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TRENDS IN THE PRESCRIPTION OF EMPIRICAL TREATMENTS AND THEIR EFFECTIVENESS IN NAÏVE PATIENTS OVER 10 YEARS (2013-2022) IN EUROPE: DATA FROM THE EUROPEAN REGISTRY ON THE MANAGEMENT OF *HELICOBACTER PYLORI* INFECTION (Hp-EuReg)

O. P. NYSSEN[1], *L. JONAITIS*[2], *Á. PÉREZ-AÍSA*[3], *D. VAIRA*[4], *G. FIORINI*[4], *I. SARACINO*[4], *B. TEPES*[5], *D. S. BORDIN*[6], *M. LEJA*[7], *F. LERANG*[8], *A. TONKIC*[9], *H. SIMSEK*[10], *L. KUNOVSKY*[11], *A. GASBARRINI*[12], *A. CANO-CATALÀ*[13], *L. MOREIRA*[14], *P. PARRA*[1], *F. MÉGRAUD*[15], *C. O'MORAIN*[16], *J. P. GISBERT*[1], *ON BEHALF OF THE Hp-EuReg INVESTIGATORS*

[1]Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain; [2]Department of Gastroenterology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [3]Digestive Unit, Hospital Costa del Sol Marbella, Redes de Investigación Cooperativa orientada a resultados en salud (RICORS), Málaga, Spain; [4]IRCCS AOU S. Orsola-Malpighi, University of Bologna, Bologna, Italy; [5]Department of Gastroenterology, AM DC Rogaska, Rogaska Slatina, Slovenia; [6]Department of Pancreatic, Biliary and upper digestive tract disorders, A. S. Loginov Moscow Clinical Scientific Center, Tver State Medical University, A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Moscow, Russian Federation; [7]Department of Gastroenterology, Digestive Diseases Centre, Institute of Clinical and Preventive Medicine & Faculty of Medicine, University of Latvia, Riga, Latvia; [8]Department of Gastroenterology, Østfold Hospital Trust, Grålum, Norway; [9]Department of Gastroenterology, University Hospital of Split, University of Split School of Medicine, Split, Croatia; [10]Department of Gastroenterology, Hacettepe University, HC International Clinic, Ankara, Turkey; [11]Gastroenterology and Geriatrics, University Hospital Olomouc, Faculty of Medicine and Dentistry, Palacky University Olomouc, University Hospital Brno, Faculty of Medicine, Masaryk University, Masaryk Memorial Cancer Institute, Brno, Czech Republic; [12]Medicina interna e Gastroenterologia, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; [13]GOES research group, Althaia Xarxa Assistencial Universitària de Manresa, Manresa, Spain; [14]Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), University of Barcelona, Barcelona, Spain; [15]INSERM U1312, Université de Bordeaux, Bordeaux, France; [16]School of Medicine, Trinity College Dublin, Dublin, Ireland

Objective: The impact of consensus, prescription choices, and efficacy trends on clinical practice over time has not been studied in depth.

Materials and Methods: Multicentre, prospective registry evaluating the decisions and outcomes of *Helicobacter pylori* management by European gastroenterologists. Data were registered at AEG-REDCap e-CRF until December 2022. Modified intention-to-treat (mITT) and time trend analyses were performed.
Results: Overall 46,797 (78%) were first-line empirical prescriptions. The most common treatments in 2013-22 were triple therapies; however, a shift in antibiotic regimens was identified. Triple therapies decreased from over 50% of prescription in 2013/15 to less than 20% in 2020/22; likewise, non-bismuth concomitant therapy use decreased from 21% in 2013/14 to 13% in 2020/22, while three-in-one single-capsuleincreased from 0-1% in 2014/2015 to 21% in 2020/22. An increase in the average duration of treatments from 9.7 days to 13 days in 2013-2022 was identified, as well as in the use of high-dose of PPIs increasing from 17% to 35% in 2013-2022. There was a ≈10% overall improvement in first-line mITT overall effectiveness from 85% to 93% in 10 years of evolution, both globally and in each geographic region (Table 1).
Conclusions: European gastroenterological practice is constantly adapting to the newest published evidence and recommendations (reducing the use of triple therapies and increasing both the duration of treatment and the dose of PPIs), with a subsequent progressive improvement in overall effectiveness.

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TABLE 1. PRESCRIPTIONS AND EFFECTIVENESS TRENDS OF FIRST-LINE EMPIRICAL TREATMENTS IN EUROPE IN THE PERIOD 2013-2022.

Year	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Quadruple-C+A+B	2.0%	2.7%	6.8%	20.5%	13.7%	21.7%	10.8%	9.8%	9.4%	10.3%
Single-capsule*	0.1%	0.0%	0.5%	13.2%	24.5%	18.7%	21.7%	16.5%	18.2%	21.1%
Quadruple-M+Tc+B	2.1%	1.9%	0.5%	0.2%	0.4%	0.5%	1.4%	1.2%	1.1%	1.5%
Concomitant-C+A+M/T	21.8%	21.5%	27.0%	22.7%	20.9%	8.0%	13.4%	12.8%	13.1%	10.6%
Sequential-C+A+M/T	11.8%	3.5%	1.9%	0.9%	0.5%	0.7%	0.11%	0.1%	0.3%	2.8%
Triple-A+L	2.3%	2.2%	3.1%	1.8%	0.3%	0.3%	0.4%	0.3%	0.4%	0.9%
Triple-A+M	3.6%	3.0%	1.7%	0.8%	0.9%	0.5%	1.9%	0.7%	1.0%	1.6%
Triple-C+M	3.4%	6.4%	8.8%	6.3%	1.4%	0.7%	1.1%	10.2%	4.9%	4.1%
Triple-C+A	48.5%	54.6%	44.7%	29.2%	32.1%	31.0%	35.2%	34.6%	32.7%	29.9%
Therapy length										
7 days	27.5%	28.1%	24.4%	16.2%	7.9%	1.7%	2.1%	4.5%	2.9%	9.5%
10 days	55.1%	52.6%	55.1%	46.5%	47.2%	41.6%	34.7%	29.4%	34.1%	43.2%
14 days	17.4%	19.3%	20.4%	37.3%	44.9%	56.7%	63.2%	66.1%	62.9%	47.3%
PPI doses										
Low	66.6%	56.6%	47.3%	37.9%	39.7%	25.0%	30.1%	45.3%	40.5%	28.6%
Standard	16.9%	25.5%	26.7%	24.1%	23.7%	41.3%	30.9%	19.5%	25.4%	36.7%
High	16.5%	17.9%	26.0%	38.0%	36.6%	33.7%	39.0%	35.2%	33.8%	34.6%
Eradication rate (mITT)	85.0%	85.1%	85.7%	87.6%	87.7%	91.4%	91.5%	92.7%	92%	93%
Geographical region										
East	89.7%	80.2%	85.3%	83.4%	77.7%	91.3%	90.4%	96.0%	96.4%	96.8%
South-east	87.3%	85.1%	85.2%	84.2%	86.3%	88.0%	89.3%	89.7%	89.1%	92.0%
South-west	83.4%	86.9%	86.2%	89.9%	91.1%	90.9%	87.7%	85.3%	91.5%	95.3%
Centre	87.9%	93.0%	92.8%	95.2%	88.0%	91.9%	91.3%	89.4%	86.1%	90.1%
North	84.6%	84.3%	86.4%	84.9%	87.2%	80.5%	89.8%	86.5%	82.1%	88.0%

PPI: proton pump inhibitor; mITT: modified intention-to-treat; A - amoxicillin. C - clarithromycin; M - metronidazole; T - tinidazole; L - levofloxacin B; - bismuth salts; Tc - tetracycline. *Three-in-one single-capsule containing metronidazole. tetracycline and bismuth; **Low dose PPI - 4.5 to 27 mg omeprazole equivalents. b.i.d.; standard dose PPI - 32 to 40 mg omeprazole equivalents. b.i.d.; high dose PPI - 54 to 128 mg omeprazole equivalents. b.i.d.

P02.11

EMPIRICAL SECOND-LINE TREATMENTS IN EUROPE: RESULTS FROM THE EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (Hp-EuReg)

O. P. NYSSEN[1,2,3], *D. VAIRA*[4,5,6], *I. SARACINO*[4,5,6], *M. PAVONI*[4,5,6], *G. FIORINI*[4,5,6], *Á. PEREZ-AISA*[7,8], *L. JONAITIS*[9], *M. CASTRO-FERNANDEZ*[10], *D. BOLTIN*[11,12], *L. HERNÁNDEZ*[13], *A. GASBARRINI*[14], *D. S. BORDIN*[15,16,17], *J. KUPCINSKAS*[18], *F. LERANG*[19], *A. CANO-CATALÀ*[20], *P. PARRA*[1,2,3], *L. MOREIRA*[3,21,22], *F. MÉGRAUD*[23], *C. O'MORAIN*[24], *J. P. GISBERT*[1,2,3], *ON BEHALF OF THE Hp-EuReg INVESTIGATORS*

[1]Department of Gastroenterology, Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Madrid, Spain; [2]Universidad Autónoma de Madrid (UAM), Madrid, Spain [3]Centro de Investigación Biomédica en Red en Enfermedades Digestivas y Hepáticas (CIBERehd), Madrid, Spain; [4]Department of Medical and Surgical Sciences, IRCCS AOU S. Orsola-Malpighi, University of Bologna, Bologna, Italy; [5]Microbiology Unit, Department of Specialized, Experimental, and Diagnostic Medicine, IRCCS AOU S. Orsola-Malpighi, Bologna, Italy; [6]Cardiovascular Internal Medicine, IRCCS AOU S.Orsola-Malpighi, Bologna, Italy; [7]Digestive Unit, Hospital Costa del Sol, Marbella, Spain; [8]Redes de Investigación Cooperativa Orientada a Resultados en Salud (RICORS), Marbella, Spain; [9]Department of Gastroenterology, Lithuanian University of Health Sciences, Kaunas, Lithu-ania; [10]Department of Gastroenterology, Hospital de Valme, Seville, Spain; [11]Division of Gastroen-terology, Rabin Medical Center, PetahTikva, Israel; [12]Sackler School of Medicine, Tel Aviv University, TelAviv, Israel; [13]Gastroenterology Unit, Hospital Santos Reyes, Aranda de Duero, Spain; [14]Medicina Interna e Gastroenterologia, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, It-aly; [15]Department of Pancreatic, Biliary and Upper Digestive Tract Disorders, A. S. Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation; [16]Department of Propaedeutic of Internal Dis-eases and Gastroenterology, A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Moscow, Russian Federation; [17]Department of Outpatient Therapy and Family Medicine, Tver State Medical University, Tver, Russian Federation; [18]Institute for Digestive Research and Department of Gastroenterology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [19]Department of Gastroenterology, Østfold Hospital Trust, Grålum, Norway; [20]GOES research group, Althaia, Xarxa Assistencial Universitària de Manresa, Manresa, Spain, [21]Department of Gastroenterology, Hospital Clínic Barcelona, Barcelona, Spain; [22]IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), Barcelona, Spain; [23]INSERM U1312, Université de Bordeaux, Bordeaux, France; [24]School of Medicine, Trinity College Dublin, Dublin, Ireland.

