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Re-Evaluating Therapeutic Strategies for *Helicobacter pylori*: Limitations of Current Approaches and Emerging Alternatives in High-Burden Kenyan Settings

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Abstract

Helicobacter pylori remains a major public health challenge in Kenya, where persistently high infection rates, socioeconomic vulnerabilities, and limited diagnostic capacity contribute to substantial gastrointestinal morbidity and an elevated risk of gastric cancer. This narrative review synthesizes fragmented evidence published over the past 16 years to provide an integrated overview of *H. pylori* epidemiology, diagnostic practices, treatment barriers, and emerging therapeutic innovations within the Kenyan context. A targeted search of major scientific databases and grey literature identified 12 relevant studies conducted across diverse Kenyan regions. Diagnostic approaches varied considerably, although stool antigen testing was most frequently employed. Across 11 studies reporting prevalence data (1526/3229 samples), a simple sample-size-weighted prevalence of 47.3% (95% CI: 45.6% - 49.0%) was observed, highlighting a substantial national burden. Reported risk factors included low socioeconomic status, limited hygiene awareness, reliance on untreated water sources, and household crowding. Management remains complicated by rising antimicrobial resistance, empirical treatment practices, and restricted access to culture and susceptibility testing. A range of emerging biologic and non-antibiotic modalities, such as bacteriophage therapy, engineered endolysins, and other innovative therapeutic platforms, is gaining attention. These modalities show

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promising *in vitro* activity, and subsequent sections focus on the specific scientific, translational, and regulatory considerations that shape their feasibility within Kenya's health-system constraints. By consolidating dispersed findings and situating them within Kenya's health-system realities, this review highlights critical gaps in surveillance, diagnostics, and therapeutic innovation, underscoring the need for strengthened research capacity and targeted evaluation of emerging therapies.

Keywords

Helicobacter pylori, Antibiotic Resistance, Gastric Cancer, Peptic Ulcer, Prophages

1. Introduction

Helicobacter pylori is one of the most common chronic bacterial infections worldwide and remains a major public health concern, particularly in low- and middle-income countries (LMICs) [1] [2]. The bacterium colonizes the gastric mucosa and is the primary etiological agent of chronic gastritis, peptic ulcer disease, mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric adenocarcinoma [3]. Owing to its strong causal association with gastric cancer, one of the leading causes of cancer-related mortality globally, *H. pylori* has been classified as a Group I carcinogen by the World Health Organization (WHO) [4] [5]. More than half of the global population is estimated to be infected, with LMICs, especially those in Sub-Saharan Africa (SSA), bearing a disproportionately high burden [6] [7]. Chronic *H. pylori* infection increases the risk of gastric cancer up to sixfold, contributing to the more than one million new gastric cancer cases and approximately 769,000 related deaths reported globally in 2020, over 70% of which occurred in developing countries [5].

Recent estimates show that the pooled prevalence of *H. pylori* in East Africa is approximately 50.98% (95% CI: 45.05 - 56.90), with country-level rates ranging from 7.7% to 94.5%. Sudan reports the highest prevalence (61.3%), while Uganda reports the lowest (40.7%) [7]. The prevalence of *H. pylori* has declined to 43.9% in adults but remains high at 35.1% among children and adolescents according to global reports [8]. In Kenya, infection remains highly endemic, driven by socioeconomic challenges, inadequate sanitation, unsafe water sources, and household crowding are profound [9].

Despite the significant disease burden, effective management of *H. pylori* infection remains challenging. Standard therapy, a combination of proton pump inhibitors and antibiotics such as clarithromycin and amoxicillin, has become increasingly unreliable due to rising antimicrobial resistance, poor treatment adherence, and the degradation of antibiotics in the acidic gastric environment [10] [11]. Limited diagnostic capacity and the difficulty of culturing the bacteria further com-

plicate treatment in many LMICs, including Kenya, often necessitating empirical therapy and hindering routine antimicrobial susceptibility testing [9] [12]. As a result, treatment failures are becoming more frequent, and 10% - 20% of patients are now classified as refractory after multiple unsuccessful eradication attempts [11]. These growing challenges highlight the urgent need for alternative or adjunctive therapeutic strategies [13].

To date, no comprehensive review of *H. pylori* epidemiology, diagnostics, antimicrobial resistance, and emerging therapies has been published from Kenya. Existing literature consists mainly of primary studies, narrow clinical overviews, and Africa-wide analyses that do not address the country's patterns. This narrative review therefore fills a critical gap by synthesizing dispersed evidence and contextualizing it within Kenya's health-system realities. It focuses on prevalence estimates derived from symptomatic, healthcare-seeking populations, drawing primarily from cross-sectional studies conducted in hospital and clinic settings. These data provide detailed insight into infection patterns among individuals presenting for clinical care, and the pooled prevalence is interpreted within this clearly defined, facility-based scope. This includes burden, challenges associated with its detection, treatment regimens and potential emerging technologies in management as alternatives or complementary therapeutic strategies for improving eradication outcomes.

2. Genetic Traits, Pathogenicity and Virulence of *H. pylori*

H. pylori possesses a streamlined but highly effective set of virulence determinants that enable lifelong colonization of the gastric mucosa and drive the progression from gastritis to ulceration and gastric cancer. Its survival in the acidic stomach is primarily mediated by urease-driven neutralization of gastric acid, coupled with flagella-based motility that allows the bacterium to penetrate the mucus layer and reach the epithelial surface. Stable colonization is maintained through a series of adhesins, including *BabA*, *SabA*, *HopQ*, and *OipA*, which anchor the organism to gastric epithelial cells and facilitate intimate host-pathogen interactions [14].

Disease severity is strongly influenced by two major toxins. Strains carrying the cag pathogenicity island (cagPAI) inject the CagA oncoprotein into host cells via a type IV secretion system, triggering pro-inflammatory signaling and cellular changes associated with carcinogenesis. In parallel, the secreted cytotoxin *VacA* induces epithelial injury and modulates immune responses, enabling persistent infection. Additional immune-evasion strategies, such as modification of lipopolysaccharide to mimic host antigens, further support chronic colonization [15].

Beyond these classical factors, *H. pylori* exhibits substantial genomic plasticity driven by recombination, horizontal gene transfer, and prophage elements. This genetic diversity underlies strain-specific differences in virulence and contributes to the pathogen's adaptability within the gastric niche. The organism also forms biofilms and can transition into coccoid, non-culturable forms, both of which enhance survival under stress and contribute to treatment failure [16]. These virulence

features allow *H. pylori* to persist for decades within the human stomach and create the chronic inflammatory environment that underlies its role in peptic ulcer disease and gastric cancer. These virulence determinants vary widely across global *H. pylori* populations, making geographical context essential for understanding disease patterns.

