

EUROPEAN HELICOBACTER AND MICROBIOTA STUDY GROUP



**EHMSG – 36th International Workshop on Helicobacter
& Microbiota in Inflammation & Cancer**

September 7-9, 2023
Antwerp, Belgium

Accepted Abstracts

www.microbiotajournal.com

DOI: 10.26355/mhd_20239_857

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Contributions of up to EUR 10.000. -(or equivalent value in kind) per year per entity are considered “Modest”. Contributions above EUR 10.000.-per year are considered “Significant”.

Missing abstracts within the consecutive presentation numbers represent withdrawn papers.

WORKSHOPS

SESSION 02: NEWS ON GASTRITIS

02.05

GASTROPANEL, GHRELIN AND LEPTIN FOR NON-INVASIVE DIAGNOSIS OF ADVANCED GASTRIC ATROPHY AND INTESTINAL METAPLASIA

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Objective: Patients with advanced corpus-predominant gastric atrophy and intestinal metaplasia are at increased risk of gastric cancer. GastroPanel, a serologic panel of markers related to stomach physiology, has been proposed as non-invasive screening test for advanced atrophic gastritis, but its sensitivity is limited. The role of the digestive hormones Ghrelin and Leptin for non-invasive detection of advanced gastric lesions is uncertain.

Patients and Methods: In n=351 individuals with histopathologic characterization of the gastric mucosa and standardized grading of gastritis (OLGA/OLGIM), serum levels of Pepsinogen I (PGI), Pepsinogen II (PGII), Gastrin17, *H. pylori* antibodies (GastroPanel), Ghrelin and Leptin were measured. Logistic regression models were developed for OLGA/OLGIM stages 3/4 using different combinations of serum parameters. ROC curves were built to compute the AUC and determine the diagnostic performance of the respective parameters.

Results: The individual serum markers reach a maximum diagnostic power for OLGA/OLGIM 3/4 of AUC = 0.645 (Ghrelin). Combining the parameters of GastroPanel in a logistic regression model reaches an AUC = 0.633, accuracy = 84.6%, sensitivity = 90.5%, specificity = 22.2%. A logistic regression model using Ghrelin and Leptin reaches an AUC = 0.628, accuracy = 89.4%, sensitivity = 96.8%, specificity = 11.1%. Adding Ghrelin and Leptin to the GastroPanel model reaches an AUC = 0.708, accuracy = 85.6%, sensitivity = 91.6%, specificity = 22.2%. This increase in AUC fails statistical significance ($p=0.398$).

Conclusions: GastroPanel has limited diagnostic value in detecting advanced gastric lesions and its combination with serum Ghrelin and Leptin does not improve it. More sensitive and specific non-invasive markers for non-invasive screening of gastric preneoplastic lesions are needed.

L. Macke: None. R. Vasapoli: None. N. Koch: None. P. Malfertheiner: None. C. Schulz: None. K. Schütte: None. A. Link: None.

02.06

REAL-TIME GASTRIC JUICE ANALYSIS FOR DETECTION OF *HELICOBACTER PYLORI* INFECTION: IS IT USEFUL IN DAILY CLINICAL PRACTICE?

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Objective: EndoFaster[®] measures real time concentration of ammonia (NH₃) and pH in gastric juice, allowing *Helicobacter pylori* (Hp) detection during upper gastrointestinal endoscopy (EGD). The aim of the present study was to validate and compare this technology with other diagnostic methods (molecular and fecal antigen assays) in daily clinical practice.

Materials and Methods: Prospective, unicenter cohort study. All patients who underwent EGD and had an indication for Hp testing were included. Patients with prior evidence of no Hp infection or with insufficient gastric juice were excluded. The gold standard for Hp infection diagnosis was the histological analysis.

Results: A total of 99 patients were included (male-46.7%; mean age-60 years, IQR 46-68). Hp infection was detected in 30% of the patients. Univariate analysis showed that all diagnostic methods had a significant association with histological diagnosis ($p < 0.001$) and EndoFaster[®] had an area under the curve of 0.9, followed by PCR-0.87 and faecal antigens-0.73. The sensitivity, specificity, positive predictive value and negative predictive value of EndoFaster[®] at a cut-off value of 67 ppm/mL for NH₃ were 79.2%, 84.1%, 76%, 86.5%, for PCR 93.3%, 84.6%, 87.5%, 91.7%, and for faecal antigens 77.8%, 88.2%, 87.5%, 79%, respectively.

Conclusions: Endofaster[®] is a method with high accuracy in detecting Hp. The high negative predictive value of EndoFaster[®] may eliminate the need to perform gastric biopsies if their only goal is to investigate Hp.

A.C. Trigo: None. M.J. Temido: None. N. Almeida: None. E. Gravito-Soares: None. M. Gravito-Soares: None. L. Santos: None. C. Chaves: None. D. Feijó: None. M.I. Viegas: None. M.M. Donato: None. A. Carmo: None. C. Chaves: None. F. Rodrigues: None. M.A. Cipriano: None. P.N. Figueiredo: None.

02.07

GASTRIC PATHOLOGY AND *HELICOBACTER PYLORI* VACA GENOTYPE IN INDIGENOUS COMMUNITIES OF ARCTIC CANADA

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Objective: Leaders of Arctic Indigenous communities in Canada partnered with academic researchers to learn whether characteristics of *Helicobacter pylori* (Hp) influence severity of Hp-induced disease in their communities. We estimated prevalence of Hp *vacA* genotypes and their associations with abnormal gastric pathology in 7 Indigenous communities in the Northwest Territories and Yukon, Canada.

Materials and Methods: Endoscopists performed gastroscopy in local health centers, taking 5-6 biopsies for histopathology and 2-4 for culture from each community-project participant during 2008-2017. In tissue culture, we isolated Hp from 274 participants. We assessed 204 isolates for *vacA* s, m and i genotypes using multiple PCR reactions. A single pathologist used the updated Sydney system to grade gastric abnormalities (see Table 1). We estimated prevalence of abnormalities by *vacA* genotype.

Results: Prevalence among 204 isolates was 150/204 (74%) for the s1 allele, 54 (26%) for s2, 86 (42%) for m1, 128 (63%) for m2, 97 (48%) for i1, and 122 (60%) for i2. Subtypes s1m1i1, s2m2i2, and s1m2i2 predominated at 72 (35%), 49 (24%) and 56 (27%), respectively; 10 (5%) participants' isolates had m1 and m2, suggesting mixed infections. Table 1 shows the prevalence of gastric abnormalities by *vacA* s/m genotype.

Conclusions: In Hp strains from Arctic Indigenous communities in Canada, the *vacAs*1+ genotype was highly prevalent and associated with more severe gastric pathology relative to other *vacA* genotypes.

O. Zaliavska: None. T.J. Cromarty: None. K.J. Goodman: None. S. Girgis: None. S. Veldhuyzen van Zanten: None.

TABLE 1. PREVALENCE OF GASTRIC PATHOLOGY BY Hp vacA s/m TYPE IN 204 RESIDENTS OF CANADIAN ARCTIC COMMUNITIES.

Attribute Data available for all samples unless otherwise indicated	All genotypes		s1m1		s2m2		s1m2		s1m1, m2	
	n	% of 204	n	% of 76*	n	% of 54*	n	% of 64*	n	% of 10*
Had baseline histopathology	204	100	76	100	54	100	64	100	10	100
Combined assessment of antrum & body biopsies (classified by highest score)										
Hp density [n=202]										
Hp undetected	19	9.3	5	6.5	7	13.2	5	7.8	2	22.2
Low	35	17.1	10	13.2	16	30.2	7	10.9	2	22.2
Mod	84	42.1	30	39.5	22	41.5	30	46.9	2	22.2
High	64	31.1	31	40.8	8	15.1	22	34.4	3	33.3
Missing	2		0		1		0		1	
Chronic inflammation										
None	17	8.3	4	5.3	6	11.1	5	7.8	2	20.0
Mild	13	6.4	4	5.3	6	11.1	2	3.1	1	10.0
Mod	79	38.7	24	31.6	24	44.4	29	45.3	2	20.0
Severe	95	46.6	44	57.9	18	33.3	28	43.8	5	50.0
Active inflammation[n=202]										
None	21	10.3	6	7.9	8	14.8	5	7.8	2	22.2
Mild	76	37.2	16	29.1	29	53.7	28	43.8	3	33.3
Mod	72	35.2	35	46.1	13	24.1	21	32.8	3	33.3
Severe	33	16.1	19	25.0	3	5.6	10	15.6	1	11.1
Missing	2		0		1		0		1	
Gastric atrophy										
None	116	56.8	32	42.1	34	63.0	43	67.2	7	70.0
Mild	61	29.9	26	34.2	17	31.5	17	26.6	1	10.0
Mod-severe	27	13.2	18	23.7	3	5.6	4	6.3	2	20.0
Gastric intestinal metaplasia										
None	172	84.3	60	79.0	51	94.4	52	81.3	9	90.0
Mild	17	8.3	11	14.5	1	1.9	5	7.8	0	0
Mod-severe	15	7.4	5	6.6	2	5.6	7	10.9	1	10.0

SESSION 03: MICROBIOME MECHANISMS OF ACTION (PARALLEL SESSION)

03.05

MOUTH MICROBIOME IN CHILDREN WITH AUTISM: DIAGNOSIS-RELATED DIFFERENCES AND ASSOCIATIONS WITH BEHAVIORAL DIFFICULTIES

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Objective: Next to gut-microbiome, also mouth microbiome compositions have been suggested to play an important role in the pathophysiology of autism spectrum disorder (ASD). A recent mouse experiment even demonstrated causal links between oral bacteria and ASD symptoms *via* transfer experiments from humans to mice (Qiao et al, 2022).

However, literature about differences in mouth microbiome composition between school-aged children with and without ASD and the link with behavioral difficulties is sparse.

Patients and Methods: We examined diagnoses-related differences in mouth microbiome composition in school-aged children with (n=80) and without (n=40) ASD (boys/girls 4/1), as well as associations with behavioral difficulties.

Results: Results provide important indications that both at family and genus level, the bacteria Erysipelotrichaceae, Campylobacteraceae, Ruminococcaceae and Tannerellaceae were significantly more abundant within the ASD children, in comparison with the control children. Furthermore, several bacteria that were significantly more abundant within the ASD group were significantly related to more anxiety disorders, reported by the parents (SCARED reported parents), and attachment difficulties associated with anxiety (ASCQ anxious).

Conclusions: This exploratory study underscores the potential role of the oral microbiome in diagnosis-related differences between children with ASD and age-matched controls. The promising associations with behavioral difficulties warrant further exploration of the oral microbiome's potential beyond the oral cavity and specifically with respect to neurological disorders.

Qiao, Y., Gong, W., Li, B., Xu, R., Wang, M., Shen, L., Shi, H., & Li, Y. (2022). Oral Microbiota Changes Contribute to Autism Spectrum Disorder in Mice. *Journal of Dental Research*, 002203452110704. <https://doi.org/10.1177/00220345211070470>

M. Evenepoel: None. M. Moerkerke: None. N. Daniels: None. M. Steyaert Jean: None. B. Boets: None. M. Joossens: None. K. Alaerts: None.

03.06

KVARM LOWERS *KLEBSIELLA PNEUMONIAE* COLONIZATION IN GASTROINTESTINAL TRACT WITHOUT DISRUPTION OF GUT MICROBIOTA

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Objective: Hospital-acquired infections (HAI) are one of the leading worldwide healthcare issues. *Klebsiella pneumoniae* is currently named at the top of the World Health Organisation (WHO) superbugs list, because of its widespread resistance to third-generation antibiotics. Recombinant bacteriocins, like klebicins, could be employed as oral antimicrobials to eradicate multidrug-resistant *Klebsiella* from the intestinal tract.

Material and Methods: The main goal of this study was to determine if klebicins disrupt microbiota during gastrointestinal infection treatment. Four study groups were used (5 animals/group) to compare the changes in mice microbiota during klebicin or antibiotic therapies: (G1) negative (*Klebsiella pneumoniae* 10⁷ CFU) and (G2) positive (*Klebsiella pneumoniae* 10⁷ CFU, Eudragit) control groups; (G3) first experimental group [klebicin KvarM (100 µg)] and (G4) the second experimental group (ciprofloxacin (50mg/kg)) therapy. Faecal samples were used for analysis using RT-PCR and 16s rRNA-coding gene V1-V2 hypervariable region next-generation sequencing. Afterward, bioinformatics and statistical analysis were performed.

Results: Analysis of the antimicrobial efficacy of KvarM (G3) showed significantly reduced colonization of *K. pneumoniae* (before therapy 1.4 x 10⁶ CFU/50 mg; after therapy 1.7 x 10² CFU/50 mg; *p* = 0.022) and had no changes in α-diversity compared to control groups. Whereas G4 also showed significantly reduced bacterial colonization (before therapy 8.75 x 10⁵ CFU/50 mg; after therapy 3.51 x 10³ CFU/50 mg; *p* = 0.1002), but α-diversity was clearly differentiated from control groups.

Conclusions: Our study demonstrates that colonization of mice intestinal tract by *K. pneumoniae* can be successfully reduced using KvarM without disruption of natural gut microbiota.

I. Karaliute: None. D. Tilinde: None. R. Ramonaite: None. J. Kupcinkas: None. A. Misiunas: None. E. Denkovskiene: None. D. Nikitina: None. Y. Gleba: None. A. Razanskiene: None. J. Skieceviciene: None.

03.07

GUT-VAGINA AXIS: DIET IS ASSOCIATED WITH THE VAGINAL MICROBIOME

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Microbial communities at different body sites do not function independently but are directly linked *via* microbial dispersal and indirectly *via* the host. In our citizen-science project Isala (<https://isala.be/en/>), the vaginal microbiome of 3,345 healthy women was mapped through 16S rRNA amplicon sequencing, showing that over 75% of the samples are dominated by *Lactobacillus* taxa. We detected a module of collaborating gut-specific taxa (*Bacteroides*, *Faecalibacterium*, *Blautia*) in the vaginal microbiome, corresponding to a gut-vagina axis for commensals, and found a positive correlation with the ‘healthy’ vaginal module consisting of *Lactobacillus crispatus*, *Lactobacillus jensenii* and *Limosilactobacillus*. However, we do not know yet how these gut-vagina-specific taxa are connected. It is possible that stimulating gut-specific taxa through carbohydrate provision (e.g., starch) is (indirectly) associated with higher vaginal abundances. We did find that specific dietary habits were significantly associated with the vaginal microbiome. For example, positive associations between the *L. crispatus*-module and frequent consumption of vegetables as well as associated fiber were found, whereas lower *L. crispatus*-module levels were linked to meat consumption (indicative of more protein fermentation). Finally, to investigate the presence of food components in the vagina, we performed metabolic profiling of 64 vaginal supernatant samples using Liquid Chromatography-Mass Spectrometry. Surprisingly, various food metabolites were detected in the vagina, suggesting a food-vagina axis. It remains to be explored whether food components reach the vagina *via* the perineum and thus impact the microbiome or indirectly *via* intestinal absorption. Nevertheless, our findings create a new perspective to improve vaginal health through (personalized) dietary advice.

I. Erreygers: None. S. Condori: None. T. Gehrman: None. D. Medeiros Selegato: None. M. Zimmermann: None. S. Lebeer: None. C. Allonsius: None. S. Ahannach: None. S. Wittouck: None. T. Eilers: None. V. Verhoeven: None.

SESSION 04: HELICOBACTER PYLORI GENOME PROJECT (HPGP)

04.06

COMPREHENSIVE ANALYSIS OF INTEGRATING CONJUGATIVE ELEMENTS (ICES) IN HELICOBACTER PYLORI POPULATIONS

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The highly efficient DNA transfer capabilities of *Helicobacter pylori* are the basis for its extensive core genome diversity, but also for maintaining variability in its mobile genetic repertoire. Among

several types of mobile genetic elements, two distinct integrating conjugative elements, which have been termed ICE $Hptfs3$ and ICE $Hptfs4$, may account for a substantial fraction of the non-core genome in individual strains. Generally, ICEs can be activated from their integrated states to undergo horizontal gene transfer. However, we have shown previously that non-canonical transfer mechanisms may be preferred in *H. pylori* due to their higher efficacy.

Here, as a part of the *Helicobacter pylori* Genome Project (HpGP) initiative, we have analyzed more than 1,000 genome sequences obtained by single-molecule, real-time (SMRT) technology (PacBio), with respect to their ICE content and variability. Taking advantage of high-quality, long-read sequencing data, we were able to characterize ICE gene arrangements, including repetitive sequences, chromosomal insertion sites, and population-specific variations. Our data show that both ICEs have a high overall prevalence in all populations, but also a strong tendency for gene erosion. Multiple potential ICE integration sites scattered over the chromosome highlight the mobility of these elements *via* canonical transfer mechanisms. Individual strains often contain more than one ICE type, and recombination events between conserved ICE sequences have frequently resulted in genome rearrangements or hybrid elements.

In conclusion, we provide the first comprehensive overview of *H. pylori* ICEs on a global scale, and in unprecedented detail.

W. Fischer: None. A.J. Gutiérrez-Escobar: None. Z.Y. Muñoz-Ramírez: None. F.F. Vale: None. D. Wang: None. S. Sandoval-Motta: None. J.P. Dekker: None. K. Thorell: None. M.C. Camargo: None. Y. Yamaoka: None.

SESSION 05: MICROBIOTA MODULATION FOR A HEALTHY LIFE

05.05

COMPOSITION OF INFANT GUT VIROME ASSOCIATED WITH MATERNAL ANTIBACTERIAL THERAPY AND TYPE OF DELIVERY

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Objective: The early development of gut virome is poorly understood. However, it has been considered that infant gut virome is determined by different environmental factors. The objective of the study was to determine changes in viral community of the infant faecal microbiota associated with type of delivery and maternal antibacterial therapy.

Patients and Methods: Study was performed at primary healthcare centers. The parents of children filled out a questionnaire and brought their child's faecal samples. The microbial DNA was extracted and metagenomic sequencing performed to identify the microorganism populations in faecal samples. Average relative abundance was compared among children with different types of delivery and previous maternal antibacterial therapy. Statistical analyses: SIAMCAT and phyloseq packages.

Results: Study included 92 children [63% (58/92) boys]. Mean age 8.4 (SD4.8) months. Most of the children (72/92) were born vaginally. However, 32% (28/88) of mothers received antibacterial therapy during delivery and 16% (14/87) during pregnancy. The most abundant viral components in cases of maternal usage of antibiotics were: species *Capnocytophaga*, *Soroca orthobunyavirus*, *Ectromelia virus*, *Wanchavirus*, *Lambdavirus*, *Anatolevirus*, *Punavirus*, *Cellulophaga lytica*, *Limbudunavirus*, *Kingerivirus*, *Capnytophaga* during delivery and species *Cohcovirus splanchnicus*, *Pleotrevirus*, *Lughvirus*, *Parabacteroides phage*, *Streptococcus phage*, *Lambdavirus*, *Saliphagus*, genus *Rockefellerivirus* during pregnancy. The most abundant viral components in children delivered by C-section: genus *Chloriridovirus*, *Nesevirus*, *Pandoravirus*, species *Capnocytophaga*. Measurements of alpha diversity in case of maternal usage of antibiotics did not show significant differences.

Conclusions: Mostly, gut virome consists of phages. Further research is necessary to clarify factors driving shifts in phage community that could promote the knowledge for phage-driven remodeling of the gut microbiome.

E. Zelča: None. D. Gudrā: None. M. Ustinova: None. D. Kārklīņa: None. I. Daugule: None.

05.06

LONG-TERM OUTCOMES OF ORAL ANTIBIOTICS COMBINATION THERAPY FOR INDUCTION AND MAINTENANCE OF ULCERATIVE COLITIS

Y. NISHIKAWA, N. SATO, T. OHKUSA

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Objective: Dysbiosis of gut microbiota is observed in ulcerative colitis (UC). In our past study, *Fusobacterium varium* was frequently observed on the large-intestinal mucosa of UC patients. We have shown the effectiveness of an antibiotic combination therapy (ATM therapy) on UC, which consists of antibiotic agents with sensitivity to *F. varium*. In this study, we aim to investigate the long-term effectiveness of ATM therapy on a larger cohort.

Material and Methods: In a prospective open-label trial, a combination of oral amoxicillin (1500 mg), tetracycline (1500 mg) and metronidazole (750 mg) was administered to patients daily for 2 weeks in addition to their conventional medication. The primary endpoint was the response rate at 3 months after the completion of ATM therapy. The secondary endpoints were the remission rate at 3 months, both remission and response rate at completion and 1 year after the ATM therapy. All adverse events were recorded.

Results: The data from 311 active UC patients were analysed. The compliance rate was 95.7%. The response rate and remission rate were 75.2% and 30.9% at completion, 62.7% and 29.6% at 3 months, 35.4% and 24.4% at 12 months, respectively. In the patient group with severe disease activity, the response rate was statistically higher at 6 months ($p=0.0299$). Adverse events were reported in 60.8% of participants. The most frequent adverse events were diarrhea (19.0%) and fever (14.8%). No life-threatening adverse event was observed.

Conclusions: 2 weeks administration of ATM therapy induces response and remission of UC and maintains the symptom for long-term.

Y. Nishikawa: None. N. Sato: None. T. Ohkusa: None.

05.07

PERCEPTIONS AND PRACTICES ON CLINICAL USE OF PROBIOTICS: A NATIONAL SURVEY OF HEALTHCARE PRACTITIONERS

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Objective: Probiotics have the potential to be used for the prevention and treatment of various medical conditions. In Greece, perceptions and practices concerning the clinical use of probiotics remain uncertain.

Material and Methods: A closed-ended, 20-item, online questionnaire was distributed *via* email to HCPs throughout Greece, aiming to evaluate how healthcare practitioners (HCPs) perceive and use probiotics in clinical practice.

Results: From 725 questionnaires sent, 185 (25.5%) HCPs provided feedback. The majority (97.5%) were gastroenterologists, most (60%) running their practice in the private sector. Fifty-one percent considered probiotics “definitively safe” and 31% “probably safe”. The most commonly recognized therapeutic indications were irritable bowel syndrome (IBS; 87.6%), prevention of antibiotic-as-

sociated diarrhea (84.3%), pouchitis (55.1%), prevention of *Clostridiodes difficile* infection (50.3%) and acute diarrhea (41.1%). The most commonly prescribed strains were *Saccharomyces boulardii* (69.2%), *Lactobacillus acidophilus* (68.1%), and *Bifidobacterium bifidum* (57.8%). Thirty-one percent reported to “always” prescribe probiotics in association to antibiotics, 25.9% “only during protracted antibiotic courses” and 17.3% “only in patients with a history of gastrointestinal symptoms”. Forty-six percent reported to “always” prescribe probiotics during *Helicobacter pylori* eradication and 22.3% “frequently”. Concerning IBS, 24.9% reported to “frequently” prescribe probiotics as first-line treatment and 23.2% “sometimes”, most commonly for the IBS-diarrhea (78.4%) and mixed IBS (38.9%) subtypes.

Conclusions: HCPs recommend probiotics for a wide range of gastrointestinal conditions and consider them safe. However, apparent discrepancies in practice patterns underscore the need for continuous medical education and the development of consensus recommendations, aiming to guide the rationale use of probiotics in clinical practice.

V. Papastergiou: None. S.D. Georgopoulos: None. D. Christodoulou: None. I.S. Papanikolaou: None. K. Ekmektzoglou: None. C. Kalantzis: None. E.J. Giamarellos-Bourboulis: None. K. Triantafyllou: None.

SESSION 06: GASTRIC CARCINOGENESIS (PARALLEL SESSION)

06.05

THE HUMANIZED LEB MOUSE MODEL WITH GASTRIC CANCER CAUSED BY LIFE-LONG *H. PYLORI* INFECTION

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Objective: There are no animal models for chronic *H. pylori* infection that efficiently reproduce development of overt gastric disease and cancer. Our ambition was to develop a mouse model which faithfully follows the recognized Correa gastric cancer cascade. Since *H. pylori* attachment drives the gastric inflammation processes, we applied the transgenic Leb mouse, which expresses a humanized ABO/Leb antigen in the gastric epithelium, for the establishment of life-long-inflammatory *H. pylori* infection.

Materials and Methods: We infected 30 Leb mice with the onco-strain *H. pylori* USU101, with 12 non-infected mice as controls. After 12 months, the development of gastric pathology was evaluated by histology. This series was reproduced with another group of 34 Leb mice over 12 months.

Results: In two series, 40%, vs. 56% of the Leb-mice developed gastric cancer and another 27% vs. 18% mice with gastric dysplasia. The total incidence of gastric malignancies was 67% vs. 74%. The intestinal-adenocarcinoma type of cancer and dysplasia were located in the corpus region. All stages of the Correa cancer cascade were represented in tissue samples. The non-infected animals all remained healthy with no gastric disease nor inflammation. The gastric cancer mucosa demonstrated 3-fold higher inflammatory infiltration compared to mice with merely gastritis.

Conclusions: We have developed the humanized Leb mouse model of gastric cancer where life-long-inflammatory *H. pylori* infection is the causative agent for cancer development. The model demonstrates unprecedented high incidence of gastric cancer, which follows the Correa cascade caused by *H. pylori* and chronic mucosal inflammation.

A. Piddubnyi: None. J.A. Bugaytsova: None. I. Tkachenko: None. R. Moskalenko: None. L. Hammarström: None. T. Borén: None.

06.06

STUDY OF *LACTOBACILLUS* SPP. EFFECTS ON GASTRIC CARCINOGENESIS IN THE CONTEXT OF *HELICOBACTER PYLORI* INFECTION

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Objective: The occurrence of gastric adenocarcinoma linked with *Helicobacter pylori* infection is influenced by different factors including the digestive microbiota. Lactic acid bacteria role on digestive carcinogenesis are discussed and some *Lactobacillus* species have been shown to act against *H. pylori*-induced inflammation and colonization, but their effects on *H. pylori*-related carcinogenesis have not yet been studied. The effects of *Lactobacillus* spp. on the epithelial-to-mesenchymal transition (EMT), cancer stem cells properties (CSC) and the inflammation in response to *H. pylori* infection were investigated.

Materials and Methods: A co-culture model was used with AGS cells infected with *H. pylori* associated with 20 different probiotic strains candidates. Different indicators of EMT and CSC properties were studied, including hummingbird phenotype quantification, tumorsphere formation assay, ZO-1 and Integrin β 1 expression with western-blot and immunofluorescence assays. Effect of the *Lactobacillus* spp. on the inflammation in response to *H. pylori* was also evaluated by quantifying IL8, IL6 and TNF α production with ELISA assay.

Results: Among the strains tested, a significant decrease of the hummingbird phenotype induced by *H. pylori* was observed in presence of *Lactobacillus gasserii* and *Lactobacillus rhamnosus* with a reduction of 65% and 70% respectively ($p < 0.0001$). *L. gasserii* and *L. rhamnosus* also decreased the number of tumorspheres formed (reduction of 24% and 50% respectively, $p < 0.001$). IL-8 production was also significantly reduced in presence of *L. gasserii* and *L. rhamnosus*.

Conclusions: These results suggest that *L. rhamnosus* and *L. gasserii* may have an inhibitory effect on carcinogenesis induced by *H. pylori*.

M. Jauvain: None. G. Lepied: None. C. Varon: None. P. Lehours: None. E. Bessède: None.

06.07

BENEFICIAL EFFECT OF SODIUM HYDROSULFIDE, THE HYDROGEN SULFIDE (H₂S) DONOR ON *HELICOBACTER PYLORI* (HP)-INFECTED FIBROBLASTS *IN VITRO*. A KEY TO THERAPEUTIC INHIBITION OF HP-CARCINOGENESIS?

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Recent epidemiological evidence indicates gastric cancer (GC)-associated *Helicobacter pylori* (Hp) infection continues to be one of the world's highest-mortality tumors due to metastasis and recurrence. Hp penetrates into the deeper layers of the mucosa and may interact with fibroblasts. Gaseous mediator hydrogen sulfide (H₂S) possesses anti-inflammatory and antioxidant properties but whether NaHS, a fast H₂S-donor, can inhibit the Hp-infected cancer-associated fibroblasts (CAFs) remains unknown. Herein, we evaluated the effect of NaHS co-incubation with fibroblasts isolated from surgical gastric specimens of patients with the laparoscopic sleeve gastrectomy and infected *in vitro* with 1x10⁹ live Hp (cagA+; vacA+) per plate for 120 hrs. CAFs were co-incubated with NaHS (50 μ M) or TGF β signaling inhibitor, SB-431542 (10 μ M). CAFs markers and pathways were determined by RT-PCR, Western Blot and immunofluorescence. Hp-infection upregulated a subset of genes typical for CAFs phenotype. The α -SMA was upregulated and incorporated into stress fibres, similarly

as observed for TGF β 1 ($p < 0.05$). Hp-infection triggered inflammatory pathways including the significant increase in TLR2, TLR4, STAT3 and NF κ B (relA) mRNAs ($p < 0.05$). The Snail⁺Twist⁺ phenotype with subsequent incorporation of Twist and Snail into the nucleus was observed. Expression of TLR2, relA and STAT3 genes was dependent on autocrine TGF β 1 signaling. Co-incubation of CAFs with NaHS evoked downregulation of TLR2 and TLR4, STAT3, NF κ B (p65) and Twist ($p < 0.05$). We conclude that H₂S donor is a promising anti-inflammatory agent inhibiting CAFs activation during Hp-infection thereby limiting the risk of Hp-induced GC development and perhaps, serving as a future adjuvant in Hp eradication therapy.

G. Krzysiek-Maczka: None. A. Targosz: None. M. Wierdak: None. M. Strzalka: None. U. Szczyrk: None. J. Czyz: A. Employment (full or part-time); Significant; Jagiellonian University, Department of Cell Biology, The Faculty of Biochemistry, Biophysics and Biotechnology. T. Brzozowski: None. A. Ptak-Belowska: None.