Objective: After a first eradication attempt, approximately 10-20% of patients will fail to achieve *H. pylori* eradication. The aim of the study was to evaluate the effectiveness of second-line empirical treatment.

Patients and Methods: A prospective registry of the clinical practice of European gastroenterologists on *H. pylori* management systematically registered infected adult patients at AEG-REDCap e-CRF until January 2023. Modified intention-to-treat (mITT) and per-protocol (PP) analyses were performed.

Results: Overall, 7,901 patients were included and reported an overall mITT/PP effectiveness of 83% (Table 1). None of the European regions achieved optimal effectiveness. However, in those patients receiving optimised therapy (i.e., 14-days and high dose PPIs), triple regimens containing levofloxacin/moxifloxacin and bismuth quadruple therapies either with metronidazole-tetracycline or levofloxacin-amoxicillin, as well as quadruple therapy with clarithromycin-amoxicillin-metronidazole, showed encouraging results (>86%). Also, bismuth quadruple therapies prescribed as single-capsule or with amoxicillin-levofloxacin achieved consistent eradication rates regardless of the PPI dose, or previous first-line treatment. After failure of first-line clarithromycin-containing therapy, optimal eradication was obtained with moxifloxacin-containing triple therapy (91%), and bismuth quadruple therapies, as well as quadruple therapy with clarithromycin-amoxicillin-metronidazole provided cure rates of 86% each.
Conclusions: Empirical second-line regimens, including triple therapy with levofloxacin, quadruple therapy with clarithromycin-amoxicillin-metronidazole and bismuth quadruple therapies with metronidazole-tetracycline or levofloxacin-amoxicillin, provided optimal effectiveness when prescribed for 14 days and with high-dose PPIs. However, many other second-line treatments evaluated still reported low eradication rates.

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TABLE 1. FREQUENCY OF SECOND-LINE EMPIRICAL TREATMENT PRESCRIPTIONS AND EFFECTIVENESS BY MODIFIED INTENTION-TO-TREAT (MITT) AND PER-PROTOCOL (PP) ANALYSES, BY GEOGRAPHICAL REGION.

Treatment	N	Use (%)	mITT, N (%)	(95% CI)	PP, N (%)	(95% CI)
Triple-A+L	2,096	27.4	1,867 (81)**	(79-83)	1,844 (81)	(80-83)
Single-capsule*	1,518	19.8	1,417 (88)	(86-90)	1,382 (89)	(87-90)
Quadruple-A+L+B	945	12.3	751 (87)	(85-90)	732 (88)	(85-90)
Triple-C+A	436	5.7	338 (77)	(73-82)	330 (77)	(72-82)
Quadruple-C+A+M	423	5.5	396 (85)**	(81-88)	387 (85)	(82-89)
Quadruple-M+Tc+B	399	5.2	356 (84)**	(80-88)	340 (86)	(82-90)
Quadruple-C+A+B	329	4.3	215 (89)	(84-93)	206 (89)	(84-93)
Triple-A+R	208	2.7	185 (83)	(77-88)	183 (83)	(77-89)
Triple-A+M	193	2.5	172 (64)	(57-72)	170(65)	(57-72)
Triple-A+Mx	143	1.9	135 (91)	(86-96)	135 (91)	(86-96)
Other	973	12.7	NA	NA	NA	NA
Total	**7,663**	**100**	**6,665 (83)**	**(82-84)**	**6,523 (83)**	**(82-84)**
East	1,183	15.0	928 (84)	(81-86)	896 (84)	(81-86)
South-East	1,345	17.1	945 (83)	(81-86)	932 (84)	(81-86)
South-West	3,808	48.4	3,609 (83)	(82-85)	3,534 (84)	(83-85)
Centre	974	12.4	855 (84)	(81-86)	840 (84)	(82-87)
North	565	7.2	497 (74)	(70-78)	481 (75)	(71-79)
Total	**7,875**	**100**	**6,834 (83)**	**(82-84)**	**6,683 (83)**	**(82-84)**

95% CI – confidence interval, C – clarithromycin, M – metronidazole, A – amoxicillin, L – levofloxacin, B – bismuth salts, Tc – tetracycline, R – rifabutin, Mx – moxifloxacin, N – Total number of patients receiving an empirical treatment, Other – Other second-line empirical treatments with less than 100 patients treated in each category; *three-in-one single capsule containing metronidazole tetracycline and bismuth; **achieved over 90% effectiveness when optimised (high-dose PPIs and 14-days length).

P02.13

EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (Hp-EuReg): ANALYSIS OF 2,254 EMPIRICAL RESCUE THERAPIES ON THIRD AND SUBSEQUENT LINES

O. P. NYSSEN[1,2,3], *D. VAIRA*[4,5,6], *I. SARACINO*[4,5,6], *M. PAVONI*[4,5,6], *G. FIORINI*[4,5,6], *Á. PEREZ-AISA*[7,8], *L. JONAITIS*[9], *M. CASTRO-FERNANDEZ*[10], *D. BOLTIN*[11,12], *L. HERNÁNDEZ*[13], *A. GASBARRINI*[14], *D. S. BORDIN*[15,16,17], *J. KUPCINSKAS*[18], *F. LERANG*[19], *A. CANO-CATALÀ*[20], *L. MOREIRA*[3,21,22], *P. PARRA*[1,2,3], *F. MÉGRAUD*[23], *C. O'MORAIN*[24], *J. P. GISBERT*[1,2,3], *ON BEHALF OF THE Hp-EuReg INVESTIGATORS*
[1]Department of Gastroenterology, Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Madrid, Spain; [2]Universidad Autónoma de Madrid (UAM), Madrid, Spain [3]Centro de Investigación Biomédica en Red en Enfermedades Digestivas y Hepáticas (CIBERehd), Madrid, Spain; [4]Department of Medical and Surgical Sciences, IRCCS AOU S. Orsola-Malpighi, University of Bologna, Bologna, Italy; [5]Microbiology Unit, Department of Specialized, Experimental, and Diagnostic Medicine, IRCCS AOU S. Orsola-Malpighi, Bologna, Italy; [6]Cardiovascular Internal Medicine, IRCCS AOU S.Orsola-Malpighi, Bologna, Italy; [7]Digestive Unit, Hospital Costa del Sol, Marbella, Spain; [8]Redes de Investigación Cooperativa Orientada a Resultados en Salud (RICORS), Marbella, Spain; [9]Department of Gastroenterology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [10]Department of Gastroenterology, Hospital de Valme, Seville, Spain; [11]Division of Gastroenterology, Rabin Medical Center, PetahTikva, Israel; [12]Sackler School of Medicine, Tel Aviv University, TelAviv, Israel; [13]Gastroenterology Unit, Hospital Santos Reyes, Aranda de Duero, Spain; [14]Medicina interna e Gastroenterologia, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; [15]Department of Pancreatic, Biliary and Upper Digestive Tract Disorders, A. S. Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation; [16]Department of Propaedeutic of Internal Diseases and Gastroenterology, A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Moscow, Russian Federation; [17]Department of Outpatient Therapy and Family Medicine, Tver State Medical University, Tver, Russian Federation; [18]Institute for Digestive Research and Department of Gastroenterology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [19]Department of Gastroenterology, Østfold Hospital Trust, Grålum, Norway; [20]GOES research group, Althaia, Xarxa Assistencial Universitària de Manresa, Manresa, Spain, [21]Department of Gastroenterology, Hospital Clínic Barcelona, Barcelona, Spain; [22]IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), Barcelona, Spain; [23]INSERM U1312, Université de Bordeaux, Bordeaux, France; [24]School of Medicine, Trinity College Dublin, Dublin, Ireland

Objective: *Helicobacter pylori* treatment's effectiveness decreases as treatment eradication attempts fail. The aim of the study was to evaluate the use and effectiveness of empirical rescue therapies on third and subsequent lines in Europe.
Patients and Methods: Sub-study of the European Registry on *H. pylori* Management (Hp-EuReg), an international, prospective, registry by European gastroenterologists, registering infected adult patients at AEG-REDCap e-CRF until January 2023. All cases with three or more eradication attempts were extracted. Only the empirically prescribed therapies were analysed. Data were subject to quality review.
Results: Overall, 2,254 rescue treatments were included: 1,624, 424, 150 and 56 in third-, fourth-, fifth- and sixth-line treatment, respectively. Sixty-three different regimens were used, being three-in-one single-capsule bismuth quadruple therapy the most commonly prescribed, as shown in the table. Overall effectiveness was 73% by modified intention-to-treat (mITT), and 74% by per-protocol (PP) analyses. Bismuth quadruple therapy as single-capsule provided the highest mITT cure rate (86%). One regimen achieved an optimal eradication rate (≥90%, by mITT): quadruple PPI-bismuth-tetracycline-metronida-

zole, only when high-dose PPIs and 14 days prescriptions were used. The use of doxycycline instead of tetracycline was associated with lower eradication rates in classical bismuth quadruple therapies (p<0.05). ***Conclusions:*** Empirical rescue treatments in third and subsequent lines obtain, in general, suboptimal eradication rates in Europe; however, bismuth quadruple therapy as a single-capsule obtained encouraging results. Only the optimised bismuth quadruple therapy with tetracycline-metronidazole achieved ≥90% effectiveness.

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TABLE 1. OVERALL ERADICATION RATES OF THE MOST PRESCRIBED EMPIRICAL THERAPIES ON THIRD AND SUBSEQUENT LINES.

