NATIONAL REFERENCE CENTER FOR *HELICOBACTER PYLORI*

Surveillance report 2024

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List of Abbreviations

HP: Helicobacter pylori

EUCAST: European Committee on Antimicrobial Susceptibility Testing

MIC: Minimum Inhibitory Concentration

MDR: Multidrug-resistant

NRC: National Reference Center

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1. Introduction

The activity of the NRC for *Helicobacter pylori* (HP) is primarily focused on microbiological diagnosis (culture/antibiogram, PCR for the identification and detection of mutations (chromosomal genes) associated with resistance to antibiotics (mainly macrolides), antigen detection in stool and serodiagnosis.

The NRC is regularly contacted by clinical biology laboratories and clinicians (gastroenterologists) for diagnostic recommendations, interpretation of results, and requests for therapeutic advice. The NRC is consulted previously for the Belgian Edition of the Sanford Guide to Antimicrobial Therapy, and recently by the Scientific Committee for the Belgian Infectious Diseases Therapy Guidelines (IGGI), for its expertise in the field of epidemiological surveillance of *H. pylori* resistance to antibiotics and for the revision and updates of the therapeutic recommendation schemes included in the guide. The NRC also collaborates with the French Helicobacter Study Group (GEFH) and at the European level with the European Helicobacter Study Group (EHSG) in multicenter studies to monitor antibiotic resistance or to evaluate/standardize diagnostic methods and/or techniques, including the organization of external quality control assays.

In 2018, the results of a surveillance study of *H. pylori* resistance to antibiotics in several European countries and the correlation observed between resistance rates and antibiotic consumption in the different countries were published (F. Mégraud et al., Gut 2021). The Belgian NRC was represented as senior author and co-principal investigator of this work.

This report summarizes the data analysis up to 2024 of the national microbiological surveillance on the antimicrobial resistance in *Helicobacter pylori*.

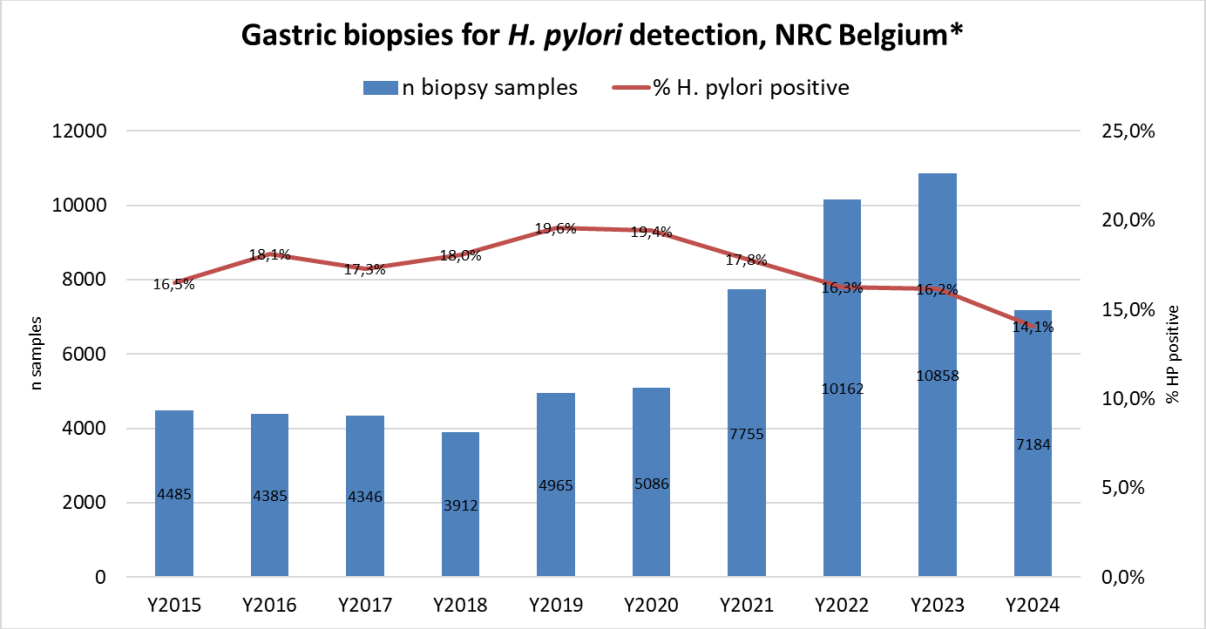
2. Characteristics of samples and patients

