; **55:** 2280–82.

29 Berçot B, Charreau I, Rousseau C, et al. High prevalence and high rate of antibiotic resistance of *Mycoplasma genitalium* infections in men who have sex with men: a substudy of the ANRS IPERGAY pre-exposure prophylaxis trial. *Clin Infect Dis* 2021; **73:** e2127–33.

30 Björnelius E, Magnusson C, Jensen JS. *Mycoplasma genitalium* macrolide resistance in Stockholm, Sweden. *Sex Transm Infect* 2017; **93:** 167–68.

31 Blanco P, Rachline A, Tarantola A, et al. Prevalence of *Mycoplasma genitalium* and other sexually transmitted pathogens in male urethritis in a sexual health centre in New Caledonia. *Int J STD AIDS* 2022; **33:** 792–98.

32 Braam JF, Slotboom B, Van Marm S, et al. High prevalence of the A2058T macrolide resistance-associated mutation in *Mycoplasma genitalium* strains from the Netherlands. *J Antimicrob Chemother* 2017; **72:** 1529–30.

33 Braam JF, Zondag HCA, van Dam AP, et al. Prevalence of fluoroquinolone resistance-associated mutations in *Mycoplasma genitalium* among clients of two sexual health centres in the Netherlands: a cross-sectional study. *BMJ Open* 2022; **12:** e066368.

34 Bradley I, Varma R, Knight V, et al. Prevalence of rectal *Mycoplasma genitalium* and macrolide resistance in men who have sex with men attending Sydney Sexual Health Centre. *Sex Health* 2020; **17:** 114–20.

35 Brehony C, Eogan M, Lambert JS, Drew RJ. Evaluation of molecular testing for *Mycoplasma genitalium* for symptomatic women. *Ir J Med Sci* 2022; **191:** 1771–75.

36 Broad CE, Furegato M, Harrison MA, et al. High prevalence of coinfection of azithromycin-resistant *Mycoplasma genitalium* with other STIs: a prospective observational study of London-based symptomatic and STI-contact clinic attendees. *Sex Transm Infect* 2021; **97:** 63–68.

37 Chambers LC, Hughes JP, Glick SN, et al. Resolution of symptoms and resumption of sex after diagnosis of nongonococcal urethritis among men who have sex with men. *Sex Transm Dis* 2019; **46:** 676–82.

38 Chernesky M, Jang D, Martin I, et al. *Mycoplasma genitalium, Chlamydia trachomatis,* and *Neisseria gonorrhoeae* detected with Aptima assays performed on self-obtained vaginal swabs and urine collected at home and in a clinic. *Sex Transm Dis* 2019; **46:** e87–89.

39 Chernesky M, Jang D, Martin I, et al. Comparison of assays for the diagnosis of *Mycoplasma genitalium* and macrolide resistance mutations in self-collected vaginal swabs and urine. *Sex Transm Dis* 2020; **47:** 705–11.

40 Chernesky MA, Jang D, Martin I, et al. *Mycoplasma genitalium* antibiotic resistance-mediating mutations in Canadian women with or without *Chlamydia trachomatis* infection. *Sex Transm Dis* 2017; **44:** 433–35.

41 Cheung C, Bourne C, Varma R. *Mycoplasma genitalium*: test positivity in syndromic presentations and clinicians' adherence with treatment guidelines at Sydney Sexual Health Centre. *Int J STD AIDS* 2021; **32:** 1174–77.

42 Chrisment D, Charron A, Cazanave C, Pereyre S, Bébéar C. Detection of macrolide resistance in *Mycoplasma genitalium* in France. *J Antimicrob Chemother* 2012; **67:** 2598–601.

43 Chua TP, Bodiyabadu K, Machalek DA, et al. Prevalence of *Mycoplasma genitalium* fluoroquinolone-resistance markers, and dual-class-resistance markers, in asymptomatic men who have sex with men. *J Med Microbiol* 2021; **70:** 001429.

44 Conway RJ, Cook S, Malone C, Bone S, Hassan-Ibrahim MO, Soni S. Resistance-guided treatment of *Mycoplasma genitalium* infection at a UK sexual health centre. *Int J STD AIDS* 2021; **32:** 758–65.

45 Coorevits L, Traen A, Bingé L, et al. Macrolide resistance in *Mycoplasma genitalium* from female sex workers in Belgium. *J Glob Antimicrob Resist* 2018; **12:** 149–52.

46 Couldwell DL, Jalocon D, Power M, Jeoffreys NJ, Chen SC, Lewis DA. *Mycoplasma genitalium*: high prevalence of resistance to macrolides and frequent anorectal infection in men who have sex with men in western Sydney. *Sex Transm Infect* 2018; **94:** 406–10.

47 Day MJ, Cole MJ, Fifer H, Woodford N, Pitt R. Detection of markers predictive of macrolide and fluoroquinolone resistance in *Mycoplasma genitalium* from patients attending sexual health services. *Sex Transm Infect* 2022; **98:** 215–18.

48 De Baetselier I, Kenyon C, Vanden Berghe W, et al. An alarming high prevalence of resistance-associated mutations to macrolides and fluoroquinolones in *Mycoplasma genitalium* in Belgium: results from samples collected between 2015 and 2018. *Sex Transm Infect* 2021; **97:** 297–303.

49 De Baetselier I, Vuylsteke B, Cuylaerts V, et al, and the CohMSM-PrEP Study Group. *Mycoplasma genitalium* and antimicrobial resistance among a cohort of West African men who have sex with men using preexposure prophylaxis (CohMSM-PrEP ANRS 12369-Expertise France Study). *Open Forum Infect Dis* 2022; **9:** ofac615.

50 de Salazar A, Barrientos-Durán A, Espadafor B, Fuentes-López A, Chueca N, Garcia F. Macrolide and fluoroquinolone resistance of *Mycoplasma genitalium* in southern Spain, 2018-2019. *Sex Transm Infect* 2021; **97:** 8–10.