SESSION 07: MICROBIOTA MODULATION BY FMT

07.06

DOUBLE-BLINDED RANDOMIZED CONTROLLED TRIAL ASSESSING THE EFFECT OF TRIPLE FAECAL MICROBIOTA TRANSPLANTATION ON HEPATIC STEATOSIS IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Objective: This double-blinded randomized controlled trial assesses the effect of three consecutive faecal microbiota transplantations (FMT) on hepatic steatosis as a potential treatment strategy for NAFLD.

Material and Methods: Patients with NAFLD, diagnosed by ultrasound or VCTE FibroScan were recruited from hepatology outpatient clinics of the Leiden University Medical Center and affiliated hospitals. Participants were randomized 1:1 to three (t=0; t=3; t=6 weeks) autologous or allogeneic FMTs. Material was derived from two carefully selected FMT-donors (1:1). We assessed changes in hepatic steatosis (MRI-PDFF), glucose tolerance (oral tolerance test), liver biochemistry, and gut-microbiome composition over a 12-week period.

Results: In total, 20 patients participated (10:10). We found no significant change in MRI-PDFF in patients receiving allogeneic [18.6% (SD 9.1%) to 17.7% (SD 9.8%) ($p=0.37$)] or autologous FMT [15.7% (SD 8.4%) to 15.4% (SD 7.4%) ($p=0.59$)] (between-group difference: -0.54%, $p=0.63$) after 12 weeks. Triglycerides decreased over time after allogeneic FMT (coeff: -0.46, 95%CI [-0.9--0.02], $p=0.04$) compared to autologous FMT, whilst no difference was observed in glucose tolerance (tAUC) ($p=0.24$), ALAT ($p=0.21$), ASAT ($p=0.76$), ALP ($p=0.91$), gGT ($p=0.33$), bilirubin ($p=0.86$) and gut-microbial alpha diversity ($p=0.19$). Interestingly, allogeneic FMT was associated with a different microbiome composition at week 12 compared to autologous FMT ($p=0.002$).

Conclusions: Triple allogeneic FMT decreased plasma triglycerides in NAFLD patients over the course of 12 weeks, but did not significantly affect hepatic steatosis, glucose tolerance, liver biochemistry and gut-microbial alpha diversity. Additional clinical and metagenomic analyses are needed to further elucidate the role of the gut microbiome in NAFLD.

B. Groenewegen: None. M.M. Ruissen: None. K.C. van Son: None. J.K. Sont: None. J.J. Keller: None. E.M. Terveer: None. M.E. Tushuizen: None.

07.07

COMPARATIVE EFFICACY OF ENCAPSULATED FECAL MICROBIOTA TRANSPLANTATION (FMT) AND FMT VIA RECTAL ENEMA FOR IRRITABLE BOWEL SYNDROME (IBS): A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED STUDY (CAP-ENEMA FMT TRIAL)

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Objective: Gut dysbiosis is an important potential mechanism linked to pathogenesis of IBS. Limited studies compared efficacy between different routes of FMT administration. This study aimed to compare efficacy of encapsulated FMT, FMT *via* rectal enema, and placebo in IBS patients.

Patients and Methods: Patients aged 18-70 years with IBS were enrolled between April 2021-November 2022 from tertiary care center in Thailand. Patients were randomized into 3 groups: 1) encapsulated FMT (6 capsules twice daily for 2 consecutive days), 2) FMT *via* rectal enema, or 3) placebo. Fifty grams of stool material were used for encapsulation or rectal enema. Encapsulated FMT and placebo capsules were identical. Primary outcome was clinical response defined by decrease in IBS-symptom severity score (IBS-SSS) by ≥ 50 points at 4 weeks. Patients' stool before and after FMT was collected for microbiome analysis.

Results: Thirty-four IBS patients were randomized to receive encapsulated FMT (N=11), FMT *via* rectal enema (N=12), or placebo (N=11). The mean age was 49.5 years and 38.2% of patients were males. Baseline characteristics, IBS subtypes, and mean IBS-SSS at baseline were comparable between groups. Encapsulated FMT provided significant improvement of IBS-SSS (170.0 ± 86.1 vs. 273.6 ± 75.1 , $p=0.007$), overall clinical response (81.8% vs. 18.2%, $p=0.003$), and quality of life (30.7 ± 4.8 vs. 24.9 ± 4.5 , $p=0.003$) at 4 weeks compared with placebo. Moreover, FMT *via* rectal enema demonstrated better IBS-SSS (155.8 ± 102.6 vs. 273.6 ± 75.1 , $p=0.005$), clinical response (83.3% vs. 18.2%, $p=0.002$), and quality of life (29.4 ± 4.9 vs. 24.9 ± 4.5 , $p=0.033$) than placebo. No serious adverse event was observed.

Conclusions: Encapsulated FMT provided high efficacy of overall clinical response, IBS-SSS and quality of life in IBS patients. Administration of either encapsulated FMT or FMT *via* rectal enema is safe and effective with favorable outcomes.

N. Aumpan: None. S. Chonprasertsuk: None. B. Pornthisarn: None. S. Siramolpiwat: None. P. Bhanthumkomol: None. P. Nunanan: None. N. Issariyakulkarn: None. P. Bongkotvirawan: None. V. Mahachai: None. R. Vilaichone: None.

07.08

MYCOBIAL COMMUNITY IN MONOZYGOTIC AND DIZYGOTIC TWINS

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Objective: Twins provide a unique model for assessing the interaction of genetics and environmental factors in microbial dynamics. While there is a growing body of knowledge on the bacterial community, there is limited data on the mycobiome, which is increasingly implicated in the development of several diseases. In this work, we performed an in-depth analysis to elucidate a fungal community in twin cohorts and assess its relationship with associated genetic and environmental factors.

Patients and Methods: A twin cohort of 106 pairs (n=212 faecal samples) was included for analysis. After DNA extraction, the ITS1-ITS2 region was amplified, sequenced and linked to microbiome data for the V1-V2 region of the 16 rRNA gene.

Results: Total reads from the fungal community showed a high degree of variation. Total abundance was independent of twin zygosity status (monozygotic vs. dizygotic) and also independent of sex, mode of delivery, breastfeeding, or household sharing. Compared to bacterial community, fungal abundance tended to be low, with the highest readings for *Candida* and *Geotrichum* and more scattered for the others (e.g., *Saccharomyces*, *Cladosporium*, *Penicillium*). Investigation of the relationship between different factors and individual fungal genera revealed that *Candida* and *Geotrichum* were not correlated with age or household sharing, but were associated with specific bacterial species with high negative correlations, e.g., with *Bifidobacterium* ($p < 0.0001$).

Conclusions: Insights into the dynamics of the fungal community in the twin subjects revealed a unique pattern of variation, distinct from that identified for the bacterial community in the lower GI tract of this population.

K. Lehr: None. J. Skieceviniene: None. N.M. Hipler: None. C. Thon: None. D. Schanze: None. M. Zenker: None. J. Kupcinskas: None. A. Link: None. A. Gecioniene: None.

SESSION 09: H. PYLORI MANAGEMENT

09.05

USE OF MACHINE LEARNING MODELS TO PREDICT FAILURE OF *HELICOBACTER PYLORI* ERADICATION THERAPY: A TWO COUNTRY VALIDATION STUDY

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Objective: The success rate of clarithromycin-containing *H. pylori* eradication has been declining globally due to emergence of antibiotic resistance. The aim of the study was to explore the role of different machine learning algorithms in predicting failure of *H. pylori* eradication therapy based on pre-treatment clinical features.

Patients and Methods: We included 84,609 adult patients who had received the first course of clarithromycin-containing triple therapy in Hong Kong (HK) from 2003 to 2013 as training set. Results were validated in 27,736 HK patients who had received *H. pylori* eradication between 2014 and 2017 (internal cohort); and 18,050 patients in the United Kingdom IMRD database who had received similar triple therapy between 2012 and 2017 (external cohort). The performance of 11 available machine learning algorithms, based on a total of 27 pre-treatment clinical parameters, in predicting the failure of triple therapy was compared.

Results: The eradication failure rate in the training, internal and external validation cohort was 5.9%, 9.5% and 6.1%, respectively. The best performance in terms of highest AUC was achieved by the Extra-Tree Classifier model (internal validation set: 0.88, 95% CI 0.87-0.88 and external validation set: 0.85, 95% CI, 0.85-0.86). Top features of importance in predicting eradication failure included the time interval between the prior antibiotic use and triple therapy (48.8%), patient's age (29.1%) and type of triple therapy given (6.28%).

Conclusions: Machine learning algorithm, based on simple pre-treatment clinical parameters, could help to identify patients at high risk of failure from clarithromycin-containing triple therapy for *H. pylori*.

W.K. Leung: None. F. Jiang: None. T.K.L. Lui: None. W.C.Y. Lau: None.

09.06

SUSCEPTIBILITY GUIDED TREATMENT OF *HELICOBACTER PYLORI* INFECTION: SERBIAN STUDY EXPERIENCE

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Objective: The high prevalence of *Helicobacter pylori* (*H. pylori*) infection and its growing antibiotic resistance rates have made the eradication of this pathogen a global problem. Considering antibiotic resistance has been recognized as the leading cause of treatment failure, efforts have been made to overcome this problem. Our aim was to evaluate the results of tailor-made eradication therapy.

Material and Methods: A retrospective interventional study including 180 *H. pylori*-positive patients was conducted. Pretreatment susceptibility to clarithromycin and fluoroquinolones was assessed using the real-time PCR molecular test. Therapy was prescribed based on the individual antibiotic susceptibility results.

Results: The overall eradication rate was 86.1%. The most commonly prescribed regimen in treatment-naïve patients was quadruple-clarithromycin+amoxicillin+metronidazole (60%), followed by single-capsule Pylera[®] (19%), triple-levofloxacin-based therapy (11%), and dual amoxicillin therapy (9%). Overall, the first-line eradication rate was 93%, with optimal results obtained in both quadruple regimens with and without bismuth (94% and 100%, respectively). In the second line, most patients were treated with triple-levofloxacin-based therapy (50%), followed by single-capsule Pylera[®] (34%), quadruple-clarithromycin+amoxicillin+metronidazole (12%), while dual amoxicillin therapy was prescribed in 4% of patients. Acceptable eradication rates were obtained only in the bismuth quadruple therapy group (86%).

Conclusions: Our results imply that non-bismuth clarithromycin-based quadruple therapy can be a good first-line therapy option if pretreatment susceptibility testing is obtained. Susceptibility testing and tailor-made therapy should be implemented in order to avoid treatment failure and subsequent multiple eradication attempts, which in turn further increase antibiotic resistance.

V. Milivojevic: None. D. Kekic: None. L. Ranin: None. T. Milosavljevic: None.

09.07

RIFABUTIN-CONTAINING TRIPLE THERAPY VERSUS BISMUTH QUADRUPLE THERAPY FOR *HELICOBACTER PYLORI* RESCUE TREATMENT: A MULTICENTER, RANDOMIZED CONTROLLED TRIAL

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Objective: To compare the efficacy and safety of rifabutin-containing triple therapy with bismuth quadruple therapy for rescue treatment of *Helicobacter pylori* (*H. pylori*).

Patients and Methods: This was a non-inferiority study trial of *H. pylori* treatment for subjects who had failed at least two prior treatments. Subjects were randomly assigned to receive rifabutin triple therapy with 14-day esomeprazole (20 mg bid), amoxicillin (1.0 g bid) and rifabutin (150 mg bid) or bismuth quadruple therapy with esomeprazole (20 mg bid), bismuth (220 mg bid), plus metronidazole (400 mg qid) and tetracycline (500 mg qid). Antimicrobial susceptibility was assessed by agar dilution and E-test methods.

Results: From May 2021 to October 2022, a total of 364 subjects were randomized. The eradication rates by intention-to-treat, per-protocol, and modified intention-to-treat were 89.0% (162/182, 95% confidence interval (CI) 83.6%-92.8%), 94.0% (157/167, 95% CI 89.3%-96.7%) and 93.6% (162/173, 95% CI 89.0%-96.4%) for rifabutin triple group. For bismuth quadruple group, they were 89.6% (163/182, 95% CI 84.3%-93.2%), 95.3% (143/150, 95% CI 90.7%-97.7%) and 93.7% (163/174, 95% CI 89.0%-96.4%).

Conclusions: The rifabutin triple therapy is an alternative to classical bismuth quadruple therapy for the rescue treatment of *H. pylori* with lower side effects and higher compliance.

H. Lu: None.

SESSION 10: DISEASES & MICROBIOTA

10.05

CAGA DETERMINES THE MICROBIOME CHANGES AND RISK OF COLORECTAL CANCER ELICITED BY *HELICOBACTER PYLORI* INFECTION

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Infection with *Helicobacter pylori* CagA-positive strains is the most important risk factor for gastric cancer development, but epidemiological data also show an increased risk for infected individuals to develop colorectal cancer (CRC). However, a direct causal and functional link between *H. pylori* infection, its virulence factor CagA and CRC was so far lacking. We infected Apc-mutant mouse models with *H. pylori* and conducted a comprehensive analysis of *H. pylori*-induced changes in intestinal immune responses and microbial signatures. In addition, Apc-mutant mice were infected with an *H. pylori* CagA-mutant strain to assess its impact on colon tumorigenesis. *H. pylori* infection accelerated tumor development in Apc-mutant mice and altered the immune response in the intestinal epithelium. We identified a pro-inflammatory and mucus-degrading microbial signature together with the loss of goblet cells. These tumor-promoting effects were also seen after stool transfer in germ-free Apc-mutant mice, which underlines a strong dependency on the microbiota. Notably, a CagA-mutant strain was not as potent in inducing the pro-carcinogenic and pro-inflammatory phenotype in Apc-mutant mice as the CagA-proficient strain. This phenotype was also transmissible *via* stool transfer, which suggests a CagA-dependent shaping of the intestinal microbiota. Our studies provide evidence that *H. pylori* infection is a strong causal promoter of colorectal carcinogenesis and that these tumor-promoting effects are largely dependent on its virulence factor CagA and modulation of the intestinal microbiome. Therefore, implementation of *H. pylori* and CagA status into CRC prevention programs should be considered. All authors exclude any conflict of personal and funding interests.

V. Engelsberger: None. A. Ralser: None. R. Mejías-Luque: None. M. Gerhard: None.

10.06

LACTOBACILLUS - A NEW KEY PLAYER IN GASTRIC CARCINOGENESIS?

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Objective: Besides *Helicobacter pylori*, other bacteria seem to be associated with gastric adenocarcinoma (GC). We aimed to identify what bacteria are significantly linked to GC in a high-risk Han Chinese population through a microbiota survey. Given that lactic acid bacteria (LAB) are frequently observed in GC, we also determined for the first time the true impact of three LAB on gastric precancerous lesions (GPLs) and GC, through a meta-analysis.

Materials and Methods: Microbiota from gastric biopsies samples (GC = 17 and functional dyspepsia [FD] = 155) was sequenced using 16S rRNA gene (DNA) and transcript (cDNA) amplicon sequencing (Illumina MiSeq 2x250 bp). For the meta-analysis, the literature search was performed on PubMed, Scopus, and Science Direct. Relative abundance (RA) and standard deviation data was collected from 20 studies. Statistical analyses included pooled effect size estimation, publication bias, heterogeneity, and sensitivity analysis.

Results: Alpha and beta diversity differed significantly between GC and FD subjects. The *Lactobacillus* RA was significantly higher in GC across all analyses, independently of *H. pylori* status, in both DNA and cDNA subgroups. The meta-analysis, comprising 1,298 subjects, showed that the pooled mean RA of LAB was significantly increased in cases (GPLs+GC) compared to controls ($p=0.040$). Particularly, the *Lactobacillus* pooled mean RA was higher in GC ($p<0.001$) and dysplasia ($p=0.014$) patients from high GC risk populations.

Conclusions: There is significant enrichment of *Lactobacillus* in GC, which has been validated through our comprehensive meta-analysis, indicating that this is an important dysbiotic signature of gastric carcinogenesis.

K. Vinasco: None. N. Castaño-Rodriguez: None. N.O. Kaakoush: None. S. Lo: None. E. Kalluzhathil: None.

10.07

URINARY LITHOGENIC PROFILE AND GUT AND URINARY MICROBIOTA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Objective: Nephrolithiasis (NL) is a common extra-intestinal complication of inflammatory bowel diseases (IBD), often induced by enteric hyperoxaluria. Growing evidence highlights the association between gut microbiota and NL, emphasising the role of some oxalate-degrading bacteria, representing the mainstay of the so-called “gut-kidney axis”. Recent studies hypothesise the involvement of urinary microbiota, but no data on IBD patients are available. Our study aims to analyse the urinary lithogenic profile in IBD patients and its relationship with gut and urinary microbiota.

Patients and Methods: Consecutive adult patients with IBD were prospectively enrolled. Ileoanal pouch, ileostomy, colostomy or short-bowel syndrome were exclusion criteria. All patients underwent abdominal ultrasound, blood tests and 24h-urine collection for lithogenic profile analysis, including calcium oxalate relative saturation ratio (RSR_{CaOx}). In a subgroup of patients, urinary and faecal microbiota were analysed through 16S rRNA sequencing.

Results: 48 patients were enrolled – 25 affected by Crohn Disease (CD) and 23 by Ulcerative Colitis (UC). NL was more frequent in CD than in UC (32% vs. 13%). Gut microbiota analysis was performed on 22 patients, stratified based on median RSR_{CaOx} (higher or lower than the median). Significantly different β -diversity was observed between the two groups ($p=0.025$) and patients with an elevated RSR_{CaOx} showed a higher relative abundance of Bacteroidetes and a lower abundance of Firmicutes (p -value <0.05). No statistically significant difference was found in urinary microbiota composition.

Conclusions: Our study reports an association between NL development and Firmicutes/Bacteroidetes imbalance in gut microbiota, suggesting possible further studies to identify patients at higher risk of NL.

I. Mignini: None. L. Masucci: None. F. De Maio: None. V. Blasi: None. C. Agrillo: None. F.R. Monzo: None. L. Laterza: None. F. Scaldaferrri: None. C. Settanni: None. D. Napolitano: None. E. Schiavoni: None. D. D'Amato: None. G. De Ninno: None. S. Baroni: None. M. Garcovich: None. L. Riccardi: None. A. Gasbarrini: None. P.M. Ferraro: None. A. Papa: None.

POSTER

POSTER SESSION 01: *HELICOBACTER* 1

P01.03

EVALUATION OF IN VITRO BIOFILM FORMATION BY *HELICOBACTER PYLORI*

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Objective: The survival of *Helicobacter pylori* in water systems may be due to its association on surfaces attached to biofilms, which would explain its survival, transmission and infection through reclaimed water and drinking water distribution systems. The ability of *H. pylori* to form biofilms in environments where there are variations in environmental conditions, such as temperature and nutrient availability has not been demonstrated. Therefore, the aim of this study was to assess the ability of this pathogen to form biofilms under different stressful environmental conditions.

Material and Methods: *H. pylori* NCTC11637 was used for this study. Biofilm formation assays were performed according to previously described methods (Yonezawa et al, 2009) and biofilm was measured by Crystal Violet method. It was also evaluated if nutrient availability and/or oxygen conditions affected the formation of *H. pylori* biofilms. The values of OD 570 “basic” and OD₅₇₀ “biofilm” were used to determine the rate of biofilm formation.

Results: The results showed that *H. pylori* has a “strong” *in vitro* biofilm formation ability when nutrient availability is optimal (100%), microaerophilic conditions and 37°C. When nutrient availability was limited, the results indicated weak formation of biofilms. Under aerobic conditions, *H. pylori* formed biofilms only under optimal nutritional conditions. *H. pylori* cannot replicate under nutritional scarcity and then it is not able to form biofilms. The presence of oxygen seems not to be affected to growth and form biofilms. Supported by the Spanish Ministerio de Ciencia, Innovación y Universidades (PID2019-105691RB-I00 / AEI / 10.13039/501100011033).

Y. Moreno: None. I. Hortelano: None. L.T. Hansen: None. M.A. Ferrús: None.

P01.04

INDIVIDUALIZED DIAGNOSIS AND ERADICATION THERAPY FOR *HELICOBACTER PYLORI* INFECTION BASED ON GENE DETECTION OF CLARITHROMYCIN RESISTANCE IN STOOL SPECIMENS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objective: Empiric therapy for *Helicobacter pylori* infection results in significantly increased antibiotic resistance and decreased eradication efficacy. The genotypic testing of clarithromycin resistance from stool specimens is a promising method for individualized diagnosis and treatment. This study aimed to determine the status of research and application on this method through a systematic review and meta-analysis.

Materials and Methods: PubMed, Embase, MEDLINE, and WAN FANG databases, were searched for relevant literature. The quality of included diagnostic articles was evaluated using the quality Assessment of Diagnostic Accuracy Studies-2 tool. A bivariate random-effect model was conducted to calculate the diagnostic accuracy of genotypic testing of clarithromycin resistance.

Results: A total of 16 diagnostic-related were included and analyzed after exclusions. The pooled sensitivity and specificity of diagnostic meta-analysis were 0.93 (95% confidence interval [CI]: 0.90-0.96) and 0.98 (95% CI: 0.93-1.00), respectively. The area under the curve (AUC) of the summary receiver operating characteristic was 0.97 (95%CI: 0.95-0.98). The genotypic testing in stool samples had heterogeneous sensitivity ($Q=37.82$, $p<0.01$, $I^2=37.82$) and specificity ($Q=60.34$, $p<0.01$, $I^2=93.72$) in detecting clarithromycin resistance. Purification method, stool sample weight, real-time PCR and antimicrobial susceptibility testing as reference accounted for the heterogeneity of pooled sensitivity, while patient age, purification method, stool sample weight and real-time PCR for the heterogeneity of pooled specificity.

Conclusions: The genotypic testing of clarithromycin resistance from stool specimens is an accurate, convenient, non-invasive and rapid detection technology, providing a definitive diagnosis of clarithromycin resistance and guiding the rational antibiotic selection.

X. Ren: None. Y. Shi: None. B. Suo: None. X. Yao: None. H. Lu: None. C. Li: None. Y. Zhang: None. L. Zhou: None. X. Tian: None. Z. Song: None.

P01.05

INCIDENCE OF *HELICOBACTER PYLORI*-RELATED PEPTIC ULCER DISEASE HAVE DECREASED FOR LAST 10 YEARS: A MULTICENTER STUDY USING A COMMON DATA MODEL IN KOREA

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Objective: The recent clinical characteristics of peptic ulcer disease (PUD) have not well been studied in the past decades. We aimed to evaluate the changing trend and characteristics of PUD in Korea.

Patients and Methods: We analyzed large-scale 7 hospital databases converted into Observational Medical Outcomes Partnership-Common Data Model. We assessed newly-diagnosed PUD *via* combination of ICD-10 code, esophagogastroduodenoscopy, and exposure of proton pump inhibitor. We classified PUD patients who tested rapid urease test or *Helicobacter pylori* (*H. pylori*) serologic test as three groups [*H. pylori*-related, drugs (NSAIDs or aspirin)-related, and idiopathic (*H. pylori*/NSAID/aspirin- negative)] and compared incidence among three groups.

Results: A total of 26,785 patients in 7 databases between 2010 and 2019 were included. The total number of PUD patients showed no declining pattern across databases ($p=0.69$ for trend). The old age (≥ 65 years) were included in 38.8% of total patients, and 58% were male. Of 19,601 patients, 41.8% were *H. pylori*-related, 36.1% were drug-related, and 22.1% were idiopathic PUD. The *H. pylori*-related PUD showed decreasing trend after 2014 ($p=0.01$ for trend), and drug-related PUD showed increasing trend only in the old age group ($p=0.001$ for trend). There were more patients with chronic liver disease in the idiopathic PUD (idiopathic vs. drugs-related vs. *H. pylori*-related; 8.1% vs. 6.3% vs. 2.7%; $p<0.001$).

Conclusions: The incidence of *H. pylori*-related PUD decreased whereas drug-related PUD increased over past 10 years, especially, in older adult. Given the aging population increases, we should focus on the control of drugs-related PUD.

W. Shin: None. S. Seo: None. Y. Choi: None. T. Kim: None.

P01.06

THE CURRENT JAPANESE PREVALENCE OF *HELICOBACTER PYLORI* INFECTION IN CHOLECYSTIC BILE

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Objective: The relationship between *Helicobacter pylori* (*Hp*) infection of human biliary system and biliary diseases has been indicated. But the prevalence of *Hp* infection in bile has been a discrepancy between reports. Today, the rate of *Hp* infection in Japan has been rapidly reduced because of an approval of eradication therapy for *Hp*-infected-gastritis by the Japanese medical insurance system from February 2013. There has been a lack of information regarding the prevalence of *Hp* infection in current Japanese bile.

Patients and Methods: The objectives of this cross-sectional study were to investigate whether *Hp* could be detected in the cholecystic bile by using the *Hp*-specific-stool-antigen test (HpSA), and to evaluate the prevalence of *Hp* infection in bile. We enrolled consecutive 30 patients undergoing cholecystectomy in our hospital from November 2022 to February 2023. Bile was aspirated by puncturing the needle into the gall-bladder during surgery or soon after resection, and immediately screened with HpSA (Testmate Rapid Pylori Antigen[®]; Wakamoto Pharmaceutical Co., Ltd). They were divided into 3 groups: *Hp*-current-infected-stomach, *Hp*-past-infected-stomach, *Hp*-never-infected-stomach, depending on assessments including a history of eradication for *Hp*, serum *Hp* antibody, and findings of Upper gastrointestinal endoscopy.

Results: *Hp* was found in 16 (53 %) of total 30 patients; in 4 (100%) of *Hp*-current-infected-stomach (N=4), in 6 (75%) of *Hp*-past-infected-stomach (N=8), and in 6 (33.3%) of *Hp*-never-infected-stomach (N=18).

Conclusions: Although the prevalence of *Hp* infection in bile was higher in *Hp*-current or *Hp*-past-infected-stomach than *Hp*-never-infected-stomach, *Hp* in bile was unexpectedly present in 33.3 % of *Hp*-never-infected-stomach.

Y. Fukuda: None. T. Sakamoto: None. Y. Shoji: None. N. Moriyama: None. K. Nakamichi: None. S. Matsubayashi: None. K. Nabeshima: None. Y. Nakagawa: None. K. Sakamoto: None. R. Nakamura: None. K. Komiya: None. H. Ureshino: None. F. Ishii: None. S. Ito: None. M. Morimoto: None. Y. Yoshida: None. T. Noritomi: None. S. Noda: None.

P01.07

MANAGEMENT OF *HELICOBACTER PYLORI* INFECTION IN A CENTER FROM THE NORTH-EAST REGION OF ROMANIA

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Objective: *Helicobacter pylori* (*H. pylori*) infection is one of the most widespread in the world. A study carried out in the North-East Region of Romania showed a prevalence of *H. pylori* infection of 39.9%. It is necessary to identify an individualized treatment management of *H. pylori* infection depending on resistance to antibiotics in the region.

Material and Methods: 117 patients hospitalized in Bacău County Emergency Hospital, Gastroenterology department, October 2019-November 2020, identified with *H. pylori* infection by non-invasive method (faecal antigen) performed upper digestive endoscopy and collection of 2 biopsies for the isolation of *H. pylori* strains. 90 positive cultures were obtained and examined for antibiotic susceptibility for amoxicillin (AMX), clarithromycin (CLR), metronidazole (MTZ), levofloxacin (LEV), tetracycline (TET), rifampicin (RIF). The diffusimetric method with E-tests according to the EUCAST guideline was used. The results were analysed based on demographic criteria and the patients' background.

Results: The highest antibiotic resistance of the *H. pylori* strains obtained was recorded in: MTZ (65/90, 72.2%), CLR (27/90, 30%), AMX (24/90, 26.7%). The highest resistance to CLR was observed in the female sex (21/45, 46.7%), in the 30-49 age group (8/15, 53.3%), in urban patients (13/43, 30.2%).

Conclusions: A different management of the treatment of *H. pylori* infection can be made in the North-East Region of Romania: thus, men, from rural areas, aged over 49 years have high chance of response to standard eradication therapy (PPI+AMX+CLR). For women, from the urban environment, quadruple therapy with Bismuth salts should be used as the first line of treatment.

E.L. Popovici: None. A.E. Oros: None. M. Indreas: None. I.L. Baltatescu: None.

P01.08

GENOMIC DIVERSITY OF GASTRIC/ENTERIC PATHOGENS THROUGH HIGH-END COMPUTING: IMPLICATIONS FOR GLOBAL INFECTION CONTROL PRIORITIES

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Multiple drug resistance in bacteria is a functional trait leading to fitness optimization. Acquisition and transmission of drug resistance in bacteria in different global lineages could be best studied by whole genome sequencing and mapping of functional consequences of genetic polymorphisms on an epidemiological scale. Machine learning-based approaches can further enhance the analysis of genetically diverse pathogens, allowing the identification of key factors involved in antimicrobial resistance (AMR). We analyzed whole genome sequencing data comprising approximately twenty thousand genome sequences of different gastric/enteric pathogens (*Helicobacter pylori*, *Escherichia coli*, *Salmonella enterica*, *Klebsiella pneumoniae*, and *Vibrio cholerae*) in conjunction with microbiological data such as resistance phenotypes. Further, we carried out an extensive survey of plasmid sequences. With the help of artificial intelligence (AI) and machine learning (ML) algorithms, this survey and other genomic features were harnessed to glean evolutionary trends of fitness traits and virulence repertoires across different species and lineages. We obtained the first extensive data on the prevalence of genetic coordinates (AMR genes, mutations, and plasmid backbones) directly or indirectly associated with drug resistance through high-resolution genomics of studied sequences. Compared to traditional subtyping methods, such as MLST and genotyping, AI/ML based comparative genomics facilitated lineage-specific identification of virulence factors such as toxin-antitoxin systems and AMR encoding genes, and provided a framework to assign hitherto unknown isolates to defined lineages. We believe these approaches and findings would be helpful in understanding and analyzing the spread of drug resistant pathogens, thereby strengthening the global infection control priorities and policies.