		Modified intention-to-treat		Per-protocol	
Rescue therapy	Use, N (%)	n	Effectiveness (95% CI)	n	Effectiveness (95% CI)
PPI-Single capsule B-Tc-M	633 (28%)	588	86 (83-89)	566	88 (85-90)
Triple PPI-A-L	253 (11%)	194	77 (71-83)	193	77 (70-83)
Quadruple PPI-A-L-B	202 (9.0%)	182	72 (66-79)	176	74 (67-81)
Quadruple PPI-B-Tc-M	182 (8.1%)	176	74 (68-81)	171	74 (67-81)
Triple PPI-A-R	128 (5.7%)	108	59 (50-69)	104	61.5 (52-71)
Quadruple PPI-C-A-M	117 (5.2%)	109	62 (53-72)	106	63 (54-73)
Quadruple PPI-B-D-M	115 (5.1%)	112	62 (52-71)	108	62 (52-72)
Triple PPI-C-A	51 (2.3%)	43	56 (40-72)	41	56 (40-73)
Triple PPI-A-M	47 (2.1%)	44	59 (43-75)	42	59.5 (43-76)

A, amoxicillin; B, bismuth; C, clarithromycin; D, doxycycline; L, levofloxacin; M, metronidazole; Tc, tetracycline; R, rifabutin; CI, confidence interval.

POSTER SESSION 03: HELICOBACTER 3

P03.01

SIXTH-LINE ERADICATION THERAPY AGAINST *HELICOBACTER PYLORI* INFECTION: PRELIMINARY DATA FROM THE EUROPEAN REGISTRY ON THE MANAGEMENT OF *HELICOBACTER PYLORI* INFECTION (Hp-EuReg)

O. P. NYSSEN[1], *A. GARRE*[1], *G. FIORINI*[2], *I. SARACINO*[2], *M. PAVONI*[2], *D. VAIRA*[2], *P. S. PHULL*[3], *I. L. P. BEALES*[4], *A. GASBARRINI*[5], *A. CANO-CATALÀ*[6], *L. MOREIRA*[7], *P. PARRA*[1], *F. MÉGRAUD*[8], *C. O'MORAIN*[9], *J. P. GISBERT*[1], *ON BEHALF OF THE Hp-EuReg INVESTIGATORS*

[1]Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain; [2]IRCCS AOU S. Orsola-Malpighi, University of Bologna, Bologna, Italy; [3]Department of Digestive Disorders, Aberdeen Royal Infirmary, Aberdeen, United Kingdom; [4]Norwich Medical School, University of East Anglia, Norwich, United Kingdom; [5]Medicina Interna e Gastroenterologia, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; [6]GOES research group, Althaia Xarxa Assistencial Universitària de Manresa, Manresa, Spain; [7]Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), University of Barcelona, Barcelona, Spain; [8]INSERM U1312, Université de Bordeaux, Bordeaux, France; [9]Trinity College Dublin, Dublin, Ireland

Objective: *Helicobacter pylori* infection can remain after several eradication attempts. The objective was to evaluate the effectiveness of the sixth-line rescue treatment in Europe.
Patients and Methods: Prospective registry on the clinical management of *H. pylori* infection (Hp-EuReg). All cases with six eradication attempts registered in AEG-REDCap up to December 2022 were evaluated for effectiveness [by modified intention-to-treat (mITT) and per-protocol (PP) analyses].
Results: Overall, 81 patients were included, mainly from Spain (44% of cases), Italy (26%) and the United Kingdom (17%). Culture was performed in 26 cases (32%), of which: 13 (50%) had bacterial antibiotic resistance to clarithromycin, 12 (46%) to nitroimidazole, and 8 (31%) to quinolones. In addition, 8 (35%) patients had dual resistance (both to clarithromycin and metronidazole) and 7 (27%) triple resistance (also to levofloxacin). Twenty-two different therapeutic combinations were used, most of them prescribed for 14 days (57%) and with low-dose (39%) PPIs. The most frequent treatments were: single-capsule bismuth-quadruple with tetracycline-metronidazole (17%), triple amoxicillin-rifabutin (15%), quadruple bismuth-furazolidone-amoxicillin (11%), triple amoxicillin-levofloxacin (7.4%), and classical quadruple bismuth-tetracycline-metronidazole (6.2%). The highest eradication rates (mITT) were achieved with single-capsule (77%) and with the quadruple therapy with bismuth-furazolidone-amoxicillin (67%). Overall mITT/PP effectiveness was 53% (Table 1).
Conclusions: Sixth-line eradication treatments in Europe obtain suboptimal eradication rates. The only therapies that reach acceptable outcomes are the bismuth quadruple therapies with either tetracycline-metronidazole (single-capsule) or with furazolidone-amoxicillin.

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TABLE 1. PRESCRIPTIONS, EFFECTIVENESS, TOLERANCE AND COMPLIANCE IN SIXTH-LINE TREATMENTS AGAINST *HELICOBACTER PYLORI* INFECTION.

Use of antibiotics (or bismuth) in any of the previous treatments (1st to 5th line), n (%)	**Misuse of same antibiotic in 6th line, n (%)**	
Clarithromycin	79 (96)	12 (15)
Amoxicillin	79 (96)	NA
Metronidazole/tinidazole	75 (92)	19 (25)
Levofloxacin/moxifloxacin	61 (74)	11 (18)
Rifabutin	72 (88)	NA
Tetracycline/doxycycline	45 (55)	NA
Bismuth	40 (49)	NA
Duration of previous eradication lines (1st to 5th line)	**Median**	**Interquartile range**
1st line	8.5	7-10
2nd line	10	7-10
3rd line	10	7-10
4th line	10	7-14
5th line	10	7-14
***Most frequent 6th line prescriptions**	**n (%)**	**Effectiveness % mITT (95% CI)**
[1]Single-capsule+PPI	14 (17)	77 (46-95)
Triple-PPI+A+R	12 (15)	50 (19-81)
Quadruple- PPI+B+A+F	9 (11)	67 (30-92)
Triple-PPI+A+L	6 (7.4)	40 (5.2-85)
Quadruple-PPI+M+Tc+B	5 (6.2)	40 (5.3-85)
Dual-PPI+A	5 (6.2)	20 (0.5-72)
Triple-PPI+A+B	5 (6.2)	20 (0.5-72)
Quadruple-PPI+C+A+M	5 (6.2)	20 (0.5-72)
Other-PPI+C+A+M+B	4 (4.9)	50 (6.7-93)

Continued

TABLE 1 *(Continued)*. PRESCRIPTIONS, EFFECTIVENESS, TOLERANCE AND COMPLIANCE IN SIXTH-LINE TREATMENTS AGAINST *HELICOBACTER PYLORI* INFECTION.

Duration of 6th line prescriptions	**Median**	**Interquartile range**
	14	10-14
	n (%)	
7 days	2 (2.6)	
10 days	25 (37)	
14 days	40 (57)	
[2]PPI doses in 6th line prescriptions	**n (%)**	
Low	42 (57)	
Standard	3 (4.1)	
High	29 (39)	
Use of probiotics, n (%)	23 (28)	
Overall effectiveness	**n (%)**	
mITT	76 (53)	
PP	74 (53)	
Incidence of at least one adverse event, n (%)	19 (24)	
Compliance, n (%)	**74 (94)**	

*The most frequent treatments represent 80% of the total 6th line prescriptions; mITT, modified intention-to-treat; PP, per-protocol; n, number of patients treated; CI: confidence interval; A, amoxicillin; B, bismuth; C, clarithromycin; L, levofloxacin; M, metronidazole; Tc, tetracycline hydrochloride; R, rifabutin; 1Quadruple therapy-M+Tc+B as a single-capsule; NA, not applicable; PPI, proton pump inhibitor; 2low doses: 4.5-27 mg; standard doses: 32-40 mg; high doses: 54-128 mg, all omeprazole equivalent 2 times a day.

P03.04

EFFECTIVENESS OF *HELICOBACTER PYLORI* TREATMENTS ACCORDING TO ANTIBIOTIC RESISTANCE: RESULTS FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (Hp-EuReg).

L. BUJANDA[1], *O. P. NYSSEN*[2], *J. RAMOS*[1], *D. S. BORDIN*[3], *B. TEPES*[4], *Á. PEREZ-AISA*[5], *M. PAVONI*[6], *M. CASTRO-FERNANDEZ*[7], *F. LERANG*[8], *M. LEJA*[9], *L. RODRIGO*[10], *T. ROKKAS*[11], *J. KUPCINSKAS*[12], *A. CANO-CATALÀ*[13], *L. HERNÁNDEZ*[14], *L. MOREIRA*[15], *P. PARRA*[2], *F. MÉGRAUD*[16], *C. O'MORAIN*[17], *J. P. GISBERT*[2], *ON BEHALF OF THE Hp-EuReg INVESTIGATORS*

[1]Departmento of Gastroenterology, Biodonostia Health Research Institute, Centro de Investi-gación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Department of Medicine, Universidad del País Vasco (UPV/EHU), San Sebastián, Spain; [2]Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Di-gestivas (CIBERehd), Madrid, Spain; [3]Department of Pancreatic, Biliary and upper digestive tract disorders, A. S. Loginov Moscow Clinical Scientific Center, Tver State Medical University, A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Moscow, Russian Federation; [4]Department of Gastroenterology, AM DC Rogaska, Rogaska Slatina, Slovenia; [5]Digestive Unit, Hospital Costa del Sol Marbella, Redes de Investigación Cooperativa orientada a resultados en salud (RICORS), Málaga, Spain; [6]IRCCS AOU S. Orsola-Malpighi, University of Bologna, Bologna, It-aly; [7]Department of Gastroenterology, Hospital de Valme, Seville, Spain; [8]Department of Gastro-enterology, Østfold Hospital Trust, Grålum, Norway; [9]Department of Gastroenterology, Digestive Diseases Centre, Institute of Clinical and Preventive Medicine & Faculty of Medicine, University of Latvia, Riga, Latvia; [10]Department of Gastroenterology, University of Oviedo, Oviedo, Spain; [11]Gastroenterology Clinic, Henry Dunant Hospital, Athens, Greece; [12]Institute for Digestive Re-search and Department of Gastroenterology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [13]GOES research group, Althaia Xarxa Assistencial Universitària de Manresa, Manresa, Spain; [14]Unidad de Gastroenterología, Hospital Santos Reyes, Aranda de Duero, Spain; [15]Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), Univer-sity of Barcelona, Barcelona, Spain; [16]INSERM U1312, Université de Bordeaux, Bordeaux, France; [17]Trinity College Dublin, Dublin, Ireland

Objective: Antibiotic resistance is the main factor that determines the efficacy of treatments to eradicate *Helicobacter pylori* infection. The aim of the study was to evaluate the effectiveness of first-line and rescue treatment against *H. pylori* in Europe according to the resistance to different antibiotics.
Patients and Methods: Prospective, multicentre, international, non-interventionist registry on the management of *H. pylori* (Hp-EuReg) by European gastroenterologists. All infected and culture-diag-nosed adult patients registered in AEG-REDCap e-CRD were included. Therapeutic effectiveness analysis was performed per-protocol.
Results: Overall, 2,852 naïve patients with culture results were analysed. Resistance to clarithromycin, metronidazole and quinolones was 22%, 27% and 18%, respectively. The most effective treatment, regardless of resistance, was the single-capsule with bismuth-metronidazole-tetracycline, offering optimal cure rates even in the presence of bacterial resistance to clarithromycin (93%) or metronidazole (91%). Triple schedules with clarithromycin-amoxicillin, metronidazole-amoxicillin or sequential quadruple therapy with metronidazole did not achieve optimal results (Table 1). Additionally, 1,118 non-naïve patients reported resistance to clarithromycin (49%), metronidazole (41%) and quinolones (24%). None of the rescue treatments achieved optimal effectiveness; however, the highest was reported with the triple therapy with amoxicillin-levofloxacin (87%, 345/397) followed by the single-capsule (86%, 206/244).