3. Geographical Variation

Globally, *H. pylori* exhibits substantial geographical variation in virulence, driven by differences in strain populations, host genetics, and environmental pressures. The most widely studied virulence determinants, CagA, *VacA*, and key adhesins such as *BabA* and *SabA*, show marked regional heterogeneity that correlates with disease risk [17]. East Asian strains, for example, predominantly carry the more oncogenic East Asian-type CagA, which is associated with higher gastric cancer incidence, whereas Western populations harbor a mix of CagA-positive and CagA-negative strains with more variable pathogenic potential. Similarly, the *VacA s1*/*m1* genotype, linked to severe gastric pathology, is more common in high-risk regions such as East Asia and parts of South America [18].

In Sub-Saharan Africa (SSA), the picture is more complex. Despite high *H. pylori* prevalence, the region paradoxically experiences lower gastric cancer rates, a phenomenon often referred to as the "African enigma" [19]. Several hypotheses have been proposed, including the predominance of less virulent *VacA* genotypes, differences in CagA phosphorylation motifs, early-life microbial exposures that modulate immune responses, and host genetic factors that may attenuate inflammation. African strains also show high genomic diversity and frequent recombination, which may dilute the dominance of highly virulent lineages seen elsewhere. However, systematic characterization of virulence profiles in SSA remains limited, and the true distribution of high-risk genotypes is still poorly defined [20].

In Kenya, available data suggest a pattern consistent with broader SSA trends: high infection prevalence but relatively low gastric cancer incidence compared to East Asian or Andean populations. Studies indicate that Kenyan isolates include both CagA-positive and CagA-negative strains, with variable *VacA* allelic combinations [4]. The limited genomic studies conducted so far point to substantial strain heterogeneity, shaped by recombination and mobile genetic elements, including prophages. This diversity may contribute to the wide clinical spectrum observed in Kenyan patients, ranging from asymptomatic infection to peptic ulcer disease. However, comprehensive virulence profiling in the country remains sparse, and the distribution of high-risk CagA and *VacA* variants is not yet fully mapped [9].

To our knowledge, only one study in Kenya has done whole-genome sequencing *H. pylori* isolate KE21, described as a typical African strain isolated from a gastric biopsy from a native female Kenyan patient diagnosed with gastric cancer [21]. In addition, other African studies show that local strains cluster predomi-

nantly within the hpAfrica1 lineage, a phylogeographic population distinct from European, Asian, and the East African hpAfrica2 strains [15] [21]. KE21, for example, carries a 1.65 Mb genome encoding approximately 1590 predicted genes, comprising both a conserved core genome and an accessory gene pool that may support regional adaptation. Kenyan isolates consistently harbor classical virulence determinants, including an intact cag pathogenicity island with Western-type CagA EPIYA-ABC motifs and a mixture of *VacA* genotypes, most commonly the virulent s1m1 allele alongside the less pathogenic s2m2 variant. Surveillance studies indicate year-to-year variation in circulating strains, reflecting ongoing genomic diversification within the population. Despite the presence of high-risk virulence factors such as cagPAI and *VacA s1m1*, Kenya continues to report comparatively low gastric cancer incidence, suggesting a complex interplay between bacterial diversity, host factors, and environmental influences [4]. Although global patterns are well described, Kenya lacks comprehensive virulence profiling, limiting the ability to predict disease severity or guide tailored therapies.

Overall, while global patterns clearly link specific virulence genotypes to disease severity, the situation in SSA, and Kenya in particular, remains insufficiently characterized, highlighting the need for more detailed molecular epidemiology. Clarifying how local strain diversity interacts with host and environmental factors will be essential for predicting disease risk and guiding future therapeutic strategies, including phage-based interventions. Yet even with these virulence differences, treatment outcomes in Kenya are increasingly shaped not by strain type but by rising antimicrobial resistance.

4. Antimicrobial Resistance Patterns of *H. pylori*

Data on *H. pylori* antimicrobial resistance (AMR) in Kenya remain limited, with most evidence derived from earlier studies reporting low resistance to clarithromycin (0% - 6.4%), tetracycline (0% - 2%), and amoxicillin (0% - 4.6%), alongside highly variable metronidazole resistance ranging from 4.6% to 100% [22] [23]. Recent community-based data similarly indicate low resistance to metronidazole (3.5%) and amoxicillin (1%), although overall AMR across all tested isolates, including co-pathogens, is reported to be at 64.2% [24]. Evidence from neighboring African regions points to emerging high-level amoxicillin resistance, as demonstrated in clinical isolates from the Democratic Republic of the Congo [25]. African meta-analyses incorporating Kenyan data report substantially higher pooled resistance estimates: clarithromycin 27% - 29.2%, metronidazole 75.8% - 91%, amoxicillin 38% - 72.6%, tetracycline 48.7%, and quinolones 17.4% [26]-[28]. Globally, *H. pylori* resistance has become a major public health concern, with rising resistance across all key antibiotic classes; clarithromycin and quinolones show the most alarming increases, mirroring emerging trends across Africa [29]. These patterns point to a continent-wide escalation in *H. pylori* AMR, suggesting that Kenya may be experiencing similar upward shifts despite historically lower resistance levels [28].

5. Drivers of Antimicrobial Resistance and Diagnostic Challenges in *H. pylori* in Kenya

Antimicrobial resistance in *H. pylori* is strongly influenced by treatment-related and health-system factors that determine how the organism encounters antibiotics. Without local AMR data, clinicians rely on standard regimens that may not match circulating resistance patterns, inadvertently selecting for resistant strains. Evidence from high-resistance settings shows that susceptibility-guided therapy achieves higher eradication rates than empirical treatment [30]. Resistance selection is further amplified by widespread antibiotic use for dyspepsia or "heartburn" without confirming *H. pylori* infection, exposing the bacterium to unnecessary or sub-therapeutic drug levels [31]. Prior antibiotic exposure for unrelated infections also contributes to the emergence of resistant subpopulations [32]. Poor adherence to multidrug eradication regimens facilitates bacterial persistence and adaptation, as incomplete therapy allows partially suppressed organisms to acquire resistance mutations [31] [33]. Limited diagnostic capacity and the absence of routine culture- or PCR-based resistance testing reinforce reliance on empirical prescribing, perpetuating a cycle that accelerates resistance development [34].

