Mind the gaps: Systematic review and meta-analysis to assess publicly available *Neisseria gonorrhoeae* isolates with whole-genome sequences linked to antimicrobial resistance data

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Background: Pathogen whole-genome sequencing (WGS) linked to antimicrobial resistance (AMR) data and patient metadata improves insights into mutations associated with resistance and transmission. *Neisseria gonorrhoeae* (NG), a WHO high-priority pathogen, is increasingly resistant to last-line treatments, underscoring the need for comprehensive genomic surveillance.

Methods: PubMed, EMBASE, WoS, and Scopus publications from January 2012 to March 2024 were searched systematically using search terms related to NG, WGS, and minimum inhibitory concentration (MIC). Studies describing clinical isolates with linked MIC results for at least one clinically relevant antibiotic (ceftriaxone, cefixime, ciprofloxacin, azithromycin, penicillin, gentamicin, and spectinomycin) were included. Unique isolates with downloadable WGS and linked MIC were analysed using EUCAST clinical breakpoints and WGS quality standards. Associated metadata (anatomical site, demographics, geographical location) was collated. AMR prevalence from individual patient data was estimated using a random-effect inverse method.

Results: Of 152 identified studies (38,543 genomes), only 22 provided publicly accessible, WGS-MIC data (9,640 unique isolates), with 9,404 isolates (97.5%) passing WGS quality control. Meta-analysis estimated low prevalence of resistance to extended-spectrum cephalosporins (ceftriaxone 0.8%, cefixime 7.7%), plus moderate and high prevalence of resistance to azithromycin (10.5%) and ciprofloxacin (49.5%) respectively. Metadata completeness varied among isolates: 51.1% had sexual orientation data (2,659 gay/bisexual; 2,266 heterosexual), 48.3% had gender (4,597 male; 52 female), 25.5% had collection site (2,138 urogenital, 216 anorectal, 69 oropharyngeal), and 11.8% had age (median 27 years). Geographic location was reported for 8,649 isolates (89.7%), with 7,278 from the USA or EU.

Conclusions: Although NG WGS-MIC data is increasing, critical gaps remain - especially for women who bear the highest disease burden, for oropharyngeal infections where resistance is prevalent, and for regions like Africa and the Western Pacific where resources for AMR are limited. Enhanced data capture and reporting are essential to improve genomic surveillance in the fight against NG AMR.

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