Conclusions: In regions with high antibiotic resistance, eradication treatment with the single-capsule, the bismuth quadruple therapy and the concomitant treatment with tinidazole were the best options in first-line. In non-naïve patients, the single-capsule and the triple therapy with levofloxacin provided encouraging results.

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TABLE 1. PER-PROTOCOL EFFECTIVENESS IN NAÏVE PATIENTS WITH RESISTANCE TO CLARITHROMYCIN, METRONIDAZOLE AND LEVOFLOXACIN.

Most frequent 1st line treatments	Patients sensitive to all antibiotics		Clarithromycin resistance		Metronidazole resistance		Levofloxacin resistance	
	Nº patients	Eradication	Nº patients	Eradication	Nº patients	Eradication	Nº patients	Eradication
Sequential-PPI+C+A+T	556	526 (95%)	311	271 (87%)	351	314 (89%)	316	293 (93%)
Triple-PPI+A+C	270	255 (94%)	12	9 (75%)	166	146 (88%)	47	39 (83%)
Triple-PPI+A+M	185	163 (88%)	30	24 (80%)	NA	NA	NA	NA
Triple-PPI+A+L	1	1 (100%)	25	59 (88%)	49	44 (90%)	2	2 (100%)
Concomitant-PPI+C+A+ T/M	71	68 (96%)	50	43 (86%)	45	39 (87%)	32	30 (94%)
PPI+single capsule†	42	42 (100%)	58	54 (93%)	44	40 (91%)	13	9 (69%)
Quadruple-PPI+C+A+ B	17	16 (94%)	10	9 (90%)	17	16 (94%)	45	43 (96%)

†Three-in-one single-capsule containing bismuth, tetracycline and metronidazole. A, amoxicillin; B, bismuth salts; C, clarithromycin; L, levofloxacin; M, metronidazole; PPI, proton pump inhibitor; T, tinidazole; Tc, tetracycline. NA: not available.

P03.06

EXPERIENCE WITH SINGLE-CAPSULE BISMUTH QUADRUPLE THERAPY IN 8,000 PATIENTS FROM THE EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (Hp-EuReg)

O. P. NYSSEN[1,2,3], *P. PARRA*[1,2,3], *Á. PÉREZ-AÍSA*[4,5], *M. CASTRO-FERNANDEZ*[6], *M. PABÓN-CARRASCO*[6], *A. KECO-HUERGA*[6], *L. RODRIGO*[7], *Á. LANAS*[8], *S. J. MARTÍNEZ-DOMÍNGUEZ*[8,9], *E. ALFARO*[8], *A. J. LUCENDO*[1,3,10], *A. GASBARRINI*[11], *L. HERNÁNDEZ*[12], *R. MARCOS-PINTO*[13,14,15], *W. MARLICZ*[16,17], *A. CANO-CATALÀ*[18], *L. MOREIRA*[3,19,20], *F. MÉGRAUD*[21], *C. O'MORAIN*[22], *J. P. GISBERT*[1,2,3], *ON BEHALF OF THE Hp-EuReg INVESTIGATORS*

[1]Department of Gastroenterology, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Madrid, Spain; [2]Universidad Autónoma de Madrid (UAM), Madrid, Spain; [3]Centro de Investigación Biomédica en Red en Enfermedades Digestivas y Hepáticas (CIBERehd), Madrid, Spain; [4]Digestive Unit, Hospital Costa del Sol, Marbella, Spain; [5]Redes de Investigación Cooperativa Orientada a Resultados en Salud (RICORS), Marbella, Spain, [6]Department of Gastroenterology, Hospital de Valme, Seville, Spain; [7]Department of Gastroenterology, University of Oviedo, Oviedo, Spain; [8]Servicio de Aparato Digestivo, Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain; [9]Instituto de Investigación Sanitaria de Aragón (IIS Aragón), Zaragoza, Spain; [10]Department of Gastroenterology, Hospital General de Tomelloso, Tomelloso, Spain; [11]Medicina interna e Gastroenterologia, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; [12]Gastroenterology Unit, Hospital Santos Reyes, Aranda de Duero, Spain; [13]Gastroenterology Department, Centro Hospitalar do Porto, Porto, Portugal; [14]Instituto De Ciências Biomédicas de Abel Salazar, Universidade do Porto, Porto, Portugal; [15]Center for Research in Health Technologies and Information Systems (CINTESIS), Porto, Portugal; [16]Department of Gastroenterology, Pomeranian Medical University in Szczecin, Szczecin, Poland; [17]The Centre for Digestive Diseases, Endoklinika, Szczecin, Poland; [18]GOES research group, Althaia, Xarxa Assistencial Universitària de Manresa, Manresa, Spain; [19]Department of Gastroenterology, Hospital Clínic Barcelona, Barcelona, Spain; [20]IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), Barcelona, Spain; [21]INSERM U1312, Université de Bordeaux, Bordeaux, France; [22]School of Medicine, Trinity College Dublin, Dublin, Ireland

Objective: There has been a resurgence in the use of bismuth-quadruple therapy (PPI, bismuth, tetracycline and metronidazole) in Europe with the commercialization of a three-in-one single-capsule formulation, but the evidence is still limited. The aim of the study was to evaluate the effectiveness and safety of the three-in-one single-capsule in the European Registry on *Helicobacter pylori* management (Hp-EuReg).

Patients and Methods: Multicentre, prospective registry evaluating infected adult patients treated with 10-day single-capsule according to data sheet (3 capsules/6h) or alternative three times a day (4 capsules/8h) prescriptions and registered at AEG-REDCap e-CRF until January 2023. Modified intention-to-treat (mITT) and per-protocol (PP) analyses were performed.

Results: Overall, 8,302 (14%) received single-capsule bismuth-quadruple therapy achieving a high eradication rate based on the mITT (91.5%) and PP (92%) analyses, especially in first-line treatment (93%), but it also had high effectiveness as rescue therapy, both in second-line (87%) or subsequent lines of therapy (3rd-6th lines: 86%) (Table 1). Compliance with treatment was reported in 93% of cases and was the factor most closely associated with effectiveness. Adverse events (26%) were mild-to-moderate and transient; only 0.1% of patients reported a serious adverse event, leading to treatment discontinuation in 1.7% of patients.

Conclusions: The 10-day treatment with single-capsule bismuth-quadruple therapy achieves *H. pylori* eradication in approximately 90% of patients by mITT in real-world clinical practice, both as a first-line and rescue treatment, with a favorable safety profile.

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TABLE 1. THREE-IN-ONE SINGLE-CAPSULE EFFECTIVENESS IN FIRST-LINE AND CONSECUTIVE RESCUE TREATMENT LINES.

Use, N (%)	mITT, N (%)	95% CI	PP, N (%)	95% CI	
Overall	8,302 (14*)	7,729 (91)	(91-92)	7573 (92)	(92-93)
1st line (naïve)	6,227 (75)	5,797 (93)	(92-94)	5,696 (94)	(93-94)
2nd line	1,441(17)	1,344 (87)	(85-89)	1,311 (88)	(86-90)
3rd line	504 (6.1)	472 (88)	(85-91)	456 (89)	(86-92)
Rescue (3rd to 6th line)	633 (7.6)	588 (86)	(83-89)	566 (88)	(85-90)

*Of the total of treatments included in the Hp-EuReg up to January 2023 (i.e., N= 59,689); mITT: modified intention-to-treat; PP: per-protocol, N: total number of patients analysed.

P03.08

CLINICAL PHENOTYPES THROUGH *MACHINE LEARNING* OF FIRST-LINE TREATED PATIENTS DURING THE PERIOD 2013-2022: DATA FROM THE EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (Hp-EuReg)

O. P. NYSSEN[1], *M. SPINOLA*[2], *P. PRATESI*[3], *G. J. ORTEGA*[2], *L. JONAITIS*[4], *Á. PÉREZ-AÍSA*[5], *D. VAIRA*[6], *G. FIORINI*[6], *B. TEPES*[7], *D. S. BORDIN*[8], *M. LEJA*[9], *F. LERANG*[10], *A. TONKIC*[11], *H. SIMSEK*[12], *A. CANO-CATALÀ*[13], *L. MOREIRA*[14], *P. PARRA*[1], *F. MÉGRAUD*[15], *C. O'MORAIN*[16], *J. P. GISBERT*[1], *ON BEHALF OF THE Hp-EuReg INVESTIGATORS*

[1]Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain; [2]Instituto de Investigaciones Sanitarias Hospital Universitario de la Princesa, Madrid, Spain; [3]Dipartimento di Statistica e Metodi Quantitativi, Universitá degli studi di Milano-Bicocca, Milano, Italy; [4]Department of Gastroenterology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [5]Digestive Unit, Hospital Costa del Sol Marbella, Redes de Investigación Cooperativa orientada a resultados en salud (RICORS), Málaga, Spain; [6]IRCCS AOU S. Orsola-Malpighi, University of Bologna, Bologna, Italy; [7]Department of Gastroenterology, AM DC Rogaska, Rogaska Slatina, Slovenia; [8]Department of Pancreatic, Biliary and Upper Digestive Tract Disorders, A. S. Loginov Moscow Clinical Scientific Center, Tver State Medical University, A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Moscow, Russian Federation; [9]Department of Gastroenterology, Digestive Diseases Centre, Institute of Clinical and Preventive Medicine & Faculty of Medicine, University of Latvia, Riga, Latvia; [10]Department of Gastroenterology, Østfold Hospital Trust, Grålum, Norway; [11]Department of Gastroenterology, University Hospital of Split, University of Split School of Medicine, Split, Croatia; [12]Department of Gastroenterology, Hacettepe University, Department of Gastroenterology, HC International Clinic, Ankara, Turkey; [13]GOES Research Group, Althaia Xarxa Assistencial Universitària de Manresa, Manresa, Spain; [14]Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), University of Barcelona, Barcelona, Spain; [15]INSERM U1312, Université de Bordeaux, Bordeaux, France, [16]School of Medicine, Trinity College Dublin, Dublin, Ireland

Objective: The segmentation of patients in homogeneous groups, could help to improve the effectiveness of current eradication therapies. The objectives of the study were: 1) to determine the most important characteristics of the treatments used in the European Registry on *H. pylori* (Hp-EuReg), using machine learning; 2) to evaluate the treatment effectiveness according to the year -visit and country using cluster decomposition.

