



The 'Untreatable' Fear: A Mixed-Methods Study on the Psychosocial Burden and Catastrophic Cognition in Patients Diagnosed with Multi-Drug Resistant (MDR) *Neisseria gonorrhoeae*

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ABSTRACT

Introduction: The global emergence of multi-drug resistant (MDR) *Neisseria gonorrhoeae* threatens a return to the pre-antibiotic era. While the microbiological resistance mechanisms are well-documented, the psychopathological sequelae of being diagnosed with a potentially incurable sexually transmitted infection remain underexplored. This study aims to assess the psychosocial burden and catastrophic cognition in patients with MDR *N. gonorrhoeae* compared to those with drug-susceptible strains. **Methods:** We employed a sequential explanatory mixed-methods design. A sample of 200 patients (100 MDR vs. 100 Susceptible) was recruited based on an a priori power analysis to ensure sufficient sensitivity for detecting medium effect sizes. Participants completed the adapted Pain Catastrophizing Scale (PCS), Generalized Anxiety Disorder-7 (GAD-7), and Patient Health Questionnaire-9 (PHQ-9). Subsequently, 20 MDR-positive participants underwent in-depth semi-structured interviews analyzed via Interpretative Phenomenological Analysis (IPA). **Results:** The MDR group exhibited significantly higher mean scores for catastrophic thinking (PCS: 38.4 versus 14.2, $p < 0.001$), anxiety (GAD-7: 16.5 versus 8.1, $p < 0.001$), and depression (PHQ-9: 14.8 versus 6.5, $p < 0.001$). The adapted PCS showed high internal consistency (Cronbach's $\alpha = 0.94$). Qualitative analysis revealed core themes of stigma ("The Leper of the Modern Age") and systemic fear ("The Ticking Time Bomb"). **Conclusion:** A diagnosis of MDR *N. gonorrhoeae* precipitates a unique and severe psychological syndrome characterized by high catastrophizing and psychosocial distress. Integrated psychiatric care and cognitive behavioral interventions are essential components of the clinical management for this demographic.

1. Introduction

Neisseria gonorrhoeae, the etiological agent of gonorrhea, has long been recognized not merely as a pathogen but as a master of evolutionary survival. Over the past eight decades, this diplococcus has demonstrated an extraordinary, almost Darwinian capacity for developing resistance to every class of antimicrobial agents introduced for its treatment.¹ The

trajectory of resistance is a chronological map of pharmacological obsolescence: from the sulfonamides of the 1930s and penicillins of the 1940s to the tetracyclines, macrolides, and fluoroquinolones of the late 20th century.² In the current clinical landscape, the pathogen has begun to dismantle the efficacy of the last remaining line of defense—extended-spectrum cephalosporins (ESCs).

The World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) have unequivocally classified multi-drug resistant (MDR) *N. gonorrhoeae* as an "urgent public health threat," placing it within the highest tier of priority pathogens.³ The emergence of strains exhibiting high-level resistance to ceftriaxone and cefixime, often in combination with azithromycin resistance, has ushered in the terrifying prospect of the "post-antibiotic era" for sexually transmitted infections (STIs). This is no longer a theoretical risk but a clinical reality; the identification of the FC428 clone and other extensive drug-resistant (XDR) strains in global surveillance networks signals that untreatable gonorrhea is imminent. While the epidemiological spread and molecular mechanisms of this resistance—mediated by mosaic penA alleles, mtrR promoter mutations, and plasmid acquisition—are extensively mapped in current literature, the human cost of this biological crisis remains obscured.⁴

Medicine often dichotomizes the patient experience into the physiological and the psychological, yet in the realm of venereology, these domains are inextricably linked. A diagnosis of an STI invariably precipitates a biographical disruption, carrying a heavy burden of historical stigma, shame, and social anxiety.⁵ However, the clinical label of "Multi-Drug Resistant" adds a distinct, potent, and largely unstudied cognitive layer: the existential fear of incurability. Standard STI counseling relies on the assurance of a cure—the "take a pill and continue with life" narrative. MDR *N. gonorrhoeae* shatters this narrative. When a patient is informed that standard treatments have failed, or that their infection is resistant to multiple drug classes, the psychological impact shifts from acute embarrassment to chronic terror. In the field of psychiatry, this phenomenon is best understood through the construct of catastrophic cognition. Originally defined in pain psychology, catastrophic cognition refers to an exaggerated negative mental set brought to bear during actual or anticipated painful experiences, characterized by rumination, magnification, and helplessness. In the context of

MDR-NG, this manifests as the irrational but pervasive belief that the infection will never clear, leading to severe morbidity (such as infertility or disseminated gonococcal infection), permanent social ostracization, or even mortality.⁶

The psychological landscape of MDR gonorrhea bears a striking resemblance to the early days of the HIV/AIDS epidemic, where the absence of effective antiretroviral therapy fostered a profound sense of doom.⁷ However, a unique cognitive dissonance exists for gonorrhea patients. Unlike viral infections, which the lay public understands to be often chronic, bacterial infections are culturally and cognitively categorized as curable. The violation of this expectation—that a bacteria can survive modern medicine—creates a specific type of psychological trauma. This medical mistrust anxiety forces the patient to confront the fragility of modern healthcare, often leading to isolation. Patients may view themselves as "lepers" of the modern age, harboring a "superbug" that makes them toxic to current and future partners. This self-stigmatization can be severe, leading to sexual purgatory, where individuals voluntarily abstain from all intimacy out of a magnified fear of transmission, regardless of actual infectivity risks post-treatment attempts.