In Kenya, empirical therapy remains common because routine antimicrobial susceptibility testing is rarely available [35]. Diagnostic capacity for *H. pylori* remains critically inadequate, with heavy reliance on non-invasive tests whose performance is inconsistent. The stool antigen test, despite being the most widely used [24] [36]-[39], shows reduced accuracy after recent antibiotic or PPI exposure [40], while continued use of serology inflates prevalence estimates by failing to distinguish active from past infection [41]. Gold-standard invasive diagnostics are largely inaccessible outside major urban centres [37], and culture remains technically demanding with low yields even in optimized laboratories [42], effectively preventing routine susceptibility testing and crippling AMR surveillance. Limited availability of urea breath testing and molecular assays [43], combined with LMIC-specific challenges such as poor cold-chain maintenance and inconsistent reagent quality, further erodes diagnostic reliability. As a result, treatment failures often go undetected, empirical therapy persists, and national surveillance systems continue to underestimate both infection burden and resistance trends [41] [44].

6. Current Treatment and Management Therapies for *H. pylo*ri and Its Limitations

The standard first-line treatment for *H. pylori* infection remains 14-day triple therapy with a proton pump inhibitor (PPI), amoxicillin, and clarithromycin [45]. Bismuth-containing quadruple therapy (BQT) offers a comparable alternative [46]. However, rising global and regional antimicrobial resistance, including single-drug, multidrug, and heterogeneous resistance, has substantially reduced eradication success [47] [48]. In Kenya and much of SSA, eradication rates remain suboptimal, with intention-to-treat (ITT) outcomes of 48% - 68% and pooled Af-

rican averages falling below 80% in high-resistance settings [28] [43] [49]. Clarithromycin-based triple therapy now achieves <80% ITT globally and is no longer recommended where clarithromycin resistance exceeds 15% [50]-[52]. SSA data show clarithromycin resistance averaging ~27% and metronidazole resistance frequently surpassing 75% - 90%. Even optimized BQT regimens, high-dose PPI, ≥1200 mg bismuth, ≥1500 mg metronidazole, and tetracycline for 14 days, often demonstrate reduced real-world effectiveness due to resistance and adherence challenges [43].

Multiple microbial and host factors contribute to treatment failure. Amoxicillin's acid-labile nature necessitates high dosing [47], while *H. pylori* biofilms and coccoid forms hinder antibiotic penetration and immune recognition [48]. Clarithromycin resistance, often driven by 23S rRNA mutations such as A2143G/A2142G, markedly increases failure risk, particularly in multidrug-resistant strains [53]. In Kenya, unregulated antibiotic use, high pill burden, adverse effects (e.g., nausea, diarrhea, black tongue with BQT), and socioeconomic barriers further compromise prescription adherence [43] [54] [55]. Additional contributors include inadequate acid suppression in rapid PPI metabolizers [56] and host factors such as comorbidities and smoking [57]. Refractory infection, persistence after two or more eradication attempts, affects 10% - 20% of patients globally and is likely higher in SSA, where structural inequities, poor sanitation, and overcrowding exacerbate reinfection and treatment failure [31] [43] [58]. These current therapeutic and management strategies and their limitations have been summarized in Table 1.

Table 1. Summary of therapeutic options for *H. pylori* and their applicability in high-burden settings such as Kenya.

Therapeutic strategy	Mechanism of action	Evidence base	Key limitations	Relevance to high burden settings (e.g., Kenya)
Standard Triple Therapy (PPI + clarithromycin + amoxicillin)	Acid suppression + inhibition of protein synthesis + cell wall disruption	Longstanding first-line regimen; declining global efficacy	High clarithromycin resistance; poor adherence; antibiotic degradation in acidic stomach	Widely used but increasingly ineffective due to rising AMR; limited diagnostic stewardship
Bismuth-containing Quadruple Therapy (BQT)	Multi-target antimicrobial + mucosal protection	Effective in some regions; alternative first line	Complex regimen; adherence challenges; limited availability of bismuth in some LMICs	Potentially useful but constrained by cost, availability, and adherence issues
Levofloxacin-based Regimens	DNA gyrase inhibition	Effective in areas with low fluoroquinolone resistance	Rapid emergence of resistance; safety concerns	Limited utility due to rising fluoroquinolone resistance in SSA
Probiotics (e.g., *Lactobacillus* spp.)	Modulation of gastric microbiota; inhibition of *H. pylori* adhesion	Adjunctive benefits; reduces side effects	Strain-specific effects; inconsistent eradication	Affordable and accessible but insufficient as monotherapy
Antimicrobial Peptides (AMPs)	Membrane disruption; bactericidal activity	Promising *in vitro* and animal studies	Stability issues; potential toxicity; high production cost	Early stage; requires formulation advances for LMIC use

Continued

Photodynamic Therapy (PDT)	ROS generation via endogenous porphyrins	Effective *in vitro* and small clinical studies	Requires specialized equipment; variable efficacy	Limited feasibility in low-resource settings
Nanoparticle-based Delivery Systems	Enhanced gastric retention; targeted drug release	Strong experimental evidence	High cost; limited clinical translation	Not yet feasible for routine use in Kenya
Medicinal Herbs (e.g., *Paeonia lactiflora*, oregano-cranberry extracts)	Urease inhibition; anti-inflammatory effects	Traditional use; some *in vitro* efficacy	Variable potency; safety concerns; lack of standardization	Locally acceptable but insufficient evidence for clinical adoption
Bacteriophage Therapy	Strain-specific bacterial lysis; self-amplifying	Strong efficacy in other pathogens; early *H. pylori* data	Few known lytic phages; high recombination; delivery challenges	High potential but requires local phage discovery and gastric-stable formulations
Vaccines	Induction of protective immunity	30+ years of research; several candidates tested	No licensed vaccine; antigen/adjuvant challenges	High potential impact but long-term development horizon

7. Emerging Technologies in Treatment of *H. pylori*

Given the limitations of current therapies, emerging biologic and non-antibiotic strategies are gaining attention as potential adjuncts or alternatives. These include bacteriophage (phage) therapy, *Bdellovibrio bacteriovorus*, endolysins, tailocins, probiotics, antimicrobial peptides (AMPs), micro and nanoparticles, and medicinal plants among others.

8. Bacteriophage Therapy

Bacteriophage therapy has emerged as a promising alternative to antibiotics due to its high specificity, low production cost, and ability to circumvent antimicrobial resistance [59]-[62]. However, phage-based strategies for *H. pylori* remain in their infancy, with very few lytic phages identified as of 2020 [60] (**Table 2**). Major scientific gaps persist, including the absence of complete phage genome sequences—essential for detecting lysogeny modules, toxin genes, antimicrobial resistance determinants, and recombination enzymes that underpin therapeutic safety [60]. These challenges are compounded by the exceptional genomic plasticity of *H. pylori*, partly driven by prophages that may confer adaptive advantages but remain poorly characterized [60] [63]. High strain variability limits broad-spectrum phage infectivity [64], while the acidic gastric environment poses substantial barriers to phage stability and delivery. Extensive recombination among phage core genes further highlights complex co-evolutionary dynamics that must be understood before therapeutic deployment [16] [60]. Additionally, *H. pylori*'s acid tolerance, patchy mucosal colonization, microaerophily, and culture difficulty necessitate coordinated clinical-laboratory workflows that are difficult to sustain in low-resource settings [65] [66].