51 Dean G, Soni S, Pitt R, Ross J, Sabin C, Whetham J. Treatment of mild-to-moderate pelvic inflammatory disease with a short-course azithromycin-based regimen versus ofloxacin plus metronidazole: results of a multicentre, randomised controlled trial. *Sex Transm Infect* 2021; **97:** 177–82.

52 Deborde M, Pereyre S, Puges M, et al. High prevalence of *Mycoplasma genitalium* infection and macrolide resistance in patients enrolled in HIV pre-exposure prophylaxis program. *Med Mal Infect* 2019; **49:** 347–49.

53 Deguchi T, Ito S, Yasuda M, et al. Surveillance of the prevalence of macrolide and/or fluoroquinolone resistance-associated mutations in *Mycoplasma genitalium* in Japan. *J Infect Chemother* 2018; **24:** 861–67.

54 Deguchi T, Kikuchi M, Yasuda M, Ito S. Multidrug-resistant *Mycoplasma genitalium* is increasing. *Clin Infect Dis* 2016; **62:** 405–06.

55 Desdorf R, Andersen NM, Chen M. *Mycoplasma genitalium* prevalence and macrolide resistance-associated mutations and coinfection with *Chlamydia trachomatis* in Southern Jutland, Denmark. *APMIS* 2021; **129:** 706–10.

56 Dionne-Odom J, Geisler WM, Aaron KJ, et al. High prevalence of multidrug-resistant *Mycoplasma genitalium* in human immunodeficiency virus-infected men who have sex with men in Alabama. *Clin Infect Dis* 2018; **66:** 796–98.

57 Dumke R, Spornraft-Ragaller P. Antibiotic resistance and genotypes of *Mycoplasma genitalium* during a resistance-guided treatment regime in a German university hospital. *Antibiotics* 2021; **10:** 962.

58 Dumke R, Thürmer A, Jacobs E. Emergence of *Mycoplasma genitalium* strains showing mutations associated with macrolide and fluoroquinolone resistance in the region Dresden, Germany. *Diagn Microbiol Infect Dis* 2016; **86:** 221–23.

59 Dumke R, Ziegler T, Abbasi-Boroudjeni N, Rust M, Glaunsinger T. Prevalence of macrolide- and fluoroquinolone-resistant *Mycoplasma genitalium* strains in clinical specimens from men who have sex with men of two sexually transmitted infection practices in Berlin, Germany. *J Glob Antimicrob Resist* 2019; **18:** 118–21.

60 Durukan D, Read TRH, Murray G, et al. Resistance-guided antimicrobial therapy using doxycycline-moxifloxacin and doxycycline-2.5 g azithromycin for the treatment of *Mycoplasma genitalium* infection: efficacy and tolerability. *Clin Infect Dis* 2020; **71:** 1461–68.

61 Edelstein IA, Guschin AE, Romanov AV, Negasheva ES, Kozlov RS. Genetic determinants of macrolide and fluoroquinolone resistance in *Mycoplasma genitalium* and their prevalence in Moscow, Russia. *Pathogens* 2023; **12:** 496.

62 Edelstein IA, Romanov AV, Kozlov RS. Development of a real-time PCR assay for detection of macrolide resistance mutations in *Mycoplasma genitalium* and its application for epidemiological surveillance in Russia. *Microb Drug Resist* 2023; **29:** 69–77.

63 Falk L, Enger M, Jensen JS. Time to eradication of *Mycoplasma genitalium* after antibiotic treatment in men and women. *J Antimicrob Chemother* 2015; **70:** 3134–40.

64 Fernández-Huerta M, Barberá MJ, Esperalba J, et al. Prevalence of *Mycoplasma genitalium* and macrolide resistance among asymptomatic people visiting a point of care service for rapid STI screening: a cross-sectional study. *Sex Transm Infect* 2020; **96:** 300–05.

65 Fernández-Huerta M, Bodiyabadu K, Esperalba J, et al. Multicenter clinical evaluation of a novel multiplex real-time PCR (qPCR) assay for detection of fluoroquinolone resistance in *Mycoplasma genitalium*. *J Clin Microbiol* 2019; **57:** e00886–19.

66 Fernández-Huerta M, Espasa M. *Mycoplasma genitalium* co-infection with *Chlamydia trachomatis* and *Neisseria gonorrhoeae* among asymptomatic patients: the silent wick for macrolide resistance spread. *Sex Transm Infect* 2019; **95:** 391.

67 Fernández-Huerta M, Salmerón P, Silgado A, et al. Clinical evaluation of the ResistancePlus MG FleXible test on the GeneXpert Infinity-48s instrument: a near-patient assay for simultaneous detection of *Mycoplasma genitalium* and macrolide resistance. *Diagn Microbiol Infect Dis* 2020; **97:** 115062.

68 Fernández-Huerta M, Vall M, Fernández-Naval C, et al. *Mycoplasma genitalium* macrolide resistance update: rate among a 2016-2017 cohort of patients in Barcelona, Spain. *Enferm Infecc Microbiol Clin* 2020; **38:** 99–104.

69 Fifer H, Merrick R, Pitt R, et al. Frequency and correlates of *Mycoplasma genitalium* antimicrobial resistance mutations and their association with treatment outcomes: findings from a national sentinel surveillance pilot in England. *Sex Transm Dis* 2021; **48:** 951–54.

70 Forslund O, Hjelm M, El-Ali R, Johnsson A, Bjartling C. *Mycoplasma genitalium* and macrolide resistance-associated mutations in the Skane region of Southern Sweden 2015. *Acta Derm Venereol* 2017; **97:** 1235–38.