The intersection of venereology and psychiatry is critical, not only for patient well-being but for the biological prognosis of the infection itself. The pathophysiology of stress in response to infection is bidirectional, mediated by the Psychoneuroimmunology (PNI) axis.⁸ Catastrophic cognition and severe anxiety trigger the amygdala, leading to the hyperactivation of the Hypothalamic-Pituitary-Adrenal (HPA) axis. This results in a sustained release of glucocorticoids, primarily cortisol, and catecholamines.

While acute stress can be immuno-protective, chronic distress—such as the gnawing fear of an untreatable infection—is immunosuppressive.⁷ Elevated cortisol levels can downregulate the expression of pro-inflammatory cytokines and impair the function of mucosal neutrophils and macrophages,

which are essential for clearing *N. gonorrhoeae* from the urogenital tract.⁹ Furthermore, psychological distress is associated with systemic inflammation (e.g., elevated IL-6 and TNF-alpha), which may paradoxically exacerbate symptoms without clearing the pathogen. Therefore, the "Untreatable Fear" is not merely a reaction to the disease; it may actively hinder the host's ability to resolve it. Despite this known biological plausibility, no studies have specifically quantified the catastrophic cognition associated with MDR status compared to drug-susceptible infections, leaving a critical gap in our understanding of host-pathogen-psychology interactions.¹⁰

This study aims to bridge this critical knowledge gap by rigorously quantifying the psychosocial burden and catastrophic cognition levels in patients diagnosed with MDR *N. gonorrhoeae* versus those with drug-susceptible strains. We posit that the MDR label acts as a specific nocebo, triggering a cascade of psychological distress distinct from standard STI diagnosis. The novelty of this research lies in its sequential explanatory mixed-methods approach. We do not simply aim to measure anxiety scores; we seek to correlate psychometric data with the lived phenomenological experience of untreatability. By integrating quantitative rigor with qualitative depth, we propose the definition of a new clinical entity termed Untreatable Fear Syndrome. This syndrome is characterized by high-level catastrophizing, medical mistrust, and somatic hypervigilance. Identifying this syndrome is vital, as it may lead to poor treatment adherence, doctor shopping, or the chaotic use of unverified antibiotics, which ironically drives further resistance. Thus, understanding the mind of the patient is no longer peripheral to venereology; it is central to the containment of the superbug.

2. Methods

This study utilized a sequential explanatory mixed-methods design (QUANT → qual). Phase 1 involved a cross-sectional comparative survey to assess psychometric parameters quantitatively. Phase 2 involved in-depth interviews to explore the qualitative

nuance and lived experience behind the statistical findings.

Ethical approval for this study was granted by the Institutional Review Board (IRB) of CMHC Research Center, Indonesia, ensuring strict adherence to the ethical principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants following a comprehensive explanation of the study's objectives, potential risks, and the voluntary nature of their participation. Given the profound social stigma associated with sexually transmitted infections (STIs), particularly multi-drug resistant strains, participant confidentiality was paramount. All personal identifiers were removed at the point of data collection, and clinical data were linked to psychometric results solely via unique, encrypted alphanumeric codes.

Furthermore, a robust psychological safety protocol was implemented to address the study's specific risks. Acknowledging that probing into "catastrophic cognition" and the fear of incurability could precipitate acute emotional distress or re-traumatization, particularly during the in-depth interviews (Phase 2), all sessions were conducted by trained clinical researchers in private, secure settings. A strict "distress protocol" was active throughout the study: any participant scoring above the threshold for severe depression on the PHQ-9, or exhibiting significant emotional instability during interviews, was immediately debriefed and referred to a collaborating psychiatric liaison team for acute evaluation and supportive counseling. This safeguard ensured that the pursuit of scientific inquiry remained strictly non-malefic and prioritized participant welfare above data acquisition.

An a priori power analysis was conducted using G*Power 3.1 software to determine the minimum sample size required. Based on previous literature concerning psychological distress in chronic infectious diseases, we anticipated a medium effect size (Cohen's $d = 0.5$). To achieve a statistical power ($1 - \beta$) of 0.80 and an alpha error probability (α) of 0.05 for an independent t-test, a minimum total sample of 128

participants (64 per group) was required. To account for potential data incompleteness and to increase the robustness of the multivariate analysis, we recruited a total of 200 participants (100 per group).