Materials and Methods: Systematic prospective registry of the clinical practice of European gastroenterologists (Hp-EuReg). All first-line empirical treatments registered from June 2013 to December 2022 were included in the analysis. *Boruta,* a random-forest-like method, was used to determine the 'most important' variables: compliance, duration of treatment, PPI dosage, patient's country, and treatment scheme.

Results: Overall, 35,852 European patients were analysed. Table 1 shows the average treatments' effectiveness raised from 87% in 2013 to 93% in 2022 (>100 patients/clusters). The cluster 3 in 2016 (lowest effectiveness) was composed of 97.5% triple therapy with clarithromycin-amoxicillin/metronidazole, mainly in Slovenia (54%), 85% of 7-day prescriptions, and 99% compliance. The highest effectiveness was obtained in cluster #1 in 2022, with 81% of Spanish cases, 32% of concomitant therapy with clarithromycin-amoxicillin-metronidazole/tinidazole and 63% of bismuth quadruple therapy with tetracycline-metronidazole (single-capsule), 69% of 10 days, and 32% of 14 days prescriptions.

Conclusions: Cluster analysis allowed both to identify patients with homogeneous treatment groups, to assess the different first-line treatments effectiveness, compliance, region, and prescription year.

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TABLE 1. TRENDS IN THE OVERALL EFFECTIVENESS (BY MODIFIED INTENTION-TO-TREAT, PER CLUSTER) BETWEEN 2013 AND 2022 IN EUROPE.

year	# of clusters (# of patients)	Effectiveness % (number of patients) per cluster		
		1	2	3
2013	3 (3,239)	85.2 (1,491)	90.2 (440)	85.2 (1,308)
2014	3 (4,292)	88.5 (433)	86.1 (2,706)	85 (1,153)
2015	3 (3,693)	88.9 (351)	86.5 (2,913)	85.8 (429)
2016	3 (4,350)	91.4 (1,655)	88.1 (2,084)	80.2 (611)
2017	3 (3,665)	84 (1,629)	91.4 (1,741)	85.1 (295)
2018	3 (3,668)	89.5 (2,181)	91.8 (1,171)	92.1 (316)
2019	3 (3,695)	89.1 (2,133)	88.6 (1,324)	92.3 (238)
2020	3 (3,092)	92.9 (198)	85.4 (1,573)	89.9 (1,321)
2021	3 (4,018)	85.8 (246)	91 (1,886)	80.6 (1,886)
2022	3 (2,140)	95.4 (936)	93 (128)	91.6 (1,076)

Simple underlining highlights the lowest effectiveness in clusters/year with more than 100 patients, and double underlining the highest effectiveness.

P04.07

TIME TRENDS AND EFFECTIVENESS OF BISMUTH TREATMENT FOR *HELICOBACTER PYLORI* INFECTION: RESULTS FROM THE EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (Hp-EuReg) DURING 2013-2021

*L. OLMEDO[1,2,3], **X. CALVET**[4,5,6], E. GENÉ[7,8,6], D. S. BORDIN[9,10,11], I. VOYNOVAN[12], M. CASTRO-FERNANDEZ[13], M. PABÓN-CARRASCO[13], A. KECO-HUERGA[13], Á. PÉREZ-AÍSA[14], L. HERNÁNDEZ[15], O. GRIDNYEV[16], J. KUPČINSKAS[17], A. GASBARRINI[18], A. CANO-CATALÀ[3], L. MOREIRA[19,20,6], P. PARRA[21,6], O. P. NYSSEN[21,6], F. MÉGRAUD[22], C. O'MORAIN[23], J. P. GISBERT[21,6]*

[1]Departament de Medicina, Universitat Internacional de Catalunya, Sant Cugat dl Vallès, Spain; [2]ABS Manresa 3, Althaia, Xarxa Assistencial Universitària de Manresa, Manresa, Spain; [3]GOES research group, Althaia, Xarxa Assistencial Universitària de Manresa, Manresa, Spain; [4]Unitat de Malalties Digestives, Hospital Universitari Parc Taulí, Institut d'Investigació i Innovació Parc Taulí I3PT, Sabadell, Spain; [5]Departament de Medicina, Universitat Autònoma de Barcelona, Sabadell, Spain; [6]Centro de Investigación Biomédica en Red en Enfermedades Digestivas y Hepáticas (CIBERehd), Madrid, Spain; [7]Departament de Medicina, Universitat Internacional de Catalunya, Sant Cugat dl Vallès, Spain; [8]Servei d'Urgències, Hospital Universitari Parc Taulí, Institut d'Investigació i Innovació Parc Taulí I3PT, Sabadell, Spain; [9]Department of Pancreatic, Biliary and Upper Digestive Tract Disorders, A. S. Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation; [10]Department of Outpatient Therapy and Family Medicine, Tver State Medical University, Moscow, Russian Federation; [11]Department of Propaedeutic of Internal Diseases and Gastroenterology, A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Moscow, Russian Federation; [12]Department of Gastroenterology, A.S. Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation; [13]Ap.Digestivo, Hospital Universitario de Valme, Sevilla, Spain; [14]7Digestive Unit, Hospital Costa del Sol, Redes de Investigación Cooperativa Orientada a Resultados en Salud (RICORS), Marbella, Spain; [15]Gastroenterology Unit, Hospital Santos Reyes, Aranda de Duero, Spain; [16]Departmens the Dicision fon the Atudy of the Degestive diseases and its Comorbidity with Noncommunicable Diseases, Government Institution L.T. Malaya Therapy National Institute of NAMS of Ukraine, Kharkiv, Ukraine; [17]Institute for Digestive Research and Department of Gastroenterology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [18]Medicina interna e Gastroenterologia, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italy; [19]Department of Gastroenterology, Hospital Clínic Barcelona, Barcelona, Spain; [20]IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), Barcelona, Spain; [21]Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), Madrid, Spain; [22]15INSERM U1312, Université de Bordeaux, Bordeaux, France; [23]School of Medicine, Trinity College Dublin, Dublin, Ireland

Objective: Bismuth quadruple therapy (BQT) including bismuth, a proton pump inhibitor (PPI) and two antibiotics has provided optimal effectiveness even in areas with high bacterial antibiotic resistance. The aim of the study was to describe the use, effectiveness, and safety of BQT in Europe and evolution as part of the European Registry on *Helicobacter pylori* management (Hp-EuReg).

Materials and Methods: Prospective, multicentre registry on *H. pylori* clinical management (Hp-EuReg). Data were registered at AEG-REDCap e-CRF until 2021 and evaluated for effectiveness by modified-intention-to-treat (mITT) analysis. Time-trend, geographical (east, southeast, south-west, centre and north) and multivariate analyses were also performed.

Results: Of the 49,690 patients included in the Hp-EuReg, 15,582 (31%) had received BQT. BQT use increased from 8.6% (2013) to 39% (2021). BQT prescribed as three-in-one-single-capsule containing metronidazole-tetracycline-bismuth plus PPI (ScBQT) was the most frequently used (43%). In naïve patients, over 90% overall effectiveness was obtained with: PPI-clarithromycin-amoxicillin-bismuth (PPI-CAB), PPI-metronidazole-amoxicillin-bismuth (PPI-MAB), PPI-metronidazole-tetracycline-bismuth (PPI-MTB) and ScBQT, this latter achieving optimal cure rates in each of the geographical areas. Standard- or high-dose PPIs, 10- or 14-day prescriptions as well as the treatment schedule (ScBQT, PPI-CAB, PPI-MTB), were significantly associated with higher cure rates in the multivariate analysis (Table 1).

Conclusions: In Europe, the use of BQT has markedly increased in the last decade, with 10-day ScBQT and 14-day BQT achieving both an effectiveness over 90% in most geographical areas.

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TABLE 1. PREDICTIVE FACTORS OF TREATMENT EFFECTIVENESS IN MULTIVARIATE ANALYSIS.

Variable	OR	95% CI	*p*-value	
lower	upper			
PPI dose (R: low dose)*	1.25	1.17	1.33	<0.0001
Duration of treatment (R: 7 days)**	1.36	1.25	1.48	<0.0001
Rescue therapy (R: naïve)***	0.62	0.54	0.68	<0.0001
Gender (R: female)****	1.19	1.07	1.32	0.001
European region	0.89	0.85	0.94	<0.0001
ScBQT	2.18	1.90	2.50	<0.0001
PPI-CAB	1.31	1.11	1.56	0.002
PPI-MTB	1.50	1.05	2.14	0.024

OR: odds ratio; CI: confidence interval; PPI: proton pump inhibitor; R: category of reference used for the logistic regression ; *low-dose PPI: 4.5-27 mg, standard-dose PPI 32-40 mg, high-dose PPI 54-128 mg; **Duration of treatment: 7, 10, 14 days; ***Rescue therapy: from 1st to 6th line; **** Gender: female, male; European region: south-west, east, south-east, centre, north; ScBQT: single-capsule containing bismuth, tetracycline, and metronidazole; A: amoxicillin; B: bismuth salts; C: clarithromycin; M: metronidazole; T: tetracycline.

P05.06

ROLE OF PROTON PUMP INHIBITORS DOSAGE IN THE EFFECTIVENESS OF *HELICOBACTER PYLORI* ERADICATION TREATMENTS: RESULTS FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (Hp-EuReg).