Table 2. Identified phages for *H. pylori*.

Phage(s)	Phage type	Objective	Country/ region	Sample source	Conclusion	Reference
HPy1R	Lytic	Genomic and phenotypic characterization of a new *H. pylori* phage	Portugal	Clinical isolates	HPy1R remained stable at 37˚C and pH 3 - 11 for 24 hours.	[68]
KHP30, KHP40	Lytic	Report complete genome sequences Determine capsid structure via cryo EM	Japan	Clinical isolates	• Complete genomes of KHP30 and KHP40 were obtained. • KHP30 is acid-stable and replicates efficiently in its host. • Capsid mutations may enhance immune evasion and gastric persistence.	[69]-[71]
Unnamed faecal phage	Lytic	Develop a screening procedure for *H. pylori* phages and characterisation	Portugal	Human faeces	Screening procedure successfully isolated a lytic phage and sequencing.	[63] [67]
HPE1, HPE2	Lytic	Isolate and characterize bacteriophages from wastewater	Egypt	Wastewater	Four *H. pylori* strains showed susceptibility to these phages.	[72]
Unnamed lytic phage	Lytic	Investigate a non-toxic therapy inhibiting colonization	Italy	Gastric biopsies	Lactoferrin HA nanoparticles enhanced phage activity fourfold by protecting it from acidity.	[73]
Prophage	Prophage	Identify prophage via *H. pylori* genome sequencing	France	Gastric biopsy	Discovery of a 24.6 kb prophage integrated into the bacterial chromosome.	[79]
PhiHp33	Prophages	Assess prophage impact on diversity & virulence	Chile	*H. pylori* genomes	Prophages significantly influence *H. pylori*, genetic diversity and fitness.	[60]
1961P	Prophage	Genomic characterization	Taiwan region	Gastric biopsy	Prophage discovery.	[80]
HP1	Temperate	Characterize *H. pylori* phage HP1	Germany	Clinical isolates	First report documenting a phage infecting *H. pylori*.	[74]

9. Characterized *H. pylori* Phages

Several *H. pylori* bacteriophages have been identified across diverse regions (Table 2). Lytic phages have been isolated in Portugal [67] [68], Japan [69]-[71], Egypt [72], and Italy [73]. These phages exhibit features such as acid stability, structural adaptations to the gastric niche, and strain-specific lytic activity. In contrast, temperate and prophage elements have been reported in Germany [74] and Chile [60], where integrated phage genomes contribute to *H. pylori* diversity and virulence. Collectively, the most promising candidates for therapeutic development remain the lytic phages φHPE1 and φHPE2, HPy1R, and KHP30/KHP40, highlighting the need for further therapeutic exploration.

10. Regulatory and Translational Barriers for *H. pylori* Phages

To overcome gastric instability or the harsh conditions of the upper gastrointes-

tinal tract (UGI), hydrogels and encapsulation systems have been proposed as protective delivery platforms, though rigorous genomic characterization and clear regulatory frameworks remain essential [66]. No *H. pylori*-specific phage products have been approved for clinical use; phage therapy remains restricted to compassionate use in Western countries [75], and regulatory uncertainty persists in SSA. Although the European Medicines Agency classified phages as medicinal products in 2011 and the European Pharmacopoeia introduced a dedicated category in 2021 [76], existing commercial phage products such as Bafasal™ and Listex™ P100 remain limited to food safety and veterinary applications [77] [78].

11. Potential Role of Endolysins for *H. pylori*

Unlike many other bacteria, such as *Staphylococcus*, *Streptococcus*, and *Pseudomonas*, *H. pylori* has very few known lytic phages and none of their endolysins have been purified or evaluated independently. Its Gram-negative outer membrane, together with the highly acidic gastric environment, further restricts the activity of natural lysins compared with whole-phage therapy [81]. Despite these constraints, several studies have demonstrated that heterologous lysins from other Gram-negative bacteria, including PlyF307-like enzymes, can kill *H. pylori in vitro* when paired with membrane-permeabilizing agents [82]. Although no native *H. pylori* phage endolysin has been characterized, several engineered lysins have demonstrated *in vitro* activity against *H. pylori*, particularly when fused to membrane-disrupting peptides or delivered via nanoparticle systems [83]. Building on this concept, engineered or fusion lysins have been developed to overcome the outer-membrane barrier and enhance stability under harsh conditions. Foundational work on Artilysins® has shown that fusing lysins to cationic or antimicrobial peptides enables efficient outer-membrane penetration and potent bactericidal activity [84] [85]. Additional engineering strategies have produced lysins capable of killing Gram-negative pathogens without chemical permeabilizers [86] and with improved stability for mucosal delivery [87]-[89]. Genomic analyses also reveal that *H. pylori* prophages encode putative lysis modules, offering additional targets for future enzyme engineering [60] [81]. Collectively, these findings position engineered lysins as a promising and underexplored therapeutic strategy for *H. pylori*, especially when paired with delivery systems that enhance acid stability and mucosal penetration.

12. The Potential of *Bdellovibrio bacteriovorus* in Eliminating *H. pylori*

Bdellovibrio bacteriovorus is a highly motile, Gram-negative bacterial predator that has attracted growing interest as a biological alternative to conventional antimicrobials [90] [91]. Unlike bacteriophages, which rely on highly specific receptor interactions, *B. bacteriovorus* is itself a living bacterium that actively seeks out and invades a broad range of Gram-negative prey. Its biphasic life cycle begins with a free-swimming attack phase, during which it locates susceptible bacteria, attaches

to the outer membrane, and penetrates the periplasm. Once inside, it establishes a protected niche where it degrades host cellular components, replicates, and ultimately lyses the prey cell to release progeny. This physical mode of predation enables *B. bacteriovorus* to target diverse Gram-negative pathogens and to penetrate biofilms more effectively than many phages, whose activity can be constrained by narrow host ranges or limited access to embedded cells. Notably, recent work shows that *B. bacteriovorus* can also kill prey without periplasmic invasion: strains lacking the MIDAS adhesive molecule deliver predatory proteins externally in a "kiss-of-death" mechanism, expanding its known killing strategies beyond classical invasion-dependent lysis [92].

While phages depend on precise molecular recognition and are therefore exquisitely specific, *B. bacteriovorus* offers a comparatively broad predatory spectrum and a low propensity for resistance development. These contrasting strategies highlight the complementary potential of bacterial predators and phages as innovative antimicrobial tools, each with distinct advantages and translational challenges [93]. Supporting its therapeutic relevance, *B. bacteriovorus* exhibits antimicrobial activity against several gastrointestinal pathogens in liquid culture, including *Campylobacter jejuni*, *Helicobacter pylori* [94], *Salmonella typhimurium*, and *E. coli* O157:H7 [93]. The distinct differences between Bdellovibrio and phages have been highlighted in **Table 3**.