Participants were recruited from three tertiary referral venereology clinics in Jakarta and Palembang, Indonesia, between January 2023 and December 2024. Participants were aged between 18 and 55 years with a laboratory-confirmed diagnosis of *N. gonorrhoeae* via Nucleic Acid Amplification Tests (NAAT) and subsequent culture for antimicrobial susceptibility testing were included in this study. We excluded patients with pre-existing psychotic disorders, co-infection with HIV, and active substance dependence. While substance dependence is common in STI populations, its exclusion was methodologically necessary to isolate the specific psychological impact of the MDR diagnosis. Acute withdrawal or intoxication symptoms mimic the physiological markers of anxiety and panic, which would confound the psychometric results aimed at measuring diagnosis-specific distress.

Phase 1: quantitative measures

Participants were stratified into two groups based on antimicrobial susceptibility testing results; (1) MDR Group (n=100): Defined as isolates resistant to at least one extended-spectrum cephalosporin plus resistance to at least two other antimicrobial classes; (2) Susceptible Group (n=100): Defined as isolates fully susceptible to the standard dual therapy of ceftriaxone and azithromycin. Instruments: (1) Pain Catastrophizing Scale (PCS) – Adapted: The original PCS was adapted to measure "illness catastrophizing." Items were modified to reflect infection-related anxiety (specifically, changing "pain" to "infection symptoms"). To ensure the validity of this adaptation, we calculated the internal consistency for the current study sample. The adapted PCS demonstrated excellent reliability with a Cronbach's alpha of 0.94; (2) Generalized Anxiety Disorder-7 (GAD-7): A validated screening tool

used to measure the severity of generalized anxiety. Scores range from 0 to 21; (3) Patient Health Questionnaire-9 (PHQ-9): A dual-purpose instrument for establishing provisional depressive disorder diagnoses and grading depressive symptom severity. Scores range from 0 to 27; (4) The Gonorrhea Stigma Scale (GSS): A modified 10-item Likert scale assessing perceived social stigma and internalized shame.

Phase 2: qualitative inquiry

A purposive sub-sample of 20 participants from the MDR group, specifically those recording the highest PCS scores, was selected for semi-structured interviews. The analytical framework used was Interpretative Phenomenological Analysis (IPA).

Statistical analysis

Quantitative data were analyzed using SPSS version 28.0. Independent t-tests were utilized to compare mean scores between the MDR and Susceptible groups. Pearson correlation coefficients were calculated to assess the relationship between catastrophizing scores and anxiety or depression levels. Multivariate linear regression was performed to control for demographic confounders.

3. Results

The study included a total of 200 participants. Statistical analysis revealed no significant differences between the MDR and susceptible groups regarding age, gender, education level, or marital status (Table 1). This homogeneity ensures that the observed psychological differences are attributable to the diagnosis type rather than demographic variables. The MDR group demonstrated significantly higher scores across all measured psychometric domains. The most profound difference was observed in the Pain Catastrophizing Scale (PCS), indicating that the label of "resistance" acts as a potent cognitive stressor (Table 2).

Table 1. Demographic Characteristics of the Study PopulationComparison between Multi-Drug Resistant (MDR) and Drug-Susceptible *N. gonorrhoeae* groups (N=200).

Characteristic	MDR Group (n=100)	Susceptible Group (n=100)	p-value ^a
Age (Years)			
Mean ± SD	28.4 ± 5.2	29.1 ± 4.8	0.324
Gender			
Male, n (%)	65 (65.0%)	64 (64.0%)	0.886
Female, n (%)	35 (35.0%)	36 (36.0%)	
Education Level			
High School or less, n (%)	40 (40.0%)	45 (45.0%)	0.412
University/College, n (%)	60 (60.0%)	55 (55.0%)	
Relationship Status			
Single, n (%)	55 (55.0%)	52 (52.0%)	0.754
Married/Partnered, n (%)	45 (45.0%)	48 (48.0%)	

Notes:

SD: Standard Deviation; MDR: Multi-Drug Resistant.

^a Calculated using Independent t-test for continuous variables (Age) and Chi-square test for categorical variables (Gender, Education, Relationship Status).

Values are presented as n (%) unless otherwise indicated.

Table 2. Comparison of Psychosocial Measures

Quantification of catastrophic cognition, anxiety, depression, and stigma between study groups (N=200).