71 Gardette M, Hénin N, Le Roy C, et al. Clinical performance of three commercial molecular diagnostic assays for the detection of fluoroquinolone resistance-associated mutations in *Mycoplasma genitalium*. *J Clin Microbiol* 2022; **60:** e0113522.

72 Gesink D, Racey CS, Seah C, et al. *Mycoplasma genitalium* in Toronto, Ont: estimates of prevalence and macrolide resistance. *Can Fam Physician* 2016; **62:** e96–101.

73 Gesink DC, Mulvad G, Montgomery-Andersen R, et al. *Mycoplasma genitalium* presence, resistance and epidemiology in Greenland. *Int J Circumpolar Health* 2012; **71:** 1–8.

74 Getman D, Jiang A, O'Donnell M, Cohen S. *Mycoplasma genitalium* prevalence, coinfection, and macrolide antibiotic resistance frequency in a multicenter clinical study cohort in the United States. *J Clin Microbiol* 2016; **54:** 2278–83.

75 Gossé M, Lysvand H, Pukstad B, Nordbø SA. A novel SimpleProbe PCR assay for detection of mutations in the 23S rRNA gene associated with macrolide resistance in *Mycoplasma genitalium* in clinical samples. *J Clin Microbiol* 2016; **54:** 2563–67.

76 Gossé M, Nordbø SA, Pukstad B. Bacterial load in daily urine samples of patients infected with *Mycoplasma genitalium*, mutation analysis, and response to treatment. *Infect Dis Obstet Gynecol* 2016; **2016:** 8382469.

77 Gratrix J, Plitt S, Turnbull L, et al. Prevalence and antibiotic resistance of *Mycoplasma genitalium* among STI clinic attendees in Western Canada: a cross-sectional analysis. *BMJ Open* 2017; **7:** e016300.

78 Guiraud J, Helary M, Le Roy C, Elguero E, Pereyre S, Bébéar C. Molecular typing reveals distinct *Mycoplasma genitalium* transmission networks among a cohort of men who have sex with men and a cohort of women in France. *Microorganisms* 2022; **10:** 1587.

79 Gullsby K, Lindh L, Adriaenssens R, Herrmann B. Comparison of three real-time PCR methods for detection of macrolide-resistant *Mycoplasma genitalium* in Sweden. *Diagn Microbiol Infect Dis* 2021; **100:** 115349.

80 Guschin A, Ryzhikh P, Rumyantseva T, Gomberg M, Unemo M. Treatment efficacy, treatment failures and selection of macrolide resistance in patients with high load of *Mycoplasma genitalium* during treatment of male urethritis with josamycin. *BMC Infect Dis* 2015; **15:** 40.

81 Hadad R, Golparian D, Lagos AC, et al. Macrolide and fluoroquinolone resistance in *Mycoplasma genitalium* in two Swedish counties, 2011-2015. *APMIS* 2018; **126:** 123–27.

82 Hamasuna R, Le PT, Kutsuna S, et al. Mutations in ParC and GyrA of moxifloxacin-resistant and susceptible *Mycoplasma genitalium* strains. *PLoS One* 2018; **13:** e0198355.

83 Harrison MA, Harding-Esch EM, Marks M, et al. Impact of mass drug administration of azithromycin for trachoma elimination on prevalence and azithromycin resistance of genital *Mycoplasma genitalium* infection. *Sex Transm Infect* 2019; **95:** 522–28.

84 Hart T, Tang WY, Mansoor SAB, Chio MTW, Barkham T. *Mycoplasma genitalium* in Singapore is associated with *Chlamydia trachomatis* infection and displays high macrolide and fluoroquinolone resistance rates. *BMC Infect Dis* 2020; **20:** 314.

85 Hay B, Dubbink JH, Ouburg S, et al. Prevalence and macrolide resistance of *Mycoplasma genitalium* in South African women. *Sex Transm Dis* 2015; **42:** 140–42.

86 Hilmarsdóttir I, Arnardóttir EM, Jóhannesdóttir ER, et al. Prevalence of *Mycoplasma genitalium* and antibiotic resistance-associated mutations in patients at a sexually transmitted infection clinic in Iceland, and comparison of the S-DiaMGTV and Aptima *Mycoplasma genitalium* assays for diagnosis. *J Clin Microbiol* 2020; **58:** e01084–20.

87 Hokynar K, Hiltunen-Back E, Mannonen L, Puolakkainen M. Prevalence of *Mycoplasma genitalium* and mutations associated with macrolide and fluoroquinolone resistance in Finland. *Int J STD AIDS* 2018; **29:** 904–07.

88 Hu M, Souder JP, Subramaniam A, et al. Prevalence of *Mycoplasma genitalium* infection and macrolide resistance in pregnant women receiving prenatal care. *Int J Gynaecol Obstet* 2023; **160:** 341–44.

89 Jary A, Teguete I, Sidibé Y, et al. Prevalence of cervical HPV infection, sexually transmitted infections and associated antimicrobial resistance in women attending cervical cancer screening in Mali. *Int J Infect Dis* 2021; **108:** 610–16.

90 Jonduo ME, Vallely AJ, Whiley DM, et al. *Mycoplasma genitalium* macrolide and fluoroquinolone resistance in pregnant women in Papua New Guinea. *Sex Transm Infect* 2023; **99:** 71–72.

91 Ke W, Li D, Tso LS, et al. Macrolide and fluoroquinolone associated mutations in *Mycoplasma genitalium* in a retrospective study of male and female patients seeking care at a STI Clinic in Guangzhou, China, 2016-2018. *BMC Infect Dis* 2020; **20:** 950.

92 Khosropour CM, Jensen JS, Soge OO, et al. High prevalence of vaginal and rectal *Mycoplasma genitalium* macrolide resistance among remale sexually transmitted disease clinic patients in Seattle, Washington. *Sex Transm Dis* 2020; **47:** 321–25.