Table 3. Comparison of *Bdellovibrio bacteriovorus* and bacteriophages.

Feature	*Bdellovibrio bacteriovorus*	Bacteriophages
Biological nature	Predatory Gram-negative bacterium	Virus that infects bacteria
Target range	Broad range of Gram-negative bacteria	Typically narrow; strain- or species-specific
Mode of action	Physical invasion of prey periplasm →* digestion → replication → lysis	Adsorption → genome injection → replication → lysis
Life cycle	Biphasic: attack phase + intraperiplasmic growth phase	Lytic or lysogenic cycles
Host dependency	Requires live Gram-negative prey for replication	Requires specific bacterial receptors
Resistance development	Rare and often transient	Common; receptor mutations, CRISPR, restriction systems
Biofilm activity	Strong penetration and disruption	Variable; some phages limited by matrix or receptor access
Safety in humans	Non-pathogenic; does not infect human cells	Safe; do not infect human cells
Therapeutic challenges	Survival in host tissues, immune clearance, delivery	Narrow host range, regulatory complexity
Use cases	Environmental biocontrol, experimental therapeutics	Clinical phage therapy, food safety, diagnostics

Key: *→: Process flow.

Despite its broad predatory activity against Gram-negative bacteria, the therapeutic application of *B. bacteriovorus* faces several challenges that distinguish it

from phages. Because it relies on direct physical contact with prey, it must withstand host-associated barriers such as immune clearance, fluctuating oxygen levels, and viscous or compartmentalized tissues, all of which can restrict predation [95]. Its replication also depends on adequate prey density and successful periplasmic invasion, making its activity less predictable than phages, which can amplify rapidly at infection sites and diffuse more readily through tissues [90] [95]. Regulatory development is similarly complex, as *B. bacteriovorus* is a live bacterial agent with potential ecological and microbiome impacts, whereas phages benefit from more established production pipelines and clearer regulatory pathways [95]. These constraints highlight the practical and translational hurdles that must be addressed before *B. bacteriovorus* can be deployed alongside or in place of phage therapy.

13. Potential Role of Tailocins in Eliminating *H. pylori*

Although tailocins, phage-derived, protein-based bacteriocins have emerged as potent precision antimicrobials against several Gram-negative pathogens, their application to *H. pylori* remains almost entirely unexplored. In principle, their ability to bind specific outer-membrane receptors and induce lethal membrane disruption offers an attractive alternative to broad-spectrum antibiotics, with the potential for strain-specific killing that minimizes disruption of the gastric microbiota [96]. Mechanistically, tailocins in other bacteria recognize conserved surface structures, deploy a contractile sheath, and puncture the cell envelope to trigger rapid depolarization and cell death [97]; engineered variants could theoretically be adapted to target *H. pylori* if suitable receptors, such as conserved porins or adhesins like *BabA* or *SabA*, were identified. However, *H. pylori*'s unique cell envelope architecture, reduced LPS, extensive phase variation, and microaerophilic physiology raise fundamental uncertainties about receptor accessibility and killing efficiency. These biological constraints are compounded by practical barriers: the organism's fastidious growth complicates the identification of endogenous tailocin producers and limits high-throughput screening, while the gastric niche, characterized by acidity, mucus viscosity, and proteolytic activity, poses major challenges for protein stability and delivery [98]. Achieving meaningful *in vivo* activity would likely require encapsulation strategies, pH-responsive coatings, or mucolytic co-delivery, alongside solutions for manufacturing consistency and immunogenicity [96]. Consequently, although tailocins represent a theoretically compelling precision-antimicrobial strategy, their feasibility for *H. pylori* remains highly speculative, highlighting a substantial and largely unaddressed research gap.

14. Other Emerging Technologies

Probiotics, particularly *Lactobacillus* spp., demonstrate immunomodulatory and anti-pathogen effects and may reduce *H. pylori* colonization, but optimal dosing, treatment duration, and interactions with antibiotics remain poorly defined, limiting their integration into standardized regimens [51] [52] [99].

Antimicrobial peptides such as cathelicidin-like peptides, bicarinalin, fusion human neutrophil peptide-1, and epinecidin-1 show potent activity against drug-resistant strains through membrane disruption, yet issues of stability, production cost, and potential immunogenicity continue to impede clinical translation [100].

Photodynamic therapy (PDT), which exploits endogenous porphyrins to generate reactive oxygen species without exogenous photosensitizers [101]-[103], remains limited by its dependence on specialized equipment and procedural expertise, restricting scalability in routine care [104] [105].

Micro- and nanoparticles offer targeted antimicrobial delivery due to their high surface-to-volume ratio [106], with chitosan-based systems providing mucoadhesion, biocompatibility, and intrinsic antimicrobial activity [102] [107]. However, challenges in manufacturing reproducibility, scale-up, and regulatory approval continue to hinder their advancement [108].

Despite decades of effort, vaccine candidates, including whole-cell, flagellar, antigen-based, and urease-based formulations, have failed to achieve commercial approval due to incomplete protection and variable host responses [109] [110]. Similarly, medicinal herbs such as *Paeonia lactiflora*, *Calophyllum brasiliense*, and oregano-cranberry extracts exhibit anti-*H. pylori* and anti-urease activity [111] [112], yet inconsistent potency, cytotoxicity concerns, and the absence of rigorous clinical trials undermine their therapeutic reliability.

15. Animal Models for *H. pylori*

Because *H. pylori* is so highly adapted to the human stomach, animal models provide only partial approximations of human disease. Although pigs, rodents, mice, Mongolian gerbils, and guinea pigs can be experimentally colonized, *H. pylori* infects non-human gastric mucosa poorly, and no model reproduces the chronicity, immune dynamics, or gastric physiology of natural human infection [113] [114]. This limited fidelity complicates evaluation of novel interventions, including phage-based approaches, and highlights the need for more physiologically relevant systems [113]. However, phage therapy has shown robust efficacy in other preclinical systems, including murine models and *Galleria mellonella*, demonstrating that phages can achieve meaningful *in vivo* bacterial clearance when supported by an appropriate host environment.

Among existing models, Mongolian gerbils offer the closest parallel to human pathology, developing chronic gastritis, metaplasia, and even adenocarcinoma, and have been central to defining virulence factors such as *BabA*, *OipA*, *AlpAB*, and the *cagPAI*. However, no phage studies have been conducted in this model, with research instead focused on antibiotics, vaccines, probiotics, and rice-derived antimicrobial indices [115] [116]. Mice provide unmatched genetic tools but are naturally less permissive, requiring transgenic or knockout strains, such as INS-GAS, IL-1β transgenic, IL-10 knockout, and *CagA*-transgenic mice, to model progressive gastric pathology [113]. Guinea pigs offer a human-like gastric epithelium and IL-8 response, while non-human primates most closely mimic human gastric physiology but are limited by ethical and logistical constraints [117].