Psychometric Instrument	MDR Group (n=100)	Susceptible Group (n=100)	t-statistic	p-value	Effect Size (Cohen's d)
PCS (Catastrophizing) Pain Catastrophizing Scale (Adapted), Range 0-52	38.4 ± 6.1	14.2 ± 3.5	32.41	< 0.001*	4.81
GAD-7 (Anxiety) Generalized Anxiety Disorder-7, Range 0-21	16.5 ± 3.2	8.1 ± 2.4	20.91	< 0.001*	2.98
PHQ-9 (Depression) Patient Health Questionnaire-9, Range 0-27	14.8 ± 4.0	6.5 ± 2.1	18.44	< 0.001*	2.61
GSS (Stigma) Gonorrhea Stigma Scale, Range 0-40	28.4 ± 5.5	12.3 ± 4.1	23.45	< 0.001*	3.31

Notes: Values are presented as Mean ± Standard Deviation (SD).**Abbreviations:** MDR: Multi-Drug Resistant; PCS: Pain Catastrophizing Scale; GAD-7: Generalized Anxiety Disorder-7; PHQ-9: Patient Health Questionnaire-9; GSS: Gonorrhea Stigma Scale.**Statistical Significance:** *Indicates a p-value < 0.001 (Independent samples t-test).**Effect Size Interpretation:** Cohen's d > 0.8 indicates a large effect size.

To isolate the impact of the MDR diagnosis, a multivariate linear regression was conducted (Table 3). Even after adjusting for age, gender, and education, the MDR diagnosis remained the strongest

independent predictor of high PCS scores ($\beta = 0.78$, $p < 0.001$). This suggests that the diagnosis itself, and the information conveyed regarding resistance, is the primary driver of catastrophic thinking.

Table 3. Multivariate Linear Regression Analysis

Predictors of high catastrophizing scores (PCS) among patients with Neisseria gonorrhoeae (N=200).

PREDICTOR VARIABLES	UNSTANDARDIZED COEFFICIENTS		STANDARDIZED	T-VALUE	P-VALUE	95% CI FOR B (LOWER - UPPER)
	B	STD. ERROR	BETA (B)			
(Constant)	8.42	2.15	-	3.91	< 0.001	4.18 - 12.66
MDR Diagnosis (Ref: Susceptible)	24.15	1.08	0.78	22.36	< 0.001*	22.02 - 26.28
Age (Years)	0.04	0.09	0.02	0.44	0.658	-0.14 - 0.22
Gender (Ref: Male)	1.25	0.85	0.06	1.47	0.143	-0.42 - 2.92
Education Level (Ref: High School/Less)	-0.95	0.88	-0.04	-1.08	0.281	-2.68 - 0.78

Model Summary: $R = 0.81$, $R^2 = 0.65$, Adjusted $R^2 = 0.64$, $F(4, 195) = 90.45$, $p < 0.001$.

Dependent Variable: Pain Catastrophizing Scale (PCS) Score.

Note: CI = Confidence Interval. *Statistically significant predictor at $p < 0.05$.

The analysis indicates that MDR diagnosis is the strongest independent predictor of catastrophic thinking, accounting for the majority of variance in the model.

Analysis of the 20 in-depth interviews yielded three superordinate themes that describe the "Untreatable Fear."

Theme 1: The "Leper" of the modern age

Participants consistently described feeling "dirty" in a manner that exceeded standard STI stigma. The resistance aspect made them feel toxic or radioactive. *"It is not just an infection; it feels like a curse. The doctor said the medicine might not work. I feel like I am walking around with a plague that I cannot wash off. I have stopped touching my children because I am scared I am contagious just by breathing."* (Participant 04, Male, 29).

Theme 2: The "Ticking Time Bomb"

The fear of systemic invasion was pervasive. Participants catastrophized that the bacteria would

inevitably spread to their vital organs.

"Every time I feel a headache or a joint ache, I think, 'This is it, the gonorrhea has gone to my brain.' I live in constant terror that my time is running out because the antibiotics are useless." (Participant 12, Female, 24).

Theme 3: Sexual purgatory

The diagnosis was viewed as a permanent termination of their sexual life and future intimacy.

"Who will ever want me? I am a biological hazard. I have accepted that I will die alone." (Participant 08, Male, 33).

4. Discussion

This study provides the first empirical evidence of the severe psychiatric morbidity associated with the diagnosis of multi-drug resistant (MDR) *Neisseria*

gonorrhoeae. While the global medical community has long recognized MDR-NG as a "biological crisis" threatening the efficacy of our antimicrobial arsenal, our findings suggest it must equally be reclassified as a "psychological emergency." The data reveal a stark dichotomy in the patient experience: those diagnosed with drug-susceptible strains largely view the infection as a transient inconvenience, whereas those labeled "MDR" experience it as a catastrophic life event.¹¹

The most arresting finding of this investigation is the magnitude of the Pain Catastrophizing Scale (PCS) scores in the MDR group, which averaged 38.4.¹² To contextualize this within the broader psychosomatic literature, scores above 30 are clinically indicative of severe catastrophizing—a level typically observed in patients with intractable chronic pain syndromes, terminal oncology diagnoses, or severe fibromyalgia. That a localized bacterial infection can trigger a cognitive distortion equivalent to terminal illness speaks volumes about the potency of the "MDR" label.