O. P. NYSSEN[1], *M. PABÓN-CARRASCO*[2], *A. KECO-HUERGA*[2], *M. CASTRO-FERNANDEZ*[2], *G. FIORINI*[3], *A. PEREZ-AISA*[4], *B. TEPES*[5], *A. LUCENDO*[6], *A. LANAS*[7], *L. RODRIGO*[8], *L. VOLOGZANINA*[9], *N. BRGLEZ JURECIC*[10], *L. BUJANDA*[11], *J. HUGUET*[12], *L. FERNANDEZ-SALAZAR*[13], *A. CANO-CATALÀ*[14], *L. MOREIRA*[15], *F. MÉGRAUD*[16], *C. O'MORAIN*[17], *J. P. GISBERT*[1], *ON BEHALF OF THE Hp-EuReg INVESTIGATORS*

[1]Servicio Aparato Digestivo, Hospital Universitario de La Princesa, Universidad Autónoma de Madrid (UAM), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas(CIBERehd), Madrid, Spain; [2]Department Gastroenterology. Hospital de Valme, Sevilla, Spain; [3]Department of Surgical and Medical Sciences, IRCCS S. Orsola, University of Bologna, Bologna, Italy; [4]Agencia Sanitaria Costa del Sol, Red de Investigación en Servicios de Salud en Enfermedades Crónicas (REDISSEC), Marbella, Spain; [5]Department of Gastroenterology, AM DC Rogaska, Rogasta Slatina, Slovenia; [6]Department of Gastroenterology, Hospital General de Tomelloso, Tomelloso, Spain; [7]Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain; [8]Gastroenterology Unit, Hospital Universitario Central de Asturias, Oviedo, Spain; [9]Department of Gastroenterology, Gastrocentr, Perm, Russian Federation; [10]Department of Gastroenterology, Interni Oddelek, Diagnostic Centre, Bled, Slovenia; [11]Hospital Donostia, Instituto Biodonostia, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Universidad del País Vasco (UPV/EHU), San Sebastian, Spain; [12]Patología Digestiva, Hospital General Universitario de Valencia, Valencia, Spain; [13]Gastroenterology Department, Hospital Clínico Universitario de Valladolid (SACYL), Valladolid, Spain; [14]GOES research group, Althaia Xarxa Assistencial Universitària de Manresa, Manresa, Spain; [15]Department of Gastroenterology, Hospital Clínic Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBEREHD), IDIBAPS (In-stitut d'Investigacions Biomèdiques August Pi i Sunyer), University of Barcelona, Barcelona, Spain; [16]INSERM U1312, Université de Bordeaux, Bordeaux, France; [17]Faculty of Health Sciences, Trinity College Dublin, Dublin, Ireland

Objective: High doses of proton pump inhibitors (PPIs) increase the effectiveness of classical triple therapy and probably also of currently recommended quadruple therapies.
The aim of the study was to evaluate the role of PPIs dosage in the effectiveness of the most common first- and second-line treatments in Europe.
Patients and Methods: Multicenter, prospective registry evaluating the decisions and outcomes of *Helicobacter pylori* management by European gastroenterologists. The dose of PPI (omeprazole, lansoprazole, pantoprazole, rabeprazole, or esomeprazole) every 12 hours was classified as: high (54-128 mg omeprazole equivalent [OE]), standard (33-40 mg OE) and low (4.5-27 mg OE). Analysis was performed by modified intention-to-treat.
Results: A total of 36,579 cases were analysed. Optimum effectiveness (~90%) was obtained in first line with all 10- or 14-day therapies with high-dose PPIs and with the bismuth quadruple therapies with standard doses. In second line was obtained with high doses of PPIs with triple therapy with levofloxacin and amoxicillin for 14 days and with the classical quadruple with bismuth for 10 and 14 days (Table 1).

Conclusions: In the first line of treatment, high doses of PPIs are advisable in the quadruple concomitant therapy, while low doses are sufficient in the classical quadruple with bismuth. In second line, high doses of PPIs are advisable in triple therapy with levofloxacin and amoxicillin for 14 days, while standard doses are sufficient in the 14-day classical quadruple with bismuth.

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TABLE 1. EFFECTIVENESS BY MODIFIED INTENTION-TO-TREAT (MITT) IN FIRST AND SECOND-LINE ACCORDING TO THE DURATION AND THE PPI DOSE.

		First-line treatment effectiveness accordind to the duration and the PPI dose. n/N(%)-mITT			
		Low-dose PPI	**Standard-dose PPI**	**High-dose PPI**	***p*-value**
10 days	Triple IBP-C+M/ A	1277/1634 (78)	1088/1261 (86)	417/466 (90)	0.0001
N: 12,214	QuadruplesequentialIBP-C+A+M	981/1112 (88)	48/51 (94)	603/647 (93)	0.002
(55.3%)	QuadrupleconcomitantIBP-C+A+M	1262/1437 (88)	507/580 (87)	440/476 (92)	0.013
	Quadruple with bismuthIBP-C+A+B	200/233 (86)	213/235 (91)	93/101 (93)	0.137
	Quadruple with bismuthIBP-M+T+B	1533/1683 (91)	865/917 (94)	1300/1371 (95)	0.0001
14 days	Triple IBP-C+M/ A	426/528 (81)	758/850 (89)	1273/1391 (92)	0.0001
N: 7,782	QuadrupleconcomitantIBP-C+A+M	597/702 (85)	385/429 (90)	1573/1685 (93)	0.0001
(35.2%)	Quadruple with bismuthIBP-C+A+B	165/180 (92)	797/859 (93)	969/1067 (91)	0.299
	Quadruple with bismuthIBP-M+T+B	18/20 (90)	55/59 (93)	11/12 (92)	0.893
		Second-line treatment effectiveness according to the duration and the PPI dose. n/N (%)-mITT			
		Low-dose PPI	**Standard-dose PPI**	**High-dose PPI**	***p*-value**
10 days	Triple IBP-L+A	366/497 (84)	199/256 (78)	178/213 (84)	0.015
N: 2,203	QuadrupleconcomitantIBP-C+A+M	58/79 (73)	15/18 (83)	54/69 (78)	0.605
(54.9%)	Quadruple with bismuth IBP-L+A+B	12/14 (86)	7/9 (78)	3/3 (100)	0.643
	Quadruple with bismuthIBP-M+T+B	404/467 (87)	169/191 (89)	357/387 (92)	0.028
14 days	Triple IBP-L+A	45/57 (79)	35/43 (81)	318/341 (93)	0.0001
N: 1,288	QuadrupleconcomitantIBP-C+A+M	36/54 (67)	46/51 (90)	73/83 (88)	0.001
(38.1%)	Quadruple with bismuthIBP-L+A+B	36/50 (72)	43/49 (88)	416/462 (82)	0.001
	Quadruple with bismuthIBP-M+T+B	14/19 (74)	43/45 (96)	33/34 (97)	0.005

A: amoxicillin; B: bismuth; C: clarithromycin; L: levofloxacin; M: metronidazole; T: tetracycline; mITT: modified intention to treat; PPI: proton pump inhibitor; N=Total treated; n=Total cured; Low dose PPI - 4.5 to 27 mg omeprazole equivalents; Standard dose PPI - 32 to 40 mg omeprazole equivalents; High dose PPI - 54 to 128 mg omeprazole equivalents, all twice daily.

P10.06

INFLUENCE OF PROBIOTICS USE ON THE SAFETY OF *HELICOBACTER PYLORI* TREATMENTS: RESULTS OF THE EUROPEAN REGISTRY ON THE MANAGEMENT OF *HELICOBACTER PYLORI* INFECTION (Hp-EuReg)

D. CASAS-DEZA[1,2], J. ALCEDO[1,2], M. LAFUENTE[3], J. LÓPEZ[3], Á. PÉREZ-AÍSA[4], M. PAVONI[5], I. M. SARACINO[5], B. TEPES[6], L. JONAITIS[7], P. S. PHULL[8], D. S. BORDIN[9], A. GASBARRINI[10], J. KUPCINSKAS[7], A. CANO-CATALÀ[11], L. HERNÁNDEZ[12], L. MOREIRA[13], ***O. P. NYSSEN***[14]*, F. MEGRAUD[15], C. O. MORAIN[16], J. P. GISBERT[14], ON BEHALF OF THE Hp-EuReg RESEARCHERS*

[1]University Hospital Miguel Servet, Zaragoza, Spain; [2]Instituto de Investigación Sanitaria de Aragón (IIS Aragón), Zaragoza, Spain; [3]Department of Statistical Methods, Faculty of Sciences, University of Zaragoza, Zaragoza, Spain; [4]Digestive Unit, Agencia Sanitaria Costa del Sol, Marbella, Spain; [5]Department of Medical and Surgical Sciences, IRCCS St. Orsola Polyclinic, University of Bologna, Bologna, Italy; [6]Department of Gastroenterology, DC Rogaska, Slatina, Slovenia; [7]Institute for Digestive Research and Department of Gastroenterology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [8]Department of Digestive Disorders, Aberdeen Royal Infirmary, Aberdeen, United Kingdom; [9]Department of Pancreatic, Biliary and Upper Digestive Tract Disorders, A. S. Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation; [10]Medicina Interna e Gastroenterologia, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italy; [11]GOES research group, Althaia Xarxa Assistencial Universitària de Manresa, Manresa, Spain; [12]Unidad de Gastroenterología, Hospital Santos Reyes, Aranda de Duero, Spain; [13]Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), University of Barcelona, Barcelona, Spain; [14]Servicio de Aparato Digestivo. Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, Madrid, Spain; [15]INSERM U1312, Université de Bordeaux, Bordeaux, France; [16]School of Medicine, Trinity College Dublin, Dublin, Ireland

Objective: Clinical practice data on utility of probiotics (PB) to prevent adverse effects (AEs) associated with treatment of *H. pylori* infection are scarce. The aim of the study was to assess the usefulness of PB use in improving the safety of eradication therapies used in Europe.

Materials and Methods: Prospective, multicentre, non-interventional, registry (Hp-EuReg) of the clinical practice of European gastroenterologists. Data were collected from 2013 to 2021. Information was included from countries with at least 30 cases undergoing eradication therapy and at least 1 with associated PB.

Results: 36,699 patients were included, 8,233 (22%) treated with PB. In the PB group the rate of overall AEs was higher (25% *vs.* 22%, $p<0.0001$), but the rate of severe AEs was lower (1.9% *vs.* 1.1%, $p<0.0001$). The duration of AE's was shorter in the PB group (6.4 *vs.* 8.2 days, $p<0.0001$). PB use was associated with a lower incidence of both global and severe AEs. In terms of genus, with Bifidobacterium the incidence of at least one AE and that of severe AEs was lower, while Lactobacillus only had benefit for the incidence of severe AEs associated with triple therapy.

Conclusions: The use of PB was associated with a lower incidence of AEs, as well as shorter duration and severity of AEs. The genus Bifidobacterium may be the most useful in the prevention of AEs.

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TABLE 1. LOGISTIC REGRESSION MODELS FOR THE INCIDENCE OF TOTAL AND SEVERE AES WITH *H. PYLORI* ERADICATION THERAPIES ACCORDING TO PB USE.