Despite these limitations, animal models have been indispensable for defining how microbial, host, and environmental factors shape disease. Gerbil and mouse studies show that high-salt diets, iron deficiency, and micronutrient deprivation accelerate atrophy, metaplasia, dysplasia, and carcinoma, and they have supported preclinical testing of antimicrobials, nano-formulations, mucoadhesive delivery systems, and immunomodulatory therapies. Collectively, these systems have advanced understanding of *H. pylori* persistence and carcinogenesis, yet their incomplete fidelity underscores the need for more human-relevant platforms to guide translational research.

16. Methodology

16.1. Article Search Strategy

Because published data on *H. pylori* in Kenya are highly fragmented and have not been compiled in a single source for at least the past 15 years, a targeted literature search was undertaken to identify studies reporting prevalence, diagnostic approaches, and related epidemiological patterns. The search included studies published between 2010 and 2026, with the final search conducted on 16 February 2026. English-language articles were searched in PubMed, Google Scholar, Academia Biology, and African Journals Online (AJOL), supplemented by a handsearch through Google to capture additional grey literature (thesis only). The search used combinations of Medical Subject Headings (MeSH) and free-text terms, including ("*Helicobacter pylori*" OR *H. pylori* OR "Helicobacter infections") AND, ("Gastritis" OR "Peptic Ulcer") AND, ("Kenya prevalence" OR "Diagnosis" OR "antibiotic resistance"), AND "Kenya". From the studies identified, key information was extracted, such as study region, reported prevalence or incidence, diagnostic methods, risk factors, study design, and study period, to provide an integrated overview of the available evidence (Table 4). Three reviewers (authors) independently screened all records and manually removed duplicates. Studies were excluded if they were not conducted in Kenya, did not contain primary data, or were available only as theses when a peer-reviewed published version existed. Prioritizing published articles ensured that the synthesis was grounded in the most rigorously vetted and widely accessible evidence. This approach was intended to synthesize dispersed findings, summarize reported prevalence estimates, and highlight emerging patterns rather than to produce an exhaustive or systematic review.

Table 4. Prevalence of *H. pylori* infections in Kenya.

Region	Prevalence (n/N, %)	*H. pylori* identification test	Study period	Study type	Risk factors	Reference
Aga Khan University Hospital, Nairobi	469/696, 67.5	Rapid urease test (RUT), histological, stool antigen and culture	-	Cross-sectional observational study	Associated gastric pathologies	[22]

Continued

Moi Teaching and Referral Hospital (MTRH), Eldoret	83/156, 53	RUT and culture	Apr 2014 and Feb 2015	Cross-sectional descriptive study (thesis)	-	[121]
Kipsamoite, Mosop Sub-County, Nandi County	35/105, 33.3	IgG* antibody (serology)	2017	Retrospective case-control	-	[122]
Mbagathi Hospital, Nairobi	176/381, 46.2	Stool antigen test	Sep 2016-Jun 2019	Cross-sectional (thesis)	Contaminated drinking and household water, age (31 - 40 yrs), gender (female)	[36]
Chuka	27/227, 11.9	Stool antigen test	June-Aug 2019	Retrospective descriptive	Lack of hygiene awareness Drinking water unsuitable for consumption	[37]
Aga Khan University Hospital, Nairobi	199/487, 40.86	Culture method	Jan 2018-Feb 2019	Prospective	Previous *H. pylori* infection, age (41 - 50 yrs), epigastric pain (lower odds, gender (male)	[9]
Getrude Children Hospital and Githogoro Outreach Clinic, Nairobi	95/212, 45	Stool antigen test	Jun 2015-Oct 2015	Cross-sectional study (thesis)	Water source and number of people sharing a house	[123]
Mbagathi and Mutuini Hospitals, Nairobi	117/328, 34	Stool antigen test	Jan 2020-2022	Cross-sectional	-	[38]
Nairobi, Kisumu and Mombasa	46/143, 32.1	Histology and PCR*	2012-2019	Case-control laboratory-based study	-	[4]
Kibwezi West, Makueni	109/344, 32	Stool antigen test	-	Analytical cross-sectional method	Lower education level; unsafe or untreated water sources, and diabetes mellitus (type 2)	[39]
Garissa County	170/290, 58.6	IgG antibody (serology)	Jan-June 2021	Descriptive cross-sectional	Lower economic status, untreated water and poor sanitation conditions	[124]
-	671/1248, 53.8	Stool antigen test	Jan 2021-Dec 2022	Cross-sectional study	Lower education level, shared housing > 3 people per room, history of dyspeptic symptoms and untreated water sources	[125]

Key: -: Not given; N: No. of eligible participants; *IgG: Immunoglobulin G; *PCR: Polymerase Chain Reaction.

16.2. Sample Pooled Prevalence

To enable contextual comparison with global trends and given the limited number of documented prevalence studies from Kenya, a simple sample-size-weighted summary prevalence was calculated using studies that reported both numerator (n_i) and denominator (N_i) values (*i.e.*, $\hat{p} = \sum n_i / \sum N_i$). This descriptive aggre-

gation combined raw counts across studies to provide an overall indication of prevalence in the Kenyan context. It is intended solely as a pragmatic summary measure and does not constitute a formal meta-analysis, as no variance modeling, weighting adjustments, or heterogeneity assessments were performed [118] [119]. Eleven studies were selected for the pooled prevalence, as one of the studies did not document the study region.

16.3. Quality and Risk-of-Bias (ROB) Evaluation

A simplified quality assessment of the included studies was conducted to enhance transparency and to gauge confidence in the synthesized prevalence estimates and associated findings [120]. It involved a brief evaluation of key methodological aspects, including study population, sampling approach, setting, diagnostic methods, and potential sources of bias (**Supplementary** Table S1).

17. Results

The available Kenyan literature on *H. pylori* spans a 16-year period and remains limited, with only 12 studies identified across diverse regions of the country. Most investigations were conducted in Nairobi, while others originated from Uasin Gishu, Nandi, the Mount Kenya region, Makueni, Mombasa, and Garissa; one study did not specify its location (**Table 4** and **Figure 1**). Diagnostic approaches varied considerably, though stool antigen testing—with or without culture—was the most frequently used method, whereas IgG serology, rapid urease testing, and histology were applied less often. Study designs were predominantly cross-sectional, supplemented by a small number of case-control, prospective, and descriptive studies, and included both published articles and postgraduate theses.