Since 2019, all gastroduodenal biopsies received were screened for the presence of HP and the mutations of the 23S rRNA (A2142C/G, A2143G) for clarithromycin resistance by real-time PCR directly on the grinded biopsies. The results of the PCR screening allow rapid report of the absence/presence of HP and the clarithromycin susceptibility (CLA-S) usually within 3 working days (much shorter than by classic cultures). These rapid results allow the initiation of targeted eradication therapy that is usually based on a clarithromycin-included regimen.

In 2024, the NRC performed PCR screening on a total of 7818 gastric and duodenal biopsy samples (patients median age 52.6 years; range: 2-97 years). Clinical specimens were sent by 28 digestive endoscopy departments (16 in Wallonia; 1 in Brussels; 11 in Flanders), including 7 hospital-associated centers (6 in Wallonia, 1 in Brussels) together representing more than 90% of all clinical samples sent to the NRC.

For the year 2024 among the 7 main centers, the HP positive rate by PCR was 14.1% (1011 cultures out of 7184 samples analyzed). The prevalence of HP has been gradually decreasing in the population over the years (during the decade 1990-2000; the average prevalence rate was 25-30%) in parallel with the decrease in the incidence of peptic ulcer disease in the population. The positivity rate for HP fluctuated annually between 15 and 20% before 2020 and has further continuously decreased since 2020 in parallel with the increase of number of samples analyzed suggesting a more common practice of sampling with microbiological analysis becoming more systematic (Figure 1).

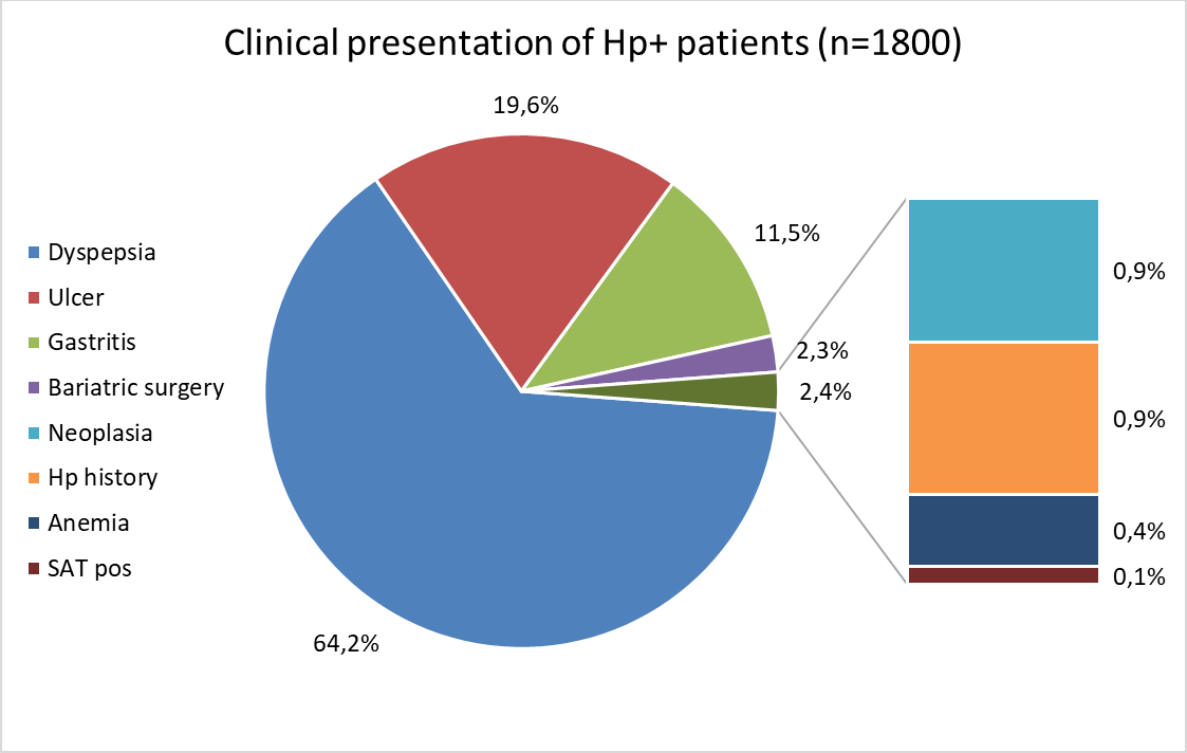
Figure 1. Number of gastric biopsies analyzed and positivity rates for *H. pylori*