N. Ahmed: None.

P01.09

H. PYLORI PREVALENCE IS ASSOCIATED WITH HIGH ALTITUDE IN A POPULATION OF DYSPEPTIC PATIENTS IN NEPAL**M. A. TRUBSHAW¹, J. BORNSCHEIN¹, M. E. TRUBSHAW²**¹University of Oxford, Oxford, United Kingdom; ²MEDyARTE Foundation, Leatherhead, United Kingdom

Objective: A high proportion of patients who attend the high-altitude MEDyARTE Foundation Clinic in the Himalayan Nar-Phu Valley, Nepal, present with dyspepsia. Previous studies estimated the prevalence of *H. pylori* in Nepalese regions at 24%-71%. We aimed to evaluate the distribution of infection according to altitude and offer explanations for findings.

Material and Methods: Four general medical clinics (two at high altitude 3000 m, two at ultra-high altitude 4000 m) were held in Himalayan villages in the Manang district of Nepal. A patient was considered 'likely gastritis' if they exhibited at least 1 major and 3 minor symptoms from the criteria established by Du et al (2014). A point-of-care *H. pylori* stool antigen test was performed on these patients.

Results: 396 patients visited the clinics, 227 with dyspeptic symptoms. 82% of these were *H. pylori* positive. A higher proportion of positives was seen in ultra-high compared to high regions (98% vs. 63%; $p < 0.001$). People in ultra-high regions lived in wooden houses together with livestock, an open fire, a shared water source and no sewage treatment. Their diet consisted of rice, pickles and daal, with little access to meat or fresh produce. In high villages, people lived in more modern houses with gas heaters, treated water, and had a more varied diet with access to fresh produce.

Conclusions: This study provides further evidence to support the hypothesis that *H. pylori* infection is associated with low socio-economic status and harsh living conditions. Further work is required to determine the implications of these findings on population health.

M.A. Trubshaw: None. J. Bornschein: None. M.E. Trubshaw: None.

P01.10

PREVALENCE AND SEVERITY OF GASTROESOPHAGEAL REFLUX DISEASE IN JAPAN OVER THE PAST 10 YEARS**M. HOJO, S. OKI, T. TAKEDA, K. UEDA, N. SUZUKI, Y. AKAZAWA, H. UEYAMA, T. SHIBUYA, S. WATANABE, A. NAGAHARA**

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Objective: In recent years, the number of Japanese currently infected with *H. pylori* has been decreasing. It is conceivable that the intragastric pH of the Japanese population would be lower than before. On the other hand, the use of proton pump inhibitor has increased in recent years. Therefore, in a context of changing intragastric pH in the Japanese population, the changes of gastric acid-related diseases over time have not been fully investigated in clinical practice.

The aim of the study was to clarify the changes in the prevalence of reflux esophagitis (RE) and non-erosive gastro-esophageal reflux disease (NERD) over time.

Patients and Methods: The subjects of this study are patients who underwent upper endoscopy at our department from January 2012 to December 2021. In each year, data on age, gender, BMI, *H. pylori* infection rate, history of taking acid secretion inhibitors, and the prevalence of RE and NERD was extracted retrospectively from the database and medical records. We examined changes over time with respect to the extracted data.

Results: The total number of patients examined was 61,590, mean age 68.3 years, mean male ratio 53.5%, mean BMI 24.1 kg/m², mean *H. pylori* infection rate 15.8%, RE prevalence 10.3% (mild 9.7%, severe 0.6%), NERD prevalence 39.5%. There was no change over time in age, male ratio, BMI, or prevalence and severity of RE. However, *H. pylori* infection rate and NERD prevalence were confirmed to decrease significantly and progressively ($p < 0.001$).

Conclusions: The prevalence and severity of RE did not change over time, but the prevalence of NERD significantly decreased.

M. Hojo: None. S. Oki: None. T. Takeda: None. K. Ueda: None. N. Suzuki: None. Y. Akazawa: None. H. Ueyama: None. T. Shibuya: None. S. Watanabe: None. A. Nagahara: None.

P01.11

BISMUTH-BASED QUADRUPLE THERAPY FOR THE FIRST-LINE TREATMENT OF CLARITHROMYCIN-RESISTANT *HELICOBACTER PYLORI* INFECTION: A PROSPECTIVE RANDOMIZED COMPARISON OF 7-DAY OR 14-DAY TREATMENT DURATION

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Objective: Bismuth-based quadruple therapy (BQT) is a treatment option for clarithromycin-resistant *Helicobacter pylori* (HP) infections. This study aimed to investigate the effectiveness of 7-day vs. 14-day BQT as a first-line treatment for clarithromycin-resistant HP infections.

Patients and Methods: In total, 162 subjects with peptic ulcer disease who were HP treatment-naïve and confirmed to have clarithromycin-resistant HP infection by dual-priming oligonucleotide-based multiplex polymerase chain reaction (DPO-PCR) were enrolled. The enrolled subjects were prospectively randomized to receive 7-day or 14-day BQT. HP eradication was assessed with ¹³C-urea breath test. The eradication, compliance, and adverse event rates of the two groups were investigated.

Results: The overall eradication rates in intention-to-treat (ITT) and per-protocol (PP) analyses were 83.0% (95% CI 77.2-88.9%, 132/159) and 89.8% (95% CI 84.9-94.7%, 132/147), respectively. The eradication rates in the ITT analysis were 79.0% (95% CI 70.1-87.9%, 64/81) in the 7-day group and 87.2% (95% CI 79.8-94.6%, 68/78) in the 14-day group ($p = 0.170$). The eradication rates in the PP analysis were 86.5% (95% CI 78.7-94.3%, 64/74) in the 7-day group and 93.2% (95% CI 87.4-99.0%, 68/73) in the 14-day group ($p = 0.182$). Clinically significant adverse events occurred in 18.2% of patients. No statistically significant differences were found in the rates of individual adverse events or all adverse events between the two groups.

Conclusions: Both 7-day and 14-day BQT were effective and safe as first-line therapy in HP infections identified as resistant to clarithromycin with a DPO-PCR assay. Fourteen-day BQT may be preferable as first-line therapy for clarithromycin-resistant HP infections.

J. Oh: None. C. Lim: None. S. Lee: None.

POSTER SESSION 02: HELICOBACTER 2

P02.01

HELICOBACTER PYLORI FOUND INCIDENTALLY DURING UPPER ENDOSCOPY PERFORMED FOR DIAGNOSIS OF COMMON PEDIATRIC GASTROINTESTINAL DISEASES

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Objective: *Helicobacter pylori* (*H. pylori*) gastritis may be an incidental finding during upper endoscopy performed to diagnose Celiac disease (CeD), Inflammatory bowel disease (IBD), and Eosinophilic esophagitis (EoE). We aimed to describe the incidence of *H. pylori* in children undergoing endoscopy for CeD, IBD and EoE and determine the indications for treatment.

Materials and Methods: A retrospective, single center study based on the review of endoscopy reports of pediatric patients, diagnosed with CeD, IBD and EoE, between 1/2017 and 12/2021. Data collected included; age, gender, hematologic parameters, endoscopic, histologic and *H. pylori* culture results, information on eradication treatment.

Results: *H. pylori* gastritis was diagnosed in 120/558 (21.5%) children, [72 (60%) female, mean age 10.6 years] during gastroscopy performed for the diagnosis of other GI diseases. *H. pylori* was present in 87/404 (21.5%) CeD, 27/113 (23.9%) IBD and 6/41 (14.6%) EOE patients ($p=0.46$). The main indication for treatment was the presence of ulcers, 4/120 (3.3%), and erosions in 17/120 (14.2%). Eradication treatment was recommended in 22/120 (18.3%) patients, 8/87 (9.2%) CeD, 10/27 (37%) IBD and 4/6 (66.7%) EoE patients, $p<0.001$. Four independent positive treatment predictors were identified; age above 10 years, (OR=10.57 [95%CI 1.88-59.36], $p=0.007$), the presence of nodular gastritis (OR=5.03 [95%CI 1.09-23.15], $p=0.38$), erosions (OR=49.21 [95%CI 8.19-295.83], $p<0.000$) and ulcers (OR=22.69 [95%CI 1.25-410.22], $p=0.035$). CeD was a strong negative predictor for treatment (OR=0.23 [95%CI 0.002-0.241], $p=0.002$).

Conclusions: *H. pylori* gastritis is a common incidental finding during endoscopy. The indications for treatment are not well defined and should be further investigated.

M. Kori: None. Y. Dolstra: None.

P02.02

PRE-CLINICAL VALIDATION OF NANOPYL®: A BIOENGINEERED APPROACH FOR HELICOBACTER PYLORI MANAGEMENT

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Objective: *Helicobacter pylori* resistance to antibiotics increased over the last decade up to 40%¹. Previously, we developed lipid nanoparticles (NanoPyl®) able to specifically impair *H. pylori* viability and biofilms *in vitro*^{2,3,4}. Here, we report NanoPyl® pre-clinical validation.

Material and Methods: NanoPyl® was prepared as described^{3,4}. Infection was established in C57BL/6 male mice with *H. pylori* SS1 strain by oral gavage (1×10^{10} CFU/mL) over 4 weeks⁵. After, NanoPyl® was administered (2vmg/mL) *via* oral gavage or *ad libitum*. In the *ad libitum* protocol, higher NanoPyl® dosages (4 and 8 mg/mL) were tested. After 14-days treatment, mice were euthanized and stomachs processed⁵. Gut microbiome of mice was analyzed in feces by sequencing data-analysis, comparing the microbiome composition before and after NanoPyl®. The microbial community was identified by amplification of the 16S rRNA gene using the Ion 16STM Metagenomics Kit and the Ion S5XL system.

Results: NanoPyl® achieved an eradication rate of 50% and reduced the bacterial load in at least 90%, independently of the administration protocol. Increasing NanoPyl® concentration did not enhance the overall anti-*H. pylori* performance. NanoPyl® was well tolerated and did not induce dysbiosis or relevant changes in mice's gut microbiome.

Conclusions: NanoPyl® is a safe and effective strategy for *H. pylori* infection management.

Acknowledgments: FCT for CEECIND/01210/2018; La Caixa Foundation(Caixa Research Validate 2022)

P. Parreira: None. C. Martins: None. L. Pereira: None. C.L. Seabra: None. C. Nunes: None. N. Pedro: None. S. Reis: None.

P02.03

MINOCYCLINE VS. TETRACYCLINE IN BISMUTH-CONTAINING QUADRUPLE THERAPY FOR *HELICOBACTER PYLORI* RESCUE TREATMENT: A MULTICENTRE, RANDOMIZED CONTROLLED TRIAL

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Objective: To compare the efficacy and tolerability of minocycline vs. tetracycline in bismuth-containing quadruple therapy for *Helicobacter pylori* (*H. pylori*) rescue treatment.

Materials and Methods: This study was a multicenter, randomized controlled, non-inferiority trial. *H. pylori*-infected subjects with multiple treatment failure were randomly (1:1) allocated to receive 14-day therapy with esomeprazole 20 mg b.i.d, bismuth 220 mg b.i.d, plus metronidazole 400 mg q.i.d and minocycline 100 mg b.i.d (minocycline group) or tetracycline 500 mg q.i.d (tetracycline group). Primary outcome was *H. pylori* eradication rate evaluated by 13 C-urea breath test at least 6 weeks after the end of treatment. Antibiotic resistance was determined using E test method.

Results: 368 subjects were randomized. The eradication rates in minocycline group and tetracycline group were 88.0% (162/184, 95% CI 83.3-92.8%) and 88.6% (163/184, 95% CI 83.9-93.2%) in intention-to-treat analysis, 98.0% (149/152, 95% CI 95.8-100%) and 97.4% (150/154, 95% CI 94.9-99.9%) in per-protocol analysis, 93.1% (162/174, 95% CI 89.3-96.9%) and 93.1% (163/175, 95% CI 89.4-96.9%) in modified intention-to-treat analysis. Minocycline, tetracycline and metronidazole resistance rates were 0.7%, 1.4% and 89.6%, respectively. Non-inferiority of minocycline was confirmed ($p < 0.025$). Metronidazole resistance did not affect the efficacy of either therapy. The two therapies exhibited comparable frequencies of adverse events (55.4% vs. 53.3%). Dizziness was the most common adverse events in the minocycline group.

Conclusions: Minocycline can be an alternative to tetracycline in bismuth-containing quadruple therapy for *H. pylori* empirical rescue treatment, irrespective of metronidazole resistance. However, relatively high incidence of adverse events in both regimens should be emphasized.

H. Lu: None.

P02.04

MOLECULAR DIAGNOSIS OF *HELICOBACTER PYLORI*: VALIDATION OF ALLPLEX *H. PYLORI* AND CLARIR ASSAY

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Objective: We aimed to validate Allplex™ *H. pylori* and ClariR Assay (Seegene) for the detection of *Helicobacter pylori* (Hp) and of clarithromycin (Clari) resistance determination in gastric biopsies according to the ISO15189 certification requirements.

Materials and Methods: Precision was assessed against QCMD external quality evaluation. Reproducibility was evaluated using Hp culture-negative (n=1), -positive/ClariR (n=3) and -positive/ClariS (n=1) samples. Methods comparison was performed on consecutive gastric biopsies with Amplidiag® *H. pylori* + ClariR (Mobidiag) previously ISO15189-certified. Discrepancies were investigated by Hp-selective culture and Clari result by MIC determination using Etest (BioMérieux) or by Sanger sequencing.

Results: Allplex reached 100% in precision and reproducibility. Compared to Amplidiag, of the 898 samples analyzed (758 Hp negative, 112 Hp ClariS, 28 Hp ClariR), 867 (96.5%) were fully concordant. 20 biopsies were negative for Hp by Amplidiag and positive by Allplex (all culture neg), while 7 biopsies were Amplidiag Hp+ and Seegene Hp- (one sample was culture positive). Regarding clarithromycin status, 2/112 Amplidiag ClariS samples were considered ClariR by Allplex (one was sequenced as WT and the other with Ct (39.8) failed at sequencing. Both were not cultivable), while 2/28 Amplidiag ClariR were considered Clari S by Allplex (one was sequenced A2143G and Etest-confirmed ClariR and the other was WT and not cultivable).

Conclusions: Amplidiag and Allplex are two robust molecular detection kits for Hp and ClariR. According to our ISO15189 certification criteria, Allplex showed equivalent performance to Amplidiag. Allplex has the advantage of being automated on Hamilton StarLet including extraction and PCR setup improving traceability.

P. Bogaerts: None. M. Hoebeke: None. C. Berhin: None. I. Wallemme: None. W. Bouchahrouf: None. O. Denis: None. T.D. Huang: None.

P02.05

HIPPO PATHWAY DYSREGULATION ON *HELICOBACTER PYLORI*-RELATED GASTRIC CANCER

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Objective: *Helicobacter pylori* is known to mediate chronic inflammatory cascade in gastric epithelial cells. The role of YAP/TAZ, a major signal in Hippo pathway in *H. pylori*-mediated gastric cancer is unclear. The purpose of this study was to investigate the role of Hippo pathway in the gastric carcinogenesis.

Materials and Methods: Gastric organoids, human gastric cancer cell lines (AGS, MKN74, GES-1), and *H. pylori* strains Hp 60190 [CagA (+) and CagA (-)] were used. We evaluated the effects of YAP/TAZ on inflammatory response, EMT, invasion and gastric cancer-associated tumorigenic properties. Organoids were cultured long-term in media containing various growth factors. A 2D organoid model was used for the *H. pylori* infection system in organoids. Electron microscopy images and TEER were measured in infected 2D organoids.

Results: We have shown that YAP was co-expressed with LGR5, a gastric stem cell marker with self-renewal ability. *H. pylori* infection caused inflammation lasting more than 72 hours, and IL-8, an inflammatory mediator, was preferentially expressed in epithelial cells infected by CagA positive strains. It was confirmed that *H. pylori* infection induces overexpression and nucleus translocation of YAP/TAZ, which may induce the epithelial mesenchymal transformation (EMT). YAP/TAZ overexpression was significantly correlated with the junction protein ZO-1 expression.

Conclusions: *H. pylori* infection may participate in gastric carcinogenesis through Hippo pathway dysregulation. These findings help to understand the regulatory circuits of inflammation, leading to gastric carcinogenesis.

Y. Lee: None. B. Yu: None. S. Lee: None. B. Hwang: None. K. Nam: None.

P02.06

THE PRESENCE OF GASTRIC AUTO-ANTIBODIES COULD BE RELATED WITH THE RE-INFECTION OF *HELICOBACTER PYLORI*

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Objective: Gastric auto-antibodies including anti-parietal cell antibody and anti-intrinsic factor antibody are an advantageous tool for screening for autoimmune atrophic gastritis, and their target is the protein of the secretory canaliculi of gastric parietal cells. It wondered whether the presence of auto-antibodies might be a marker of gastric neoplasia and *Helicobacter pylori* (*H. pylori*) would be a potential trigger of autoimmune gastritis.

Patients and Methods: We analyzed 1,518 patients who diagnosed non-ulcer dyspepsia (NUD) (n=603) and gastric neoplasia (n=915) at St. Vincent Hospital from May 2019 to May 2021. All of them checked auto-antibodies, and compared the frequencies between non-ulcer dyspepsia (NUD) and gastric neoplasia. Among patients with NUD, screening endoscopic examinations and *H. pylori* state were evaluated simultaneously (n=295).

Results: The rate of positive auto-antibodies were 43 of NUD and 41 patients of gastric neoplasia ($p=0.07$). According to *H. pylori* infection state, there was no statistical difference ($p=0.44$). When 295 patients with NUD had screening endoscopic exams and they were divided into two groups - *H. pylori*-naive ($n=211$) and history of eradication ($n=84$), the positive rate of auto-antibodies was the higher in patients with history of eradication ($p<0.01$). Among 8 patients with re-infection of *H. pylori*, 6 patients had positive results of auto-antibodies (6/8, 75%, $p<0.01$).

Conclusions: It was unlikely that the presence of auto-antibodies was a marker of gastric neoplasia. *H. pylori* could be a potential trigger of autoimmune gastritis. In patients with history of eradication, the presence of autoantibodies could predict the re-infection of *H. pylori*.

G. Jeon: None.

P02.07

TEN-YEAR EVOLUTION OF PRIMARY ANTIMICROBIAL RESISTANCE AMONG *HELICOBACTER PYLORI* IN BELGIUM

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Objective: This epidemiological update aimed to summarize the primary antimicrobial resistance rates of *Helicobacter pylori* in Belgium over a decade.

Materials and Methods: Between 2013 and 2022, 9375 *H. pylori* were detected from 52837 gastric biopsy specimens (mean positivity rate of 18%) at the national reference centre. About 90% of the specimens were collected from six large endoscopy clinics located in Brussels and Wallonia. *In vitro* susceptibility testing to clarithromycin (CLA), metronidazole (MTZ), levofloxacin (LVX), amoxicillin (AMX) and tetracycline (TET) was performed using Etest strips (Biomérieux) and interpreted according to EUCAST clinical breakpoints. Isolates from patients known to have received previous eradication therapy were excluded from the analysis.

Results: The number of biopsy samples analysed more than doubled from 2013 ($n=3906$) to 2022 ($n=10162$). The mean primary resistance percentages during the 2013-2022 period were: 34.5% for MTZ, 31.7% for LVX and 23.5% for CLA. Resistance rates to AMX and TET remained constantly low ($\leq 1\%$). Over the 10-year surveillance period, resistance to CLA (27.6% to 20.8%; X^2 trend =41.8, $p<0.001$) and LVX (28.5% to 25%; X^2 trend =6.9, $p=0.009$) decreased significantly. Double and triple drug resistance remained stable between 2017 and 2022.

Conclusions: High resistance rates to CLA, MTZ and LVX were observed in Belgium suggesting that antibiotic susceptibility guided therapy of *H. pylori* infection should be favoured to empirical treatment especially if clarithromycin-containing regimens are considered. Continuous monitoring of resistance rates for *H. pylori* provides information to optimize the therapeutic strategies.

T.D. Huang: None. O. Denis: None. M.C. Montesinos: None. M. Hoebeke: None. C. Berhin: None. W. Bouchahrouf: None. I. Wallemme: None. P. Bogaerts: None.

P02.08

COMPARISON OF *HELICOBACTER PYLORI* ERADICATION RATES BETWEEN 7 AND 14 DAYS OF TAILORED THERAPY ACCORDING TO CLARITHROMYCIN RESISTANCE TEST: A RANDOMIZED, MULTICENTER, NON-INFERIORITY STUDY

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Objective: Recently, simple tailored therapy according to clarithromycin resistance has been implemented as *Helicobacter pylori* eradication therapy. However, despite tailored therapy and frequent drug adverse events, studies on the treatment period are lacking. Therefore, we compared the *H. pylori* eradication rate of the 7-day and 14-day regimens of tailored therapy according to the clarithromycin resistance.

Patients and Methods: This multicenter prospective randomized non-inferiority trial included *H. pylori* positive patients. Enrolled patients are randomly assigned to 7-day and 14-day therapy, respectively, depending on the presence or absence of clarithromycin resistance by 23S rRNA gene point mutation. Standard triple therapy (rabeprazole 20 mg, amoxicillin 1 g, and clarithromycin 500 mg twice daily) or bismuth quadruple therapy (rabeprazole 20 mg twice daily, metronidazole 500 mg thrice daily, and bismuth 120 mg and tetracycline 500 mg 4 times daily) have assigned by the clarithromycin resistance.

Results: In total of 314 and 278 patients were included in the intention-to-treat and per-protocol analyses, respectively. Both 7-day and 14-day regimens showed an acceptable eradication rate in the ITT (7-day 78.3% vs. 14-days 78.3%, $p > 0.99$) and PP (87.9% vs. 89.1%, $p=0.851$) analyses. Non-inferiority in the eradication success rate between 7-day and 14-day regimens was confirmed. Subgroup analyses according to the clarithromycin resistance, no significant difference in eradication rates was observed between 7-day and 14-day standard triple therapy (90.0% vs. 90.1%, $p > 0.99$) and bismuth quadruple therapy (82.5% vs. 86.5%, $p=0.757$), respectively.

Conclusions: Seven-day triple or quadruple therapy according to the clarithromycin resistance showed similar eradication rate compared with 14-day group.

S. Jee: None. K. Jung: None. M. Lee: None. M. Koh: None. S. Kim: None. J. Lee: None. S. Seol: None.

P02.09

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)

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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-capsule increased 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.

O.P. Nyssen: Other; Significant; Mayoly and Allergan. L. Jonaitis: None. Á. Pérez-Aísa: None. D. Vaira: None. G. Fiorini: None. I. Saracino: None. B. Tepes: None. D.S. Bordin: None. M. Leja: None. F. Lerang: None. A. Tonkic: None. H. Simsek: None. L. Kunovsky: None. A. Gasbarrini: None. A. Cano-Català: None. L. Moreira: None. P. Parra: None. F. Mégraud: None. C. O'Morain: None. J.P. Gisbert: Other; Significant; Mayoly, Allergan, Diasorin, Gebro Pharma, and Richen.

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.

P02.10

CLINICAL EVALUATION OF A NOVEL MOLECULAR DIAGNOSIS KIT BASED ON QPROBE FOR DETECTING *HELICOBACTER PYLORI* USING STOOL SAMPLE

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Objective: To diagnose *Helicobacter pylori* (*H. pylori*), the culture and antibiotic susceptibility test plays a key role in determining the most effective *H. pylori* eradication regimen. However, it is a complicated method and takes several days to obtain results. A new *H. pylori* diagnosis kit using stool sample is simpler and requires only an hour to get a result. In this study, we report the clinical evaluation of point-of-care testing (POCT) kit, a novel kit for detecting *H. pylori* and CAM resistance.

Materials and Methods: 75 participants suspected of *H. pylori* infection were enrolled and were diagnosed for *H. pylori* infection and CAM resistance-associated mutation. In diagnosis of *H. pylori* infection, the POCT kit and conventional diagnostic methods (urea breath test, stool antigen test, culture test, and real-time polymerase chain reaction [PCR]) were compared. For CAM-resistant associated mutation detection, the concordance between the diagnostic kit and antibiotic susceptibility test was measured.

Results: The diagnosis of *H. pylori* infection with the POCT kit showed significant correlations with conventional diagnostic methods. Especially in the control culture, the sensitivity was 96.1% (49/51), the specificity was 100% (24/24). The detection of CAM resistance-associated mutations had a strong concordance rate, 98.0% (48/49), compared with the antibiotic susceptibility test.

Conclusions: The *H. pylori* molecular POCT kit using stool samples is a time-efficient and reliable diagnosis method for *H. pylori* infection and to detect CAM resistance-associated mutations. This novel kit could replace other conventional methods in selecting the most effective eradication regimen for *H. pylori*.

M. Tsuda: None. Y. Watanabe: None. R. Oikawa: None. S. Hayasaka: None. I. Tanaka: None. K. Eto: None. K. Kubo: None. H. Yamamoto: None. M. Kato: None.

P02.11

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

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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.

O.P. Nyssen: Other; Significant; Mayoly and Allergan. D. Vaira: None. I. Saracino: None. M. Pavoni: None. G. Fiorini: None. Á. Perez-Aisa: None. L. Jonaitis: None. M. Castro-Fernandez: None. D. Boltin: None. L. Hernández: None. A. Gasbarrini: None. D.S. Bordin: None. J. Kupcinskis: None. F. Lerang: None. A. Cano-Català: None. P. Parra: None. L. Moreira: None. F. Mégraud: None. C. O'Morain: None. J.P. Gisbert: Other; Significant; Mayoly, Allergan, Diasorin, Gebro Pharma, and Richen.

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).

P02.12

HELICOBACTER PYLORI AND NON-HELICOBACTER PYLORI HELICOBACTER INFECTION RATES SHOWED MARKEDLY DIFFERENT ASSOCIATIONS WITH UPPER GASTROINTESTINAL DISEASES AMONG ASIAN COUNTRIES

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Objective: To determine the influence of the socioeconomic, religious, and dietary backgrounds on the development of *Helicobacter pylori* (Hp) and non-Hp Helicobacter (NHPH) infection.

Materials and Methods: PCR and histological studies were conducted in Asian countries, including Nepal (243 cases from 2004 to 2007), Bangladesh (417 cases from 2008 to 2011), Myanmar (172 cases from 2006 to 2012), Mongolia (225 cases, 2013), and Japan (385 cases from 2006 to 2009). Approximately half of the included patients suffered from upper gastrointestinal diseases; however, the disease pattern differed across countries. Immunohistochemical studies using antibodies against Hp and *H. suis* (Hs) were conducted.

Results: The rates of Hp and NHPH infections were 55% and 0.8% in Nepal, 27% and 3.8% in Bangladesh, 49% and 4.9% in Myanmar, 68% and 17.7% in Mongolia and 69% and 1.6% in Japan. Most of the cases of NHPH were caused by Hs based on the PCR results. In addition, the coinfection accounted for more than half of the NHPH positive cases. Hp and NHPH infections were independently related to the formation of gastric ulcers in Bangladesh, and atrophic gastritis in Myanmar. Mongolia, Myanmar and Bangladesh showed higher NHPH infection rates than Japan, although pork consumption is reported to be low in these countries. This suggests the existence of the NHPH reservoir other than pigs.

Conclusions: Hp and NHPH had the different infection rates and diverse associations with gastrointestinal diseases among Asian countries, suggesting the influence of socioeconomic backgrounds and ethnical differences.

M. Nakamura: None. A. Øverby: None. S. Takahashi: None. S.Y. Murayama: None. T. Matsuhisa: None. Y. Yamaoka: None. H. Suzuki: None.

P02.13

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

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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 $\geq 90\%$ effectiveness.

O.P. Nyssen: Other; Significant; Mayoly and Allergan. D. Vaira: None. I. Saracino: None. M. Pavoni: None. G. Fiorini: None. Á. Perez-Aisa: None. L. Jonaitis: None. M. Castro-Fernandez: None. D. Boltin: None. L. Hernández: None. A. Gasbarrini: None. D.S. Bordin: None. J. Kupcinkas: None. F. Lerang: None. A. Cano-Català: None. L. Moreira: None. P. Parra: None. F. Mégraud: None. C. O'Morain: None. J.P. Gisbert: Other; Significant; Mayoly, Allergan, Diasorin, Gebro Pharma, and Richen.

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

Rescue therapy	Use, N (%)	Modified intention-to-treat		Per-protocol	
		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)

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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-Eu-Reg). 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.

O.P. Nyssen: Other; Significant; Mayoly and Allergan. A. Garre: None. G. Fiorini: None. I. Saracino: None. M. Pavoni: None. D. Vaira: None. P.S. Phull: None. I.L.P. Beales: None. A. Gasbarrini: None. A. Cano-Català: None. L. Moreira: None. P. Parra: None. F. Mégraud: None. C. O'Morain: None. J.P. Gisbert: Other; Significant; Mayoly, Allergan, Diasorin, Gebro Pharma, and Richen.

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 (1 st to 5 th line), n (%)	Misuse of same antibiotic in 6 th 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 (1 st to 5 th line)	Median	Interquartile range
1 st line	8.5	7-10
2 nd line	10	7-10
3 rd line	10	7-10
4 th line	10	7-14
5 th line	10	7-14
*Most frequent 6 th 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 6 th 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 6 th 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.

P03.02

HELICOBACTER PYLORI CAG A PERTURBS NON-CANONICAL WNT/PLANAR CELL POLARITY (PCP) SIGNALING, WHICH MEDIATES LINEAGE SPECIFICATION OF EPITHELIAL STEM CELLS

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Objective: Once delivered into gastric epithelial cells *via* bacterial type IV secretion, *Helicobacter pylori* CagA interacts with a number of host proteins and thereby disturbs multiple intracellular signaling pathways to promote gastric carcinogenesis.

