

## #82 - QUADRUPLE THERAPIES ARE SUPERIOR TO STANDARD TRIPLE THERAPY FOR HELICOBACTER PYLORI ERADICATION. A MULTICENTER OBSERVATIONAL STUDY IN EUROPEAN AND LATIN AMERICAN COUNTRIES (LEGACY STUDY)

<https://doi.org/10.46613/congastro2023-82>

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**Introduction:** Gastric cancer is one of the most lethal malignancies worldwide. Eradication of *Helicobacter pylori* (*H. pylori*) infection, its primary cause reduces the risk of gastric cancer. There is limited information comparing eradication rates of antibiotic schemes that includes European and Latin American populations.

**Objective:** To compare the effectiveness of Standard Triple Therapy (STT), Quadruple non-bismuth Concomitant Therapy (QCT), and Quadruple Bismuth Therapy (QBT) in six centers in Europe and Latin America: Portugal, Spain, Chile, Mexico, and Paraguay.

**Methods:** This is a retrospective study based on the LEGACY registry from 2017 to 2022 in Portugal, Spain, Chile, Mexico, and Paraguay. The inclusion criteria were being diagnosed as *H. pylori*-positive individuals, receiving eradication treatment, and having undergone an eradication test at least one month after treatment. The outcome variable was the eradication rate, and the main independent variable was the scheme used. To compare the *H. pylori* treatment schemes, the statistical approach used was through Poisson multilevel multivariate regression, including sex, age, and ecological country-specific variables from available evidence, including *H. pylori* antibiotic resistance (clarithromycin, metronidazole, and amoxicillin), and the proportion of *CYP2C19* polymorphism corresponding to extensive metabolizer for proton pump inhibitors (Table 1).

**Results:** The study included 873 patients, 64% females, with a mean age of 54 years (52.6-54.7). The *H. pylori* eradication rates were 75.2% for STT, 89.3% for QCT, and 91.3% for QBT. Both therapies (QCT-QBT) had statistically significant differences vs. STT, with an Incidence Risk Ratio (IRR) of 1.25 (p-value: <0.01) for QCT and an IRR of 1.24 (p-value: <0.01) for QBT.

**Conclusions:** Quadruple therapies (both with and without bismuth) are superior to STT for *H. pylori* eradication regardless of country-specific *H. pylori* antibiotic resistance and *CYP2C19* polymorphism in a sample of individuals belonging to five different countries and two continents.

Table 1. Sample characteristics, treatment eradication rates, and Poisson multilevel multivariate model to eradication per scheme. The model incorporated as covariates age, sex, country's clarithromycin resistance prevalence, country's metronidazole resistance prevalence, country's amoxicillin resistance prevalence, and country's *CYP2C19* rapid metabolizers prevalence. The grouping variable (for multilevel analysis) was the LEGACY center where the patients were treated. STT: Standard Triple Therapy, QCT: Quadruple Concomitant Therapy, and QBT: Quadruple Bismuth Therapy. PUC: Pontificia Universidad Católica de Chile, INCLIVA: Fundación para la Investigación del Hospital Clínico de la Comunidad Valenciana, GENPAT: GenPat Laboratory, INCAN: Instituto Nacional de Cancerología, IPATIMUP: Institute of Molecular Pathology and Immunology of the University of Porto, VHIO: Vall d'Hebron Institute of Oncology. *H. pylori* resistance data and *CYP2C19* rapid metabolizer prevalence is from scientific papers. \*Obtained from the analysis of a sample of LEGACY participants from GENPAT because there is not found in scientific papers as for the other countries.

Center characteristics and eradication rate per scheme												
Center	Country	City	N	Gender Female % (N)	Age Mean (I 95%)	<i>H. pylori</i> resistance to Clarithromycin country prevalence	<i>H. pylori</i> resistance to metronidazole country prevalence	<i>H. pylori</i> resistance to amoxicillin country prevalence	<i>CYP2C19</i> rapid metabolizer country prevalence	STT eradication rate % (N)	QCT eradication rate % (N)	QBT eradication rate % (N)
PUC	Chile	Santiago	210	66.3 (115)	52.7 (50.8-54.7)	26.0	49.0	2.0	20.5	81.8 (108)	91.6 (33)	97.6 (42)
GENPAT	Paraguay	Asunción	144	64.5 (95)	49.2 (46.7-51.7)	2.0	32.6	2.0	0.0 *	74.7 (71)	92.8 (26)	100.0 (2)
INCAN	Mexico	Ciudad de Mexico	150	63.3 (95)	58.4 (55.6-61.2)	12.0	58.6	1.8	14.3	77.7 (28)	100.0 (9)	90.9 (10)
IPATIMUP	Portugal	Porto	154	62.9 (97)	52.8 (50.7-55.0)	48.0	34.4	0.6	28.8	68.0 (17)	88.8 (16)	94.4 (10)
INCLIVA	Spain	Valencia	149	65.1 (97)	50.7 (48.1-53.2)	27.0	30.5	0.2	29.5	54.1 (13)	84.4 (85)	75.0 (21)
VHIO	Spain	Barcelona	66	60.6 (40)	63.6 (60.5-66.8)	27.0	30.5	0.2	29.5	66.6 (18)	100.0 (10)	83.3 (15)
Total	-	-	873	64.4 (563)	53.7 (52.6-54.7)	-	-	-	-	75.2 (255)	89.3 (159)	91.3 (101)

  

Poisson multilevel multivariable model to eradication per scheme		
Scheme	IRR eradication (95% CI)	p-value
STT	Reference	-
QCT	1.25 [1.14 - 1.37]	<0.01
QBT	1.24 [1.17 - 1.32]	<0.01