*Analysis from the top 7 centers

The clinical presentations of patients with HP detected in gastric biopsies are summarized in Figure 2. Dyspepsia, gastro-duodenal ulcer and gastritis represent 95% of the clinical presentations of HP infection, while the bariatric surgery, history (including family) of gastric neoplasia or of HP infection, investigation of anemia and positive result of stool antigen test (SAT) for HP are the other clinical contexts of HP positivity.

Figure 2. Clinical presentation of patients infected by *H. pylori*



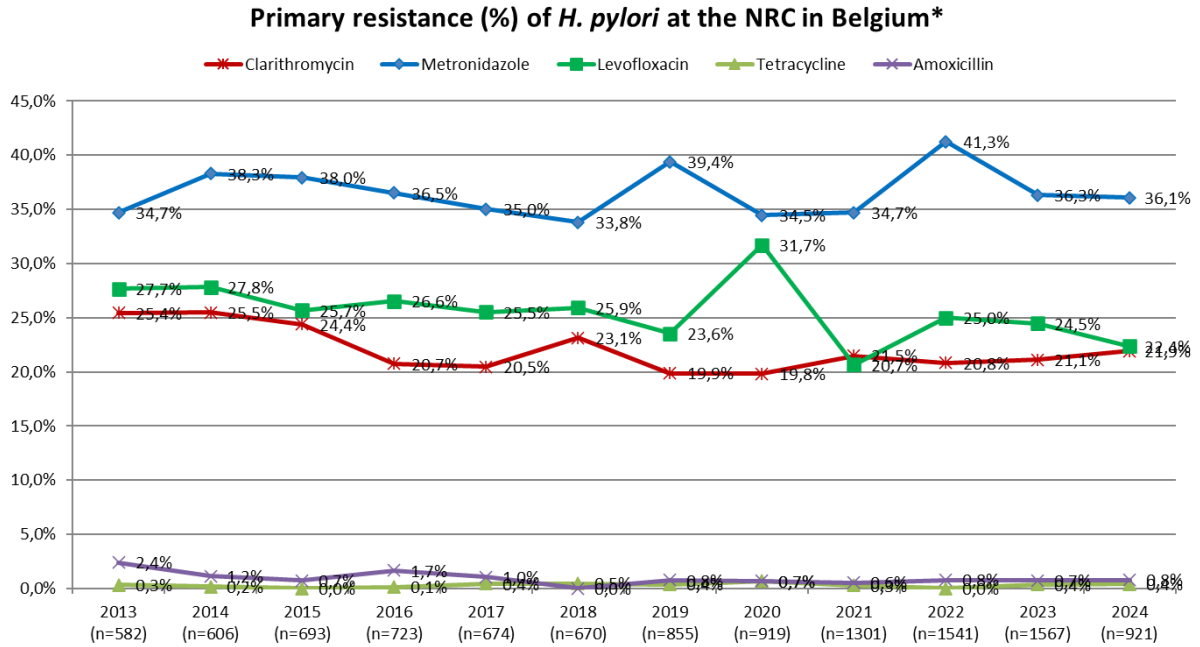
3. Primary resistance

To report resistance rates, a distinction is made between the primary resistance (in the absence of known patient exposure to a specific treatment aimed at eradicating HP infection), and the secondary resistance (observed after failure to eradicate the infection in patients who have previously received specific anti-HP treatment). This distinction is of importance because the primary resistance rates reported in the population have a direct impact on the choice of first-line probabilistic treatments that will be prescribed in the absence of microbiological sampling.

Resistance to clarithromycin was based on the detection of mutations of the 23S rRNA by real-time PCR directly on all biopsies. Extensive antimicrobial susceptibility testing (AST) was performed by the gradient strip diffusion method using Etest for metronidazole, levofloxacin, tetracycline and amoxicillin and interpreted according to the 2024 EUCAST guidelines (Breakpoint tables for interpretation of MICs and zone diameters. Version 14.0).

In 2024, the total numbers of PCR Hp positive samples or HP strains analyzed for primary resistance rate were 921 for clarithromycin, and of 255 (isolates) for metronidazole, levofloxacin, tetracycline and amoxicillin.

Figure 3. Primary resistance to 5 antibiotics for *H. pylori* in Belgium



Primary resistance of HP mainly affects metronidazole, clarithromycin (cross-resistance to all macrolides), and levofloxacin (cross-resistance to all fluoroquinolones) showing resistance rates of 36.1%, 21.9% and 22.4%, respectively in 2024. Resistance to these three classes of antibiotics has a major impact in clinical practice and significantly reduces the efficacy of treatment regimens using these molecules. This is particularly true for macrolide resistance (reduction in treatment efficacy by >50% on average in cases of resistance). Resistance to amoxicillin or to tetracycline is very rare (<1%), and its clinical impact has not been clearly demonstrated.

Overall, observed resistance levels have remained stable over the past three years, with some slight fluctuations. Given the sample size, the limited number of providing centers and the presence of bias in patient selection (endoscopy services attached to a hospital, leading to a greater risk of recruitment of patients already treated and referred to second line by their treating physician), these rates are not necessarily representative of the entire general population.