Materials and Methods: Microinjection of mRNA into *Xenopus laevis* embryos has been widely utilized as a powerful experimental tool for investigating the role of a protein of interest in signaling pathways involved in the process of embryonic development. To investigate a hitherto unidentified intracellular signaling pathway that is subverted by delivered CagA, we examined the effect of *H. pylori* CagA on *Xenopus* embryogenesis by injecting wild-type or mutant *cagA* mRNA.

Results: *H. pylori* CagA ectopically expressed in *Xenopus* embryos subverted blastopore formation during gastrulation, followed by a failure of neural tube closure with a shortened anteroposterior axis. Furthermore, animal cap explants of *Xenopus* embryos expressing CagA displayed impaired convergent extension movements, suggesting that the bacterial oncoprotein dampens planar cell polarity (PCP) formation. Mechanistically, the structured N-terminal CagA was found to interact with the C-terminal cytoplasmic tail of the tetraspanins Van Gogh-like protein 1 (VANGL1) and VANGL2, the unique core components of the non-canonical Wnt/PCP pathway. CagA-VANGL1/2 interaction competitively inhibited Dishevelled (Dvl)-VANGL1/2 interaction that sequesters Dvl from the Wnt/PCP receptor FRIZZLED, causing perturbation of Wnt/PCP signaling that plays a crucial role in epithelial cell fate specification.

Conclusions: *H. pylori* CagA may contribute to the development of gastric cancer by subverting Wnt/PCP-mediated cell-lineage specification of gastric epithelial stem cells in conjunction with other oncogenic CagA actions.

A. Takahashi-Kanemitsu: None. M. Lu: None. M. Hatakeyama: None.

P03.03

FREQUENCY OF BLOOD GROUP ANTIGEN BINDING (*BAB*) GENES VARIES ACROSS *HELICOBACTER PYLORI* POPULATIONS AND PHYLOGENY REVEAL THEY GROUP FOLLOWING A POPULATION STRUCTURE

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Objective: *Helicobacter pylori* utilizes Blood group Antigen Binding Adhesin (BabA) for persistent colonization in the gastric niche, contributing to disease risk. Paralogs BabB and BabC may participate in recombination events to regulate BabA activity. We aimed to investigate the frequency and sequence relationships of *bab* genes in worldwide *Helicobacter pylori* genomes.

Materials and Methods: *bab* genes were retrieved from 1,011 genomes sequenced by SMRT/PacBio and part of the *Helicobacter pylori* Genome Project (HpGP) dataset. TBLASTN identified *bab* gene using Bab proteins from OMP database, with >90% identity, >80% coverage, and 10⁻⁹ e-value. Sequences were aligned, and phylogenetic trees constructed. Genetic distances and networks were calculated and visualized using the core-genome subpopulation assignment.

Results: Frequencies of *bab* genes varied across populations. *babA* was present in 100% hpEAsia strains, over 75% of Asian and African subpopulations, <70% of Europeans, and <20% of hpNEAfrica strains. *babB* was prevalent in around 50% of African and Asian populations but lower in European subpopulations. *babC* was less frequent, and notably, the Asian population, including hspIndigenousAmerica and hspAfrica1SAfrica lacked *babC*. Phylogeny analyses grouped *babA* and *babB* by population. Distance network analyses of *babA* showed that European strains had a strong interaction with most other populations, while Latin American subpopulations were rather dispersed.

Conclusion: Frequency of *Bab* genes varies among *H. pylori* populations, with *babA* as the more prevalent and phylogeny grouped *bab* gene by population. Network interactions suggest old-world populations *babA* has evolved to form tight groups, whereas in America is evolving to reach well-formed clusters.

Z.Y. Munoz-Ramirez: None. S. Sandoval-Motta: None. J. Torres: None. M. Camargo: None. K. Thorell: None.

P03.04

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

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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-diagnosed 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.

L. Bujanda: None. O.P. Nyssen: Other; Significant; Mayoly and Allergan. J. Ramos: None. D.S. Bordin: None. B. Tepes: None. Á. Perez-Aisa: None. M. Pavoni: None. M. Castro-Fernandez: None. F. Lerang: None. M. Leja: None. L. Rodrigo: None. T. Rokkas: None. J. Kupcinskis: None. A. Cano-Català: None. L. Hernández: None. L. Moreira: None. P. Parra: None. F. Mégraud: None. C. O'Morain: None. J.P. Gisbert: Other; Significant; Mayoly, Allergan, Diasorin, Gebro Pharma, and Richen.

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

Most frequent 1 st 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.

P03.05

INDEX OF GASTRIC EPITHELIOCYTES PROLIFERATION IN *HELICOBACTER PYLORI*-POSITIVE PATIENTS WITH ATROPHIC GASTRITIS DEPENDING ON THE PRESENCE OF COMPLETE OR INCOMPLETE INTESTINAL METAPLASIA

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Objective: Incomplete intestinal metaplasia (IM) in the gastric mucosa is known to increase the gastric cancer risk (Gupta et al, 2020). But the mechanism of this process is not clear enough.

Material and Methods: The study included 20 patients with non-atrophic gastritis (group A), 20 patients with atrophic gastritis without IM (group B), 20 patients with atrophic gastritis with complete IM (group C), and 20 patients with atrophic gastritis with incomplete IM (Group D). The study included only patients with *Helicobacter pylori* infection. Biopsy sampling and determination of atrophic gastritis severity and IM were performed using the OLGA (Rugge et al, 2006) and OLGIM (Capelle et al, 2010) systems. Hematoxylin stain, alcian blue stain and PAS reaction were used for typing of IM foci. Proliferation activity was studied by immunohistochemistry on the nuclear protein Ki67 expression.

Results: The total Ki67 expression index in gastric epitheliocytes was 26.7±1.8% in group A and 50.2±1.6% in group B ($p<0.001$). In group C, this indicator was 4.8±0.1% in the complete IM foci and 22.4±2.8% in the mucosa without IM foci ($p<0.001$). The Ki67 expression index in the IM foci in group D (38.7±2.6%) was significantly higher than in the IM foci in group C ($p<0.001$). The proliferation index in the gastric mucosa without IM foci did not differ in patients of groups C and D ($p=0.26$).

Conclusions: Proliferation activity in incomplete intestinal metaplasia foci in patients with atrophic gastritis is significantly increased, which greatly increases the developing gastric cancer risk.

V.V. Tsukanov: None. R.V. Ryabokon: None. V.A. Khorzhevskiy: None. A.V. Vasyutin: None. J.L. Tonkikh: None.

P03.06

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

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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.

O.P. Nyssen: Other; Significant; Mayoly and Allergan. P. Parra: None. Á. Pérez-Aísa: None. M. Castro-Fernandez: None. M. Pabón-Carrasco: None. A. Keco-Huerta: None. L. Rodrigo: None. Á. Lanás: None. S.J. Martínez-Domínguez: None. E. Alfaro: None. A.J. Lucendo: None. A. Gasbarrini: None. L. Hernández: None. R. Marcos-Pinto: None. W. Marlicz: None. A. Cano-Català: None. L. Moreira: None. F. Mégraud: None. C. O'Morain: None. J.P. Gisbert: Other; Significant; Mayoly, Allergan, Diasorin, Gebro Pharma, and Richen.

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

P03.07

INDEX OF GASTRIC EPITHELIOCYTES APOPTOSIS IN *HELICOBACTER PYLORI*-POSITIVE PATIENTS WITH ATROPHIC GASTRITIS DEPENDING ON THE PRESENCE OF HIGH OR LOW DEGREE DYSPLASIA

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Objective: There is no doubt about the importance of dysplasia in the process of carcinogenesis, but the details of the pathology development need further study (Kinami et al, 2022).

Material and Methods: The study included 20 patients with non-atrophic gastritis (group A), 20 patients with atrophic gastritis and low-grade dysplasia (group B), and 20 patients with atrophic gastritis and high-grade dysplasia (group C). The study included only patients with *Helicobacter pylori* infection. Biopsy sampling and determination of the severity of atrophic gastritis were carried out according to the OLGA system (Rugge et al, 2006). Diagnosis of gastric mucosa dysplasia was carried out according to the WHO classification guidelines (Nagtegaal et al, 2020). Apoptosis activity was studied by the expression of the p53 protein by immunohistochemistry method.

Results: The total p53 expression index in gastric epitheliocytes was 6.5±1.2% in group A. The apoptosis index was significantly increased in dysplasia foci in group B patients (55.7±3.6%; $p_{A-B} < 0.001$) and group C persons (225.3±3.1%; $p_{A-C} < 0.001$; $p_{B-C} < 0.001$). The apoptosis index in the epithelial cells of the surrounding mucosa in groups B and C did not differ from those in group A and was 4.3±0.6% and 5.0±0.9%, respectively.

Conclusions: A significant increase in the apoptosis index in the foci of low and high dysplasia was obtained, which indicates pronounced disturbances in the processes of cell renewal in these patients.

R.V. Ryabokon: None. V.V. Tsukanov: None. V.A. Khorzhevskiy: None. A.V. Vasyutin: None. J.L. Tonkikh: None.

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)

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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.

O.P. Nyssen: Other; Significant; Mayoly and Allergan. M. Spinola: None. P. Pratesi: None. G.J. Ortega: None. L. Jonaitis: None. Á. Pérez-Aísa: None. D. Vaira: None. G. Fiorini: None. B. Tepeš: None. D.S. Bordin: None. M. Leja: None. F. Lerang: None. A. Tonkic: None. H. Simsek: None. A. Cano-Català: None. L. Moreira: None. P. Parra: None. F. Mégraud: None. C. O'Morain: None. J.P. Gisbert: Other; Significant; Mayoly, Allergan, Diasorin, Gebro Pharma, and Richen.

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.

P03.09

THE PROTECTION OF TISSUE-RESIDENT MEMORY T CELLS DURING *HELICOBACTER PYLORI* INFECTION

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Tissue-resident memory cells (TRM) were recently reported to provide immediate protection after antigen reencounter in different bacterial and viral infections. However, the function of TRM in the gastric tissue during *Helicobacter pylori* infection remains unclear. Using a robust mouse model of *H. pylori* infection, we traced the origin and development of TRM cells induced by *H. pylori* infection, which largely depends on the presence of the virulence factor CagA. Importantly, we could show that gastric Hobit⁺TRM cells confer full protection after eradication and subsequent re-infection with *H. pylori*. RNA-seq experiments allowed us to map the transcriptional profiles of these protective TRM during infection, eradication, and re-infection settings. Together, we identify and characterize gastric TRM cells, which possess characteristic transcriptional signatures and are important for protection. This knowledge will be valuable for the development of prophylactic and therapeutic vaccination approaches.

R. Gong: None. A. Ralser: None. V. Friedrich: None. R. Mejías-Luque: None. M. Gerhard: None.

P03.10

THE ROLE OF MITOCHONDRIAL MODULATION IN INNATE IMMUNITY AND TUMORIGENESIS DURING *HELICOBACTER PYLORI* INFECTION

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Objective: *Helicobacter pylori* frequently colonizes the human stomach and is the major risk factor for stomach adenocarcinoma. Many environmental stressors, including infections, may affect mitochondrial function and structure, have short- and long-term effects on mitochondrial and host physiological processes. Previous studies have shown DNA-damage-induction by *H. pylori* *in vitro* and affection of mitochondrial functions and structure. We hypothesized that a low-level activation of mitochondrial apoptosis signaling in the absence of cell death may contribute to the DNA-damage-induction, mitochondrial modulation, and host cell response.

Materials and Methods: We generated several human epithelial cell lines with specific defects in components of the apoptosis-system or depleted of their mitochondrial DNA to investigate their potential contribution to DNA-damage and mitochondrial modulation induced by *H. pylori*.

Results: *H. pylori* induced DNA-damage in cell culture, which was dependent on a low-level activation of the mitochondrial apoptosis system and the caspase-dependent DNase (CAD) and occurred in the absence of cell death. Depleting the cells from mitochondrial DNA had similar impact on DNA-damage. Inflammatory cytokine secretion during *H. pylori* infection was partly dependent on low-level apoptosis activation.

Conclusions: Mitochondrial DNA depletion attenuated the mitochondrial sublethal apoptosis signaling as well as cytokine production. Low-level mitochondrial apoptosis activation and alteration of mitochondrial dynamics can therefore be a part of the immune reaction to *H. pylori*-infection.

M. Badr: None. B. Dörflinger: None. M. Metzler: None. A. Haimovici: None. G. Häcker: None.

P03.11

EFFECT OF *HELICOBACTER PYLORI* TREATMENT ON RECURRENCE OF UPPER GASTROINTESTINAL BLEEDING IN ATRIAL FIBRILLATION PATIENTS WITH ANTITHROMBOTIC AGENTS

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Objective: The risk of recurrent gastrointestinal bleeding (GIB) in atrial fibrillation (AF) patients on anti-thrombotic after *H. pylori* (HP) eradication remains poorly defined. We characterized the incidences of hospitalizations for all recurrent GIB in antithrombotic users according to HP eradication therapy.

Patients and Methods: Based on the nationwide claims and health database, we identified all AF patients newly diagnosed with upper GIB between 2010 and 2017. Patients were divided into three cohorts according to the anti-thrombotic use after AF diagnosis: warfarin, NOAC, and anti-platelets. The primary outcome was incident rebleeding after index GIB during follow-up.

Results: Among a total of 2,670 AF patients with upper GIB, the warfarin group (94 pairs), NOAC group (98 pairs), and anti-platelet group (218 pairs) were compared for recurrent GIB after propensity matching for the treatment of HP. During 5 years follow-up, HP treatment was closely related to recurrent GIB with marginal trend toward significance in warfarin group (hazard ratio [HR] 0.77, 95% CI 0.51-1.18) and anti-platelet group (HR 0.89, 95% CI 0.72-1.09). Whereas HP treatments were independently related with a lower risk of all-cause mortality in the warfarin group (HR 0.28, 95% CI 0.09-0.87) and anti-platelet group (HR 0.79, 95% CI 0.67-0.93).

Conclusions: AF patients with GIB were not significantly associated with a lower risk for recurrent GIB after HP treatment, irrespective of the kinds of anti-thrombotic taken. However, for AF patients on anti-platelet, HP treatment reduced the risk of all-cause mortality during 5-years follow-up.

B. Kim: None. D. Lee: None. S. Shin: None.

P03.12

NEUTROPHIL MIGRATION IN RESPONSE TO EXPOSURE OF *HELICOBACTER PYLORI* OUTER MEMBRANE VESICLES IN A POLARIZED GASTRIC EPITHELIAL CELL MODEL

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H. pylori shed outer membrane vesicles (OMVs) that contain many of the surface elements of the bacteria. Neutrophil transmigration across mucosal surfaces contributes to the dysfunction of epithelial barrier properties, a characteristic underlying *H. pylori* infection. Although *H. pylori*-derived OMVs may contribute to the pathogenesis of *H. pylori* infection, the roles of neutrophil transmigration in OMVs have not been elucidated. In the present study, we investigated whether *H. pylori* OMVs can

induce neutrophil transepithelial migration. Employing an established *in vitro* model, we demonstrated that *H. pylori* OMVs induced the migration of neutrophils across polarized monolayers of NCI-N87 gastric cell lines. *H. pylori* OMVs increased phosphorylated forms of ERK1/2, p38, and JNK proteins in NCI-N87 116 cells. However, pretreatment with chemical inhibitors, such as PD98059, SB203580, or SP600125 did not significantly change the *H. pylori* OMV-induced neutrophil transepithelial migration. *H. pylori* OMVs increased protein kinase C (PKC) activity in gastric epithelial cells. The pretreatment with chelerythrine chloride (pan-PKC inhibitor) significantly decreased the OMV-induced neutrophil transepithelial migration. In addition, the PKC- δ activity was associated with OMV-induced neutrophil transepithelial migration. Furthermore, we found that phospholipase A2 (PLA2) and 12/15-lipoxygenase (12/15-LOX) were involved in the regulation of OMV-induced transepithelial migration. These results suggest that *H. pylori* OMVs can induce the migration of neutrophils across the gastric epithelial layer to the infection site, in which the neutrophil transepithelial migration may be associated with the activation of PKC- δ and the 12/15-LOX pathway.

J. Kim: None.

POSTER SESSION 04: HELICOBACTER 4

P04.01

EFFICACY OF CULTURE-BASED TAILORED THERAPY AS PRIMARY TREATMENT OF *HELICOBACTER PYLORI* INFECTION: A MULTICENTER PROSPECTIVE STUDY

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Objective: The low eradication rate and high drug resistance rate of *Helicobacter pylori* remain problematic. Here, we report the updated results of a multicenter prospective study comparing culture-based tailored therapy and empirical therapy as primary treatment of *H. pylori* infection.

Material and Methods: We prospectively enrolled 312 treatment-naïve patients with *H. pylori* infection from 4 hospitals in Korea. The patients were randomly assigned to the tailored group and the empirical group at a ratio of 3:1. The tailored group was treated with either a clarithromycin-based triple regimen, metronidazole-based triple regimen, or bismuth quadruple regimen according to the antibiotic susceptibility test. The empirical group was treated with a concomitant regimen.

Results: After randomization, 30 (9.6%) patients dropped out. The *H. pylori* eradication rates in the tailored and empirical groups were 83.8% and 83.3% ($p=1.000$) in the ITT analysis and 92.9% and 91.5% ($p=0.794$) in the PP analysis, respectively. Moderate-to-severe adverse events on daily activity were significantly less common in the tailored group than in the empirical group (11.3% vs. 33.3%, $p<0.001$). Taste alteration, constipation, dizziness, insomnia and fatigue of grade 2 or higher were less common in the tailored group as well (4.3% vs. 12.0%, $p=0.026$ and 0% vs. 4.0%, $p=0.014$, 1.3% vs. 8.0%, $p=0.008$, 0.4% vs. 5.3%, $p=0.014$, 1.3% vs. 6.7%, $p=0.024$ respectively).

Conclusions: Culture-based tailored therapy seems to be effective and safe as a primary treatment for *H. pylori* infection.

J. Lee: None. B. Min: None. E. Gong: None. J. Kim: None. H. Jung: None. J.J. Kim: None. H. Na: None. J. Ahn: None. D. Kim: None. K. Choi: None.

P04.02

PREVALENCE OF *HELICOBACTER PYLORI* INFECTION AMONG GASTROENTEROLOGISTS AND GASTROENDOSCOPISTS IN BRAZIL

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Objective: The aim of the study was to determine *Helicobacter pylori* (HP) prevalence in gastroenterologists and gastroendoscopists in Brazil.

Patients and Methods: During the 2022 Brazilian Digestive Disease Week meeting (SBAD), participants were invited to undergo a 13C-urea breath test (UBT) to investigate their HP status. The participants were requested to complete a questionnaire regarding demographic data and information about medical specialties (gastroenterology or gastroendoscopists). 286 participants, 160 women, 126 men, mean age 42, SD 13, range 25-83 years, agreed to participate. 13C-urea breath test: preceding the study, all participants abstained from taking PPI and H2 blockers within one week and antibiotics for four weeks, respectively. The test was performed after, at least, one-hour fasting, using BreathID HP Lab System® (Exalenz Bioscience, Israel, now Meridian Bioscience, USA), and a delta over baseline (DOB) ≥ 5‰ indicated HP infection.

Results: The observed overall prevalence of HP infection was 23.8%. Table 1 summarizes the obtained results. As 67 out of 286 participants informed previous successful treatment for *H. pylori* infection, if we exclude all of them from the analysis, the real prevalence among the 219 remaining participants would be 25.1%. If we consider these 67 participants previously treated as belonging to *H. pylori*-positive group, the prevalence will reach 42.7% of the participants.

Conclusions: HP infection has a moderate/high prevalence among Brazilian gastroenterologists. Endoscopy procedures seem not to increase the risk of acquiring the infection.

L.G.V. Coelho: None. D. Chinzon: None. L.T. Ribeiro: None. A. Delgado: None. O.R. Trindade: None. L.A. Leão: None. T. Barreto: None. M. Sylvio: None. E.G. Vilela: None.

TABLE 1. ASSOCIATION BETWEEN *H. PYLORI* PREVALENCE AND VARIABLES STUDIED (N=286).

Variable	n	<i>H. pylori</i> prevalence
Age range Chi-square (p-value = 0.007)		
25-34 years	107	14.4%
35-44 years	90	24.4%
45-54 years	31	25.8%
55-64 years	33	36.4%
>64 years	25	44.0%
Body mass index (BMI) Chi-square (p-value= 0.035)		
Underweight and normal weight (BMI < 24.9 kg/m ²)	158	19.0%
Overweight and obesity (BMI > 25.0 kg/m ²)	128	26.3%
Gastroenterologists and gastroendoscopists Chi-square (p-value = 0.243)		
Gastroenterologists	177	21.5%
Gastroendoscopists	109	27.5%

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

P04.03

THE IMPACT OF CO-INFECTIOUS RATE OF CLARITHROMYCIN-SUSCEPTIBLE AND RESISTANT *H. PYLORI* STRAINS FOR THE EFFICACY OF ERADICATION TREATMENT INCLUDING CLARITHROMYCIN**M. KATO**¹, **M. TSUDA**¹, **K. KUBO**², **Y. WATANABE**^{3,4}¹Public Interest Foundation Hokkaido Cancer Society, Sapporo, Japan; ²National Hospital Organization Hakodate National Hospital, Hakodate Japan, Hakodate, Japan; ³Kawasaki Rinko General Hospital, Kawasaki, Japan, Kawasaki, Japan; ⁴St. Marianna University School of Medicine, Kawasaki, Japan

Objective: The heterogeneity of clarithromycin-susceptible and resistant *H. pylori* strains has been reported to differ within individuals. We have already shown that pyrosequencing analysis enabled to quantify gene mutations at positions 2,142 and 2,143 of *H. pylori* 23S rRNA using intragastric fluid. To evaluate the impact of co-infectious rates with clarithromycin-susceptible and resistant *H. pylori* strains on efficacy of CAM-containing eradication therapy, we performed a quantitative analysis of the mutation rate by pyrosequencing analysis and compared it with the outcome of eradication therapy.

Patients and Methods: Sixty-four *H. pylori*-positive subjects who received CAM-based eradication therapy consists of vonoprazan and amoxicillin were enrolled. *H. pylori* culture and CAM susceptibility test were performed using biopsy samples, intragastric fluid was used real-time PCR and pyrosequencing analysis. Ethical approval and written informed consents were obtained.

Results: The success rate of CAM-based eradication therapy was 61.9% (13/21) for CAM-resistant strains, 95.1% (39/41) for sensitive strains. The distribution of CAM-resistant mutations using pyrosequencing analysis showed that the mutation rate at position 2,142 was 25% (16/64) and that (>20%) at position 2,143 was 31% (20/64). The relationship between the mutation rate of CAM-resistant gene and eradication results showed the success rate of 90% or more with a mutation rate of 20% or less for both position 2,142 and 2,143. On the other hand, when the mutation rate was 20% or higher, the success rates decreased to 60%.

Conclusions: The mutation rate of CAM-resistant gene by pyrosequencing analysis influences the outcome of CAM-based eradication therapy.

M. Kato: None. M. Tsuda: None. K. Kubo: None. Y. Watanabe: None.

P04.04

USEFULNESS OF TEXTURE AND COLOR ENHANCEMENT IMAGING IN THE EVALUATION OF ENDOSCOPIC FINDINGS OF GASTRITIS**S. OKI**, **T. TAKEDA**, **M. HOJO**, **A. NAGAHARA**

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Objective: Texture and color enhancement imaging (TXI), which was newly developed for image-enhanced endoscopy, allows easy recognition of differences in mucosal color and structure. Our aim was to evaluate the visibility of endoscopic findings of gastritis using TXI.

Material and Methods: A single-center prospective clinical study was performed to investigate whether the visibility of the endoscopic findings of *Helicobacter pylori* gastritis according to the Kyoto Classification of Gastritis improved using TXI compared with white light imaging (WLI). Patients who underwent esophagogastroduodenoscopy with WLI and TXI from February 2021 to March 2022 at our hospital were enrolled. Three experts and three trainees rated the visibility on TXI compared with WLI on a scale of 5 (improved) to 1 (decreased), and we calculated the percentage of cases with improved visibility. The intra-class correlation coefficient (ICC) was assessed as a measure of inter-rater reliability.

Results: Thirty-eight cases of diffuse redness, 26 cases of spotty redness, 32 cases of map-like redness, 39 cases of patchy redness, 36 cases of intestinal metaplasia, 42 cases of atrophy and 44 cases of red streak were included. The percentage of cases with improved visibility of each finding on TXI compared with WLI was 78.9, 80.8, 84.4, 84.6, 22.2, 83.3, and 77.3 (%), respectively, in the experts and 68.4, 96.2, 90.6, 71.8, 55.6, 88.1, and 40.9 (%), respectively, in the trainees. The ICCs for inter-rater reliability on TXI overall were 0.50-0.65 among all endoscopists.

Conclusions: TXI compared with WLI improved visibility of endoscopic findings for both trainees and experts.

S. Oki: B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; Olympus Co., Ltd. M. Hojo: C. Other Research Support (supplies, equipment, receipt of drugs or other in-kind support); Significant; Olympus Co., Ltd. T. Takeda: C. Other Research Support (supplies, equipment, receipt of drugs or other in-kind support); Significant; Olympus Co., Ltd. A. Nagahara: C. Other Research Support (supplies, equipment, receipt of drugs or other in-kind support); Significant; Olympus Co., Ltd.

P04.05

ASSESSMENT OF RISK FACTORS FOR A POSITIVE ¹³C-UREA BREATH TEST IN THE UKRAINIAN POPULATION

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Objective: Ukraine remains a country with a high prevalence of *Helicobacter pylori* infection. Our aim was to identify important risk factors for positive ¹³C-UBT as the most accurate diagnosis.

Patients and Methods: The study was conducted from 2006 to 2019 on 972 men (mean age±SD -40.47±14.92) and 1,120 women (age 42.09±15.55) who either never received eradication therapy (1,280 persons) or already received one (control test – 814). The regression analysis was performed by using logistic model (enter method).

Results: 56.7% of primary and 43.3% of control tests were HP-positive. The large number of positive control tests was explained by the passing of the study by individuals who were dissatisfied with the previous results. AUC of logistic model ROC-curve was 0.68 (95%CI 0.657 to 0.701) and percent of cases correctly classified was 64.84 (Table 1).

We found a significantly smaller increase in HP-positive individuals with a large mass – Spearman's coefficient of rank correlation = -0.326 (95%CI -0.391 to -0.257). This could be a suspicion to offer them a larger dose of isotope-labeled urea. However, analysis proved that individuals with increased weight were more likely to have positive results, and these fears are redundant.

Conclusions: We proved a consistent decrease in the prevalence rate of HP-infection in Ukraine (Vinnytsya region as an example). A fact that contradicts most previous studies is the reduced risk of HP-infection among Ukrainian men.

S. Melashchenko: None. I. Paliy: None. S. Zaika: None. I. Chernova: None.

TABLE 1. PARAMETERS OF LOGISTIC REGRESSION ANALYSIS MODEL (ENTER METHOD).

Variable	Coefficient	Std. Error	p	Odds ratio (95% CI)
Primary test -0; Control -1	-1.16951	0.10649	<0.0001	0.3138 (0.2550 to 0.3861)
Year of test (2006-2019)	-0.063577	0.012052	<0.0001	0.9400 (0.9183 to 0.9622)
Body weight (kg)	0.011726	0.0037270	0.0017	1.0118 (1.0044 to 1.0192)
Dyspeptic symptoms (0 or 1)	0.20884	0.22656	0.3567	1.2322 (0.7904 to 1.9211)
Male gender (m=1; f=0)	-0.36776	0.12405	0.0030	0.6940 (0.5443 to 0.8849)
Height (cm)	0.0054344	0.0049702	0.2742	1.0055 (0.9957 to 1.0153)
Age (years)	0.0021307	0.0035866	0.5525	1.0023 (0.9953 to 1.0094)
Constant	126.0764			

P04.06

BRAZILIAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-BRAZILREG): ANALYSIS OF 640 FIRST-LINE TREATMENTS

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Objective: Little is known about the first-line regimens used and their outcomes in real-life studies in Brazil. The aim of the study was to evaluate the effectiveness of the first-line eradication treatments in Brazil, as part of the Brazilian Registry on *Helicobacter pylori* management (Hp-BrazilReg).

Materials and Methods: Multicenter, prospective registry evaluating outcomes of *H. pylori* management by Brazilian gastroenterologists. Data were registered at e-CRF AEG-REDCap from March 2022 to April 2023. The effectiveness was evaluated by modified intention-to-treat. Data were subject to quality review.

Results: Up to now, 879 Brazilian patients were included (mean age 52 years, 64% women, and 2.3% penicillin allergy). Treatment indications were: 62% dyspepsia with normal endoscopy and 12% gastroduodenal ulcers. Endoscopy was performed in 96% of the cases to diagnose the infection, employing histology (91.5%) and the rapid urease test (16%). No pre-treatment resistance test was performed. Regarding first-line treatments, 640 patients were included. The main first-line regimens were triple-clarithromycin+amoxicillin (89%), and dual-amoxicillin (2.2%), with 14-day prescriptions in 97% of patients, low-dose and standard-dose PPIs in 37% each, and high-dose PPIs in 27% of cases. Probiotics were used in 18%. 99% were compliant (>90% drug intake). Confirmation of the eradication was mainly performed by endoscopy (74%), histology (70%), ¹⁴C-urea breath test (14%), and rapid urease test (12%). Overall, both intention-to-treat and per-protocol effectiveness were 88%. 27% presented at least one adverse event, mainly nausea (10%) and diarrhea (7.2%).

Conclusions: Triple-clarithromycin+amoxicillin accounts for the vast majority of prescriptions in Brazil and achieves an acceptable eradication rate (88%).