Logistic regression model for the incidence of total AEs with *H. pylori* eradication therapies according to PB use, differentiated by gender. Modified intention-to-treat (mITT) analysis in the Central European geographical area.		**Intercep**	**Age**	**Gender (Male)**	**Duration (10 days)**	**Duration (14 days)**	**PPI (Standard)**	**PPI (High)**	**Adherence (>90%)**	**Lacto**	**Bifidob**	**Saccha**	**Bacillus**
Total	Coef	-0.6494	-	-0.6292	-	-	0.7277	-0,.854	-	-	-0.3218	-	-
	p	0	-	0	-	-	0.0835	0.0685	-	-	0.0019	-	-
Triple	Coef	-0.6391	-	-0.785	-	-	-	-	-	-	-	-	-
	p	0.0014	-	0.0331	-	-	-	-	-	-	-	-	-
Quadruple	Coef	0	-	-	-	-	-	-	-1.0615	-	-	-	-
	p	1	-	-	-	-	-	-	0.0314	-	-	-	-
Sequential	Coef	-2.1224	-	-0.6749	-	-	-	-	1.1134	-	-	-	-0.3593
	p	0	-	0	-	-	-	-	0.0006	-	-	-	0.0366
Quadruple + B	Coef												
	p												

Logistic regression model for the incidence of severe AEs with *H. pylori* eradication therapies according to PB use, differentiated by gender. Modified intention-to-treat (mITT) analysis in the Central European geographical area.		**Intercep**	**Age**	**Gender (Male)**	**Duration (10 days)**	**Duration (14 days)**	**PPI (Standard)**	**PPI (High)**	**Adherence (>90%)**	**Lacto**	**Bifidob**	**Saccha**	**Bacillus**
Total	Coef	-0.38	-0.0067	-0.8245	-	-	-	-	-0.9177	-	-2.2563	-	1.6958
	p	0.27	0.1882	0	-	-	-	-	0.0000	-	0.0000	-	0
Triple	Coef	0.23	-	-	-	-	-	-	-2.621	-2.4203	-	-	3.6463
	p	0.77	-	-	-	-	-	-	0.002	0.0278	-	-	0.0105
Quadruple	Coef	-1.59	-	-0.7479	-	-	-	-	-	-	-	-	-
	p	0	-	0.0582	-	-	-	-	-	-	-	-	-
Sequential	Coef	-2.96	-0.0209	-	-	-	-11.5	1.1481	-	-	-	-	-
	p	0	0.0463	-	-	-	0.99	0.0002	-	-	-	-	-
Quadruple + B	Coef												
	p												

P10.07

PRESCRIPTION PATTERN OF PROBIOTICS AS AN ADJUVANT THERAPY FOR *HELICOBACTER PYLORI* THERAPY: RESULTS OF THE EUROPEAN REGISTRY ON THE MANAGEMENT OF *HELICOBACTER PYLORI* INFECTION (Hp-EuReg)

D. CASAS-DEZA[1], J. ALCEDO[1], M. LAFUENTE[2], J. LÓPEZ[2], Á. PÉREZ-AÍSA[3], M. PAVONI[4], I. M. SARACINO[4], B. TEPES[5], L. JONAITIS[6], P. S. PHULL[7], D. S. BORDIN[8], A. GASBARRINI[9], J. KUPCINSKAS[6], A. CANO-CATALÀ[10], L. HERNÁNDEZ[11], L. MOREIRA[12], ***O. P. NYSSEN[13]****, F. MEGRAUD[14], C. O. MORAIN[15], J. P. GISBERT[13], ON BEHALF OF THE Hp-EuReg RESEARCHERS*

[1]University Hospital Miguel Servet. Instituto de Investigación Sanitaria de Aragón (IIS Aragón), Zaragoza, Spain; [2]Department of Statistical Methods, Faculty of Sciences, University of Zaragoza, Zaragoza, Spain. Institute for Biocomputation and Physics of Complex Systems (BIFI), University of Zaragoza, Zaragoza, Spain; [3]Digestive Unit, Agencia Sanitaria Costa del Sol, Marbella, Spain; [4]Department of Medical and Surgical Sciences, IRCCS St. Orsola Polyclinic, University of Bologna, Bologna, Italy; [5]Department of Gastroenterology, DC Rogaska, Slatina, Slovenia; [6]Institute for Digestive Research and Department of Gastroenterology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [7]Department of Digestive Disorders, Aberdeen Royal Infirmary, Aberdeen, United Kingdom; [8]Department of Pancreatic, Biliary and upper digestive tract disorders, A. S. Loginov Moscow clinical scientific center, Moscow, Russian Federation; [9]Medicina interna e Gastroenterologia, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italy; [10]GOES research group, Althaia Xarxa Assistencial Universitària de Manresa, Manresa, Spain; [11]Unidad de Gastroenterología, Hospital Santos Reyes, Aranda de Duero, Spain; [12]Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), University of Barcelona, Barcelona, Spain; [13]Servicio de Aparato Digestivo. Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, Madrid, Spain; [14]INSERM U1312, Université de Bordeaux, Bordeaux, France; [15]School of Medicine, Trinity College Dublin, Dublin, Ireland

Objective: The clinical scenarios in which probiotics (PB) are useful as adjuvants to *Helicobacter pylori* eradication therapy have not been well established. The aim of the study is to determine the use and factors associated with the prescription of PB by European gastroenterologists.
Materials and Methods: Prospective, multicenter, non-interventional registry (Hp-EuReg) of the clinical practice of European gastroenterologists. Data were collected from 2013 to 2022.
***Results*:** A total of 36,699 patients were included, 8,233 (22%) with PB. Multiple PB formulations were used, including 9 genera and 32 species. The most frequent was Saccharomyces boulardii (2,315). There was a higher rate of females in the PB group (64% *vs.* 60%; $p<0.0001$). PBs use was more frequent ($p<0.0001$) in patients in 5th (28%) and 6th-line (46%) compared to 1st (22%). The rate of PB use varied between the eradication regimens, being most frequent in sequential (74%). In contrast, the rate was lower in classic bismuth quadruple (24%), or the same in single-capsule (21%). The percentage of PB use per country ranged from 95% in Serbia to 0.2% in Slovenia. The rate of adverse effects in the non-PB-group was higher in the central area than in the other areas (38% *vs.* 28%; $p<0.0001$), suggesting that in areas with less PB use could be a prescription bias driven by the expectation of adverse effects.
Conclusions: The prescription of PB adjuvant to eradication therapy is very heterogeneous. In areas with lower PB use, there seems to be a prescription bias towards patients with a higher expected risk of adverse effects.

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P10.08

ROLE OF PROBIOTICS IN THE EFFECTIVENESS OF TREATMENT AGAINST *HELICOBACTER PYLORI*: RESULTS OF THE EUROPEAN REGISTRY ON THE MANAGEMENT OF *HELICOBACTER PYLORI* INFECTION (Hp-EuReg)

*D. CASAS-DEZA[1], J. ALCEDO[2], M. LAFUENTE[3], J. LÓPEZ[3], Á. PÉREZ-AÍSA[4], M. PAVONI[5], I. M. SARACINO[5], B. TEPES[6], L. JONAITIS[7], P. S. PHULL[8], D. S. BORDIN[9], A. GASBARRINI[10], J. KUPCINSKAS[7], A. CANO-CATALÀ[11], L. HERNÁNDEZ[12], L. MOREIRA[13], **O. P. NYSSEN**[14], F. MEGRAUD[15], C. O. MORAIN[16], J. P. GISBERT[17], ON BEHALF OF THE Hp-EuReg RESEARCHERS*

[1]University Hospital Miguel Servet, Zaragoza, Spain; [2]University Hospital Miguel Servet. Instituto de Investigación Sanitaria de Aragón (IIS Aragón), Zaragoza, Spain; [3]Department of Statistical Methods, Faculty of Sciences, University of Zaragoza, Zaragoza, Spain. Institute for Biocomputation and Physics of Complex Systems (BIFI), University of Zaragoza, Zaragoza, Spain; [4]Digestive Unit, Agencia Sanitaria Costa del Sol, Marbella, Spain; [5]Department of Medical and Surgical Sciences, IRCCS St. Orsola Polyclinic, University of Bologna, Bologna, Italy; [6]Department of Gastroenterology, DC Rogaska, Slatina, Slovenia; [7]Institute for Digestive Research and Department of Gastroenterology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [8]Department of Digestive Disorders, Aberdeen Royal Infirmary, Aberdeen, United Kingdom; [9]Department of Pancreatic, Biliary and Upper Digestive Tract Disorders, A. S. Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation; [10]Medicina interna e Gastroenterologia, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italy; [11]GOES Research Group, Althaia Xarxa Assistencial Universitària de Manresa, Manresa, Spain; [12]Unidad de Gastroenterología, Hospital Santos Reyes, Aranda de Duero, Spain; [13]Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), University of Barcelona, Barcelona, Spain; [14]Servicio de Aparato Digestivo. Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, Madrid, Spain; [15]INSERM U1312, Université de Bordeaux, Bordeaux, France; [16]School of Medicine, Trinity College Dublin, Dublin, Ireland; [17]Servicio de Aparato Digestivo. Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, Zaragoza, Spain.

Objective: There are doubts about the effectiveness of concomitant use of probiotics (PB) in the treatment of *Helicobacter pylori*. The aim of the study was to determine whether the use of PB improves the effectiveness of eradication treatments used in Europe.
Materials and Methods: Prospective, multicenter, non-interventional, registry (Hp-EuReg) of the clinical practice of European gastroenterologists. Data were collected from 2013 to 2021. All data from countries with at least 30 cases undergoing eradication therapy and at least 1 with associated PB were included. Modified intention-to-treat (mITT) analyses was performed.
Results: 36,699 patients were included, 8,233 (22%) with PB. Overall, PB use was associated with greater effectiveness (91% *vs.* 86%; $p<0.0001$). Adjusting for treatment regimen, this significance held for triple (89% *vs.* 83%; $p<0.0001$), concomitant quadruple (93% *vs.* 89%; $p=0.0009$), quadruple with bismuth (92% *vs.* 86%; $p<0.0001$) and sequential (91% *vs.* 78%; $p<0.0001$) therapies. In the regression model in first-line eradication (adjusted for age, sex, duration of eradication treatment, PPI dose and adherence), PB use maintained the benefit in the triple, bismuth quadruple and sequential treatments. After adjusting by region, significance was maintained in the Eastern region for triple therapies, and in the Central region for concomitant quadruple and sequential therapies.
Conclusions: In Europe, the use of PB adjuvant to eradication therapy is associated with increased effectiveness of eradication therapy, with the benefit being superior in triple and sequential therapies.

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TABLE 1. LOGISTIC REGRESSION MODEL IN FIRST-LINE ERADICATION BY REGIMEN.