Figure 4. Number of primary antibiotic resistances for *H. pylori*

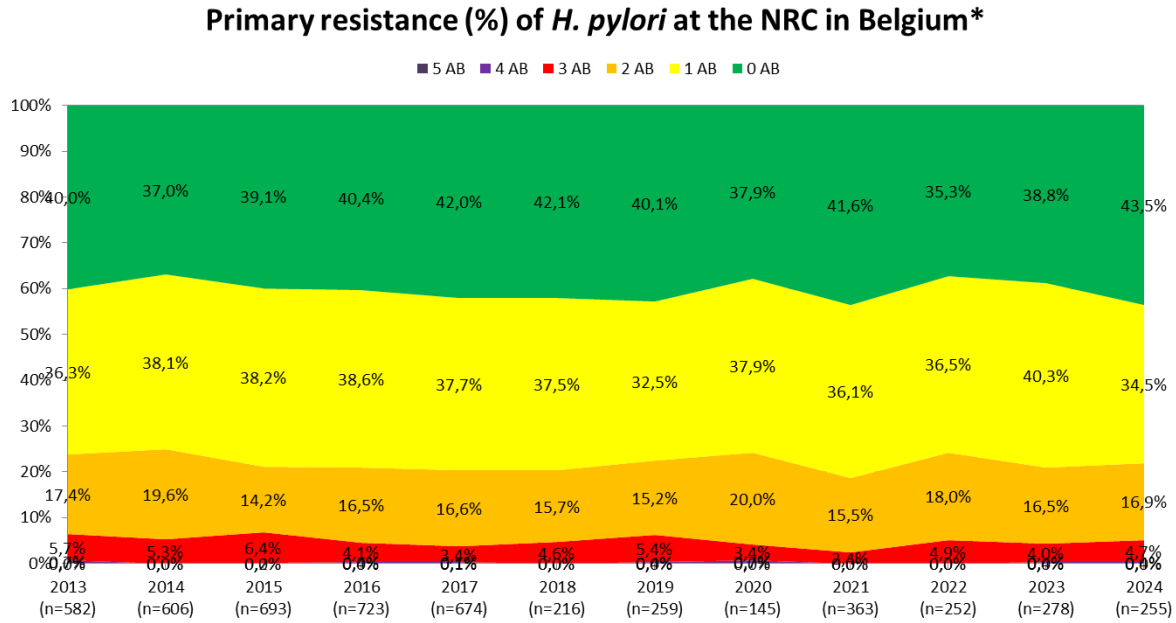
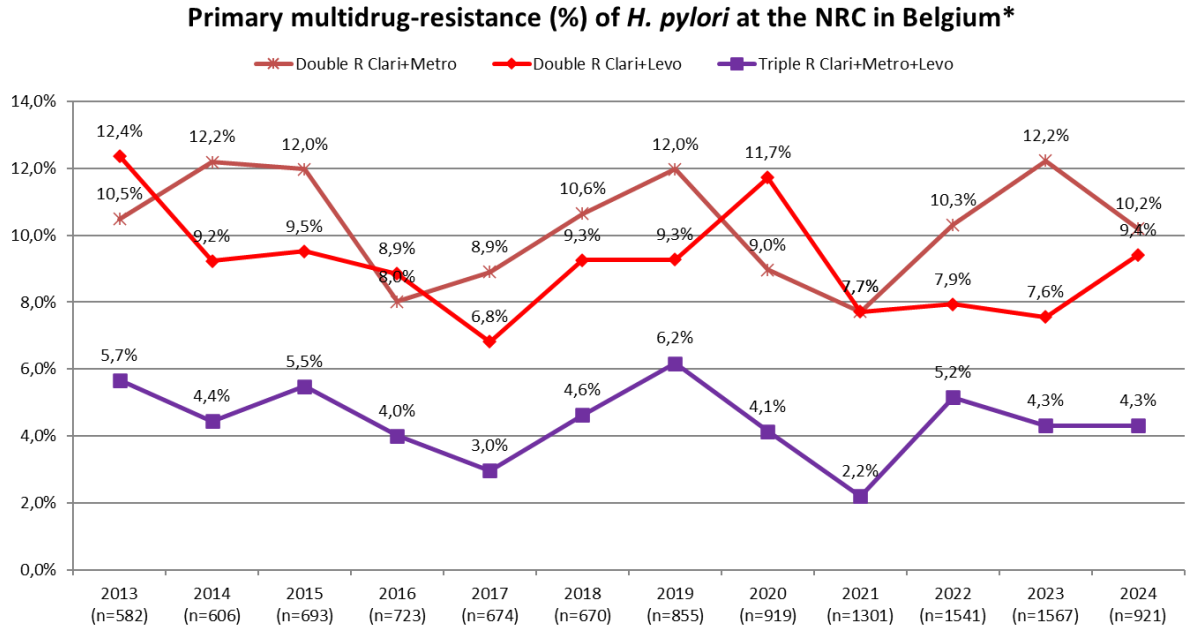


Figure 5. Primary multidrug resistance of *H. pylori*



Primary resistance is observed in nearly 60% of the HP strains tested. This resistance affects a single class of antibiotics in most cases. However, resistance affecting two antibiotics is observed in 42 patients (16.5% of cases). This double resistance combined equally either levofloxacin with metronidazole (n=17), levofloxacin with clarithromycin (n=11), or metronidazole with clarithromycin (n=14). Resistance to three different classes of antibiotics (mainly clarithromycin, metronidazole and levofloxacin) was found in 12 patients (5%). These double or triple resistances strongly suggest the probability of

resistance induced by undocumented previous treatments aimed either at the treatment of HP infection or other intercurrent infections.