B.S.F. Sanches: None. **O.P. Nyssen:** B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Modest; Mayoly, Allergan. **L.T. Ribeiro:** None. **J.C.S. Veloso:** None. **S.R. Chaves:** None. **H.P. Breyer:** None. **H. Okamoto:** None. **J.R. Marinho:** None. **G.C. Couto:** None. **L.F. Guidi:** None. **C.S. Alencar:** None. **L.A.S. Sousa:** None. **L.S. Silva:** None. **G.G.L. Cançado:** None. **H.O. Galizzi:** None. **M.J.G. Massote:** None. **L. Moreira:** None. **A. Cano-Català:** None. **J.P. Gisbert:** D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Mayoly, Allergan, Diasorin, Gebro Pharma, Richen. **L.G.V. Coelho:** D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Takeda, EMS.

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

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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.

L. Olmedo: None. X. Calvet: None. E. Gené: None. D.S. Bordin: None. I. Voynovan: None. M. Castro-Fernandez: None. M. Pabón-Carrasco: None. A. Keco-Huerta: None. Á. Pérez-Aisa: None. L. Hernández: None. O. Gridnyev: None. J. Kupčinskas: None. A. Gasbarrini: None. A. Cano-Català: None. L. Moreira: None. P. Parra: None. O.P. Nyssen: None. F. Mégraud: None. C. O'Morain: None. J.P. Gisbert: None.

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

Variable lower	OR upper	95% CI	p-value	
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.

P04.08

CONTROL OF *HELICOBACTER PYLORI* BY CD8⁺ T CELLS IS MEDIATED BY THE RECOGNITION OF CAG A

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Objective: CagA, which activates multiple pro-oncogenic pathways after translocation into epithelial cells, is the most significant virulence factor to *Helicobacter pylori* oncogenesis. By becoming an intracellular antigen, it is prone to be targeted by CD8⁺ T cells. However, CD8⁺ T cells are not yet considered to participate in the immune response to *H. pylori*.

Materials and Methods: Here, we spatiotemporally characterize gastric CD8⁺ T cell responses to *H. pylori* infection in mice and humans. Applied methods are flow cytometry, RNA sequencing, ChipCytometry, T cell depletion, *H. pylori* eradication, and ex vivo stimulation.

Results: Compared to CD4⁺ T cells, CD8⁺ T cells dominate the mucosal mononuclear infiltrate during the early response to murine *H. pylori* infection. These CD8⁺ T cells are tissue-resident memory T (T_{RM}) cells, residing within the gastric mucosa after *H. pylori* eradication. They mediate bacterial control via the release of cytotoxic T cell effector functions, including IFN- γ secretion. The induction of gastric CD8⁺ T_{RM} cells is highly depended on the ability of the infecting strain to deliver CagA. Strikingly, most CD8⁺ T cells show TCR specificity for CagA. We corroborate our findings of a CagA-dependent gastric CD8⁺ T_{RM} cell infiltration in *H. pylori*-infected patients and identify multiple CagA-derived epitopes inducing CD8⁺ T cell responses in humans.

Conclusions: Our results expose new roles for a previously neglected T cell population. Considering CagA's mode of action, cytotoxic CD8⁺ T cells targeting CagA-infected epithelium could eventually be exploited to prevent gastric cancer development.

M.R.A. Koch: None. R. Gong: None. J. Schiede: None. V. Friedrich: None. R. Mejías-Luque: None. D.H. Busch: None. V. Engelsberger: None. M. Gerhard: None. C. Schulz: None. R. Vasapolli: None.

P04.09

LONG-TERM EFFECT OF *HELICOBACTER PYLORI* THERAPY ON ATROPHIC GASTRITIS AND INTESTINAL METAPLASIA AFTER ENDOSCOPIC RESECTION OF GASTRIC NEOPLASM: A FOLLOW-UP OF A RANDOMIZED CONTROLLED TRIAL

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Objective: We previously reported that *H. pylori* therapy improved the grade of atrophic gastritis (AG) at the corpus lesser curvature (LC) at 3-year follow-up in patients who had undergone endoscopic resection for early gastric cancer or high-grade adenoma. To evaluate the long-term effect of *H. pylori* therapy on the AG and intestinal metaplasia (IM) at the corpus LC, we assessed the histologic status of the patients at extended follow-up.

Patients and Methods: In this follow-up study of a previous prospective, double-blind, placebo-controlled, randomized trial, 327 patients (162 in the *H. pylori* treatment group and 165 in the placebo group) have assessed the improvement in AG and IM grades at the closeout time endoscopy for evaluation of metachronous gastric cancer. For patients with persistent *H. pylori* infection, bismuth-containing quadruple *H. pylori* therapy was provided, and AG and IM status were re-evaluated 1-year after the therapy. The primary outcome was the follow-up improvement from baseline in AG grades at the corpus LC.

Results: During a median follow-up of 6.6 years, AG grades were improved in 83 of 157 patients (52.9%) in the treatment group and in 52 of 156 (33.3%) in the placebo group (odds ratio in the treatment group, 2.24; 95% confidence interval, 1.42-3.54; $p=0.0005$). The proportion of patients who had an improved grade of IM was higher in the treatment group than in the placebo group (37.9% vs. 23.2%, $p=0.0042$).

Conclusions: The effect of *H. pylori* therapy on the improvement of corpus AG and IM was persistent during the extended follow-up periods.

J. Lee: None. I. Choi: None. Y. Kim: None. C. Kim: None. M. Kook: None.

P04.10

COMPARISON OF FOUR DIAGNOSTIC TESTS FOR *HELICOBACTER PYLORI* INFECTION

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Objective: Due to lower operational costs, HMOs may prioritize stool antigen testing (*HpStAg*) over ¹³C-urea breath tests (¹³C-UBT) for the non-invasive diagnosis of *H. pylori* infection. We aimed to determine the relative accuracy of the diagnostic tests for *H. pylori* infection at our institution.

Materials and Methods: We performed same-day ¹³C-UBT, rapid urease test (*RUT*), histological examination, and *HpStAg* on consecutive patients presenting for gastroscopy at Rabin Medical Center. ¹³C-UBT test meal consisted of 4 g citric acid. Monoclonal stool Ag test was performed using the LIAISON Meridian chemiluminescent immunoassay (DiaSorin SpA, Italy). Histology was examined with H&E, and additional stains were performed at the pathologist's discretion. For the assessment of ¹³C-UBT the *de facto* gold standard was concordant *RUT* and histology. For the assessment of *HpStAg*, the *de facto* gold standard was defined at the result of at least two of the three remaining tests (*RUT*, histology and ¹³C-UBT).

Results: Overall, 91 patients were included [36 males (39.6%) age 50.1±18.7 years]. The indication for gastroscopy was dyspepsia in 57 (62.6%). *RUT* and histology were discrepant in 3 cases. For ¹³C-UBT and *HpStAg*, respectively. *H. pylori* positivity was 34.5% and 37.1%; sensitivity was 96.6% and 69.2%; specificity was 100% and 95.4%; PPV was 100% and 89.8%; NPV was 98% and 84%; false positive was 0% and 10.1%; and false negative was 1.8% and 16.0%.

Conclusions: The accuracy of ¹³C-UBT is superior to *HpStAg* at our institution. Clinicians should be aware of test limitations when interpreting results.

D. Boltin: None. R. Gingold-Belfer: None. T.T. Perets: None. R. Dickman: None. M. Siterman: None.

P04.11

**EMPIRICAL THERAPY VS. TAILORED THERAPY OF *H. PYLORI* IN KOREA:
A NATIONWIDE PLACEBO-CONTROLLED STUDY IN KOREA**

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Objective: The aim of this study was to compare the effect of empirical therapy and tailored therapy for *H. pylori* in Korea.

Patients and Methods: After urea breath test (UBT), subjects were randomly allocated to empirical group or tailored group. In tailored group, DPO-PCR was performed to detect wild type (clarithromycin sensitive) or mutant (clarithromycin resistant). Each group were randomly assigned to 7-day group or 14-day group. Pantoprazole 40 mg, clarithromycin 500 mg, and amoxicillin 1000 mg (PCA) were administered twice a day in empirical group. In tailored group, PCA were administer in wild type and pantoprazole 40 mg bid, metronidazole 500 mg tid, bismuth subsalicylate 300 mg qid, and tetracycline 500 mg qid was administered in mutant group. Six weeks after eradication, UBT was performed to confirm *H. pylori* eradication.

Results: The eradication rates are summarized in Table 1 and Table 2.

Conclusions: Fourteen-day therapy is necessary in empirical therapy and 7-day therapy is enough in tailored therapy.

B. Kim: None. J. Kim: None. J. Kim: None. W. Chung: None. C. Bang: None. S. Jung: None. G. Kim: None. Y. Lim: None. S. Lee: None. J. Sung: None. S. Seo: None. M. Joo: None. S. Jeon: None. H. Lee: None. W. Lee: None. S. Park: None. K. Kim: None. H. Kim: None.

TABLE 1. 7-DAY VS. 14-DAY THERAPY IN EMPIRICAL THERAPY.

	Success	Fail	p-value
7-day (N=90)	60/90 (66.7%)	30/90 (33.3%)	0.012
14-day (N=93)	77/93 (82.2%)	16/93 (17.2%)	

TABLE 2. 7-DAY VS. 14-DAY THERAPY IN TAILORED THERAPY.

		Success	Fail	p-value
Wild type	7-day	60/69 (87.0%)	9/69 (13.0%)	0.846
	14-day	59/67 (88.1%)	8/67 (11.9%)	
Mutant	7-day	18/19 (94.7%)	1/19 (5.3%)	1.000
	14-day	16/17 (94.1%)	1/17 (5.9%)	

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P05.01

THE ERADICATION RATES OF CONCOMITANT AND TAILORED THERAPY WERE HIGHER THAN SEQUENTIAL AND TRIPLE WITH PROBIOTICS AND TRIPLE THERAPY FOR *HELICOBACTER PYLORI*

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The eradication rates of the standard triple therapy have continuously decreased, mainly because of the widespread development of antibiotic resistance, particularly clarithromycin. We compared the efficacy of standard triple, triple with probiotics, sequential, concomitant, and tailored therapies for *H. pylori* eradication. This was a prospective, randomized controlled study involving 1,500 patients diagnosed with *H. pylori* infection between January 2018 and December 2022 in Yeouido St. Mary's Hospital of the Catholic University. We compared 5 treatment regimens: the triple therapy was treated with clarithromycin-based triple therapy for 7 days; the triple therapy with probiotics therapy was treated with triple therapy and lactobacillus for 7 days; the sequential therapy consisted of rabeprazole and amoxicillin for the initial 5 days, followed by rabeprazole, clarithromycin, and metronidazole for the subsequent 5 days; the concomitant therapy consisted of rabeprazole, amoxicillin, clarithromycin, and metronidazole for 7 days; the tailored therapy was treated with clarithromycin based triple therapy in the absence of 23S rRNA point mutation while clarithromycin was replaced by metronidazole when the mutation was detected. Six weeks following the completion of therapy, successful *H. pylori* eradication was defined by a negative 13C-urea breath test. The eradication rates were 91.2% in the concomitant group, 90.7% in the tailored group, 85.1% in the sequential group, 81.2% in triple with probiotics group and 76.2% in triple group ($p=0.135$). In areas where resistance of clarithromycin is high, concomitant and tailored therapy may be more effective than sequential and triple with probiotics and triple therapy for *H. pylori* eradication.

Y. Nam: None. D. Cheung: None. J. Kim: None.

P05.02

EXCELLENT ERADICATION RATE OF 14-DAY ONCE-DAILY VONOPRAZAN, LEVOFLOXACIN, CLARITHROMYCIN-MR, AND BISMUTH FOR *H. PYLORI* INFECTION IN HIGH CLARITHROMYCIN RESISTANCE AREA: A PROSPECTIVE RANDOMIZED STUDY (ONCE-VONO TRIAL)

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Objective: Vonoprazan, a novel potent acid inhibitor, has been recently introduced in *H. pylori* treatment regimen. Until now, levofloxacin has rarely been used in vonoprazan-containing regimens. This pioneer study aims to evaluate the efficacy of once-daily vonoprazan, levofloxacin, clarithromycin MR, and bismuth for *H. pylori* eradication.

Patients and Methods: This prospective randomized study was conducted to compare *H. pylori* eradication between 7-day and 14-day once-daily regimens composed of vonoprazan 40 mg, clarithromycin-MR 1 g, levofloxacin 500 mg, and bismuth subsalicylate 1,048 mg. CYP3A4/5 polymorphisms (1*/1*, 1*/3*, 3*/3*) and antibiotic susceptibility test (Epsilometer test or GenoType® HelicoDR) were also performed. Successful eradication was defined as negative 13C-UBT 4 weeks after treatment completion. Of 133 dyspeptic patients undergoing upper GI endoscopy, 39 (29%) had *H. pylori* infection and were enrolled in this study. Thirty-nine patients (15 men and 24 women with the mean age of 58.5 years) were randomized to receive 7-day (19 patients) or 14-day regimen (20 patients).

Results: Eradication rates of 7-day and 14-day regimens were 73.7% and 90.0% ($p=0.24$) by intention-to-treat analysis, respectively. Per-protocol eradication rates of 7-day and 14-day regimens were 77.8% and 94.7% ($p=0.18$), respectively. Antibiotic resistance rates were 25.6% for clarithromycin and 33.3% for levofloxacin. Minor side effects such as black stool (38.4%), bitter taste (23.1%), and nausea and vomiting (17.9%) were not different between groups. No serious adverse event was reported.

Conclusions: Once-daily 14-day vonoprazan, levofloxacin, clarithromycin-MR, and bismuth provided 94.7% eradication rate. This 14-day regimen could be safely used as an alternative first-line treatment for *H. pylori* infection in high clarithromycin resistance areas.

R. Vilaichone: None. S. Sukkamolsantiporn: None. S. Chonprasertsuk: None. B. Pornthisarn: None. S. Siramolpiwat: None. P. Bhanthumkomol: None. N. Issariyakulkarn: None. P. Nunanan: None. N. Aumpan: None. V. Mahachai: None.

P05.03

MOLECULAR TESTING GUIDED THERAPY VS. SUSCEPTIBILITY TESTING GUIDED THERAPY IN FIRST-LINE AND THIRD-LINE *HELICOBACTER PYLORI* ERADICATION – TWO MULTICENTRE, OPEN-LABEL, RANDOMISED CONTROLLED, NON-INFERIORITY TRIALS

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Objective: Whether the efficacy of molecular testing guided therapy (MTGT) is non-inferior to that of susceptibility testing guided therapy (STGT) in *H. pylori* eradication remains uncertain.

Patients and Methods: We conducted two multi-centre, open-label, randomised controlled trials. Treatment-naïve *H. pylori*-positive patients were included in Trial 1 and patients with refractory infection were included in Trial 2. Clarithromycin and levofloxacin resistance were determined by agar dilution test in the STGT group, and by PCR and direct sequencing for detection of 23S rRNA and *gyrase A* mutations in the MTGT group.

Results: A total of 560 treatment-naïve patients were recruited in Trial 1, and another 320 patients with refractory *H. pylori* infection were recruited in Trial 2. In first-line therapy (Trial 1), the eradication rates in the MTGT group and the STGT group were 86.1% (95% CI: 82.0%-90.1%) vs. 86.8% (95% CI: 82.8%-90.8%) in the ITT analysis (p -value=0.805), respectively. In third-line therapy (Trial 2), the eradication rates in the MTGT group and the STGT group were 88.1% vs. 86.9% in the ITT analysis (p -value=0.735), respectively. The difference in eradication rate between the MTGT and STGT groups was -0.7% (95% CI: -6.4%-5.0%) in Trial 1 and 1.3% (95% CI: -6.0%-8.5%) in Trial 2 by ITT analysis.

Conclusions: Molecular testing guided therapy was similar and not inferior to susceptibility testing guided therapy in first-line and third-line treatment of *H. pylori* infection, respectively.

J. Liou: None. M. Chen: None. P. Chen: None. E.M. El-Omar: None. M. Wu: None.

TABLE 1. ANTIBIOTIC RESISTANCE RATES AND ERADICATION RATES OF MOLECULAR TESTING GUIDED THERAPY (MSGT) AND SUSCEPTIBILITY TESTING GUIDED THERAPY (STGT).

	TRIAL 1 (First-Line)		TRIAL 2 (Third-Line)	
	MTGT (N=280)	STGT (N=280)	MTGT (N=160)	STGT (N=160)
Clarithromycin resistance	16.1% (39/243)	21.1% (53/251)	94.6% (140/148)	93.9% (138/147)
Levofloxacin resistance	21.0% (51/243)	17.9% (45/251)	75.7% (112/148)	70.1% (103/147)
23S rRNA mutation (tissue)	17.7% (49/277)	22.8% (63/276)	93.8% (150/160)	95.0% (151/159)
Gyrase A mutation (tissue)	19.9% (55/276)	18.9% (52/275)	75.2% (118/157)	66.5% (103/155)
ITT analysis	86.1% (241/280)	86.8% (243/280)	88.1% (141/160)	86.9% (139/160)
difference	-0.7%, 95% CI: -6.4% to 5.0%, $p=0.071$		1.3%, 95% CI: -6.0% to 8.5%, $p=0.002$	
PP analysis	90.6% (240/265)	91.6% (240/262)	90.3% (140/155)	89.1% (139/156)
difference	-1.0%, 95% CI: -5.9% to 3.8%, $p=0.059$		1.2%, 95% CI: -5.5% to 8.0%, $p=0.001$	

P05.04

EFFECTIVENESS OF LEVOFLOXACIN-CONTAINING RESCUE THERAPY IN CENTRAL SEOUL, KOREA

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Objective: Levofloxacin-containing regimens, as third-generation quinolones, are commonly employed for the rescue treatment of *Helicobacter pylori* (HP) infection. However, recent studies have demonstrated the inadequacy of levofloxacin-amoxicillin-proton pump inhibitor (PPI) regimens against *gyrA* mutation-positive HP strains and quinolone resistance. This study aimed to evaluate the efficacy of levofloxacin-amoxicillin-PPI regimens in eradicating HP in patients with first- and second-line therapy failures.

Method and Materials: A total of 33 patients with failed therapies, confirmed by UBT, were recruited from Seoul Paik Hospital. The patients underwent 7, 10, and 14-day regimens of levofloxacin 250 mg, amoxicillin 1 g, and rabeprazole 20 mg twice daily. Follow-up UBT was conducted one-month post-treatment completion.

Results: The study included 33 patients (12 males, 21 females), aged 45-88 years (mean 65.2, SD 10.1). The primary endoscopic features observed were chronic atrophic gastritis with intestinal metaplasia (13 patients), gastric polyps (8), peptic ulcers (5), early gastric cancers (4), adenomas (2), and lymphofollicular gastritis (1). The mean eradication rates were 57.6% (intent-to-treat, ITT) and 69.2% (per-protocol, PP). The ITT and PP eradication rates for the 7, 10, and 14-day regimens were 60.0% and 60.0%, 62.5% and 69.2%, and 50.0% and 62.5%, respectively. Treatment durations of 10 or 14 days showed trends favoring higher eradication rates but with poorer compliance for longer durations. No statistically significant differences were found in treatment duration or compliance.

Conclusions: Rescue therapy in central Seoul, Korea, demonstrated suboptimal efficacy in eradicating HP. No significant differences were observed between 7- and 10- and 14-day regimens.

J. Moon: None. S. Kim: None. E. Kim: None. I. Kim: None. S. Seol: None.

P05.05

THE ART OF DECEIVING: LIPID-BASED DECOYS FOR *HELICOBACTER PYLORI* INFECTION MANAGEMENTA. S. PINHO^{1,2,3}, R. PEREIRA^{1,2,4}, M. PEREIRA^{1,2}, A. RAI⁵, L. FERREIRA^{5,6}, M. C. L. MARTINS^{1,2,3}, P. PARREIRA^{1,2}

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Objective: Antibiotic-based therapy for *Helicobacter pylori* (*Hp*) fails in up to 40% of patients and has severe side-effects, as dysbiosis. *Hp* depends on the uptake of cholesterol for survival and exhibits positive chemotaxis towards it. Here we describe proof-of-concept studies using 2D and 3D models for validating surface-grafted cholesterol as a bioengineered strategy for the management of *Hp* gastric infection.

Material and Methods: 2D model surfaces (self-assembled monolayers-SAMs) were prepared using pegylated cholesterol in different ratios (Chol-SAMs; 0, 25 and 100%). Chol-SAMs were characterized as described. Specific adhesion was evaluated by incubating *Hp* J99 strain for 2h with Chol-SAMs similarly to reported. Then, 3D gold nanoparticles functionalized with cholesterol (Chol-NPs) were prepared and characterized as described. *In vitro* performance against *Hp* J99 was assessed through antibacterial, Transmission Electron Microscopy (TEM), cyto- and hemocompatibility assays. *Escherichia coli* ATCC[®] 25922 and *Lactobacillus acidophilus*-01 were tested as representative of gut microbiota.

Results: *Hp* adhered specifically to Chol-SAMs in a concentration-dependent manner. Chol-NPs minimum bactericidal concentration (MBC) was 125 µg/mL for *Hp* J99, while control-NPs (without cholesterol) required >500 µg/mL. After 2h, Chol-NPs killed *Hp* through internalization and membrane rupture (TEM). Bacteria representative of gut microbiota were unaffected by Chol-NPs. Chol-NPs were cytocompatible (human gastric adenocarcinoma cell line) at concentrations 4 times higher than the MBC, as well as nonhemolytic, highlighting their safety profile.

Conclusions: Cholesterol-functionalized biomaterials are a promising strategy worth developing.

Acknowledgments: FCT for funding (2022.12580.BD; CEECIND/01210/2018). PT2020 for funding (POCI-01-0247-FEDER-04708).

A.S. Pinho: None. R. Pereira: None. M. Pereira: None. A. Rai: None. L. Ferreira: None. M.C.L. Martins: None. P. Parreira: None.

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).

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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.

O. P. Nyssen: None. M. Pabón-Carrasco: None. A. Keco-Huerga: None. M. Castro-Fernandez: None. G. Fiorini: None. A. Perez-Aisa: None. B. Tepes: None. A. Lucendo: None. A. Lanas: None. L. Rodrigo: None. L. Vologzanina: None. N. Brglez Jurecic: None. L. Bujanda: None. J. Huguet: None. L. Fernandez-Salazar: None. A. Cano-Català: None. L. Moreira: None. F. Mégraud: None. C. O'Morain: None. J. P. Gisbert: None.

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

P05.07

EVALUATION OF MOLECULAR-BASED CLARITHROMYCIN RESISTANCE TESTING IN *HELICOBACTER PYLORI* COMPARED TO CULTURE-BASED TESTING.

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Objective: Molecular methods offer a more rapid alternative for the detection of Hp resistance to antibiotics than traditional culture-based methods. The aim of the study was to evaluate the diagnostic accuracy of molecular-based clarithromycin susceptibility testing compared to culture and E-test.

Patients and Methods: Following ethical approval and informed consent, adults were recruited prospectively from Tallaght University Hospital and Letterkenny University Hospital, Ireland, regardless of Hp treatment history. During routine gastroscopy, subjects had 1 antrum and 1 corpus biopsy taken for Hp culturing and DNA extraction. Clarithromycin susceptibility testing was performed by the Etest method (Biomerieux). The RIDA[®]GENE *Helicobacter pylori* assay (R-Biopharm AG, Germany) was used for detection of Hp and clarithromycin resistance-associated point mutations (A2146C, A2146G and A2147G).

Results: In all samples from 191 culture-positive patients [mean age 48.4 ± 15.3 years; 45.0% (N=86) female] were analysed. The rates of clarithromycin resistance detected by culture-based and molecular methods were 49.2% (N=94/191) and 38.7% (N=74/191), respectively ($p=0.05$; Fisher's exact test). Results were in agreement between both methods in 84.3% (N=161/191) of cases. The sensitivity and specificity of the RIDA[®]GENE assay compared to culture for the detection of clarithromycin resistance were 74.2% (95% CI: 64.4-82.6%) and 94.7% (95% CI: 88.0-98.3%), respectively. The positive predictive value was 93.5% (95% CI: 85.5-97.9%) and the negative predictive value was 78.1% (95% CI: 69.4-85.3%).

Conclusions: While the RIDA[®]GENE assay was easy to use and more rapid than Hp culture, the low sensitivity compared to culture in our cohort may limit its use to cases where culture-based methods are unsuccessful.

S.D. Molloy: None. T.J. Butler: None. I. Merrigan: None. V. Pariahar: None. K. Van Der Merve: None. D. McNamara: None. S.M. Smith: None.

P05.08

THE ROLE OF NANOSTRUCTURED LIPID CARRIERS (NLC) PROTEIN CORONA IN *H. PYLORI* SELECTIVITY

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Objective: With the increase of antibiotic resistance, the current therapeutic regimens against *Helicobacter pylori* (Hp) are failing, proving the need for alternative antibiotic-free therapies. Drug-free nanostructured lipid carriers (NLC) with bactericidal activity against Hp were previously developed. Here, the effect of protein corona on their specificity against Hp was studied. Additionally, the major component of the protein corona (albumin) was explored regarding its selectivity towards Hp and possible use for Hp targeting.

Material and Methods: NLC were produced using Precirol ATO5[®], Miglyol-812[®] and Tween[®]60 (NLC60)². NLC60 protein corona was analyzed by liquid chromatography-mass spectrometry (MS) and its effect on NLC activity was tested. Fluorescent albumin in solution and in nanoparticles (produced by microfluidics) was tested against Hp J99 and *Escherichia coli* ATCC[®] 25922[™] and their interaction was analyzed by imaging flow cytometry.

Results: MS analysis confirmed a protein corona on NLC surface that delays activity against Hp. This protein corona was composed by 70 proteins, being serum albumin the most abundant (>93%). After incubation with labelled albumin, only Hp interacted with this protein. The same was observed for albumin nanoparticles (imaging flow cytometry). When tested against both bacteria no bactericidal effect was observed.

Conclusion: The role of protein corona and albumin in NLC activity and Hp selectivity was demonstrated. These results aid in disclosing NLC selectivity towards Hp, and highlight the role of albumin and the potential of albumin nanoparticles for Hp targeting.

Acknowledgments: FCT for SFRH/BD/151081/2021 and CEECIND/01210/2018 and to the BiotechHealth Doctoral Program.

R. Chitas: None. C. Nunes: None. P. Parreira: None. M.C.L. Martins: None.

P05.09

PPI'S EFFECTIVENESS IN H. PYLORI ERADICATION SCHEMES DEPENDS ON THE BASAL SECRETION OF HYDROCHLORIC ACID

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Objective: Sufficient inhibition of HCl secretion is one way to improve the *Helicobacter pylori* (HP) eradication. The aim of the study was to evaluate PPI effectiveness at first day of treatment depending on the HCl basal secretion.

Patients and Methods: We analyzed 83 results of 24-h-gastro-pH-monitoring at day one of PPI taking in patients with acid-dependent gastroesophageal diseases. Primarily we performed express-gastro-pH-monitoring. The separation criterion was established previously by express-gastro-pH-monitoring indicators (X pH >2.48 units, Me pH >2.3 units, Mo pH >2.35 units).

We created two groups comparable by age, sex, height, weight, and prescribed PPI. Group I – 55 patients with indicators less than suggested. Group II – 28 patients with indicators corresponding to the proposed criteria.

We studied 24-h-gastro-pH-monitoring pH indicators (X pH, Me pH, Mo pH) for basal period-time from the start of the investigation to the first PPI dose (1 hour); time after the first PPI dose until the end of monitoring (23 h); night period (22:00-07:00).

Results: The basal period intragastric indicators X pH, Me pH, Mo pH in I group were significantly ($p < 0.01$) lower (1.9 ± 0.09 , 1.75 ± 0.07 , 1.68 ± 0.07 vs. 2.2 ± 0.09 , 2.03 ± 0.1 , 1.96 ± 0.1). 23 hours after the first PPI dose in group I indicators were significantly ($p < 0.01$) lower (4.2 ± 0.2 , 4.07 ± 0.2 , 3.6 ± 0.2 vs. 4.9 ± 0.2 , 4.9 ± 0.3 , 4.5 ± 0.3); night period indicators in the group I were significantly ($p < 0.01$) lower (4.3 ± 0.2 , 4.2 ± 0.3 , 3.9 ± 0.3 vs. 5.03 ± 0.2 , 5.02 ± 0.3 , 4.9 ± 0.4).

Conclusions: Basal gastric acidity affects PPI acid-blocking action at the first day of treatment during the 23-hour period and night period. The proposed criteria for prognostic PPI acid-blocking effect assessment before treatment are sufficient.

I. Paliy: None. S. Zaika: None. N. Kondratiuk: None. K. Ksenchyna: None.

P05.10

WATCH OUT *HELICOBACTER*: CHITOSAN NANOPARTICLES DECORATED WITH ANTIMICROBIAL PEPTIDES FOR GASTRIC INFECTION

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The available therapy for *Helicobacter pylori* (Hp), the etiological agent of ~89% of gastric cancer cases, fails in 10-40% of the individuals, mainly due to high antibiotic resistance rates, highlighting the need for alternatives.

Antimicrobial peptides (AMPs) have excellent bactericidal performance against multiresistant-bacteria. The immobilization of AMPs onto biomaterials avoids the proteolytic degradation and aggregation with proteins, while enhancing their bactericidal effect (lower AMPs concentrations are needed compared with free-AMPs).

Here, an innovative microfluidics system suitable for nanoparticles production and bioconjugation of any thiolated-AMP in a single device was developed. MSI-78A-SH (one of the few effective AMP against Hp) was directly grafted onto chitosan nanoparticles surface (AMP-NP, 113±43 nm), using the Thiol-Norbornene “Photoclick” Chemistry (reaction yield ~40%).