93 Kristiansen GQ, Lisby JG, Schønning K. 5′ nuclease genotyping assay for identification of macrolide-resistant *Mycoplasma genitalium* in clinical specimens. *J Clin Microbiol* 2016; **54:** 1593–97.

94 Latimer RL, Vodstrcil LA, Plummer EL, et al. The clinical indications for testing women for *Mycoplasma genitalium*. *Sex Transm Infect* 2022; **98:** 277–85.

95 Laumen JGE, van Alphen LB, Maduna LD, et al. Molecular epidemiological analysis of *Mycoplasma genitalium* shows low prevalence of azithromycin resistance and a well-established epidemic in South Africa. *Sex Transm Infect* 2021; **97:** 152–56.

96 Le Roux MC, Mafunise M, de Villiers BE, Ditsele RM. Antimicrobial susceptibility of *Mycoplasma genitalium* isolates from Pretoria, South Africa in 2012 and 2016. *S Afr J Infect Dis* 2018; **33:** 46–49.

97 Le Roy C, Bébéar C, Pereyre S. Clinical evaluation of three commercial PCR assays for the detection of macrolide resistance in *Mycoplasma genitalium*. *J Clin Microbiol* 2020; **58:** e01478–19.

98 Le Roy C, Bébéar C, Pereyre S. Performance of three commercial molecular diagnostic assays for the simultaneous detection of *Mycoplasma genitalium* and macrolide resistance. *J Clin Microbiol* 2021; **59:** e00020–21.

99 Guiraud J, Lounnas M, Boissière A, et al. Lower *mgpB* diversity in macrolide-resistant *Mycoplasma genitalium* infecting men visiting two sexually transmitted infection clinics in Montpellier, France. *J Antimicrob Chemother* 2021; **76:** 43–47.

100 Le Roy C, Hénin N, Pereyre S, Bébéar C. Fluoroquinolone-resistant *Mycoplasma genitalium*, southwestern France. *Emerg Infect Dis* 2016; **22:** 1677–79.

101 Le Roy C, Pereyre S, Hénin N, Bébéar C. French prospective clinical evaluation of the Aptima *Mycoplasma genitalium* CE-IVD Assay and macrolide resistance detection using three distinct assays. *J Clin Microbiol* 2017; **55:** 3194–200.

102 Lee SS, Cheng KF, Wong NS, et al. Emergence of antibiotic-resistant *Mycoplasma genitalium* as the cause of non-gonococcal urethritis in male patients at a sexually transmitted infection clinic. *Int J Antimicrob Agents* 2022; **59:** 106510.

103 Li L, Yuan Y, He W, Zheng L, Wang Q. Emerging multidrug resistance contributes to treatment failure in *Mycoplasma genitalium* infected patients in China. *Diagn Microbiol Infect Dis* 2023; **105:** 115854.

104 Li WN, Shi L, Long XY, Li Y, Zhu WB, Liu G. *Mycoplasma genitalium* incidence, treatment failure, and resistance: a retrospective survey of men of infertile couples from a hospital in China. *Andrology* 2020; **8:** 91–100.

105 Li Y, Su X, Le W, et al. *Mycoplasma genitalium* in symptomatic male urethritis: macrolide use is associated with increased resistance. *Clin Infect Dis* 2020; **70:** 805–10.

106 Li Y, Xiu L, Wang L, Zhang L, Wang F, Peng J. Rapid detection of antimicrobial resistance in *Mycoplasma genitalium* by high-resolution melting analysis with unlabeled probes. *Microbiol Spectr* 2022; **10:** e0101422.

107 Lucena Nemirosky J, Espelt R, López Grado E, et al. Macrolide resistance in *Mycoplasma genitalium* in Catalonia, Spain: a 1 year prospective study. *J Antimicrob Chemother* 2021; **76:** 2702–07.

108 Maduna LD, Peters RPH, Kingsburgh C, Strydom KA, Kock MM. Antimicrobial resistance in *Neisseria gonorrhoeae* and *Mycoplasma genitalium* isolates from the private healthcare sector in South Africa: a pilot study. *S Afr Med J* 2021; **111:** 995–97.

109 Mahlangu MP, Müller EE, Da Costa Dias B, Venter JME, Kularatne RS. Molecular characterization and detection of macrolide and fluoroquinolone resistance determinants in *Mycoplasma genitalium* in South Africa, 2015 to 2018. *Sex Transm Dis* 2022; **49:** 511–16.

110 Maldonado-Barrueco A, Rodríguez-Ayala M, Grandioso-Vas D, et al. Epidemiology and prevalence of mutations associated with resistance to macrolides and fluoroquinolones in *Mycoplasma genitalium* in a tertiary hospital from Madrid, Spain. *Rev Esp Quimioter* 2023; **36:** 310–13.

111 Martens L, Kuster S, de Vos W, Kersten M, Berkhout H, Hagen F. Macrolide-resistant *Mycoplasma genitalium* in southeastern region of the Netherlands, 2014-2017. *Emerg Infect Dis* 2019; **25:** 1297–303.

112 McAuliffe GN, Bissessor L, Basu I, Smith S, Upton A. Barriers to testing and management of *Mycoplasma genitalium* infections in primary care. *Int J STD AIDS* 2019; **30:** 1116–23.

113 McIver R, Jalocon D, McNulty A, et al. Men who have sex with men with *Mycoplasma genitalium*-positive nongonococcal urethritis are more likely to have macrolide-resistant strains than men with only female partners: a prospective study. *Sex Transm Dis* 2019; **46:** 513–17.

114 Mondeja BA, Rodríguez NM, Blanco O, Fernández C, Jensen JS. *Mycoplasma genitalium* infections in Cuba: surveillance of urogenital syndromes, 2014-2015. *Int J STD AIDS* 2018; **29:** 994–98.