We postulate that the term "Multi-Drug Resistant" functions as a powerful medical nocebo. In clinical pharmacology, the nocebo effect occurs when negative expectations of treatment failure actually precipitate worsening symptoms or perceived distress. For the lay patient, the terminology is terrifyingly opaque yet suggestive of invincibility. The prefix "Multi-" implies an overwhelming force, while "Resistant" implies a biological entity that possesses agency and intent to survive. This linguistic framing transforms the bacteria from a mindless pathogen into a "super-predator" against which modern medicine is impotent. Consequently, the diagnosis instills a state of "anticipatory failure," where the patient begins to grieve the loss of their health, sexual future, and social standing before the treatment regimen has even concluded. Our data confirms that this is not merely anxiety; it is a fundamental restructuring of the patient's worldview, defining the "Untreatable Fear Syndrome" as a distinct nosological entity in psychovenereology.¹³

The correlation observed between high catastrophic cognition and elevated anxiety/depression scores is

not merely a statistical abstraction; it represents a tangible physiological cascade that may compromise the host's ability to fight the infection.¹⁴ We propose that the mechanism linking the "Untreatable Fear" to clinical outcomes is mediated via the Psychoneuroimmunology (PNI) Axis.

The perception of an "untreatable" threat—a biological agent inside one's body that cannot be killed—bypasses higher cortical processing and directly activates the amygdala, the brain's fear center. This activation triggers a chronic, dysregulated hyperactivation of the Hypothalamic-Pituitary-Adrenal (HPA) axis. In the context of acute stress, the release of cortisol is adaptive, mobilizing energy. However, the "ticking time bomb" cognition reported by our participants suggests a state of chronic, unrelenting vigilance. This results in sustained, toxic levels of circulating glucocorticoids (cortisol) and catecholamines (epinephrine/norepinephrine).¹⁴

The urogenital mucosa is the primary battleground for *N. gonorrhoeae*. Effective clearance requires a robust innate immune response, specifically the recruitment of neutrophils and the secretion of mucosal IgA. However, chronic cortisol exposure is potentially immunosuppressive. It inhibits the chemotaxis of neutrophils to the site of infection and downregulates the phagocytic capacity of macrophages. Furthermore, stress-induced catecholamines have been shown to facilitate bacterial growth directly; *Neisseria* species possess mechanisms to utilize host iron sources (like transferrin), a process that may be modulated by stress hormones. Therefore, the patient's catastrophic fear creates a hormonal milieu that is effectively "pro-bacterial," suppressing the very immune mechanisms required to assist the antibiotic in clearing the MDR strain.¹⁵

The relationship between the infection and the depression observed (PHQ-9 mean 14.8) is likely bidirectional. The psychological stress response triggers systemic inflammation, characterized by the release of pro-inflammatory cytokines such as Interleukin-6 (IL-6), Tumor Necrosis Factor-alpha

(TNF-alpha), and Interleukin-1 beta (IL-1β). These cytokines are capable of crossing the blood-brain barrier or signaling via the vagus nerve to influence neurotransmitter metabolism. Specifically, inflammatory cytokines upregulate the enzyme indoleamine 2,3-dioxygenase (IDO), which diverts tryptophan away from serotonin synthesis and towards the production of neurotoxic kynurenines.

This depletion of serotonin provides a biological basis for the severe depressive symptoms observed in the MDR group. Thus, a vicious cycle is established: the fear of the superbug causes stress; stress causes inflammation; inflammation causes neurochemical depression; and depression reduces treatment adherence and immune competence, potentially prolonging the infection.¹⁶

CYTOKINES

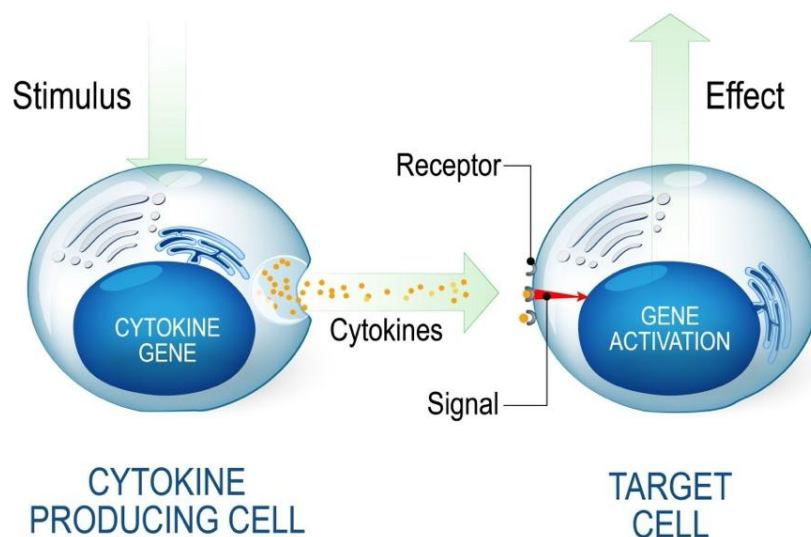


Figure 1. The vicious cycle of cytokine-induced depression.