The developed AMP-NP were stable in acidic conditions (pH 1.2) and cytocompatible against gastric adenocarcinoma cell lines (AGS & MKN74, ATCC®). AMP-NP (10¹¹ NP/mL; 96 µg/mL AMP) were bactericidal against two highly pathogenic Hp26695 & HpJ99 strains. Full eradication of Hp26695 was attained in 30 min, which may be related to an AMP concentration 3 times higher in AMP-NP than the minimum bactericidal concentration (MBC) of the free AMP (32 µg/mL). HpJ99 eradication was achieved in 24h using a lower AMP concentration in AMP-NP (96 µg/mL) than the required when AMP was free (MBC: 128 µg/mL). AMP-NP affected Hp membrane by inducing the formation of vesicles and pores and a subsequent release of intracellular content.

Overall, this strategy is a step forward in the development of non-antibiotic approaches to counteract multi-strain-Hp infection.

D. Fonseca: None. P. Alves: None. E. Neto: None. B. Custódio: None. S. Guimarães: None. M. Martins: None. A. Gomes: None. P. Gomes: None. R. Pereira: None. P. Freitas: None. P. Parreira: None. C. Martins: None.

P05.11

BIOPSIES SAMPLING IN *HELICOBACTER PYLORI* NEGATIVE PATIENTS: IS IT STILL WORTHY?

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Objective: Intestinal-type gastric carcinoma occurs from long-term atrophic/metaplastic pangastritis. *H. pylori* infection remains the main risk factor for gastric cancer. The study aimed to assess the prevalence of pangastritis and its distribution between *H. pylori* infected and uninfected dyspeptic patients who consecutively underwent upper endoscopy.

Materials and Methods: Diagnosis of *H. pylori* infection was performed by the Composite Reference Method. Histopathological analysis was performed by gastric mapping (antrum, incisura angularis and gastric body) and OLGA (Operative link on gastritis assessment) / OLGIM (Operative link on gastric intestinal metaplasia) staging.

Results: The study enrolled 709 dyspeptic patients (Mean age: 54.5; M/F: 278/431), including 208 with and 501 without *H. pylori* infection. Overall, atrophic or metaplastic pangastritis (OLGA/OLGIM: 3-4) was detected in 6 (0.8%) and 3 (0.4%) patients. The distribution of pangastritis among infected and uninfected patients is provided in Table 1, and the patterns of histological features in Table 2. No case of dysplasia was detected.

Conclusions: These results show the low probability of finding atrophy (metaplastic and non-metaplastic), in patients without *H. pylori* infection, thus laying the groundwork to start thinking about avoiding gastric mapping in this group of patients.

G. Fiorini: None. M. Pavoni: None. A. D'Errico: None. M.L. Tardio: None. I.M. Saracino: None. A. Zullo: None. C. Borghi: None. D. Vaira: None.

TABLE 1. OLGA AND OLGIM STAGING.

	HP POS31	HP NEG5
OLGA I	16	4
OLGA II	12	1
OLGA III	2	//
OLGA IV	1	//
Metaplastic atrophy		
OLGIM I	13	4
OLGIM II	11	1
OLGIM III	1	//
OLGIM IV	2	//

TABLE 2. HISTOPATHOLOGICAL OVERVIEW.

	HP POS (n: 208)		HP NEG (n: 501)	
	ANTRUM	CORPUS	ANTRUM	CORPUS
Normal	//	6	7	210
CIG + CAG	184	193	489	291
CIG/CAG + atrophy	6	2	//	//
CIG/CAG + metaplastic atrophy	18	7	5	//

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P06.01

IMPACT OF SUB-INHIBITORY CONCENTRATIONS OF ANTIBIOTICS ON THE BIOFILM DEVELOPMENT OF *HELICOBACTER PYLORI*

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Objective: For the last decade, the attention of scientists studying *Helicobacter pylori* has increasingly focused on the ability of this bacterium to form biofilms. Still, little is known about how the presence of sub-inhibitory concentrations (sub-MICs) of classically used antibiotics affects the first stages of its biofilm development.

Materials and Methods: Biofilm properties were assessed using classical methods (culture and a crystal violet staining), but also advanced equipment for creating microfluidic conditions and allowing for a real-time observation of microorganisms – the Bioflux 1000 coupled with fluorescence microscopy.

Results: Using stationary and microfluidic biofilm growth models, the modulatory effect of sub-MICs of all tested representatives of antibiotics on the amount and properties of biofilms was observed. However, This effect was achieved without impacting the bacterial cell viability. It was found that exposure of *H. pylori* strains to sub-MICs of clarithromycin reduced the rate of cell autoaggregation, as well as contrib-

uting to a decrease in the total amount of biofilm (biovolume and average thickness) and proteins constituting the biofilm matrix. On the other hand, exposing *H. pylori* strains to sub-MICs of metronidazole or levofloxacin had the opposite effect, resulting in enhanced cell autoaggregation, greater amount of biofilm formed (including the amount of biomatrix proteins and eDNA) and increased biofilm heterogeneity. **Conclusions:** Sub-inhibitory concentrations of antibiotics have a significant effect on the amount and architecture of *H. pylori* biofilm. Among the tested antibiotics, only sub-MICs of clarithromycin did not enhance the biofilm development of this bacterium.

P. Krzyżek: None. P. Migdał: None. G. Gościński: None.

P06.02

MOLECULAR EVOLUTION OF THE 16S RRNA GENE WITHIN THE HELICOBACTER PYLORI GENOME PROJECT

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Objective: *Helicobacter pylori* is etiologically associated with various gastric diseases, and co-habitation with humans has shaped the evolution of its genome. 16S ribosomal RNA (16S rRNA) sequencing is commonly used in microbiome and evolutionary studies, but the use of 16S rRNA sequencing for assessing *H. pylori* population structure has not been comprehensively evaluated.

Material and Methods: Using 1,011 genomes from the *Helicobacter pylori* Genome Project (HpGP) and reference genome ATCC-26695, we conducted the most comprehensive evaluation yet undertaken of *H. pylori* 16S rRNA, addressing population structure and genome rearrangements.

Results: The phylogenetic tree revealed a distinct clade enriched for African strains (hspAfrica1 and hspAfrica2) that was consistently observed by haplotype network analysis. Nevertheless, 16S rRNA had limited resolution for analyzing the global evolutionary history of *H. pylori* outside the African strains. Inversions and/or transpositions of the first and/or second 16S copies were observed in specific *H. pylori* populations.

Conclusions: This work reveals more extensive genomic rearrangement of *H. pylori* 16S rRNA genes than previously appreciated.

I.A. Wichmann: None. M.C. Camargo: None. J.L. Cherry: None. T.L. Cover: None. D. Wang: None. J.P. Dekker: None. P. González-Hormazábal: None. D. Falush: None. R.M. Peek: None. Y. Yamaoka: None. C.C. Abnet: None. E. Tarazona-Santos: None. R. Zamudio: None.

P06.04

PRACTICAL ADEQUACY OF THE 7-DAY TRIPLE REGIMEN FOR *HELICOBACTER PYLORI* ERADICATION ACCORDING TO THE CLARITHROMYCIN RESISTANCE-ASSOCIATED MUTATION PCR RESULTS: A SINGLE CENTERED RETROSPECTIVE STUDY

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Objective: To investigate the practical adequacy of the 1-week tailored *H. pylori* eradication strategy in the clinical field.

Patients and Methods: A retrospective review and analysis of patients who had eradication therapy from January 2019 to December 2022, at Yeouido St. Mary's hospital.

Results: 213 subjects were enrolled consecutively during the study period. The mean age was 59.7 (± 12.6) and the male proportion was 63.9%. The PCR for clarithromycin resistance was performed in 77 patients, and 22 patients had A2143G mutation (28.9%). The eradication success rate of the 1-week regimen according to PCR results was compatible with the empirical 2-week clarithromycin-based triple regimen, 93.9% and 96.5% in the PP analysis, respectively (p -value = 0.828). Two-week tailored regimen had no superiority to a 1-week regimen, 86.3% and 93.9% in the PP analysis, respectively.

Conclusions: When the regimen was selected based on a PCR test for clarithromycin resistance-associated mutation, the eradication success rate of the 1-week regimen was equivalent to the 2-week empirical regimen and when sensitive drugs were used, a 2-week tailored regimen did not show superior results compared to a 1-week tailored regimen.

Y. Nam: None. D. Cheung: None. J. Kim: None. S. Park: None.

TABLE 1. ERADICATION SUCCESS RATES ACCORDING TO THE REGIMENS.

Regimens	Eradication success rates. % (n/n)	
	Per protocol analysis	Intention-to-treat analysis
PCR-based tailored regimen		
1-week	93.9% (31/33)	79.5% (31/39)
2-week	86.3% (19/22)	73.1% (19/26)
Empirical clarithromycin-based triple regimen		
1-week	83.7% (36/43)	75.0% (36/48)
2-week	96.5% (82/85)	82/0% (82/100)

TABLE 2. COMPARISON RESULTS OF REGIMENS.

Comparison (Chi-square)	p -value
PCR-based tailored 1-week regimen vs empirical 2-week regimen	0.828
PCR-based tailored 1-week regimen and 2-week regimen	0.632

P06.05

THE ROLE OF *HELICOBACTER SUIS*, *FUSOBACTERIUM GASTROSUIS* AND THE PARS OESOPHAGEAL MICROBIOTA IN GASTRIC ULCERATION IN SLAUGHTER PIGS RECEIVING MEAL OR PELLETED FEED

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Objective: Ulceration of the non-glandular part of the porcine stomach (*pars oesophagea*) leads to economic losses and decreased animal welfare. Infections with *Helicobacter suis*, possibly in combination with *Fusobacterium gastrosuis*, may play a role in this multifactorial disease.

Material and Methods: Keeping all other environmental and genetic factors identical, 75 pigs received a pelleted feed while 75 other pigs received a meal feed. The *pars oesophagea* was macroscopically examined. (q)PCR assays for *H. suis* and *F. gastrosuis*, as well as *pars oesophagea* microbiota analyses were performed.

Results: All 150 pig stomachs showed lesions. *F. gastrosuis* was detected in 115 cases (77%) and *H. suis* in 117 cases (78%), with 92 cases (61%) of co-infection. The infectious load of *H. suis* was an independent risk factor for severe gastric lesions (OR=1.14; $p=0.038$), possibly through upregulated gastric acid secretion. The infectious load of *F. gastrosuis* was an independent risk factor for mild gastric lesions (OR=0.8; $p=0.0014$). Feed pelleting did not impact the severity of gastric lesions significantly (OR=1.72; $p=0.28$); however, there was a positive association between receiving pelleted feed and the presence of *H. suis* (OR=2.43; $p=0.058$). Preliminary differential abundance analysis of the *pars oesophagea* demonstrated a statistically and biologically significant positive association of *Helicobacter* and *Campylobacter* species and a negative association of *Lactobacillus* species with the gastric ulcer score.

Conclusions: *H. suis* infections may indeed play a role in the development of gastric lesions in the *pars oesophagea*. Improving feed management and gaining knowledge on how to control *H. suis* infection may positively impact pig health.

E. Taillieu: None. S. Taelman: None. S. De Bruyckere: None. E. Goossens: None. I. Chantziaras: None. C. Van Steenkiste: None. P. Yde: None. S. Hanssens: None. D. De Meyer: None. W. Van Criekinge: None. M. Stock: None. D. Maes: None. K. Chiers: None. F. Haesebrouck: None.

P06.06

PRESENCE OF POTENTIALLY NOVEL *HELICOBACTER PYLORI*-LIKE ORGANISMS IN GASTRIC SAMPLES FROM CATS AND DOGS

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Objective: Currently, seven gastric non-*Helicobacter pylori* *Helicobacter* (NHPH) species are known to commonly colonize the stomach of cats and dogs, with a low pathogenic significance. Reports of *H. pylori* and *H. pylori*-like organisms infecting animals have occasionally been made.

Material and Methods: Samples were collected from the corpus and antrum of 20 cats and 27 dogs. A *Helicobacter* genus-specific 16S rRNA PCR assay, *H. pylori*-specific *ureAB* and *glmM* PCR assays and a nested PCR detecting 23S rRNA in a *Helicobacter* genus-specific manner in the first step and a *H. pylori*-specific manner in the second step were performed, in combination with sequencing.

Results: Based on 16S rRNA sequence analysis, 39/47 animals (83%) appeared infected with canine/feline gastric NHPHs in the corpus and/or antrum. *H. pylori*-specific *ureAB* amplicons were obtained in samples of 22 stomachs. In three corpus samples and one antrum sample, *ureAB* amplicons showed the highest similarity to a sequence obtained from a gastric sample of a wild boar, while all other amplicons showed the highest homology to sequences obtained from human hosts. Only one antrum sample positive in the *ureAB* assay was also positive in the *H. pylori*-specific *glmM* assay, however, with a borderline percentage identity of 95%. All samples were negative in the final step of the nested 23S rRNA PCR assay. Sequence analysis of *Helicobacter* genus-specific 23S rRNA amplicons could provide further information on potentially novel *H. pylori*-like organisms.

Conclusions: Cats and dogs may be (co-)infected with gastric *Helicobacter* organisms other than the known gastric NHPHs.

E. Taillieu: None. S. De Bruyckere: None. C. Van Steenkiste: None. K. Chiers: None. F. Haesebrouck: None.

P06.07

EVALUATION OF A NEW LIQUID TYPE RAPID UREASE TEST KIT FOR DIAGNOSIS OF HELICOBACTER PYLORI

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Objective: Rapid and accurate diagnostic tool is important for *Helicobacter pylori* (*H. pylori*) infection in clinical practice. Rapid urease test (RUT) is a relatively time-saving and accurate method and is recommended as a first-line diagnostic test. The aim of this study is to evaluate the reaction time and accuracy of new liquid type RUT.

Materials and Methods: To assess the rapidity and accuracy of a new liquid rapid urease test (Helicotest[®], WON medical, Republic of Korea) compared with another commercial RUT kit (HP kit, Chong Kun Dang, Republic of Korea) and the real-time quantitative PCR-based assay (Seeplex[®] H.pylori-ClaR Detection, Seegene, Republic of Korea), consecutive dyspeptic or check-up patients referred to two tertiary center for endoscopy were prospectively studied. Rapid urease tests were read at 10, 30, 60 and 120 min.

Results: Of the 176 enrolled patients, 38.6% were infected with *H. pylori*. The positive rate of the new rapid urease test was 26.1, 35.8, 39.2 and 41.5% at 10, 30, 60 and 120 min, respectively. When compared with the HP kit, the difference according to the time to confirm positivity was 28.6 minutes (95% CI, 16.60 to 39.73, $p < 0.0001$). New rapid urease test had accuracy and sensitivity of 96.0 and 98.53%, whereas HP kit had 92.05 and 74.41%, respectively (p -value 0.1266, 0.0008).

Conclusions: Compared to the commonly used RUT test method, new liquid type RUT test presented faster results with higher sensitivity. This could result in the advancement of *H. pylori* treatment outcomes in an outpatient-based clinical setting.

H. Lee: None. S. Kim: None. J. Chung: None.

P06.08

EFFICACY AND TOLERABILITY OF BISMUTH-BASED ERADICATION THERAPY WITHOUT PROTON PUMP INHIBITORS FOR *HELICOBACTER PYLORI* INFECTION IN PATIENTS WITH CORPUS ATROPHIC GASTRITIS: A RETROSPECTIVE SINGLE-CENTER EXPERIENCE

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Objective: Efficacy of eradication-therapy-regimens (ETR) in *Helicobacter-pylori* (Hp) infection is commonly reported in association with pump-pomp-inhibitors (PPIs). In Corpus-atrophic-gastritis (CAG)-patients, PPIs are not indicated. This study aimed to assess the eradication rate (ER) and safety of modified-ETR with single-pill bismuth-based therapy without PPIs (SPBTnoPPIs) for 13-days, 3-pills t.i.d compared to (i) other ETR, amoxicillin-based therapy, without PPIs (ABTnoPPIs) in CAG-patients, and (ii) ETR with SPBT with PPIs (SPBTandPPIs) in no-CAG patients, in the first-line-treatment of Hp-infection.

Materials and Methods: A total of 113 consecutive-patients histologically Hp-positive were included between 2001-2020: CAG was diagnosed in 76-patients [77.6%-females, median-age 58.5 years (26-88)], and 37 patients were not affected by CAG [51.4%-females, median-age 58 (22-81)]. The efficacy of Hp-treatment was assessed by histopathology (according to updated-Sydney-system) in all patients at 6±3months after treatment. ER was expressed according to intention-to-treat (ITT) and per-protocol (PP) approach.

Results: 46 and 30 CAG-patients underwent SPBTnoPPIs and ABTnoPPIs, respectively. 3 (6.5%) patients on SPBTnoPPIs and 2 (6.7%) patients on ABTnoPPIs did not complete therapy (by patient's decision) ($p=1.00$). The 37 no-CAG patients were treated with SPBTandPPIs, and no patients interrupted the therapy. CAG-patients treated with SPBTnoPPIs compared to ABTnoPPIs showed a significantly higher ER at ITT-analysis ($p=0.02$) and at PP-analysis ($p=0.01$). CAG-patients treated with SPBTnoPPIs compared to no-CAG patients received SPBT and PPIs showed a higher ER at ITT-analysis ($p=0.07$), and a significantly higher ER at PP-analysis ($p=0.02$). 4 CAG-patients (8.7%) patients on SPBTnoPPIs reported mild adverse events, compared to 2 (6.7%) CAG-patients on ABTnoPPIs ($p=1.00$). No-CAG patients did not report any adverse events ($p=0.125$).

Conclusions: A modified SPBT-regimen without PPIs (3 days more but less pills/day) showed a high ER of about 95% in CAG-patients with good compliance and tolerability, and it may be considered as first-line therapy.

E. Dilaghi: None. L. Mosciatti: None. A. Monizzi: None. C. Millado Luciano: None. M. Toniatti: None. L. Dottori: None. I. Ligato: None. G. Esposito: None. G. Pivetta: None. B. Annibale: None. E. Lahner: None.

P06.09

ENHANCING THE THERAPEUTIC POTENTIAL OF RESVERATROL AGAINST HELICOBACTER PYLORI INFECTIONS THROUGH CHITOSAN NANOPARTICLES

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Helicobacter pylori (Hp) is the etiological agent of several gastric disorders. The increasing resistance rate to conventional antimicrobials has been propelled by several aspects, namely its ability to form biofilms (1). New strategies based on bioactives as *trans*-resveratrol (RESV), have been explored, since it can inhibit Hp growth (2). Despite its promising antimicrobial activity, RESV low solubility in

water and photosensitivity have hindered its use (3). Here we developed nanoparticles of chitosan (NP) loaded with *trans*-resveratrol (RESV-NP) by the ionic gelation method. RESV-NP characterization was done by dynamic light scattering (DLS), nanoparticle tracking analysis (NTA) and Cryogenic transmission electron microscopy (Cryo-TEM). Cryo-TEM showed RESV-NP spherically shaped. Size (110.7 ± 1.2 nm), polydispersity index (0.29) and zeta potential (17.3 ± 3.2 mV) were determined by DLS and concentration of each batch (3.12×10^{11} NP/mL) by NTA. RESV encapsulation efficiency was 72% and full release was achieved after 5 minutes (High-performance liquid chromatography). $3.9 \mu\text{g/mL}$ of RESV-NP were bactericidal against *H. pylori* J99 planktonic cells, in biofilms and in an *in vitro* infection model (4). RESV-NP were not cytotoxic against gastric cell lines (AGS and MKN-74) at bactericidal concentration (5). Overall, RESV-NP is a promising bioengineered strategy to vector RESV by oral route for *H. pylori* management.

Acknowledgments: FAPESP grants 2019/09597-6 and 2021/11681-5; CAPES Financial Code 001.

L. Spósito: None. D. Fonseca: None. R.M. Sábio: None. T.M. Bauab: None. A.B. Meneguim: None. P. Parreira: None. C. Martins: None. M. Chorilli: None.

P06.10

PREVALENCE OF *HELICOBACTER PYLORI* INFECTION IN PRESCHOOL CHILDREN BENEFITING FROM EDUCATION AND NUTRITION CENTERS AND CHILDREN'S CENTERS FOR NUTRITION AND COMPREHENSIVE CARE (CEN-CINAI) NUTRITIONAL PROGRAMS

IN COSTA RICA (2014-2016)

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Objective: *Helicobacter pylori* infection is associated with low income and lower sanitation conditions. Iron deficiency anemia has been associated with *H. pylori*, putatively due to lower serum iron availability, being a rare condition to a common infection. The aim of the study was to report the prevalence rates of *H. pylori* and correlate it to iron deficiency among Costa Rican preschool children from CEN-CINAI nutritional programs.

Patients and Methods: 2,503 children from 0-7 years old from 13 CEN-CINAI of the Central South Region of Costa Rica were surveyed in 2014-2016. Data on socioeconomic characteristics were obtained, and blood samples were collected from 2,203 of the children for measures of iron, ferritin, TIBC, vitamin D and hematologic parameters. For this study, a subsample of 435 serums was analyzed for antibodies to *H. pylori*.

Results: We estimated a prevalence of *H. pylori* infection at 15.40% (95% CI), a condition more frequent in children without proper sewage water disposal or septic tank usage with a prevalence of 22.22%. Anemia prevalence was lower in the subsample (4.5%) than the one reported in the original study (7.5%) and had no correlation with *H. pylori* infection.

Conclusions: There was no correlation between iron deficiency anemia and *H. pylori* infection in this population. Nevertheless, the seroprevalence of *H. pylori* observed is expected for Latin American countries in children <10 years old. Sewage disposal could have a major role in the infection.

V. Ramírez-Mayorga: None. J. Romero-Carpio: None. M. Granados-Zamora: None. M. Solano-Barquero: None. S. Molina-Castro: None.

P06.11

HELICOBACTER PYLORI PROTEIN SABB PROMOTES COLONIZATION AND ADHERENCE TO METAPLASTIC STOMACH TISSUE

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Helicobacter pylori infects half the world's population. *H. pylori*-driven disease manifests as chronic inflammation, which can sometimes give rise to metaplasia and neoplasia. Despite *H. pylori*'s major contribution to the global cancer burden, too little is known about the long-term interactions between pathogen and host. We used a model of gastric intestinal metaplasia to examine the impact of *in vivo* evolution of *H. pylori* to better understand its role in disease progression. Mouse infection studies of the J99 culture collection (isolates from a single human sampled over six-years) revealed genetically distinct subgroups with different abilities to colonize. We found that a single mouse infected with a poorly colonizing isolate was robustly colonized after 1 week. Sequencing of the mouse output revealed that the only genetic difference between the poor mouse colonizing "stock" isolate and the "adapted" isolate was a gene conversion in the gene encoding the putative adhesin SabB. This conversion swapped a portion of the related *sabA* gene, encoding the sialyl-Lewis^x-binding adhesin SabA. Additional experimental evolution led to this conversion reaching fixation and resulted in new polymorphisms at this locus. Deletion of *sabB* from multiple strains reduced their ability to colonize healthy mice, both alone and in competition with wildtype strains, and reduced their *ex vivo* adherence to mouse stomach tissue. These phenotypes were even stronger when metaplasia was induced. Ongoing work is investigating the functional consequences of the polymorphisms identified. Collectively, these results suggest that SabB promotes colonization and tissue adherence, especially in the metaplastic environment.

J.P. Frick: None. V.P. O'Brien: None. L.K. Jackson: None. A.E. Rodriguez Martinez: None. D.S. Jones: None. C.D. Johnston: None. N.R. Salama: None.

P06.12

EARLY-LIFE HELICOBACTER PYLORI INFECTION WORSENS METABOLIC STATE IN MICE ON HIGH-FAT DIET

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Objective: Microbial colonization of the human host begins at birth, and perturbations to the early life microbiome increase the risk of overweight and obesity later in life. The deprivation of ancestral microbial taxa is thought to have implications for the proper development of the host immune system, potentially triggering the development of autoinflammatory diseases such as obesity. We hypothesize that *H. pylori*, an ancestral member of the human microbiome, can protect against diet-induced obesity if established early in life.

Materials and Methods: We infected C57BL/6Jrj neonatal mice with *H. pylori* and subjected them to high-fat diet (HFD) after weaning. One short-term experiment was conducted to track circulating metabolic hormone and cytokine levels. A long-term experiment was performed to monitor fecal microbiome composition analysed with 16S rRNA gene sequencing.

Results: We found a bloom of Akkermansiaceae in the distal gut microbiome and higher leptin levels in newly weaned *H. pylori*-infected mice compared to controls. When switched to HFD, *H. pylori* exacerbated the negative effects of the diet in a sex-specific manner as observed in visceral fat accumulation, further perturbation of the gut microbiome composition, and higher levels of inflammatory cytokines.

Conclusions: We conclude that early-life infection with *H. pylori* accelerates metabolic decline in the face of a diet-induced obesity challenge in our model, through modulation of the inflammatory response and gut microbiome composition.

Sigri Kløve: None. Katrine B. Graversen: None. Jacob A. Rasmussen: None. Jonas Schluter: None. Martin Blaser: None. Sandra B. Andersen: None.

POSTER SESSION 07: CANCER 1

P07.01

THE INFLUENCE OF PROCEDURAL VOLUME ON THE OUTCOME OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC NEOPLASM: A NATIONWIDE POPULATION-BASED STUDY USING ADMINISTRATIVE DATA

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Objective: Endoscopic submucosal dissection (ESD) is a well-established treatment modality for gastric neoplasms. We aimed to investigate the effect of procedural volume on the outcome of ESD for gastric cancer or adenoma.

Material and Methods: Patients who underwent ESD for gastric cancer or adenoma from November 2011 to December 2017 were identified using the Korean National Health Insurance Service database. Operational definitions were created using the diagnosis and procedure codes and validated using individual hospital medical records. Outcomes included bleeding, perforation, pneumonia, 30-day mortality, composite outcome comprising all these adverse outcomes, and additional resection. Hospital volume was categorized into four groups: very high-, high-, low-, very low-volume hospitals (VHVH, HVH, LVH, VLVH). The outcomes of ESD were compared in relation to hospital volume.

Results: There were 95,411 procedures in 89,780 patients during the study period. There were 5,607 composite events, which included 5,098 bleeding, 601 perforation, and 712 pneumonia cases, respectively. Additional resection within 180 days occurred in 7,900 cases. There were significant differences in ESD-related adverse outcomes among the four hospital volume categories. Multiple logistic regression revealed that VHVH, HVH, and LVH were associated with lower risk of composite outcome, when compared to VLVH (OR, 0.627, 95% CI, 0.445-0.885, $p=0.008$; OR, 0.542, 95% CI, 0.406-0.722, $p<0.001$; OR, 0.697, 95% CI, 0.548-0.886, $p=0.003$). Similar tendencies were also shown in terms of bleeding, perforation, and pneumonia, which was not evident in additional resection.

Conclusions: Hospital volume was closely associated with adverse clinical outcomes in patients with ESD for gastric cancer or adenoma.

J. Park: None. M. Kim: None. B. Kim: None. J. Kim: None.

P07.02

ENDOSCOPIC HISTOACRYL INJECTION FOR ESOPHAGOJEJUNOSTOMY LEAKAGE AFTER TOTAL GASTRECTOMY IN PATIENTS WITH GASTRIC CANCER

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Objective: Esophagojejunostomy leakage after total gastrectomy for gastric cancer is one of the most serious and life-threatening adverse events. The purpose of this study was to evaluate complications after gastrectomy in patients with gastric cancer during the period when Histoacryl® (B. Braun, Melsungen, Germany) injection was performed. Therapeutic outcome of endoscopic Histoacryl® injection for esophagojejunostomy leakage was also determined.

Materials and Methods: This was a single-center retrospective study. Between 2016 and 2021, clinicopathologic characteristics and surgical outcomes of 205 patients who underwent total gastrectomy were investigated. Baseline characteristics and clinical outcomes of 10 patients with esophagojejunostomy leakage were also investigated.

Results: Postoperative complication and mortality rates of total gastrectomy in 205 patients were 25.4% and 0.9%, respectively. Serious complications more than Clavien-Dindo IIIb accounted for 6.3%. Ten esophagojejunostomy leakages occurred in 205 (4.9%) patients. Among ten esophagojejunostomy leakage patients, eight patients were performed endoscopic Histoacryl® injection and seven patients were successfully managed for leakage with endoscopic Histoacryl® injection (87.5%). The mean post-injection hospital stay of seven successfully managed patients was 13.8 days. They were able to drink water at 1-6 days after injection. Among eight patients with endoscopic Histoacryl® injection, six patients were injected once and two patients were injected three times. The injection took 3-10 minutes at a time.

Conclusions: Overall morbidity and mortality of 2,051 gastrectomies in patients with gastric cancer were comparable to those of previously published studies. Endoscopic Histoacryl® injection for esophagojejunostomy leakage after total gastrectomy can be considered a useful treatment for some selected cases.

S. Choi: None. M. Goh: None.

P07.03

INVESTIGATION OF GASTRIC CANCER IN THE CASES OF AUTOIMMUNE GASTRITIS.

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Objective: Autoimmune gastritis (AIG) is a special type of gastritis in which anti-parietal cell antibody against proton-pumps (H⁺/K⁺ATPase) are produced. AIG is associated with a high incidence of gastric cancer (GC) and GC associated with AIG is focused because of decrease of gastric cancer associated with *H. pylori*. The aim of the study was to investigate the characteristics of GC in AIG cases.

Patients and Methods: AIG cases in our hospital were compared with and without GC. Patients background (age, sex, autoimmune diseases), laboratory data (gastrin, antibodies), histopathology of gastric mucosa and clinicopathological features of GC were retrospectively analyzed. Diagnosis of AIG was defined as follows: (1) positive for PCA and/or intrinsic factor antibody (IFA), (2) positive for features of endoscopic AIG such as corpus-dominant gastritis and sticky mucus and (3) hypergastrinemia.

Results: Fourteen cases of AIG with GC and 21 cases of AIG without GC were compared. There were no significant differences in patient's characteristics and laboratory data between groups with and without GC. Although one case was advanced GC, almost of all the GC were elevated type and differentiated mucosal cancer. Gastric type and mixed type in mucin-phenotype were dominant.