115 Muller EE, Mahlangu MP, Lewis DA, Kularatne RS. Macrolide and fluoroquinolone resistance-associated mutations in *Mycoplasma genitalium* in Johannesburg, South Africa, 2007-2014. *BMC Infect Dis* 2019; **19:** 148.

116 Mulligan V, Lynagh Y, Clarke S, Unemo M, Crowley B. Prevalence, macrolide resistance, and fluoroquinolone resistance in *Mycoplasma genitalium* in men who have sex with men attending an sexually transmitted disease clinic in Dublin, Ireland in 2017-2018. *Sex Transm Dis* 2019; **46:** e35–37.

117 Murray GL, Danielewski J, Bradshaw CS, et al. Performance of the ResistancePlus MG diagnostic test for *Mycoplasma genitalium* using samples collected with Hologic Aptima Specimen Collection kits. *J Med Microbiol* 2020; **69:** 244–48.

118 Murray GL, Doyle M, Bodiyabadu K, et al. Evaluation of ResistancePlus MG FleXible, a 'near-patient' test for the detection of *Mycoplasma genitalium* and macrolide resistance mutations, using freshly collected clinical samples. *J Med Microbiol* 2021; **70**.

119 Naicker M, Singh R, van der Westhuizen D, Tinarwo P, Abbai NS. Lack of resistance to macrolides in *Mycoplasma genitalium* detected in South African pregnant women. *S Afr J Infect Dis* 2021; **36:** 209.

120 Ng KKM, Leung PKL, Cheung TKM. Molecular detection of *Mycoplasma genitalium* in endocervical swabs and associated rates of macrolide and fluoroquinolone resistance in Hong Kong. *Hong Kong Med J* 2020; **26:** 390–96.

121 Ngobese B, Swe Swe-Han K, Tinarwo P, Abbai NS. Low prevalence of macrolide resistance in *Mycoplasma genitalium* infections in a cohort of pregnant women living with human immunodeficiency virus. *Int J STD AIDS* 2022; **33:** 1174–82.

122 Nijhuis RH, Severs TT, Van der Vegt DS, Van Zwet AA, Kusters JG. High levels of macrolide resistance-associated mutations in *Mycoplasma genitalium* warrant antibiotic susceptibility-guided treatment. *J Antimicrob Chemother* 2015; **70:** 2515–18.

123 Nijhuis RHT, Duinsbergen RG, Pol A, Godschalk PCR. Prevalence of *Chlamydia trachomatis, Neisseria gonorrhoeae*, *Mycoplasma genitalium* and *Trichomonas vaginalis* including relevant resistance-associated mutations in a single center in the Netherlands. *Eur J Clin Microbiol Infect Dis* 2021; **40:** 591–95.

124 Nye MB, Harris AB, Pherson AJ, Cartwright CP. Prevalence of *Mycoplasma genitalium* infection in women with bacterial vaginosis. *BMC Womens Health* 2020; **20:** 62.

125 Ong JJ, Magooa MP, Chikandiwa A, et al. and the HIV in Africa Research Partnership Study Group. Prevalence and antimicrobial resistance of *Mycoplasma genitalium* infection among women living with human immunodeficiency virus in South Africa: a prospective cohort study. *Clin Infect Dis* 2019; **69:** 873–76.

126 Parmar NR, Mushanski L, Wanlin T, et al. High prevalence of macrolide and fluoroquinolone resistance-mediating mutations in *Mycoplasma genitalium*-positive urine specimens from Saskatchewan. *Sex Transm Dis* 2021; **48:** 680–84.

127 Pereyre S, Laurier-Nadalié C, Le Roy C, et al, and the investigator group. Prevalence of macrolide and fluoroquinolone resistance-associated mutations in *Mycoplasma genitalium* in metropolitan and overseas France. *Sex Transm Infect* 2023; **99:** 254–60.

128 Peters RPH, Jung HS, Muller EE, et al. Lack of macrolide resistance in *Mycoplasma genitalium* infections in a cohort of pregnant women in South Africa. *Sex Transm Infect* 2021; **97:** 624–25.

129 Philipova I, Hadad R, Levterova V, Kantardjiev T, Unemo M. *Mycoplasma genitalium* antimicrobial (azithromycin and moxifloxacin) resistance and treatment outcome in Sofia, Bulgaria, 2018-2021. *J Eur Acad Dermatol Venereol* 2023; **37:** e994–95.

130 Philipova I, Levterova V, Simeonovski I, Kantardjiev T. Azithromycin treatment failure and macrolide resistance in *Mycoplasma genitalium* infections in Sofia, Bulgaria. *Folia Med* 2022; **64:** 422–29.

131 Piñeiro L, Idigoras P, Arrastia M, Manzanal A, Ansa I, Cilla G. Increases in the macrolide resistance of *Mycoplasma genitalium* and the emergence of the A2058T mutation in the 23S rRNA gene: clonal spread? *Antibiotics* 2022; **11:** 1492.

132 Pineiro L, Idigoras P, de la Caba I, Lopez-Olaizola M, Cilla G. Guided antibiotic therapy for *Mycoplasma genitalium* infections: analysis of mutations associated with resistance to macrolides and fluoroquinolones. *Enferm Infecc Microbiol Clin* 2019; **37:** 394–97.

133 Pitt R, Unemo M, Sonnenberg P, et al. Antimicrobial resistance in *Mycoplasma genitalium* sampled from the British general population. *Sex Transm Infect* 2020; **96:** 464–68.

134 Pitt R, Fifer H, Woodford N, Alexander S. Detection of markers predictive of macrolide and fluoroquinolone resistance in *Mycoplasma genitalium* from patients attending sexual health services in England. *Sex Transm Infect* 2018; **94:** 9–13.