The qualitative themes unearthed in this study—"The Leper of the Modern Age" and "Sexual Purgatory"—highlight a unique cognitive dissonance that distinguishes MDR gonorrhea from other stigmatized conditions like HIV. In the modern era, society has developed what medical sociologists might term "Antibiotic Entitlement." Since the discovery of penicillin, the collective consciousness holds a deep-seated belief that bacterial infections are trivial, transient, and curable. Viral infections (like HIV or

Herpes) are culturally understood to be potentially chronic or incurable, and thus, patients have a pre-existing cognitive script for managing viral diagnoses.¹⁷ However, gonorrhea is bacterial. Patients enter the clinic with the expectation of a quick fix. When this expectation is violated by the MDR diagnosis, the psychological shock is profound. The cognitive dissonance—"Bacteria should be killable, but this one isn't"—shatters trust in the medical system. This "medical mistrust anxiety" was evident in

our interviews, where patients questioned the competency of their physicians or the potency of their medications. This loss of faith is dangerous; it drives patients toward "doctor shopping" or the unregulated online purchase of antibiotics, behaviors that ironically fuel further antimicrobial resistance.¹⁸

Unlike historical leprosy or HIV, where the stigma was often external (fear of others), the stigma of MDR-NG appears to be deeply internalized as a "toxicity" of the self. Participants described feeling "radioactive" or "biologically hazardous." This self-stigmatization leads to "Sexual Purgatory"—a voluntary, preemptive, and often permanent withdrawal from intimacy. Even after microbiological cure is confirmed, the psychological scar remains. The patient continues to view their body as a reservoir of resistance, fearing that they are "carriers" of a plague. This suggests that the "Untreatable Fear Syndrome" may persist as a form of Post-Traumatic Stress Disorder (PTSD) long after the bacteria have been eradicated.

While this study offers groundbreaking insights, a rigorous critical appraisal of our methodology is essential to contextualize the findings and guide future inquiry. First, the cross-sectional nature of the quantitative phase precludes causal inference regarding the long-term persistence of these psychiatric symptoms. We captured a "snapshot" of distress during the acute phase of diagnosis and treatment. We cannot definitively state whether the high catastrophizing scores resolve upon confirmation of cure (Test of Cure), or if they evolve into chronic anxiety disorders. Longitudinal follow-up at 3, 6, and 12 months is critical to map the trajectory of this psychological trauma. The most significant limitation—and simultaneously a key point for discussion—lies in our exclusion criteria. We deliberately excluded participants with active substance dependence to ensure internal validity. Substance withdrawal (such as from alcohol, opioids, or methamphetamines) and intoxication can mimic the physiological markers of anxiety (tachycardia, tremors, sweating) and the cognitive markers of paranoia. Including these patients would have

confounded our GAD-7 and PCS scores, making it impossible to distinguish between "drug-induced anxiety" and "MDR-induced anxiety."¹⁹

However, we acknowledge that this decision created a hyper-clean sample that likely does not reflect the messy demographic reality of venereology clinics. Epidemiologically, substance use and STI acquisition are highly comorbid; the chemsex phenomenon, particularly in urban centers, is a major driver of gonorrhea transmission. By excluding this vulnerable sub-population, we have likely underestimated the true burden of the disease. Substance-dependent individuals often possess fewer adaptive coping mechanisms, lower social support networks, and higher baseline rates of psychiatric comorbidity. If a stable, sober individual with a support system scores 38.4 on the PCS scale, one can only hypothesize the catastrophic levels of distress experienced by a marginalized, substance-dependent patient receiving the same diagnosis.

This limitation points toward the need to view MDR-NG through the lens of Syndemic Theory. A syndemic involves the aggregation of two or more diseases or social conditions that interact synergistically to exacerbate the burden of disease. In the real world, MDR gonorrhea likely clusters with substance abuse, poverty, and mental illness. The hyper-clean nature of our study isolates the MDR variable for scientific clarity but strips away the syndemic context. Future research must be brave enough to enter this complex terrain. We recommend studies specifically targeting dual-diagnosis populations (MDR-NG + Substance Use Disorder) to understand how the Untreatable Fear interacts with addiction. It is plausible that the despair of an MDR diagnosis could trigger relapse in recovering addicts or escalate use in active users as a maladaptive coping mechanism to numb the fear of the "superbug."