4. Secondary resistance

Figure 6. Primary and secondary resistances rates of *H. pylori*

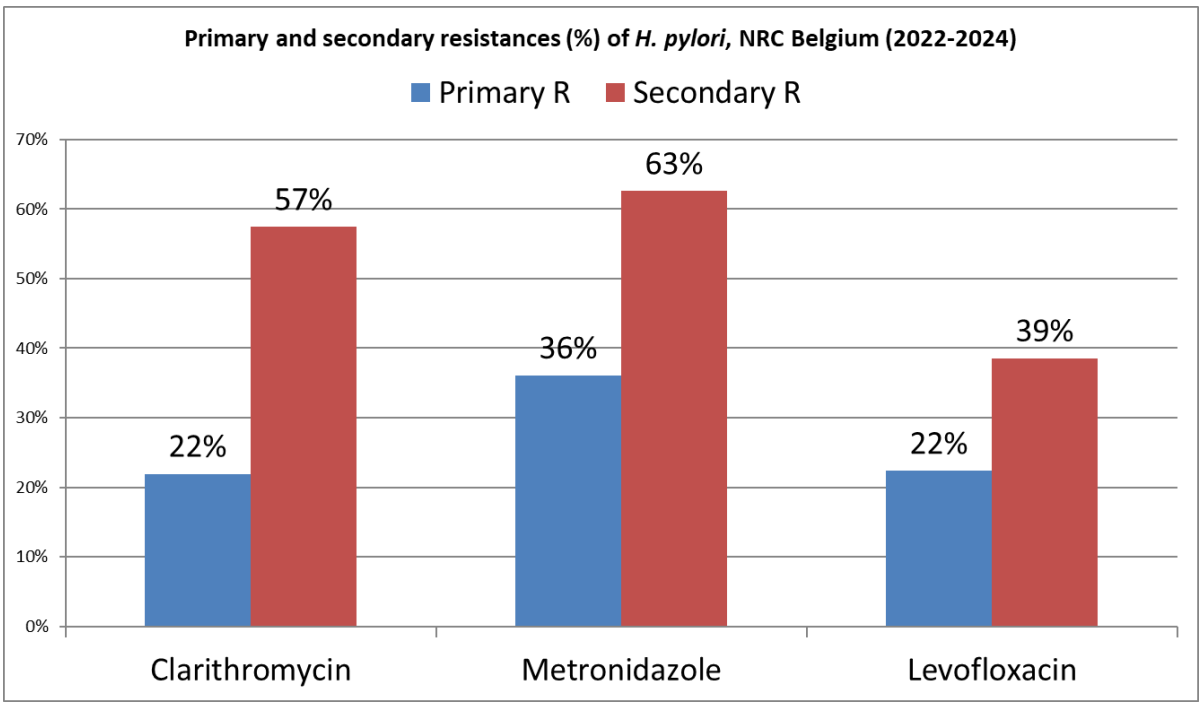
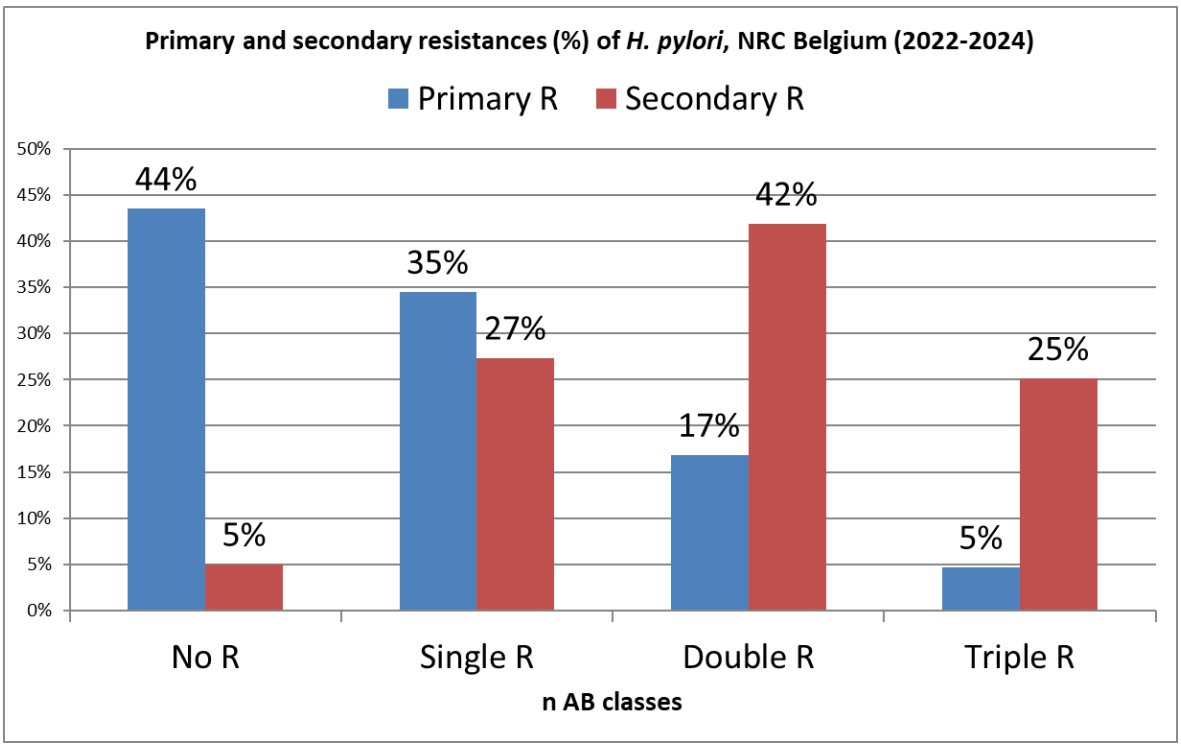