135 Pitt R, Fifer H, Woodford N, Hopkins S, Cole MJ. Prevalence of *Chlamydia trachomatis* and *Mycoplasma genitalium* coinfections and *M. genitalium* antimicrobial resistance in rectal specimens. *Sex Transm Infect* 2021; **97:** 469–70.

136 Pond MJ, Nori AV, Witney AA, Lopeman RC, Butcher PD, Sadiq ST. High prevalence of antibiotic-resistant *Mycoplasma genitalium* in nongonococcal urethritis: the need for routine testing and the inadequacy of current treatment options. *Clin Infect Dis* 2014; **58:** 631–37.

137 Read TR, Fairley CK, Tabrizi SN, et al. Azithromycin 1.5g over 5 days compared to 1g single dose in urethral *Mycoplasma genitalium*: impact on treatment outcome and resistance. *Clin Infect Dis* 2017; **64:** 250–56.

138 Read TRH, Murray GL, Danielewski JA, et al. Symptoms, sites, and significance of *Mycoplasma genitalium* in men who have sex with men. *Emerg Infect Dis* 2019; **25:** 719–27.

139 Richardson D, Lewis DA, Jeoffreys NJ, Couldwell DL. *Mycoplasma genitalium* coinfection in men with symptomatic gonococcal urethritis. *Sex Transm Infect* 2021; **97:** 363–67.

140 Ring A, Balakrishna S, Imkamp F, et al. High rates of asymptomatic *Mycoplasma genitalium* infections with high proportion of genotypic resistance to first-line macrolide treatment among men who have sex with men enrolled in the Zurich Primary HIV Infection Study. *Open Forum Infect Dis* 2022; **9:** ofac217.

141 Rivaya B, Le Roy C, Jordana-Lluch E, et al. Detection and prevalence of macrolide and fluoroquinolone resistance in *Mycoplasma genitalium* in Badalona, Spain. *Antibiotics* 2022; **11:** 485.

142 Romano SS, Jensen JS, Lowens MS, et al. Long duration of asymptomatic *Mycoplasma genitalium* infection after syndromic treatment for nongonococcal urethritis. *Clin Infect Dis* 2019; **69:** 113–20.

143 Salado-Rasmussen K, Jensen JS. *Mycoplasma genitalium* testing pattern and macrolide resistance: a Danish nationwide retrospective survey. *Clin Infect Dis* 2014; **59:** 24–30.

144 Sandri A, Carelli M, Visentin A, et al. *Mycoplasma genitalium* antibiotic resistance-associated mutations in genital and extragenital samples from men-who-have-sex-with-men attending a STI clinic in Verona, Italy. *Front Cell Infect Microbiol* 2023; **13:** 1155451.

145 Muñoz Santa A, Aramburu Arnuelos J, Bernet Sánchez A, Bellés Bellés A. *Mycoplasma genitalium*: analysis of mutations associated with macrolide resistance in Lleida, Spain. *Enferm Infecc Microbiol Clin* 2022; **40:** 209–10.

146 Scoullar MJL, Boeuf P, Peach E, et al. *Mycoplasma genitalium* and other reproductive tract infections in pregnant women, Papua New Guinea, 2015-2017. *Emerg Infect Dis* 2021; **27:** 894–904.

147 Seo Y, Park H, Lee G. Molecular mechanisms of macrolide and fluoroquinolone resistance among Korean isolates of *Mycoplasma genitalium* over a period of five years 2014-2019. *J Med Microbiol* 2021; **70**.

148 Seo Y, Park H, Lee G. *mgpB* genotyping and genetic diversity for antimicrobial resistance of *Mycoplasma genitalium*. *J Med Microbiol* 2022; **71:** 001585.

149 Shedko ED, Khayrullina GA, Goloveshkina EN, Akimkin VG. Clinical evaluation of commercial PCR assays for antimicrobal resistance in *Mycoplasma genitalium* and estimation of resistance-mediated mutation prevalence in Moscow and Moscow region. *Eur J Clin Microbiol Infect Dis* 2021; **40:** 1413–18.

150 Shilling HS, Garland SM, Costa AM, et al. *Chlamydia trachomatis* and *Mycoplasma genitalium* prevalence and associated factors among women presenting to a pregnancy termination and contraception clinic, 2009-2019. *Sex Transm Infect* 2022; **98:** 115–20.

151 Shimada Y, Deguchi T, Nakane K, et al. Macrolide resistance-associated 23S rRNA mutation in *Mycoplasma genitalium*, Japan. *Emerg Infect Dis* 2011; **17:** 1148–50.

152 Shipitsyna E, Khusnutdinova T, Budilovskaya O, et al. Performance of the first commercial dual resistance assay, AmpliSens *Mycoplasma genitalium*-ML/FQ-Resist-FL, for detection of potential macrolide and quinolone resistance-associated mutations and prevalence of *M. genitalium* resistance mutations in St. Petersburg, Russia. *Sex Transm Infect* 2023; **99:** 191–94.

153 Shipitsyna E, Kularatne R, Golparian D, et al. *Mycoplasma genitalium* prevalence, antimicrobial resistance-associated mutations, and coinfections with non-viral sexually transmitted infections in high-risk populations in Guatemala, Malta, Morocco, Peru and South Africa, 2019-2021. *Front Microbiol* 2023; **14:** 1130762.

154 Shipitsyna E, Rumyantseva T, Golparian D, et al. Prevalence of macrolide and fluoroquinolone resistance-mediating mutations in *Mycoplasma genitalium* in five cities in Russia and Estonia. *PLoS One* 2017; **12:** e0175763.

155 Spiller OB, Rees CL, Morris DJ, Davies RL, Jones LC. *Mycoplasma genitalium* prevalence in Welsh sexual health patients: low antimicrobial resistance markers and no association of symptoms to bacterial load. *Microb Pathog* 2020; **139:** 103872.