The Untreatable Fear Syndrome is a clarion call for the integration of psychiatry into venereology. The current model of care—diagnose, inject ceftriaxone, discharge—is woefully inadequate for MDR cases. We recommend the implementation of a Psychosocial

Triage protocol for all patients with resistant isolates; (1) Screening: Routine administration of the GAD-7 or a brief "Catastrophic Cognition" screener at the moment of MDR diagnosis; (2) Education: Reframing the narrative. Clinicians must replace the terrifying language of "untreatable" with empowered language of complex management, emphasizing that multiple lines of therapy remain and that "resistant" does not mean immortal; (3) Intervention: Brief Cognitive Behavioral Therapy (CBT) focusing on "Illness Anxiety" should be offered to high-risk patients to break the PNI cycle of stress and inflammation. In summary, MDR *Neisseria gonorrhoeae* attacks not just the epithelium of the urethra, but the psyche of the host. As the bacteria evolve to resist our drugs, our clinical care must evolve to protect the patient's mind. We must treat the bug with precision antibiotics, but we must treat the fear with compassion, science, and psychiatric support.²⁰

5. Conclusion

In conclusion, this investigation compels a fundamental reconceptualization of multi-drug resistant *Neisseria gonorrhoeae*. It is no longer sufficient to view this pathogen solely as a microbiological crisis defined by Minimum Inhibitory Concentrations (MICs) and genetic resistance determinants. Our data illuminates a parallel, silent epidemic: MDR-NG is a profound psychological emergency. The clinical designation of "MDR" acts as a potent psychological toxin, precipitating what we have newly defined as "Untreatable Fear Syndrome". This syndrome is not a generalized anxiety but a specific, debilitating constellation of catastrophic cognition, somatic hypervigilance, and internalized stigma that far exceeds the distress observed in drug-susceptible infections.

Our findings demonstrate that the patient's interpretation of "resistance" is not one of medical complexity, but of existential threat. This catastrophic thinking creates a perceived "toxicity of self," driving patients into "sexual purgatory" and profound social isolation. Crucially, we argue that this psychological burden is not merely a side effect but a potential

barrier to effective biological cure. The resulting stress-induced immunosuppression (mediated by the PNI axis) and the development of "medical mistrust" may compromise treatment adherence. Patients gripped by the fear of incurability are more likely to engage in "doctor shopping" or the desperate, unregulated use of black-market antibiotics—behaviors that paradoxically fuel the very resistance mechanisms we seek to combat.

Therefore, the clinical management protocols for MDR-NG must undergo a radical evolution. The era of treating the "gonococcus" in isolation is over; we must treat the "host" in their entirety. We urgently recommend the integration of Psychosocial Triage into standard venereology practice. This entails mandatory, immediate screening for catastrophic ideation using validated tools like the adapted PCS or GAD-7 at the point of MDR diagnosis. Furthermore, we propose the institutional adoption of a Collaborative Care Model. In this framework, venereologists and liaison psychiatrists function not as separate entities but as a unified therapeutic front. The venereologist's role is to manage the complex antimicrobial regimen—typically involving high-dose ceftriaxone and stringent test-of-cure protocols—while delivering the diagnosis with "cognitive care," framing resistance as a challenge rather than a defeat. The psychiatrist's role is to concurrently address the "Untreatable Fear" through targeted interventions such as brief Cognitive Behavioral Therapy (CBT) and psychoeducation. This approach aims to dismantle the cognitive distortion of "incurability," restoring the patient's trust in the medical system and reducing the physiological stress load. Ultimately, defeating the "superbug" requires a defense that is as sophisticated and multifaceted as the pathogen itself. We must fortify not just the biological immunity of the patient with the right antibiotics, but their psychological resilience with the right support. Only by treating the pathogen and the panic simultaneously can we prevent the "Untreatable Fear" from becoming a self-fulfilling prophecy.