Conclusions: Characteristics of GC in AIG cases were elevated morphology and gastric mucin phenotype, and those were different with GC associated with *H. pylori*.

S. Ono: None. M. Higashino: None. M. Inoue: None. M. Ono: None. K. Yamamoto: None. N. Sakamoto: None.

P07.04

TREATMENT OUTCOME AND SAFETY OF GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION IN OUR HOSPITAL

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Objective: Endoscopic submucosal dissection (ESD) for early gastric cancer (EGC) has recently expanded. We aimed to examine the treatment outcome and safety of gastric ESD cases at our hospital in comparison with a previous report (Japan Clinical Oncology Group study, JCOG1009/1010).

Material and Methods: The treatment outcomes and safety of patients with ESD for EGC from July 2018 to July 2022 were examined based on patient background, lesion background, procedure background, curability based on the eCura system, and complications.

Results: This study evaluated 130 (previous report: 337) patients with a median age of 76 years (previous report: 62 years). The lesions had a median size of 14 mm (previous report: 12 mm). The proportion of *en bloc* resection was 100% (previous report: 100%). Curative resection (eCura A or B) was achieved in 78% (previous report: 72%). Submucosal invasion was observed in 20% (previous report: 12%). Total complications occurred in 23.8%, including perforation in 13.1% (previous report: 3.8%) and delayed bleeding in 9% (previous report: 3.5%).

Conclusions: Our study revealed that our hospital performed ESD for EGC for older patients and obtained a slightly higher rate of perforation and delayed bleeding compared to a previous study. However, a better result was obtained in the curative resection rate, which is significantly meaningful for the diagnosis and treatment of the elderly who are intolerant to surgery.

Y. Shoji: None. N. Moriyama: None. S. Noda: None. Y. Fukuda: None. T. Sakamoto: None. K. Nakamichi: None.

P07.05

VOLATILOMIC SIGNATURES OF GASTRIC JUICE: INVESTIGATION OF POTENTIAL VOLATILE MARKERS OF GASTRIC CANCER AND *H. PYLORI* INFECTION

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Objective: Gastric cancer is the fifth most commonly diagnosed malignancy in the world, with more than 1 million new cases per year and a low survival rate. Gastric juice can be considered a promising reservoir of potential biomarkers for this cancer. The objective of this study was to investigate volatilomic signatures of gastric juice to identify alterations caused by gastric cancer and *H. pylori* infection. The study involved 78 gastric cancer patients and 176 controls from four different populations (Brazil, Colombia, Latvia, Ukraine).

Materials and Methods: Volatilomic signatures were investigated using headspace solid-phase microextraction (HS-SPME) followed by gas chromatography with mass spectrometric detection (GC-MS).

Results: Eighteen volatile organic compounds (VOCs) were statistically different between the groups of interest (Mann-Whitney U test). Ten of them, e.g., 2,3-butanedione, benzaldehyde, 2-pentylfuran, 2-ethylhexanal and phenol, were present at significantly higher levels in samples obtained from gastric cancer patients. Moreover, an ANOVA test was used to identify chemical compounds associated with *Helicobacter pylori* infection. Twelve compounds showed a good correlation with this infection (e.g., 2-pentylfuran, hexanal, mesitylene, o-xylene and n-pentadecane).

Conclusions: The VOCs at elevated levels in gastric cancer patients can be considered as potential biomarkers of this disease and assist in developing non-invasive tests for its diagnosis. The *H. pylori*-related compounds form a set of potential confounders for the recognition of gastric cancer markers. *H. pylori* infection is the risk factor for gastric cancer and the *H. pylori*-related compounds can be incorrectly associated to this disease. Nevertheless, these compounds are candidates for general *H. pylori* volatile markers.

D. Slefarska-Wolak: None. L. Mezmale: None. M. Bhandari: None. V. Veliks: None. V. Patsko: None. A. Lukashenko: None. E. Dias-Neto: None. D. Nunes: None. T. Bartelli: None. A. Pelosof: None. C. Zitron Sztokfisz: None. R. Murillo: None. C. Ager: None. A. Królicka: None. C. Mayhew: None. H. Haick: None. M. Leja: None. P. Mochalski: None.

P07.06

IS IT NECESSARY TO OBTAIN BIOPSY FROM THE INCISURA ANGULARIS FOR STAGING OF ATROPHIC GASTRITIS ACCORDING TO THE OLGA PROTOCOL?

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Objective: The OLGA protocol is widely used in clinical practice to evaluate progression of atrophic gastritis and risk of gastric cancer. The aim of this study was to establish the significance of histological changes in the gastric mucosa from the incisura angularis to assess the grade and the stage of atrophic gastritis.

Materials and Methods: 1,146 patients with clinical manifestations of chronic gastritis were examined. Biopsy material was obtained during endoscopic examination in accordance with the OLGA protocol. Histological assessment of the grade of inflammation and the stage of atrophy was carried out with the standard OLGA protocol. Then, the same samples were evaluated without taking into account histological changes in the incisura angularis.

Results: *H. pylori* histologically was revealed in 122 patients (10.6%). Grade II of inflammation was detected in 839 patients (73.2%). This score did not change if the biopsy from the incisura angularis was not tested. Severe stages of gastric mucosa atrophy (III and IV) were detected in 465 patients (40.58%). If changes in the incisura angularis were not taken into account, then severe stages of atrophy (III and IV) were detected in 460 patients (40.1%). In total, changes in the assessment of the stage of atrophy occurred in 53 patients (4.62%), and more often, this was observed in patients with stages I and II.

Conclusions: Evaluation of the histological changes in the gastric mucosa from the incisura angularis does not significantly affect the assessment of the grade and stage of chronic gastritis according to the OLGA system.

S.G. Khomeriki: B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; Moscow Center for Innovative Technologies in Healthcare. Grant #0903-1/22. **D.S. Bordin:** B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; Moscow Center for Innovative Technologies in Healthcare. Grant #0903-1/22. **N.M. Khomeriki:** None. **E.V. Parfenchikova:** B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; Moscow Center for Innovative Technologies in Healthcare. Grant #0903-1/22. **K.A. Nikolskaya:** B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; Moscow Center for Innovative Technologies in Healthcare. Grant #0903-1/22. **V.A. Ivanova:** B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; Moscow Center for Innovative Technologies in Healthcare. Grant #0903-1/22.

P07.07

AN ARTIFICIALLY INTELLIGENT DIAGNOSTIC ASSISTANT FOR GASTRIC INFLAMMATION (AIDA)

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Objective: Gastric cancer (GC) has a poor prognosis with a 5-year survival rate of only 10% to 25% in Western countries. We aim to improve the outcomes of GC patients by creating a multidisciplinary artificial intelligence (AI) assistant, called AIDA, that assists clinicians in diagnosing precancerous inflammation, providing personalised treatment and follow-up strategies, and making recommendations for monitoring patients' health status, ultimately helping to prevent GC.

Materials and Methods: In our two-phase clinical study, we are collecting and harmonising data from patients, from the European *H. pylori* Registry (Hp-EuReg) (>30 countries, >60,000 patient records), and from endoscopic/pathological images (>40,000 records) to create a personalised risk score for each patient's likelihood of developing gastric cancer. In the second phase, we will improve the AI assistant by integrating multi-omics data using state-of-the-art graph neural networks and testing its risk prediction and recommendations.

Results: AIDA is currently under development, employing a reinforcement learning strategy to analyse patient data, enhancing the success of *H. pylori* treatment. Additionally, the explainable AI workflows using semi-supervised generative adversarial neural networks are being designed to improve the detection of precancerous lesions through endoscopy and histology imaging data. Structured as a collaborative data platform, AIDA facilitates data sharing. The development of the platform is in its initial stage, with preliminary outcomes anticipated early next year.

Conclusions: In summary, our multidisciplinary AIDA assistant will enable the creation of personalised risk scores for each patient's likelihood of developing GC and thus, adapt the modalities of surveillance and clinical management for each individual patient.

J.P. Gisbert: None. O.P. Nyssen: None. A. Miralles-Marco: None. E. Jiménez: None. M. Leja: None. F. Carneiro: None. C. Figueiredo: None. L. Moreira: None. T. Matysiak-Budnik: None. J. Martin: None. J. Kupčinskas: None. M. Dinis-Ribeiro: None. M. Spaander: None. S. Sedola: None. Z. Maravic: None. K. Veselkov: None. T.C. Fleitas: None.

P07.08

SEROLOGIC TEST IN METACHRONOUS TUMORS AFTER ENDOSCOPIC RESECTION FOR GASTRIC NEOPLASM

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Objective: Endoscopic resection (ER) is a widely performed procedure for the treatment of gastric neoplasms and metachronous lesions are a major concern after ER. The aim of this study was to investigate the role of serum pepsinogen or gastrin levels in the development of metachronous tumors after endoscopic resection for gastric neoplasms.

Patients and Methods: We retrospectively reviewed 180 patients with gastric neoplasms who underwent ER from July 2017 to May 2019. Baseline characteristics and serum pepsinogen and gastrin levels were compared between patients with and without metachronous gastric tumors after ER.

Results: Of the 180 patients, 100 (55.6%) underwent ER for low-grade adenoma, 29 (16.1%) for high-grade adenoma, and 51 (28.3%) for adenocarcinoma. During the mean follow-up period of 28.3 months, 17 (9.4%) patients developed metachronous neoplasms. There were no significant differences in serum pepsinogen I, II, and I/II ratio, size, pathology and number of lesions, and *Helicobacter pylori* infection status at the time of the index ER procedure between the two groups with and without metachronous lesions. The serum gastrin level was 68.7 ± 27.6 in the group with metachronous lesions, which was significantly lower than the level of 104.5 ± 99.5 in the group without metachronous lesions ($p=0.001$). The proportion of patients with high gastrin levels also showed a lower trend in the group with metachronous lesions (5.9% vs. 27.0%, $p=0.075$).

Conclusions: In patients with metachronous tumors after ER for gastric neoplasms, serum gastrin levels were significantly lower than in patients without metachronous lesions.

S. Jung: None. S. Kim: None. A. Lee: None. S. Kim: None. D. Kim: None.

P07.09

PREDICTIVE FACTORS ASSOCIATED WITH OVERALL SURVIVAL RATE IN FEMALE GASTRIC CANCER PATIENTS: A LARGE POPULATION-BASED STUDY IN THE ASSOCIATION OF SOUTHEAST ASIAN NATIONS (FGC-ASEAN TRIAL)

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Objective: ASEAN remain to have high gastric cancer (GC) especially in female. This study aimed to compare clinical manifestations, histopathology and prognostic factors associated with overall survival rate of female gastric cancer patients in ASEAN.

Materials and Methods: This retrospective cohort study was conducted between 2007-2022 at tertiary care center in Thailand. All-important clinical information was extensively reviewed and all qualified studies in ASEAN published in PubMed and Scopus between 2000-2022 were analyzed. Young female GC defined as under 50 years.

Results: Total of 4,090 gastric cancer patients were enrolled. Age between 15-93 years, 25.2% female. Top three countries with the highest prevalence of female GC of ASEAN were Indonesia (53.8%), Malaysia (51.7%), and Thailand (51%). 195 Thai gastric cancer patients were also included with mean age 59.2 years (51% female). Common presenting symptoms were weight loss (67.7%) and dyspepsia (59.3%). In Thailand, young female GC had significantly more common diffused type than male and elderly female (79.3% vs. 39.9%, p -value=0.01 and 79.3% vs. 54.4%, p -value=0.02, respectively). Interestingly, this study demonstrated that female had significantly higher 1-year survival rate than male GC (36.7% vs. 22.3%, p -value=0.02, OR=2.01; 95% CI: 1.07-3.82). Moreover, elderly female demonstrated significantly better 1-year survival than young female GC (33.7% vs. 20.7%, p -value=0.03, OR=2.95; 95% CI: 1.07-8.15). Overall, 1-year survival rate of female GC patients was 29-32.5% in ASEAN.

Conclusions: Gastric cancer in female has become more common in ASEAN and presented at advanced stage with poor prognosis. Elderly female has the most favorable prognosis compared to male and young female GC. Early diagnosis and high suspicion in high-risk groups is crucial and will improve treatment outcomes.

R. Vilaichone: None. P. Bongkotvirawan: None. N. Aumpan: None. B. Pornthisarn: None. S. Chonprasertsuk: None. S. Siramolpiwat: None. P. Bhanthumkomol: None. P. Nunanu: None. N. Issariyakulkarn: None. V. Mahachai: None.

P07.10

GASTRIC MICROBIOME INHIBITS THE DEVELOPMENT OF PREMALIGNANT LESIONS AND GASTRIC CANCER**J. KIM, K. NAM**

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The gut microbiota contributes to biological functions, including metabolism, immune system, and pathogen resistance. Many studies about the role of microbiota were investigated in intestine, but there were few studies in stomach because of the acidic conditions. Despite the harsh condition, *Helicobacter pylori* was infected in the stomach and served as a predominant risk factor for gastric cancer (GC). Accordingly, composition of gastric bacterial community was identified through 16S rRNA sequencing. Recently, the gastric microbiota composition of *H. pylori* infected people and GC patients was different from normal people. Some studies were conducted on the role of commensal gastric microbiota in gastric tumorigenesis using Germ-free (GF) mice, but the results were controversial. Here, we investigated the effect of microbiota in gastric disease induced by MNU treatment or *Helicobacter felis* infection through comparison of specific-pathogen-free (SPF) and GF mice. *H. felis* infection was more prevalent in GF gastric tissue. Immune cell infiltration increased in *H. felis* infected GF mice antrum than SPF mice. The GO BP terms for genes response to stimulus and immune response are upregulated in GF mice at early *H. felis* infection. Gastric tumorigenesis also increased in MNU-treated GF mice. Only GF mice occurred gastric tumor at 20 weeks after MNU treat, and at 44 weeks. High tumor incidence was observed in GF mice. MNU-treated GF mice gastric tissue were upregulated tumorigenic pathways, such as PI3K-Akt pathway, cholesterol synthesis pathway and so on. Our findings reveal that gastric microbiota had protective effect in gastric tumor development.

J. Kim: None. K. Nam: None.

P07.11

HELICOBACTER PYLORI AND COLON CANCER - FROM EPIDEMIOLOGIC ASSOCIATION TO MECHANISTIC INSIGHTS**A. RALSER¹, V. ENGELSBERGER², R. MEJÍAS-LUQUE², M. GERHARD²**¹Gladstone Institutes, San Francisco, CA, United States; ²Technical University Munich, Munich, Germany

Helicobacter pylori infects more than half of the world's population, and although the bacterium exclusively colonizes the stomach, chronic infection is also associated with extragastric diseases. According to epidemiological studies, *H. pylori* infected individuals harbor a nearly twofold increased risk to develop colorectal cancer (CRC), but so far, the underlying mechanisms that confer this increased risk were unclear. Apc-mutant mouse models were infected with *H. pylori* and an extensive analysis of *H. pylori*-induced changes in tumor development and intestinal immune responses was conducted. In addition, we validated our findings in a cohort of infected patients. Apc-mutant mice infected with *H. pylori* developed twice as any tumors compared with uninfected controls and showed a pro-inflammatory and pro-carcinogenic immune signature in the murine colon. Housing of Apc-mutant mice under germ-free conditions reduced tumor numbers, and the observed phenotype was normalized by early antibiotic eradication of *H. pylori*. In addition, similar immune and epithelial alterations were found in human biopsies from *H. pylori*-infected patients, as well as an increase in pro-carcinogenic bacterial species. Importantly, *H. pylori*-eradicated patients showed an attenuated phenotype. Together, we provide evidence that *H. pylori* infection promotes colorectal carcinogenesis and that these tumor-promoting effects are ameliorated by antibiotic treatment. Therefore, implementation of *H. pylori* status into an adaptive CRC risk score should be considered and eradication of *H. pylori* might be an effective measure to reduce this risk. All authors exclude any conflict of personal and funding interests.

A. Ralser: None. V. Engelsberger: None. R. Mejías-Luque: None. M. Gerhard: None.

P07.12

PREDICTIVE VALUE OF COMBINED RISK SCORE FOR GASTRIC CANCER

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The population with an intermediate risk of developing gastric cancer (GC) is not indicated for gastroscopic screening. We proposed a DSC risk score that includes gastrin G17 (G17), IgG anti-*H. Pylori*, sex and age of patients at pepsinogen test used for the diagnosis of atrophic gastritis. The results revealed an improvement in the diagnosis of GC risk with a sensitivity of 70% and AUC of 0.72 compared to 15% and 0.47 obtained with the conventional pepsinogen test. We then selected some serum biomarkers to be included in the DSC score with the aim of increasing the specificity and sensitivity of the test. We recruited two cohorts, the first consisting of participants who were referred to gastroenterologists and the second consisting of a retrospective series of patients with a confirmed diagnosis of GC. Participants were classified using the DSC test as having negative, neutral or positive DSC results. Then we added analysis of 8 serum biomarkers (CXCL20, CXCL9, HE4, HER2, HER3, PDL-1, sCDH1 and EGF). Participants recruited in the first series were classified by gastroscopy and histological examinations for the diagnosis of GC, dysplasia, severe atrophy (OLGA stages III-IV) or zero/moderate grade atrophy (OLGA stages 0-II). Initial data collected showed a significant relationship between selected biomarkers and DSC score. Studies are ongoing to define the weight and cut-off of each marker and better understand their functions in the context of gastric injury progression. The markers will be included in the DSC score test to evaluate their effectiveness.

V. De Re: None. R. Cannizzaro: None. S. Realdon: None. M. Gian Maria: None. M. Casarotto: None. O. Repetto: None. R. Vettori: None. A. Steffan: None.

POSTER SESSION 08: CANCER 2

P08.01

LUNG MICROBIOTA COMPOSITION CHANGE IN NON-SMALL CELL LUNG CANCER

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Objective: Lung cancer is still the leading cause of cancer-related deaths worldwide (Zhao, 2021). Recent studies demonstrates that microbiota is increasingly recognized as an important player in various types of cancer onset, progression or even response to chemotherapy treatment (Pizzo, 2022). However, the role of microbiota in development and progression of lung cancer has not been fully explored. The aim of the study was to evaluate the composition of microbiota between lung tumor tissue samples and adjacent lung tumor tissue samples in patients with non-small cell lung cancer (NSCLC).

Materials and Methods: Lung tumor tissue and adjacent tumor tissue were collected during video fibrobronchoscopy. Extraction of bacterial DNA was performed using PureLink™ Microbiome DNA Purification Kit. Libraries were prepared using V1-V2 region of 16s rRNA gene was amplified and sequenced on an Illumina MiSeq platform. Bioinformatic and statistical analysis was performed in the R software environment as described previously by Camarinha Silva A et al, 2014.

Results: We enrolled 55 males and 19 females in the lung tumor biopsy group with a mean age of 70.2±8.8 years, 43 males and 20 females in the adjacent lung tumor biopsy group with a mean age of 71.8±8.9 years. The differences between the two tissues were detected at all taxonomical levels.

Conclusions: The microbiome composition of cancerous tissue in patients with non-small cell lung cancer differs from the tumor-adjacent tissue at all taxonomical levels. The differences in these groups demonstrated, that the microbiota of the lungs may change during oncogenesis.

R. Lukosevicius: None. V. Ankudavicius: None. D. Nikitina: None. J. Skieceviciene: None. J. Kupcinkas: None. S. Miliauskas: None. M. Zemaitis: None.

P08.02

NOVEL SERUM BIOMARKERS FOR EARLY DETECTION OF GASTRIC CANCER AND GASTRIC PRE-NEOPLASTIC LESIONS

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Objective: Gastric cancer is the 4th common malignant tumor worldwide. Cancer cells have high proliferation rates with high demands of nutrients and oxygen, thereby utilizing alternative metabolic pathways compared to normal cells. A pilot experiment was conducted with volunteers comprising all steps of the Correa cascade: normal mucosa, chronic gastritis, atrophic gastritis, intestinal metaplasia, and gastric cancer (GC) to detect metabolic changes between these. The goal is to identify prognostic blood biomarkers to identify and monitor patients at risk.

Material and Methods: From 115 patients undergoing endoscopy, serum and biopsy samples were collected. From these, metabolites were extracted and identified by UPLC-MS/MS. After data normalization, linear models (ANOVA + EMM) and ROC (area under the curve) analyses were used to identify a metabolite biomarker signature that discriminates the different pre-cancerous stages and GC from each other.

Results: Around 2,000 small molecules and complex lipids could be identified. Six serum and nine biopsy metabolites were identified that discriminate people with normal gastric mucosa compared to gastric cancer patients. Potential markers for the different preneoplastic stages were found in the pilot data, but the sample size needs to be increased to get valid results.

Conclusions: This approach detects metabolic serum markers to discriminate between GC and normal mucosa, as well as possibly between different preneoplastic stages of the human stomach. These results form the basis for the development of a blood-based biomarker panel to identify and monitor patients at risk to develop GC.

C. Schulz: None. N. Koch: None. R. Vasapolli: None. L. Macke: None. P. Malfertheiner: None.

P08.03

CLASSIFICATION OF GASTRIC ADENOCARCINOMAS ACCORDING TO LAUREN IN REFERENCE CENTERS IN CENTRAL BRAZIL

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Objective: Gastric adenocarcinoma (AdG) accounts for 90% of gastric cancers. One of the ways to categorize this type of neoplasm is by Lauren's classification. This study analyzed the clinicopathological profile of patients diagnosed with AdG according to Lauren.

Materials and Methods: This is a cross-sectional study carried out in oncology centers in the Central Brazil region. Patients diagnosed with AdG among 2020 and 2023 were included. The study variables were: gender, age, Lauren classification, tumor location, and depth. Descriptive analysis of categorical variables was performed using absolute and relative frequencies. The Chi-square test was used to verify statistical differences. The study was approved by the Ethics Committee No. 3,174,666.

Results: Forty-seven patients were included in the study, 29 men (61.7%) and 18 women (38.2%) with a mean age of 60 years. Regarding the clinicopathological profile of the patients, 46.8% had intestinal-type tumor, 45.6% diffuse and 8.5% mixed. Of patients with intestinal tumors, 70.6% were located in the antrum and 45.5% invaded the mucosa. As for the diffuse cases, 41.7% were located in the antrum and body and 45.4% with serosa invasion. There was a statistically significant difference between age and Lauren's classification ($p < 0.05$) between types of intestinal and mixed tumors.

Conclusions: In this study, the antral region was more affected in both histological types of Lauren. Regarding depth, the mucosa was more affected in the intestinal type and the serosa in the diffuse type.

D.V. Minaré: None. A.F.P.L. Ramos: None. A.L.S. Bizinoto: None. S.B. Santiago: None. K.V.D.D. Santos: None. G.A. Fernandes: None. M.P. Curado: None. M.S. Barbosa: None. L.T. Rasmussen: None.

P08.04

ANTIOXIDANT PROTECTION IN STOMACH CANCER

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Objective: Purpose of the study: to study the activity of antioxidant defense enzymes in gastric cancer.

Patients and Methods: 47 patients with gastric cancer and 55 apparently healthy volunteers were examined. In the blood serum, the content of malondialdehyde, the activity of superoxide dismutase and catalase enzymes were determined by spectrophotometric methods. The functional activity of neutrophils was determined by chemiluminescent methods. Statistical data processing was carried out using the Statistica for Windows 8.0 application packages. The statistical significance of differences was determined using the Mann-Whitney test ($p < 0.05$).

Results: In patients with gastric cancer, there was a decrease in the functional activity of neutrophils, while inefficient phagocytosis was accompanied by an increased production of ROS. In the blood serum of gastric cancer patients, a 50-fold increase in the content of malondialdehyde was detected, indicating significant oxidative stress in patients and a decrease in superoxide dismutase activity and an increase in catalase activity in patients with gastric cancer relative to the control group.

Conclusions: In patients with gastric cancer associated with *Helicobacter pylori* infection, pronounced oxidative stress is detected. Multidirectional changes in the superoxide dismutase-catalase system are found, superoxide dismutase activity is reduced, while high catalase activity indicates massive cell necrosis in gastric cancer, under conditions of high catalase activity, cells lining blood vessels are subjected to significant oxidative stress. A decrease in neutrophil function, inefficient phagocytosis is accompanied by a large amount of ROS, which further enhance the manifestations of oxidative stress.

O. Smirnova: None. A. Sinyakov: None.

P08.05

PHYSICAL AND BIOCHEMICAL NUCLEAR SIGNATURES:
A SECRET MESSAGE UNDERLYING GASTRIC CANCER INVASION

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Objective: Genetic and epigenetic alterations of E-cadherin (*CDH1*) occur in 60% of gastric carcinomas and result in increased cell invasion and subsequent metastasis. However, the mechanisms underlying disease aetiology are far from understood, perpetuating its poor prognosis. We aim to address the hypothesis that loss of cell-cell adhesion mediated by E-cadherin mutations causes an imbalance in mechanical loads throughout the actin cytoskeleton, inducing nucleus remodelling and a consequent invasive signature.

Material and Methods: Herein, we have established cell lines and *Drosophila* strains expressing wild-type E-cadherin or a novel variant identified in gastric cancer patients. Nuclear architectural features

and cell migration were evaluated using confocal microscopy and advanced bioimaging techniques. In addition, we have investigated the composition of the nuclei envelope from mutant and wild-type cells through high-resolution Mass Spectrometry (LC-MS).

Results: We verified that cells expressing E-cadherin mutations display increased migratory rates *in vivo*, when compared with those expressing the wild-type protein. Nuclear morphology assessment revealed that area, perimeter, and circularity are higher in nuclei from E-cadherin mutant cells, suggesting a more relaxed and flexible structure. Mutant E-cadherin further elicited delocalization of nucleus towards the epithelial basal surface, which is indicative of a closer interaction with the basement membrane. Ultimately, we identified a distinct molecular profile of the nuclear envelope from E-cadherin mutant cells. Differentially abundant proteins include critical molecules for structural integrity of the nucleus.

Conclusions: This work provides evidence that E-cadherin dysfunction generates unique physical and biochemical nuclear features, modulating the invasive phenotype of gastric cancer cells.

J. Figueiredo: None. J. Pereira: None. R.M. Ferreira: None. L. Carvalho: None. M. Gonçalves: None. S. Melo: None. P. Carneiro: None. P. Guilford: None. E. Morais-de-Sá: None. R. Seruca: None.

P08.06

DAIRY PRODUCT CONSUMPTION AND GASTRIC ADENOCARCINOMA: IS THERE AN ASSOCIATION?

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Objective: Gastric adenocarcinoma (AdG) has a multifactorial origin, and the consumption of dairy products may be associated with this neoplasm. The aim of this study was to evaluate the association of dairy consumption and the chance of AdG in the Central Brazil region.

Material and Methods: This is a case-control study, consisting of 117 cases and 200 controls. Patients between 18 and 75 years of age, of both genders, were recruited between 2019 and 2022. Dairy consumption was assessed using a food frequency questionnaire and categorized into high and low fat. Descriptive analyzes were performed using Pearson's Chi-square test and odds ratios were calculated using simple and multiple logistic regression. The study was approved by Ethics Committee No. 3,174,666.

Results: The mean age of patients with AdG was 56.5 ± 10 years. Most cases occurred in women (55.6%), aged over 60 years (44.4%). Statistical differences were observed between gender, age, education level, BMI, smoking, alcohol consumption and consumption of low-fat dairy products ($p < 0.001$). On average, cases consumed more high-fat and low-fat dairy products (175.9 ± 214.4 and 28.7 ± 52.7 g/day, respectively) than controls. Consumption of more than 125.72 g/day of high-fat dairy products (OR = 2.60, 95% CI 1.27-5.33) and consumption of more than 12.87 g/day of low-fat dairy products of fat (OR = 2.22, 95% CI 1.11-4.40) was associated with higher odds of AdG.

Conclusions: Consumption of high-fat and low-fat dairy products increased the chance of AdG by about 2.5 times.

S.B. Santiago: None. G.L. Freire: None. A.F.P.L. Ramos: None. D.V. Minaré: None. A.S. Bizinoto: None. L.T. Rasmussem: None. G.A. Fernandes: None. M.P. Curado: None. M.S. Barbosa: None.

P08.07

INFLUENCE OF *HELICOBACTER PYLORI* INFECTION ON *BACTEROIDES FRAGILIS*-INDUCED INTESTINAL CARCINOGENESIS IN C57BL/6 *APC^{MIN/+}* MICE

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Objective: Epidemiological data suggests that *Helicobacter pylori* (Hp) infection is associated with increased colorectal cancer (CRC) incidence in a subset of CRC patients. It has been documented that infection of clinical strains of enterotoxigenic *Bacteroides fragilis* (ETBF) producing *B. fragilis* toxin (a 20-kDa zinc metalloprotease) are associated with the development of CRC and can induce colon cancer in *Apc^{min/+}* mice. The aim of this study is to examine how Hp coinfection influences ETBF-induced intestinal carcinogenesis in *Apc^{min/+}* mice.

Materials and Methods: B6 *Apc^{min/+}* female mice were treated with clindamycin (0.1g/L) and streptomycin (5g/L) in water for 5 days, followed by inoculation with ETBF; a subset of ETBF-inoculated mice were gavaged with HpSS1 one week later. Mice were euthanized at 10-12 weeks post-ETBF inoculation. Gastric and intestinal tissues were collected for histopathological evaluation/polyp enumeration, and bacterial colonization/gene expression via qPCR.

Results: Major findings: (1) Hp coinfection significantly decreased the number of tumorous polyps in small intestine (SI, $p < 0.02$) but not in colon, compared to mono-ETBF infection; (2) Levels of colonic IL17A/F transcripts, a key cytokine for ETBF-induced colon cancer, trended to be higher in dually infected mice compared to mono-ETBF-infected mice; (3) ETBF coinfection did not affect Hp-induced gastric pathology; (4) Hp coinfection did not impact colonization levels of colonic ETBF.