156 Spornraft-Ragaller P, Dumke R. Prevalence and antibiotic resistance of rectal Mollicutes in HIV-infected men who have sex with men at the University Hospital of Dresden, Germany. *Infection* 2020; **48:** 259–65.

157 Stafford IA, Hummel K, Dunn JJ, et al. Retrospective analysis of infection and antimicrobial resistance patterns of *Mycoplasma genitalium* among pregnant women in the southwestern USA. *BMJ Open* 2021; **11:** e050475.

158 Su JP, Tan LY, Garland SM, et al. Evaluation of the SpeeDx ResistancePlus MG Diagnostic Test for *Mycoplasma genitalium* on the Applied Biosystems 7500 Fast Quantitative PCR Platform. *J Clin Microbiol* 2017; **56:** e01245-17.

159 Sweeney EL, Lowry K, Bletchly C, Nimmo GR, Whiley DM. *Mycoplasma genitalium* infections can comprise a mixture of both fluoroquinolone-susceptible and fluoroquinolone-resistant strains. *J Antimicrob Chemother* 2021; **76:** 887–92.

160 Sweeney EL, Mhango LP, Ebeyan S, et al. Evaluation of the resistance plus MG FleXible cartridge for near-point-of-care testing of *Mycoplasma genitalium* and associated macrolide resistance mutations. *J Clin Microbiol* 2020; **58:** e01897–19.

161 Tickner JA, Bradshaw CS, Murray GL, Whiley DM, Sweeney EL. Novel probe-based melting curve assays for the characterization of fluoroquinolone resistance in *Mycoplasma genitalium*. *J Antimicrob Chemother* 2022; **77:** 1592–99.

162 Toh E, Gao X, Williams JA, et al. Evaluation of clinical, Gram stain, and microbiological cure outcomes in men receiving azithromycin for acute nongonococcal urethritis: discordant cures are associated with *Mycoplasma genitalium* infection. *Sex Transm Dis* 2022; **49:** 67–75.

163 Touati A, Peuchant O, Jensen JS, Bébéar C, Pereyre S. Direct detection of macrolide resistance in *Mycoplasma genitalium* isolates from clinical specimens from France by use of real-time PCR and melting curve analysis. *J Clin Microbiol* 2014; **52:** 1549–55.

164 Trembizki E, Buckley C, Bletchly C, Nimmo GR, Whiley DM. High levels of macrolide-resistant *Mycoplasma genitalium* in Queensland, Australia. *J Med Microbiol* 2017; **66:** 1451–53.

165 Twin J, Jensen JS, Bradshaw CS, et al. Transmission and selection of macrolide resistant *Mycoplasma genitalium* infections detected by rapid high resolution melt analysis. *PLoS One* 2012; **7:** e35593.

166 Unemo M, Salado-Rasmussen K, Hansen M, et al. Clinical and analytical evaluation of the new Aptima *Mycoplasma genitalium* assay, with data on *M. genitalium* prevalence and antimicrobial resistance in *M. genitalium* in Denmark, Norway and Sweden in 2016. *Clin Microbiol Infect* 2018; **24:** 533–39.

167 Vesty A, McAuliffe G, Roberts S, Henderson G, Basu I. *Mycoplasma genitalium* antimicrobial resistance in community and sexual health clinic patients, Auckland, New Zealand. *Emerg Infect Dis* 2020; **26:** 332–35.

168 Wang L, Li Z, Wan C, Tian X, Liu H, Li Y. Prevalence of *Mycoplasma genitalium* infection with antimicrobial resistance mutations among gay sex workers in China. *Int J STD AIDS* 2023; **34:** 518–24.

169 Wold C, Sorthe J, Hartgill U, Olsen AO, Moghaddam A, Reinton N. Identification of macrolide-resistant *Mycoplasma genitalium* using real-time PCR. *J Eur Acad Dermatol Venereol* 2015; **29:** 1616–20.

170 Wood GE, Jensen NL, Astete S, et al. Azithromycin and doxycycline resistance profiles of US *Mycoplasma genitalium* strains and their association with treatment outcomes. *J Clin Microbiol* 2021; **59:** e0081921.

171 Xiao L, Waites KB, Van Der Pol B, Aaron KJ, Hook EW 3rd, Geisler WM. *Mycoplasma genitalium* infections with macrolide and fluoroquinolone resistance-associated mutations in heterosexual African American couples in Alabama. *Sex Transm Dis* 2019; **46:** 18–24.

172 Zhou L, Lopez Rodas A, Llangarí LM, Romero Sandoval N, Cooper P, Sadiq ST. Single gene targeted nanopore sequencing enables simultaneous identification and antimicrobial resistance detection of sexually transmitted infections. *PLoS One* 2022; **17:** e0262242.

173 Manhart LE, Leipertz G, Soge OO, et al, and the MyGeniUS Study Team. *Mycoplasma genitalium* in the US (MyGeniUS): surveillance data from sexual health clinics in four US regions. *Clin Infect Dis* 2023; **77:** 1449–59.

174 Lau A, Kong FYS, Fairley CK, et al. Azithromycin or doxycycline for asymptomatic rectal *Chlamydia trachomatis*. *N Engl J Med* 2021; **384:** 2418–27.

175 Australia Sexual Health Alliance. Australian STI management guidelines for use in primary care. January 2023. http://www.sti.guidelines.org.au (accessed Nov 17, 2023).

176 Drud ST, Anagrius C, Loré B, Elfving K, Jensen JS. Changes in prevalence of *Mycoplasma genitalium* macrolide and fluoroquinolone resistance: notes from a 13-year retrospective survey in Dalarna County, Sweden. *Sex Transm Infect* 2023; **99:** 507–12.

177 Horner PJ, Blee K, Falk L, van der Meijden W, Moi H. 2016 European guideline on the management of non-gonococcal urethritis. *Int J STD AIDS* 2016; **27:** 928–37.