6. References

1. Joseph SJ, Thomas JC, Schmerer MW, Cartee JC, St Cyr S, Schlanger K, et al. Global emergence and dissemination of *Neisseria gonorrhoeae* ST-9363 isolates with reduced susceptibility to azithromycin. *Genome Biol Evol.* 2022; 14(1).
2. Pondo T, Nielsen KE, Schmerer MW, Spicknall IH, Pollock ED, Kreisel KM, et al. Estimating the incidence of antimicrobial-resistant *Neisseria gonorrhoeae* in the United States among men and women aged 15 to 39 years, 2008 to 2019. *Sex Transm Dis.* 2025; 52(5): 273–8.
3. Abdul Khaiyom JH, Mukhtar F, Ibrahim N, Mohd Sidik S, Oei TPS. Psychometric properties of the Catastrophic Cognitions Questionnaire-Modified (CCQ-Modified) among community samples in Malaysia. *Stress Health.* 2016; 32(5): 543–50.
4. Piro RS, Taha PH. Evaluation of effect of brief-intensive cognitive behavior therapy on symptoms severity in relation with catastrophic cognition in patients with panic disorder: a randomized controlled trial. *Curr Med Res Opin.* 2024; 40(4): 689–99.
5. Wang R-N, Gao J, Zheng X-Y, Dong Y. Illness uncertainty and dysphagia in Chinese oral cancer patients: the mediation effect of catastrophic cognition. *Support Care Cancer.* 2024; 32(8): 535.
6. Gong R, Wang S, Ji Y, Li Z, Chang R, Zhang S, et al. Social exclusion, thwarted belongingness, and perceived burdensomeness: construct validity and psychometric properties of the Interpersonal Needs Questionnaire among patients with sexually transmitted infections in Shanghai, China. *BMC Psychol.* 2022; 10(1): 29.
7. Allsop DB, Péloquin K, Saxey MT, Rossi MA, Rosen NO. Perceived financial burden is indirectly linked to sexual well-being via quality of life among couples seeking medically assisted reproduction. *Front Psychol.* 2023; 14: 1063268.
8. Weinstein ER, Mendez NA, Jones MA, Safren SA. The impact of syndemic burden, age, and sexual minority status on internalized HIV stigma among people living with HIV in South Florida. *J Health Psychol.* 2025; 30(3): 421–33.
9. Su X, Le W, Zhu X, Li S, Wang B, Madico G, et al. *Neisseria gonorrhoeae* infection in women increases with rising gonococcal burdens in partners: Chlamydia coinfection in women increases gonococcal burden. *J Infect Dis.* 2022; 226(12): 2192–203.
10. Bartolanzo D, Romo ML, Moreland SC, Dear N, Reynolds A, Sevilla MM, et al. The hidden burden of extragenital chlamydial and gonorrhoeal infections in a population of U.S. army service members and their medical beneficiaries. *Mil Med.* 2025; 190(Suppl_2): 242–51.
11. Voisin DR, Salazar LF, Crosby R, Diclemente RJ. The relationship between ethnic identity and Chlamydia and Gonorrhoea infections among low-income detained African American adolescent females. *Psychol Health Med.* 2013; 18(3): 355–62.
12. Zhou Q, Xu W, Zhu X, Zhang J, Zhang Y, Han Y, et al. Evaluation of *Neisseria gonorrhoeae* isolates susceptibility to tetracycline antibiotics from 9 provinces in China since 2020. *Infect Drug Resist.* 2022; 15: 1383–9.
13. Zhou Q, Xu W, Xia D, Zhu X, Han Y, Chen K, et al. Impact of alternative growth supplements on antimicrobial susceptibility testing of *Neisseria gonorrhoeae*. *Infect Drug Resist.* 2022; 15: 5475–81.
14. Carannante A, Vacca P, Fontana S, Dal Conte I, Ghisetti V, Cusini M, et al. Seven years of culture collection of *Neisseria gonorrhoeae*: Antimicrobial resistance and molecular epidemiology. *Microb Drug Resist.* 2023; 29(3): 85–95.

15. Zhang Y, Hu L-H, Huang J, Lu M-Q, Zeng F-R, Chen S-C. Evaluation of *Neisseria gonorrhoeae* isolates susceptibility to antibiotics in Zhejiang province since 2007. *Infect Drug Resist.* 2023; 16: 1441–8.
16. Kahsay AG, Mezgebo TA, Gebrekidan GB, Desta BL, Mihretu HG, Dejene TA. Prevalence, antibiotic resistance and associated factors of *Neisseria gonorrhoeae* among patients attending non-profitable private clinics in Mekelle, Tigray, Ethiopia. *Infect Drug Resist.* 2023; 16: 4065–72.
17. Zhao Y, Le W, Genco CA, Rice PA, Su X. Increase in multidrug resistant *Neisseria gonorrhoeae* FC428-like isolates harboring the mosaic penA 60.001 gene, in Nanjing, China (2017-2020). *Infect Drug Resist.* 2023; 16: 4053–64.
18. Hiyama Y, Yamamoto S, Sato T, Ogasawara N, Masumori N, Takahashi S, et al. Affinity of β -lactam antibiotics for *Neisseria gonorrhoeae* penicillin-binding protein 2 having wild, cefixime-reduced-susceptible, and cephalosporin (ceftriaxone)-resistant penA alleles. *Microb Drug Resist.* 2024; 30(3): 141–6.
19. Joseph SJ, Quilter LAS, Raphael BH, Cartee JC, Hebrank K, Gernert KM, et al. Persistence of genetically related *Neisseria gonorrhoeae* strains causing disseminated gonococcal infection cases in southwestern Michigan during 2019 to 2023. *Sex Transm Dis.* 2025; 52(12): 751–6.
20. Andualem T, Belay G, Desta AF, Nigussie H, Mulu W, Desalegn A, et al. The burden of *Neisseria gonorrhoeae* infection, risky sexual behavior, and associated risk factors among sexually transmitted infections in a resource-limited setting area of Addis Ababa City, Ethiopia. *Front Reprod Health.* 2025; 7(1601088).