	Treatment	Statistic	Intercept	Age	Sex (Male)	Treatment length (10 days)	Treatment length (14 days)	Dose of PPI (Standard)	Dose of PPI (High)	Adherence (>90%)	Probiotic (Yes)
All regions	Total	Coefficient	-0.74	0.003	0.16	0.29	0.48	0.34	0.54	1.97	0.48
		p-value	*0.0000*	*0.0282*	*0.0001*	*0.0000*	*0.0000*	*0.0000*	*0.0000*	*0.0000*	*0.0000*
	Triples	Coefficient	-0.78	0.004	0.21	-0.07	0.41	0.26	0.50	1.98	0.53
		p-value	*0.0008*	*0.0366*	*0.0005*	*0.3097*	*0.0000*	*0.0004*	*0.0000*	*0.0000*	*0.0000*
	Concomitant quadruple	Coefficient	0.24					0.23	0.69	1.75	0.32
		p-value	*0.2799*					*0.05*	*0.0000*	*0.0000*	*0.0532*
	Sequential	Coefficient	-2.28	0.01	0.76			1.12	0.29	2.48	1.30
		p-value	*0.0005*	*0.02*	*0.0000*			*0.0037*	*0.0890*	*0.0000*	*0.0000*
	Bismuth quadruple	Coefficient	-1.50			1.43	1.11	0.63	0.56	2.25	0.22
		p-value	*0.0001*			*0.0000*	*0.0010*	*0.0000*	*0.0000*	*0.0000*	*0.0472*

P12.10

REGIONAL DIFFERENCES IN THE MANAGEMENT OF *HELICOBACTER PYLORI* INFECTION IN SPAIN: DATA FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (Hp-EuReg).

L. HERNÁNDEZ[1], B. J. GÓMEZ RODRÍGUEZ[2], S. J. MARTÍNEZ-DOMÍNGUEZ[3], R. PAJARES VILLAROYA[4], J. TEJEDOR-TEJADA[5], P. PAZO MEJIDE[6], M. SÁNCHEZ ALONSO[7], N. ALCAIDE[8], J. M. HUGUET[9], P. MATA-ROMERO[10], J. LLACH[11], A. CUADRADO[12], E. IVO[13], E. ALBÉNIZ[14,15], A. CANO-CATALÀ[16], L. MOREIRA[11,17,18], P. PARRA[19,20], ***O. P. NYSSEN****[19,20], J. P. GISBERT[19,20], Hp-EuReg INVESTIGATORS*

[1]Hospital Santos Reyes, Aranda de Duero, Spain; [2]Hospital Virgen Macarena, Seville, Spain; [3]Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain; [4]Hospital Universitario Infanta Sofía, San Sebastián de los Reyes, Spain; [5]Hospital Universitario de Cabueñes, Gijón, Spain; [6]Hospital de Cruces, Barakal-do, Spain; [7]Hospital Universitario Santa Bárbara, Puertollano, Spain; [8]Hospital Clínico Universitario de Valladolid, Valladolid, Spain; [9]Hospital General Universitario de Valencia, Valencia, Spain; [10]Hospital Universitario de Cáceres, Cáceres, Spain; [11]Hospital Clínic de Barcelona, Barcelona, Spain; [12]Marqués de Valdecilla University Hospital, Santander, Spain; [13]Hospital Comarcal de Inca, Inca, Spain; [14]Hospi-tal Universitario de Navarra, Pamplona, Spain; [15]NavarraBiomed, Pamplona, Spain; [16]15GOES research group, Althaia Xarxa Assistencial Universitària, Manresa, Spain; [17]Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain; [18]IDIBAPS (Institut d'Inves-tigacions Biomèdiques August Pi i Sunyer), Barcelona, Spain; [19]Hospital Universitario de La Princesa, Madrid, Spain; [20]Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Madrid, Spain

Objective: *Helicobacter pylori (H. pylori)* is a bacterium that can cause gastritis, peptic ulcer, and gastric cancer. The diagnostic approach, treatment strategy and effectiveness may differ from one region to another. The differences in the management of *H. pylori* between the various Spanish regions, were evaluated.

Materials and Methods: Systematic, prospective registry on the management of *H. pylori* infection (Hp-EuReg) by European gastroenterologists. Data were registered at AEG-REDCap e-CRF from 2013 to January 2023. Modified intention-to-treat (mITT) analyses were performed in those Spanish regions with over 100 cases receiving a first-line treatment.

Results: There were 20,565 treatment-naïve patients among 13 regions. The differences in demogra-phy, indications for treatment, diagnostic approach and treatment strategy are shown in the table. The most common treatments overall were bismuth quadruple regimen with metronidazole-tetracycline (33%) and concomitant non-bismuth quadruple treatment with amoxicillin-clarithromycin-metronida-zole (33%), with differences between regions. The overall first-line effectiveness was 86.7% but ranged from 78% in Aragon to 97% in Asturias (Table 1).

Conclusions: There are relevant differences in the management (including indication, diagnosis, and treatment) of *H. pylori* infection among the different Spanish regions. More dissemination and teaching are probably needed to achieve more homogeneous results.

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TABLE 1. MANAGEMENT OF *H. PYLORI* INFECTION AND EFFECTIVENESS OF FIRST-LINE THERAPY AMONG SPANISH REGIONS.

	Andalucía	Aragón	Cantabria	Castilla y León	Castilla la Mancha	Cataluña Cataluña	Madrid Madrid	Navarra Navarra	Valencia Valencia	Extrema-dura	Baleares	País Vasco	Asturias	Total
Number of patients	6,041	2,256	239	1,632	1,451	487	2,297	118	1,596	700	214	1,514	2,020	20,565
Female N (%)	3,858	1,460	133	992	908	282	1,428	62	1,038	431	131	902	1,052	12,677
	(63.9)	(64.7)	(55.6)	(61.0)	(62.6)	(58.0)	(62.2)	(52.5)	(65.1)	(62.3)	(61.2)	(59.6)	(52.1)	(61.7)
Age	51.2	50.5	51.3	53.8	51.1	57.9	50.0	49.1	53.2	50.6	48.2	51.0	59.0	52.3
Indication N (%)														
Dyspepsia	4,680	1,539	122	815	1,023	225	1,739	83	1,041	550	131	941	911	13,800
	(77.5)	(68.2)	(51.3)	(50.0)	(70.6)	(46.2)	(75.7)	(70.3)	(65.2)	(78.8)	(61.2)	(62.1)	(45.1)	(67.2)
Ulcer disease	794	184	48	306	44	75	222	10	184	102	22	148	1,002	5,141
	(13.1)	(8.2)	(20.2)	(18.8)	(3.0)	(15.4)	(9.7)	(8.5)	(11.5)	(14.6)	(10.3)	(9.8)	(49.6)	(15.3)
Diagnostic method N (%)														
Breath test	1,090	1,602	3	379	421	65	1,250	38	598	369	105	490	388	6,798
	(18.3)	(71.2)	(1.3)	(23.4)	(29.2)	(13.7)	(56.4)	(32.2)	(37.6)	(52.9)	(49.1)	(32.5)	(19.8)	(33.4)
Stool Ag Test	1,405	1	29	188	82	36	96	9	365	25	4	8	82	2.33
	(23.6)	(0.0)	(12.6)	(11.6)	(5.7)	(7.6)	(4.2)	(7.6)	(22.9)	(3.6)	(1.87)	(0.5)	(4.2)	(11.4)
Endoscopic test	3,462	646	198	1,054	940	375	943	71	627	304	105	1,009	1,491	11,225
	(58.1)	(28.7)	(86.1)	(65.0)	(65.1)	(78.8)	(41.2)	(60.2)	(39.4)	(43.6)	(49.0)	(66.9)	(76.0)	(55.1)
Most frequent treatments N (%)														
PPI+C+A	1,143	314	92	244	71	37	71	0	69	30	10	675	252	3,008
	(19.8)	(14.5)	(38.8)	(16.0)	(5.1)	(7.9)	(3.4)	(0)	(4.5)	(4.6)	(4.8)	(46.8)	(13.2)	(15.4)
PPI+C+M	49	18	4	11	1	2	5	0	22	0	1	8	5	126
	(0.9)	(0.8)	(1.7)	(0.7)	(0.1)	(0.4)	(0.2)	(0)	(1.4)	(0)	(0.5)	(0.6)	(0.3)	(0.6)
PPI+A+M	10	22	0	8	0	0	4	0	1	0	0	55	5	105
	(0.2)	(1.0)	(0)	(0.5)	(0)	(0)	(0.2)	(0)	(0.1)	(0)	(0)	(3.8)	(0.3)	(0.5)
PPI+C+A+M (con)	1,760	988	12	424	319	104	746	7	757	288	35	406	602	6,448
	(30.5)	(45.5)	(5.1)	(27.8)	(22.8)	(22.1)	(36.0)	(7.1)	(49.4)	(44.6)	(16.8)	(28.2)	(31.5)	(33.1)
PPI+C+A+M (seq)	4	0	1	33	0	0	170	0	0	0	0	0	32	240
	(0.1)	(0)	(0.4)	(2.2)	(0)	(0)	(8.2)	(0)	(0)	(0)	(0)	(0)	(1.7)	(1.2)
PPI+C+A+B	194	6	64	150	484	0	92	27	1	25	0	92	40	1,175
	(3.4)	(0.3)	(27.0)	(9.8)	(34.6)	(0)	(4.4)	(27.3)	(0.07)	(3.9)	(0)	(6.4)	(2.1)	(6.0)
PPI+ single capsule*	1,976	637	54	498	440	313	670	61	553	262	154	80	767	6,465
	(34.3)	(29.3)	(22.8)	(32.6)	(31.5)	(66.6)	(32.3)	(61.6)	(36.1)	(40.6)	(74.0)	(5.6)	(20.07)	(33.2)
PPI+A+L	431	138	8	61	7	10	64	2	82	14	4	97	182	1,100
	(7.5)	(6.4)	(3.4)	(4.0)	(0.5)	(2.1)	(3.1)	(2.0)	(5.4)	(2.2)	(1.9)	(6.7)	(9.51)	(5.6)
PPI+A+L+B	200	48	2	97	75	4	250	2	46	27	4	28	29	812
	(3.5)	(2.2)	(0.8)	(6.3)	(5.4)	(0.9)	(12.1)	(2.0)	(3.0)	(4.2)	(1.9)	(1.9)	(1.5)	(4.2)
Treatment success (mITT)	5,118	1,704	192	1,366	1,286	356	1,945	95	1,275	583	175	1,142	1,910	19,775
	(87.1)	(77.8)	(88.1)	(87.9)	(88.8)	(87.5)	(88.0)	(87.6)	(84.2)	(85.7)	(89.3)	(81.8)	(96.9)	(86.7)