178 Jensen JS, Cusini M, Gomberg M, Moi H, Wilson J, Unemo M. 2021 European guideline on the management of *Mycoplasma genitalium* infections. *J Eur Acad Dermatol Venereol* 2022; **36:** 641–50.

179 Fernández-Huerta M, Barberá MJ, Serra-Pladevall J, et al. *Mycoplasma genitalium* and antimicrobial resistance in Europe: a comprehensive review. *Int J STD AIDS* 2020; **31:** 190–97.

180 Paukner S, Gruss A, Jensen JS. *In vitro* activity of lefamulin against sexually transmitted bacterial pathogens. *Antimicrob Agents Chemother* 2018; **62:** e02380-17.

181 Read TRH, Jensen JS, Fairley CK, et al. Use of pristinamycin for macrolide-resistant *Mycoplasma genitalium* infection. *Emerg Infect Dis* 2018; **24:** 328–35.

182 Falk L, Jensen JS. Successful outcome of macrolide-resistant *Mycoplasma genitalium* urethritis after spectinomycin treatment: a case report. *J Antimicrob Chemother* 2017; **72:** 624–25.

183 Deguchi T, Ito S, Yasuda M, et al. Emergence of *Mycoplasma genitalium* with clinically significant fluoroquinolone resistance conferred by amino acid changes both in GyrA and ParC in Japan. *J Infect Chemother* 2017; **23:** 648–50.

184 Clarke EJ, Vodstrcil LA, Plummer EL, et al. Efficacy of minocycline for the treatment of *Mycoplasma genitalium*. *Open Forum Infect Dis* 2023; **10:** ofad427.

185 Doyle M, Vodstrcil LA, Plummer EL, Aguirre I, Fairley CK, Bradshaw CS. Nonquinolone options for the treatment of *Mycoplasma genitalium* in the era of increased resistance. *Open Forum Infect Dis* 2020; **7:** ofaa291.

186 Glaser AM, Geisler WM, Ratliff AE, Xiao L, Waites KB, Gaisa M. Two cases of multidrug-resistant genitourinary *Mycoplasma genitalium* infection successfully eradicated with minocycline. *Int J STD AIDS* 2019; **30:** 512–14.

187 Mondeja BA, Couri J, Rodríguez NM, Blanco O, Fernández C, Jensen JS. Macrolide-resistant *Mycoplasma genitalium* infections in Cuban patients: an underestimated health problem. *BMC Infect Dis* 2018; **18:** 601.

188 Durukan D, Doyle M, Murray G, et al. Doxycycline and sitafloxacin combination therapy for treating highly resistant *Mycoplasma genitalium*. *Emerg Infect Dis* 2020; **26:** 1870–74.

189 Vodstrcil LA, Plummer EL, Doyle M, et al. Combination therapy for *Mycoplasma genitalium*, and new insights into the utility of *parC* mutant detection to improve cure. *Clin Infect Dis* 2022; **75:** 813–23.

190 Kenyon C, Manoharan-Basil SS, Van Dijck C. Is there a resistance threshold for macrolide consumption? Positive evidence from an ecological analysis of resistance aata from *Streptococcus pneumoniae*, *Treponema pallidum*, and *Mycoplasma genitalium*. *Microb Drug Resist* 2021; **27:** 1079–86.

191 Barazzetti FH, Bazzo ML, Filho VB, et al. Antimicrobial resistance in *Mycoplasma genitalium:* preliminary results of the first Brazilian study. International Society for Sexually Transmitted Diseases 25th World Congress; Chicago, IL, USA; July 24–27, 2023.

192 Tsai MJ, Sun HY, Su LH, et al. *Mycoplasma genitalium* infection and resistance-associated mutations to macrolides and fluoroquinolones among high-risk patients in Taiwan. *J Microbiol Immunol Infect* 2024; **57:** 629–37.

193 Fortas C, Crucitti T, Harimanana A, et al. Sexually transmitted infections and bacterial vaginosis among women of child-bearing age in Antananarivo. Madagascar: prevalence and risk factors. International Society for Sexually Transmitted Diseases 25th World Congress; Chicago, IL, USA; July 24–27, 2023.

194 Biswal D, Gupta S, Sethi S, Singh S, Khanna N, Dhawan B. Macrolide and fluoroquinolone resistance associated mutations in *Mycoplasma genitalium* in men who have sex with men attending STI clinic: a pilot study from India. *Indian J Dermatol Venereol Leprol* 2024; **90:** 632–35.

195 Lam PPH, Nguyen NH, Nguyen TTT, Trinh NB, Luong BA. *Mycoplasma genitalium* prevalence, co-infection and macrolide resistance-associated mutations in Southern Vietnam. *Infez Med* 2024; **32:** 222–30.

196 Fernández-Huerta M, Serra-Pladevall J, Esperalba J, et al. Single-locus-sequence-based typing of the *mgpB* gene reveals transmission dynamics in *Mycoplasma genitalium*. *J Clin Microbiol* 2020; **58:** e01886-19.

197 Kenyon CR, Schwartz IS. Effects of sexual network connectivity and antimicrobial drug use on antimicrobial resistance in *Neisseria gonorrhoeae*. *Emerg Infect Dis* 2018; **24:** 1195–203.

198 Kenyon C, Manoharan-Basil SS, Van Dijck C. Gonococcal resistance can be viewed productively as part of a syndemic of antimicrobial resistance: an ecological analysis of 30 European countries. *Antimicrob Resist Infect Control* 2020; **9:** 97.

199 Machalek DATM, Vodstrcil LA, Asselin J, et al. *Mycoplasma genitalium*, testing, positivity and macrolide resistance patterns in Australia, sentinel surveillance data 2012–2022. Australasian Sexual and Reproductive Health Conference; Sydney, NSW, Australia; Sept 18–20, 2023.