Across the 11 studies that reported both numerator and denominator data (1526/3229 samples), the combined sample-size-weighted prevalence was 47.3% (95% Wilson score CI: 45.6% - 49.0%), reflecting a substantial burden of infection. It should be emphasized that the pooled prevalence is a descriptive summary drawn from the included studies and does not constitute a nationally representative estimate for Kenya due to variability. Considerable variability was evident across regions and populations, shaped by differences in diagnostic methods, study settings, and participant characteristics. Environmental and sociodemographic factors, including limited hygiene awareness, lower education and socioeconomic status, reliance on untreated water sources, and overcrowded living conditions, were recurrently associated with infection. Some studies also noted higher prevalence among adults aged 31 - 50 years, while associations with gender and clinical symptoms such as dyspepsia or prior infection varied across settings (**Table 4**). The risk-of-bias assessment showed that most Kenyan studies had a moderate level of bias, largely due to symptomatic, facility-based sampling and variable diagnostic methods, while a few serology-only or highly specific subgroup studies demonstrated moderate-to-high bias, limiting the overall certainty and generalizability of the pooled prevalence estimates (**Supplementary** Table S1).

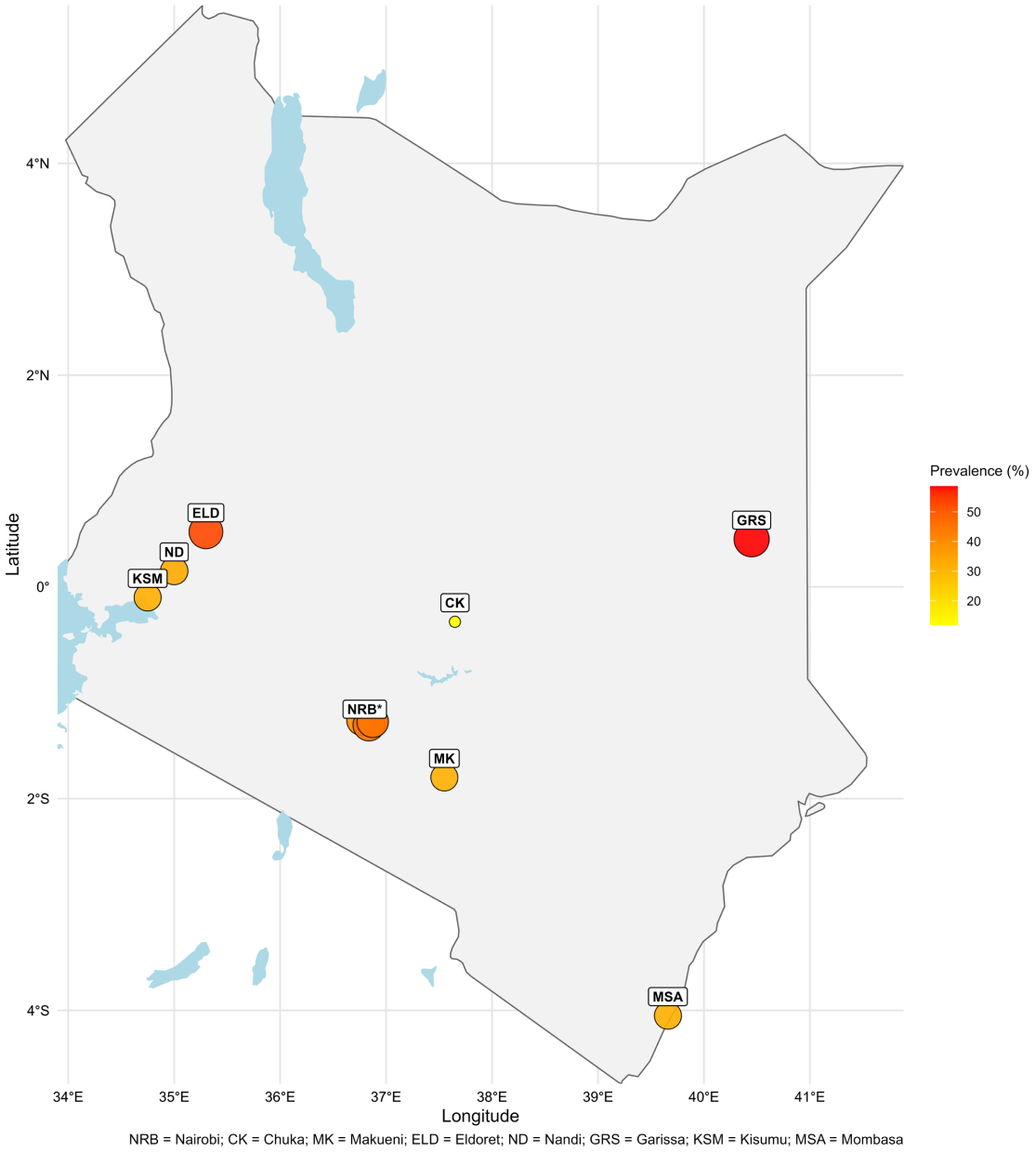

Figure 1. Geographic distribution of reported *H. pylori* studies in Kenya (2010-2025).

18. Discussion

This review establishes that *H. pylori* remains highly endemic in Kenya, with a pooled prevalence of 47.3%, slightly lower than earlier detection reports [22] [121] [124]. This difference is expected, as pooled analyses integrated data from diverse regions and diagnostic methods, moderating the higher values reported in individual studies. However, the true prevalence in Kenya is likely higher than documented, given limited diagnostic access, the concentration of studies in only a few counties, and the absence of routine screening—particularly among asymptomatic individuals. As a result, many infections remain undetected, and published estimates almost certainly underestimate the actual national burden.

Comparable findings have been reported in East Africa, where a recent meta-analysis estimated a pooled prevalence of 50.98%, with Sudan showing the highest burden and Uganda the lowest at 40.7% [7] [126]. Another regional review reported prevalence ranges of 50% - 78.5% [15]. At the continental level, SSA continues to bear the highest global burden, with overall prevalence exceeding 70%, and substantial variation across subregions, West Africa (28% - 93.1%), North Africa (51.4% - 99%), and Southern Africa (50% - 93%) [15].

Diagnostic capacity remains limited, with few facilities able to perform culture or antimicrobial susceptibility testing. Dependence on stool antigen testing, while practical, is affected by pre-analytical and laboratory variability. The absence of standardized diagnostic pathways and a national surveillance system results in inconsistent case detection and geographically skewed data. Critically, the lack of routine susceptibility testing forces clinicians to rely on empirical therapy, obscuring resistance trends and contributing to treatment failure. Strengthening laboratory networks and coordinated reporting systems is essential to improve diagnostic accuracy and epidemiological monitoring [15] [126].