Figure 7. Number of antibiotics involved in primary and secondary resistances of *H. pylori*



Secondary resistance rates (after failure of *H. pylori* eradication treatment) are very high, ranging from 40% to 80% depending on the antibiotic. Given the very high frequency of emerging resistance to macrolides, it is contraindicated to re-administer macrolide therapy in the event of prior failure with a clarithromycin-containing regimen.

The high rate of double and triple resistance after treatment also suggests that second- or third-line treatments should be adapted based on culture and antibiogram results.

5. Summary

The National Reference Center (NRC) for *Helicobacter pylori* in Belgium conducted microbiological surveillance to monitor antimicrobial resistance trends in 2024. A total of 7,818 gastric and duodenal biopsy samples were analyzed using real-time PCR and culture methods. The HP positivity rate was 14.1% in the top 7 hospital-based endoscopy units, continuing a downward trend over the past decade.

Primary resistance remains high, with nearly 60% of HP strains showing resistance to at least one antibiotic, predominantly metronidazole, clarithromycin, and levofloxacin. In particular, the clarithromycin resistance rate remained high (>20%) and should discourage the use of clarithromycin-based triple therapy as empiric treatment. On the other hand, direct PCR targeting 23S rRNA mutations directly performed on biopsies allow timely and targeted eradication therapy, which is crucial since clarithromycin resistance alone can reduce treatment efficacy by over 50%. Double resistance was observed in 17% of cases, and triple resistance in 5%. Resistance to amoxicillin and tetracycline remains rare (<1%).

Secondary resistance, found after treatment failure, was markedly higher (40–80%), especially for macrolides. This highlights the need for culture-based antibiotic susceptibility testing to guide second- or third-line therapies.

The report underscores the critical role of early detection of clarithromycin resistance in optimizing first-line treatment strategies and combating the rise of multidrug-resistant *H. pylori*.

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