Rising resistance to clarithromycin, metronidazole, and levofloxacin is a major contributor to declining eradication rates. Antibiotic misuse, over-the-counter access, incomplete treatment courses, and limited follow-up accelerate resistance development. The acidic gastric environment further reduces antibiotic stability, while empirical therapy, necessitated by the absence of susceptibility testing, reinforces ineffective prescribing patterns. Current treatment guidelines, often adapted from high-income settings, may not reflect local resistance profiles or resource constraints, increasing the risk of persistent infection and long-term complications [28] [127].

Emerging biologic and non-antibiotic therapies offer promising alternatives to conventional treatment but remain largely experimental. Bacteriophages, engineered endolysins, *Bdellovibrio bacteriovorus*, tailocins, antimicrobial peptides, probiotics, photodynamic therapy, nanoparticles and medicinal plant derivatives all demonstrate varying degrees of *in vitro* activity. However, each faces significant translational barriers, including instability in the gastric environment, delivery challenges, incomplete genomic characterization, and limited clinical validation [128].

To align with feasibility needs in Kenya, these modalities can be prioritized according to gastric-delivery stability, manufacturability, and regulatory pathway readiness. Based on these criteria, bacteriophage therapy, engineered endolysins, and probiotic-based adjuncts represent the most realistic near-term candidates. These approaches benefit from comparatively greater acid-tolerance when formulated appropriately, lower-cost microbial or fermentation-based production, and clearer regulatory pathways through existing biologics or food-supplement frameworks. In contrast, modalities such as nanoparticles, photodynamic therapy, antimicrobial peptides, tailocins, medicinal plant derivatives, and Bdellovibrio-based approaches require advanced formulation technologies, specialized delivery sys-

tems, or more complex regulatory oversight, positioning them as longer-term options for Kenya.

Animal models are essential for preclinical evaluation of these modalities but introduce important constraints. Murine and gerbil systems do not fully replicate human gastric physiology, immune responses, or chronic infection dynamics, and many *H. pylori* strains colonize animals differently from humans. These limitations complicate interpretation of preclinical findings and may overestimate therapeutic efficacy. Consequently, advancing these emerging therapies will require improved model systems and carefully designed translational studies tailored to human gastric biology and the realities of low-resource settings [91] [95].

19. Implications for Policy and Research in Kenya

Addressing the burden of *H. pylori* in Kenya will require coordinated national strategies that integrate improved diagnostics, antimicrobial stewardship, and socioeconomic interventions. Establishing a national AMR surveillance system, expanding laboratory capacity, and developing locally informed treatment guidelines are critical steps. Kenya is well-positioned to contribute to global innovation in emerging biologic therapies, particularly in phage discovery, lysin engineering, and nanoparticle-based delivery. Investments in research infrastructure, biobanking, and genomic surveillance will support this progress. Ultimately, reducing the long-term burden of *H. pylori* will require a multifaceted approach that combines biomedical innovation with strengthened health systems and improved Water, Sanitation, and Hygiene (WASH) conditions.

20. Conclusions

H. pylori remains a major public-health challenge in Kenya, sustained by high infection prevalence, rising AMR, and persistent diagnostic and treatment limitations. The fragmented nature of local data, combined with limited access to reliable diagnostics and routine susceptibility testing, continues to drive empirical therapy and contributes to suboptimal eradication outcomes. Biological factors, including strain diversity, biofilm formation, and the organism's ability to persist in harsh gastric conditions, further complicate management.

Although several emerging therapies show promise, most remain experimental and are not yet feasible for routine use in low-resource settings. Parallel investments in research capacity, genomic surveillance, and innovation in alternative therapeutics will be essential to advance locally relevant solutions. Ultimately, reducing *H. pylori*-associated morbidity and gastric cancer risk will depend on integrating biomedical advances with improvements in water, sanitation, hygiene, and antibiotic stewardship across the health system.

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CRediT Authorship Contribution Statement

TWN: Conceptualization, investigation, methodology, and writing—original draft preparation. **BN**: Conceptualization, data curation, investigation, writing—original draft preparation, and visualization. **IJM**: Conceptualization, investigation, data curation, methodology, writing—review and editing and validation. **JNO**: Investigation. **AN:** Review and editing, supervision, and validation. **JAO**: Conceptualization, formal analysis, investigation, supervision, validation, review and editing.

Data Statement

All data supporting the findings of this publication are available within this article and the references.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Supplementary

Table S1. Summary of methodological characteristics and potential sources of bias among included *H. pylori* studies conducted in Kenya.

Study	Study population/setting	Study design	Diagnostic method	Key bias concern	Overall risk of bias
Mwangi *et al.*, 2020	Dyspeptic patients undergoing endoscopy (hospital-based)	Cross-sectional	Endoscopy + biopsy/histopathology	Symptomatic/facility-based population only	Moderate
Said *et al.*, 2019	Peptic ulcer patients at Mbagathi Level V Hospital	Cross-sectional	Endoscopy/serology (not fully detailed)	Hospital-based symptomatic cohort; limited methodological transparency	Moderate-High
Machaj *et al.*, 2020	Hospitalized patients with gastritis (Chuka hospital)	Cross-sectional	Stool antigen test (main); urease/histology (comparison)	Facility-based sampling; short study period (3 months)	Moderate
Kuve *et al.*, 2022	Gastritis patients in Nairobi hospitals	Cross-sectional	Laboratory methods (serology/culture presumed)	Symptomatic hospital population only	Moderate
Muma *et al.*, 2022	Community members (Kibwezi West Sub-County)	Community cross-sectional	Serology (presumed)	Regional (rural) sampling only; limited generalizability	Moderate
Kimang'a *et al.*, 2010	Clinical samples from Kenyan patients	Cross-sectional	Culture and antibiotic susceptibility testing	Older data; limited population representation	Moderate
Churyai, 2015	Dyspeptic patients at Moi Teaching and Referral Hospital	Cross-sectional	Culture-based detection	Single-center hospital cohort	Moderate
Rono *et al.*, 2019	Children (5 - 15 years) in Western Kenya	Cross-sectional	Serology	Serology may overestimate active infection	Moderate-High
Machogu, 2020	Children (3 - 60 months) attending clinics	Cross-sectional	Serology/stool antigen test	Clinic-based pediatric population	Moderate
Mohamed *et al.*, 2022	Pregnant women attending antenatal clinic (Garissa)	Cross-sectional	Serology	Specific demographic group (pregnant women only)	Moderate
Njenga *et al.*, 2023	Gastric cancer patients (case-control, FFPE samples)	Retrospective observational	Histology + PCR genotyping	Highly specific subgroup (cancer-focused); FFPE* DNA degradation risk	Moderate-High

Key: *FFPE: Formalin-Fixed, Paraffin-Embedded.