Conclusions: Our data indicate that Hp coinfection differentially influences ETBF-induced tumorigenesis in SI versus colon. Additional investigations (such as longitudinal infection studies) will be warranted to shed light on the mechanisms underlying effects of Hp coinfection on ETBF-induced intestinal carcinogenesis.

Z. Ge: None. Y. Feng: None. N. Parry: None. Y. Lee: None. M. Guo: None. Z. Shen: None. J.G. Fox: None.

P08.08

EPIDEMIOLOGICAL PROFILE OF GASTRIC CANCER IN THE CENTRAL REGION OF BRAZIL: IS THERE A DIFFERENCE BETWEEN SEX?

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Objective: Gastric cancer (GC) is the sixth most common type of cancer in the world. Lifestyle and exposure to risk factors influence the epidemiological profile of this neoplasm among men and women. This study investigated the disparity between the sexes of individuals with GC in the Midwest region of Brazil.

Material and Methods: This is an ecological study, with the incidence of malignant neoplasm of the stomach in the period from 2013 to 2022. Population data were extracted from the Department of Informatics of the Unified Health System (DATASUS). The information was stratified by geographic region, gender, period of diagnosis and type of neoplasm (C16). Incidence rates were calculated per 100,000 inhabitants.

Results: The population of the Midwest region of Brazil is homogeneous between genders, with 50.4% women and 49.6% men. GC cases were predominantly male (mean of 2.9 males per 100,000 inhabitants) when compared to females (1.6/100,000inhabitants). The highest incidences of GC occurred between the years 2020 and 2021. During this period, there was a 1.3% increase in cases for women, compared to previous years. In 2022, there was a decline in the number of cases, for both sexes, 33.3% for women and 36.9%for men.

Conclusions: In the Midwest region there was a higher incidence of GC in men. It is considered that the epidemiological profile of cases in both sexes is probably associated with different exposure to risk factors and lifestyle.

P.M.N. Ferreira: None. A.L.S. Bizinoto: None. L.T. Rasmussem: None. G.A. Fernandes: None. M.P. Curado: None. M.S. Barbosa: None.

P08.09

HISTOLOGICAL CHARACTERISTICS AND SOCIODEMOGRAPHIC PROFILE OF PATIENTS WITH GASTRIC ADENOCARCINOMAS IN REFERENCE HOSPITALS IN BRAZIL

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Objective: Gastric adenocarcinoma (AdG) is the fourth leading cause of death from cancer in the world. The clinical and pathological aspects of this neoplasm are decisive for the patient's prognosis. AdG of the loosely cohesive type is more aggressive, while the tubular type has a better prognosis. The aim of the study was to describe the histopathological profile of patients with AdG in central Brazil.

Materials and Methods: This is a cross-sectional study carried out in reference hospitals from 2020 to 2023. Data were collected from medical records of patients with AdGs aged between 18 and 75 years, of both sexes. Patients diagnosed with AdGs more than 2 years ago, with secondary gastric cancer, metastasis or deaths were excluded. The study was approved by the Ethics Committee No. 3,174,666.

Results: 87 medical records were analyzed, 54 of which were male patients (62%) and 33 were female patients (38%), with a mean age of 59.3 years. According to the WHO classification, tubular and weakly cohesive AdGs were predominant, corresponding to 45% and 41.3% of the cases, respectively. The most frequent location of AdGs was the antrum (55%) followed by the body/fundus (26.4%). Regarding tumor grade, 12% were grade I, 25% grade II and 14% grade III.

Conclusions: In the population of Central Brazil, there was a higher incidence of AdG in men aged between 60 and 70 years. Tubular and weakly cohesive AdGs were predominant, the most common location and degree of differentiation were non-cardia and grade II, respectively.

K.V.D. Santos: None. D.V. Minaré: None. A.L.S. Bizinoto: None. A.F.P.L. Ramos: None. L.T. Rasmussen: None. M.P. Curado: None. M.S. Barbosa: None.

P08.10

IMPACT OF THE COVID-19 PANDEMIC ON HOSPITAL MORTALITY FROM GASTRIC CANCER IN BRAZIL

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Objective: Gastric cancer (GC) is the sixth most prevalent type of cancer and the fifth in mortality worldwide. The COVID-19 pandemic changed the epidemiological profile of the GC due to the interruption in the control, prevention, screening and treatment services for this neoplasm during this period. The aim of this study was to analyze hospital mortality from GC before and during the COVID-19 pandemic in Brazil.

Material and Methods: Data were collected through the country's Mortality Information System (SIM). The pre-pandemic period of the study was from May 2018 to February 2020, and during the pandemic, data were collected from March 2020 to December 2021. The analysis variables were number of hospital deaths, age group and gender.

Results: In the pre-pandemic period, there were 8,763 hospital deaths due to GC, while during the pandemic there were 8,038 deaths. Most deaths were male (63%) and aged between 60 and 69 years, in both periods. The mortality rate between the periods corresponded to 15.03/100,000 inhabitants before the pandemic and 14.22/100,000 inhabitants during COVID-19. During the pandemic period, there was an 8.35% drop in hospital deaths from gastric cancer in Brazil.

Conclusions: In both periods, most deaths occurred among men and patients aged 60 to 69 years. There was a slight reduction in the number of deaths from GC during the pandemic in Brazil. It is thought that this drop may be related to high mortality from COVID-19 and underreporting of cases from this neoplasm.

M.S. Barbosa: None. G.S.L. Machado: None. A.S. Bizinoto: None. G.A. Fernande: None. M.P. Curado: None. L.T. Rasmussen: None.

P08.11

GASTRIC CANCER MORTALITY IN DIFFERENT GEOGRAPHIC REGIONS OF BRAZIL

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Objective: Gastric cancer (GC) is the sixth most frequent cause of neoplasia in the world and fifth in mortality among all cancers. In Brazil, death rates vary according to geographic region, population profile, prevalence of risk factors and accessibility to diagnostic and treatment services. The aim of the study was to compare standardized GC mortality rates in the five regions of Brazil.

Material and Methods: Data were collected from the open access bank of the Mortality Information System (SIM), from 2010 to 2020. Information was extracted on detailed diagnosis of malignant neoplasm of the stomach (ICD-10 C.16) and the geographic region of residence, for both sexes. The calculation of the mortality rate was performed by the ratio between deaths by GC and the number of inhabitants in each region.

Results: The Southeast and South regions had the highest mortality rates (8.43 and 7.69/100,000 inhabitants), followed by the North (6.32/100,000 inhabitants), Northeast (5.79/100,000 inhabitants) and Midwest region (5.39/100,000 inhabitants). Despite the annual declines, there was homogeneity in the number of deaths in all regions, except in the North region, which had a progressive increase until 2018. The lowest mortality rates occurred from 2019 onwards in the five regions.

Conclusions: Mortality rates varied according to different regions of the country. The reductions observed over time may be related to the greater efficiency of public health policies in more developed regions.

M.S. Barbosa: None. A.S. Bizinoto: None. J.N. Germano: None. L.T. Rasmussen: None. G.A. Fernande: None. M.P. Curado: None.

POSTER SESSION 09: CANCER 3

P09.01

EARLY RETIREMENT PENSIONERS DIAGNOSED WITH STOMACH OR ESOPHAGUS CANCER IN GERMANY – CHARACTERIZATION AND UTILIZATION OF MEDICAL REHABILITATION

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Objective: In order to avoid early retirement (ER) the German statutory pension insurance fund covers the cost of rehabilitation for employees whose working capacity is endangered due to health problems. We aimed to describe the use of medical rehabilitation among persons received a disability pension due to stomach or esophagus cancer.

Materials and Methods: Analysis based on 20% random samples of administrative pension records from the Research Data Centre of the German Federal Pension Insurance (DRV FDZ 2022). We estimated risk of non-utilization of medical rehabilitation using multiple logistic regression models.

Results: The data set contains 5,358 persons who were granted an EM pension due to stomach or esophagus cancer for the first time between 2001 and 2020, of whom 3,111 (58.1%) did not receive medical rehabilitation in the five years before the granting of ER pension.

Among 2,853 (53.3%) cases the application for rehabilitation was reevaluated as an application for an ER pension. Risk factors for not receiving medical rehabilitation were male gender, foreign nationality, low

or unknown education, low income as well as low pension payment amount. For example, adjusted risk (Odds Ratio [95%-CI]) among persons with low income (1st quartile vs. 4th quartile), was 2.4 [1.8; 3.1].

Conclusions: One reason for the social inequality in the implementation of the principle “rehabilitation before pension” could be the difficulty of complying with the economic efficiency and frugality requirement [§ 13 (1) SGB VI, Federal Ministry of Justice 2022] when granting medical rehabilitation measures for economic disadvantaged persons.

M. Weyermann: None.

P09.02

EFFECT OF *HELICOBACTER PYLORI* ERADICATION ON GASTRIC CANCER PREVENTION IN KOREA – A RANDOMIZED CONTROLLED CLINICAL TRIAL (HELPER)-BASELINE RESULTS

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Objective: We report baseline data of the HELPER trial which aims to evaluate the effect of *Helicobacter pylori* eradication in reduction of gastric cancer incidence in the middle-aged general population in Korea.

Materials and Methods: Initiated in 2014, HELPER is a randomized, double-blind placebo-controlled trial of Koreans aged 40-65 who are eligible for the National Gastric Cancer Screening Program (NGC-SP). The study participants underwent endoscopic screening at baseline as part of the NGCSP and tested for *H. pylori* infection by rapid urease test or ¹³C-urea breath test (UBT). *H. pylori*-positive participants were subsequently randomized to eradication with 10-day bismuth quadruple therapy or placebo. Participants have been followed-up by biennial endoscopic screening within the NGCSP.

Results: A total of 12,724 underwent examinations and 11,798 (mean age, 52y) were enrolled from 12 study centres. As of May 2023, median follow-up time was 47.5 (IQR 35.4) months and 7,991 (70%) completed at least one follow-up examination. Among the 5,269 *H. pylori* positive participants (50% women) who received either treatment or placebo, 4,454 participants took at least one study drug and 3,508 participants completed ≥7 days of treatment or placebo. The most frequently reported treatment associated adverse events included nausea, dyspepsia, dizziness and diarrhoea. A confirmatory UBT was performed in a subgroup (n=354), of those 181 (51%) participants remained positive and 173 tested negative.

Conclusions: In this population-based randomized controlled trial, we found acceptable treatment compliance and follow-up participation. The trial continues its active follow-up and results from the interim analysis are foreseen in 2026.

J. Park: None. Y. Kim: None. J. Kim: None. S. Jeon: None. B. Kim: None. H. Kim: None. G. Baik: None. W. Shin: None. J. Kim: None. G. Kim: None. S. Kim: None. M. Park: None. M. Han: None. J. Joo: None. R. Herrero: None. I. Choi: None.

P09.03

H. PYLORI INFECTION AFFECTS THE HER2-CDH1 INTERACTION

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We showed that Wnt/ β -catenin pathway interconnects overexpression of the Human epidermal growth factor receptor 2 (HER2) with loss of E-cadherin (CDH1) in patients with metastatic gastric cancer (GC) (De Re, 2022). The aim of the present study was to investigate whether *H. pylori* infection could affect this pathway and thus the response to treatment with trastuzumab (TRAS), an anti-HER2 monoclonal antibody. We employed the human gastric cell line NCI-N87 with high HER-2 expression and created a trastuzumab-resistant clone (R). Both N87 and R-N87 cell lines were treated with EGF, TRAS and a combination of both. In addition, subclones were infected with 2 different strains of *H. pylori*: a low virulent (LV-HP) and a high virulent (HV-HP) strain for 6 hours in one study and 20 hours in another. Cells were then harvested for RNA extraction and subsequent gene expression analysis using NanoString. Major findings associated with HV-HP infection were revealed after 20 hours of co-culture, reduction on CTNNB1 and increase of RARA were among the most significant compared with non-infected cells (log2 fold change -0.346, $p=1.15E-05$ and 0.449, $p=3.56E-07$, respectively). Overall results suggest that the more virulent *H. pylori* strain affects the Wnt/ β -catenin signalling pathway, and thus possibly the treatment response. Further analyses are ongoing to better define the role of *H. pylori* in the response to treatment of metastatic GC over-expressing HER2.

M. Casarotto: None. G. Brisotto: None. P. Baldo: None. S. Zanussi: None. A. Steffan: None. R. Cannizzaro: None. V. De Re: None.

P09.04

PROTEIN CONVERTASES INHIBITION AS A NEW STRATEGY TO TARGET CANCER STEM CELLS PROPERTIES IN GASTRIC CANCER

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Objective: Proprotein convertases (PCs) are enzymes involved in the maturation of a large panel of precursor proteins implicated in fundamental cellular processes and cancer, such as proliferation, survival, invasion, immunity and metastasis. The poor prognosis of gastric adenocarcinoma (GC) is linked to cancer stem cells (CSCs) at the origin of tumor initiation, progression, chemoresistance and metastasis. The epithelial to mesenchymal transition and the Hippo signalling pathway have been involved in the control of CSC properties and GC bad prognosis. The role of PCs in the control of CSC properties remain to be elucidated in GC.

Material and Methods: Using a general chemical PCs inhibitor, we have studied the consequences of PCs inhibition on CSCs tumorigenic and invasive properties as well as on EMT and Hippo pathway in four GC cell lines *in vitro*, as well as in mouse xenografts models.

Results: PCs inhibition had a significant effect on GC CSCs ability to form tumorspheres, on invasion and on drug efflux, but without affecting CD44 and ALDH CSCs markers expression. PC inhibition also decreased the expression of ZEB1, Snail and other EMT markers as well as the transcriptional activity of YAP/TAZ/TEAD oncogenic effectors of Hippo pathway. PC inhibition reduced the ability of GC cells to form metastases *in vivo*.

Conclusions: PCs inhibition could be a potential strategy to target CSCs in GC notably by reducing their tumorigenic, drug efflux and invasive properties via the targeting of YAP/TAZ/TEAD oncogenic activity.

C. Varon: None. A. Zaafour: None. L. Seeneevassen: None. N. Nicolas: None. T. Nguyen: None. C. Genevois: None. E. Sifré: None. C. Porcheron: None. A. Giese: None. P. Dubus: None. A. Khatib: None. J. Descarpentrie: None.

P09.06

IMPROVING THE ACCURACY OF THE PEPSINOGEN TEST IN DETECTING PRECANCEROUS GASTRIC LESIONS BY ADJUSTING CUT-OFF VALUES IN CURRENT SMOKERS BY THE PRESENCE OF *HELICOBACTER PYLORI* INFECTION

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Objective: The aim was to identify factors that could be used to adjust pepsinogen (Pg) cut-off values to improve Pg test accuracy in detecting precancerous gastric lesions (PGL).

Material and Methods: Plasma Pg was measured and upper endoscopy with biopsy was performed for 1,210 participants within the “Multicentric randomized study of *Helicobacter pylori* eradication and pepsinogen testing for prevention of gastric cancer mortality: the GISTAR study”. Univariate and multivariate analysis were conducted to identify factors (sociodemographic, medical history, diet, lifestyle, *H. pylori* (HP) infection) associated with false negative (FN) cases in Pg testing (cut-off Pgl/PgII ≤2 and Pgl ≤30 ng/mL). Factor dependent effects were assessed by calculating sensitivity and specificity using the predetermined Pg cut-offs with ROC, evaluated by AUC. New Pg cut-offs were calculated using Youden’s index.

Results: Current smokers, men, and HP-positives were more likely to be FN. In the general population, sensitivity was 65.4% for Pgl/II ≤2 and 62.6% for Pgl ≤30 ng/mL. Sensitivity of Pg test was substantially lower for current smokers and was affected by HP infection: for Pgl/II in HP-positives 52.0% (37.4-66.3), AUC 0.76 vs. HP-negatives 32.3% (16.7-51.4), AUC 0.68; for Pgl in HP-positives 32.0% (19.52-46.70), AUC 0.63 vs. HP-negatives 38.7% (21.9-57.8), AUC 0.68. Calculating new cut-offs for current smokers by HP presence resulted in improved sensitivity: new cut-off, sensitivity for HP-negatives Pgl/II ≤3.0, 48.4% and Pgl ≤37.75 ng/mL, 67.7%.

Conclusions: Adjusting Pg cut-offs for smokers based on *H. pylori* status may improve the accuracy of Pg testing for precancerous gastric lesions. Supported by ESF Project Nr.8.2.2.0/201/006.

D. Razuka-Ebela: None. I. Polaka: None. I. Ebela: None. S. Parshutin: None. J. Park: None. M. Leja: None.

P09.07

SMALL INTESTINAL BACTERIAL OVERGROWTH SIBO IN PATIENTS WITH UPPER GASTROINTESTINAL CANCER: PREVALENCE AND IMPACT ON QUALITY OF LIFE

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Objective: Small intestinal bacteria overgrowth (SIBO) is a clinical disorder in which symptoms, clinical signs or laboratory abnormalities are due to an alteration in the number or composition of the bacterial population in the small intestine. The aim of the study was to assess the prevalence of SIBO and the impact of SIBO symptoms on quality of life in patients with upper GI cancer.

Materials and Methods: A standardized questionnaire covering SIBO- symptoms, concurrent medications, history of surgery was completed by patients with bloating and/or diarrhoea. On a scale from 0 (no symptoms) to 3 (severe symptoms), the effect of SIBO-symptoms on quality of life was assessed. After 30 days without antibiotics, patients with symptoms and poor quality of life (score > 1) underwent EGD with duodenal aspirate. SIBO was defined as a bacterial count greater than 10³ colony forming units per millilitre in duodenal aspirate.

Results: A total of 90 consecutive patients were enrolled (31 gastric, 32 pancreatic, 13 oesophageal and 14 biliary). SIBO-related symptoms were recorded in 60/90 people with active (N=44, 73%) or past (N=16, 27%) upper GI cancer. Bloating was reported in 21/60 (35%) cases, diarrhoea in 7/60 (11%) cases and bloating plus diarrhoea in 32/60 (54%) cases. EGD with duodenal aspirate was performed in 36 patients. SIBO was diagnosed in 19 out of 36 (53%) patients. In addition, 95% (18/19) of SIBO patients reported flatulence.

Conclusions: SIBO is present in one in two patients with cancer of the upper GI who report bloating or diarrhoea with impairment of quality of life.

R. Rosania: None. S. Sulzer: None. A. Kaasch: None. V. Keitel-Anselmino: None. M. Venerito: None.

P09.08

IMPACT OF *HELICOBACTER PYLORI* ON IMMUNOTHERAPY VERSUS MOLECULAR TARGETED THERAPY IN HEPATOCELLULAR CARCINOMA: A MULTICENTER, RETROSPECTIVE STUDY

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Objective: Immune checkpoint inhibitors (ICI) marked a breakthrough in the treatment of hepatocellular carcinoma (HCC). However, response to treatment is only seen in around 30% of patients. Immunomodulating effects of *Helicobacter pylori* (HP) have been associated with resistance to ICI in patients with lung cancer. This study aims to assess the effect of HP on the efficacy of ICI in HCC.

Patients and Methods: We conducted a retrospective, multicenter study in 170 patients with HCC divided into three cohorts based on the treatment modality: (1) ICI, (2) sorafenib, (3) radioembolization (RE) plus sorafenib. HP serostatus was determined using validated ELISA tests. OS was estimated with Kaplan-Meier analysis and log-rank test. The study was approved by the institutional review board. All patients gave written informed consent.

Results: 54 patients were treated with ICI, 57 patients with sorafenib and 59 patients with RE plus sorafenib. 19 patients were HP positive in the ICI cohort, 32 patients in the sorafenib cohort, 26 patients in the RE plus sorafenib cohort. Baseline characteristics were similar between HP positive and HP negative patients. Median OS was longer in HP negative patients treated with ICI as compared to HP positive patients (18.3 vs. 10.7 months, $p=0.15$). In patients treated with sorafenib or RE plus sorafenib, median OS was similar between both groups.

Conclusions: We observed a favorable treatment outcome in HP negative patients with HCC treated with ICI without reaching statistical significance. Larger trials are required to confirm our findings.

C. Schulz: None. N. Ben Khaled: None. M. Gerhard: None. L. Jochheim: None. R. Schinner: None. L. Macke: None. O. Öcal: None. C.M. Lange: None. E.N. De Toni: None. J. Mayerle: None. J. Ricke: None. P. Malfertheiner: None.

P09.09

NEXT GENERATION PHAGE DISPLAY MIMOTOPE-VARIATION ANALYSIS (MVA)-DEFINED ANTIBODY RESPONSE PATTERNS LINK BREAST CANCER TO *HELICOBACTER PYLORI* INFECTION

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Helicobacter pylori (*H. pylori*) a common pathogen is the primary cause of gastric ulcers and raises the risk of stomach cancer. Recent studies have suggested that *H. pylori* infection may be linked to other types of cancer including breast cancer (BC). To comprehensively map the humoral immune

response from peripheral blood and identify the features that associate with progression of BC, we employed MVA method to characterise the antibody epitope repertoire in the cohort of patients with BC (n=104) and their age- and sex-matched controls (n=172). Our data showed that antibody immune response against *H. pylori* was widespread, however specific patient subgroups had characteristic antibody epitope profiles. This allowed to develop fine descriptions of the antigenic epitopes for early and metastatic forms of BC. In case of metastatic BC, immune response against *H. pylori* was associated with epitopes of the virulence factor CagA antigen. These findings were further confirmed by HP-CagA-IgG ELISA and epitope-specific dot ELISA. From the mechanistic point of view these data suggest that chronic inflammation or the microbiota imbalance trigger by *H. pylori* infection can promote breast cancer development.

Our findings provide new insights into the immunological features of breast cancer development associated with *H. Pylori*.

K. Palm: None. H. Sadam: None. R. Maruste: None. A. Rähni: None. M. Toots: None.

P09.10

HELICOBACTER PYLORI ATTACHMENT-BLOCKING ANTIBODIES PROTECT AGAINST GASTRIC DISEASE

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Objective: The majority of the world-population carry the gastric pathogen *Helicobacter pylori*, but most individuals experience little or no symptoms. Here we report on a protective mechanism where *H. pylori* attachment and the accompanying chronic mucosal inflammation can be reduced by antibodies that are present in a vast majority of *H. pylori* carriers.

Materials and Methods: We tested ~1000 individual serum samples from *H. pylori* carriers for their individual levels of broadly blocking antibodies (bbAbs) that reduce the bacterial mucosal attachment.

Results: We found that the vast majority of individuals demonstrate bbAb titers, which can reduce the attachment of *H. pylori* to the blood group ABO glycans in the gastric mucosa. Of relevance for gastric disease, we found that patients with duodenal ulcer disease have significantly lower levels of such bbAbs. To test for possibilities to elicit a protective immune response, we found that challenge infections with *H. pylori* induced bbAbs in human volunteers. Furthermore, vaccination induced bbAbs to the critically necessary protective level/titers in both rhesus macaques and mice.

Conclusions: We believe the human immune response has identified an Achilles heel in use of bbAbs for defusing the *H. pylori* infection. The results show that the bbAbs reduce *H. pylori* adherence, reduce gastric inflammation, and reduce the risk for severe gastric disease. Our new results bring a better understanding of the homeostasis in immune responses against *H. pylori* infection and epithelial attachment and its consequences for mucosal inflammation and severe gastric disease.

<https://www.biorxiv.org/content/10.1101/2023.05.25.542131v1>,

<https://biorxiv.org/cgi/content/short/2023.05.24.542096v1>

T. Boren: None. J.A. Bugaytsova: None. A. Piddubnyi: None. I. Tkachenko: None. P. Malfertheiner: None. J.V. Solnick: None. L. Hammarström: None.

P09.11

METACHRONOUS RECURRENCE AMONG PATIENTS WHO RECEIVED ENDOSCOPIC RESECTION FOREARLY GASTRIC CANCER AT AGE ≤ 50 YEARS: COMPARED PATIENTS WITH >50 YEARS**J. PARK¹, M. JOO¹, W. KIM¹, B. LEE¹, S. KIM¹, H. CHUN²**¹Division of Gastroenterology, Department of Internal Medicine, Korea University Guro Hospital, Korea University College of Medicine, Seoul, Korea, Republic of; ²Division of Gastroenterology, Department of Internal Medicine, Korea University Anam Hospital, Korea University College of Medicine, Seoul, Korea, Republic of**Objective:** A small portion of patients are diagnosed as early gastric cancer (EGC) and undergo endoscopic submucosal dissection (ESD) at young age, however, their clinical outcomes are rarely known. We investigated clinical characteristics and outcomes of patients who underwent ESD for treatment of EGC at age under 50.**Material and Methods:** We enrolled patients who were diagnosed as EGC and underwent ESD during 2006 and 2020. We divided them either for young age (YA) group if age ≤ 50 years and other age (OA) group if >50 years. Results: We enrolled 1,349 patients (YA group: 105 patients [7.8%], OA group: 1244 [92.2%]). Compared with OA group, YA group contained more female patients (36.2 vs. 26.5%, $p=0.033$), their tumor was located at middle third (41.0 vs. 29.6%, $p=0.006$) and was depressed (40.0 vs. 28.8%, $p=0.001$), and had more undifferentiated (30.5 vs. 12.1%, >0.001) and diffuse type (22.9 vs. 7.3%, >0.001) histology. However, synchronous tumor was less frequent in YA group (2.9 vs. 12.4%, $p=0.001$). When we sorted 884 patients who achieved curative resection and were followed-up longer than 12 months, Kaplan-Meier analysis showed that metachronous neoplasm (dysplasia or cancer) and metachronous cancer were significantly less in YA group than OA group ($p=0.003$ and 0.013, respectively). However, local recurrence was not significantly different between two groups.**Conclusions:** ESD is a favorable and effective therapeutic modality for EGC patients who are aged under 50, once curative resection is achieved.**J. Park: None. M. Joo: None. W. Kim: None. B. Lee: None. S. Kim: None. H. Chun: None.****POSTER SESSION 10: HELICOBACTER 7**

P10.01

HELICOBACTER PYLORI BASE-EXCISION RESTRICTION ENZYME IN GASTRIC CANCER**M. FUKUYO¹, N. TAKAHASHI^{2,3,4}, K. HANADA⁵, K. ISHIKAWA⁶, K. YAHARA⁷, & VENCLOVAS⁸, H. YONEZAWA^{2,9}, Y. KATSURA¹⁰, H. MAKI¹¹, I. UCHIYAMA¹², N. OSADA¹³, T. OSAKI², C. CAMARGO¹⁴, C. RABKIN¹⁴, I. KOBAYASHI^{3,4,12,15}**¹School of Medicine, Chiba University, Chiba, Japan; ²Department of Infectious Diseases, Kyorin University School of Medicine, Mitaka, Tokyo, Japan; ³Department of Computational Biology and Medical Sciences, Graduate School of Frontier Sciences, University of Tokyo, Tokyo, Japan; ⁴Institute of Medical Science, University of Tokyo, Tokyo, Japan; ⁵Faculty of Medicine, Oita University, Oita, Japan; ⁶Department of Cell Biology, Institute of Life Science, Kurume University, Kurume, Japan; ⁷Antimicrobial Resistance Research Center, National Institute of Infectious Diseases, Tokyo, Japan; ⁸Institute of Biotechnology, Vilnius University, Vilnius, Lithuania; ⁹Tokyo Dental College, Chiyoda, Tokyo, Japan; ¹⁰Primate Research Institute, Kyoto University, Inuyama, Japan; ¹¹Division of Biological Science, Graduate School of Science and Technology, Nara Institute of Science and Technology, Nara, Japan; ¹²Laboratory of Genome Informatics, National Institute for Basic Biology, Okazaki, Japan; ¹³Graduate School of Information Science and Technology, Hokkaido University, Sapporo, Japan; ¹⁴Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, United States; ¹⁵Research Institute for Micro-nano Technology, Hosei University, Koganei, Tokyo, Japan

Objective: *Helicobacter pylori* has been recognized as a major risk factor for stomach (gastric) cancer, but how it changes the human genome to cause cancer remains unknown. In this and related bacteria, recent works identified a family of restriction enzymes that excise a base from its recognition sequence. At the resulting abasic site, its own endonuclease activity or a separate endonuclease activity may generate an atypical strand break not repairable by ligation.

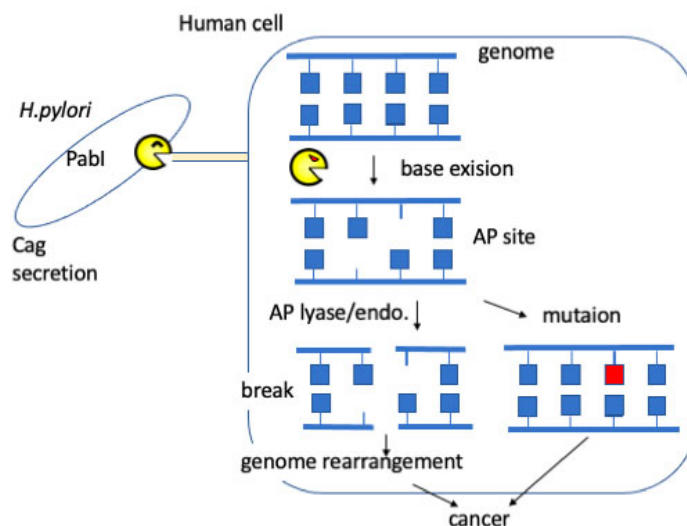
Materials and Methods: For involvement of this toxic restriction enzyme in stomach carcinogenesis, we present here multiple lines of evidence.

Results: 1. Its gene is associated with stomach cancer according to the data from *Helicobacter pylori* Genome Project. 2. Its recognition sequence (5'GTAC) is found frequently mutated in stomach cancer genomes. 3. It causes chromosomal double-strand breakage in human cells in infection and gene transfer. 4. It promotes mutagenesis in bacterial reporters. 5. It can be modeled to compactly ride on duplex DNA, which might help its transfer to human cells.

Conclusions: We expect that involvement of a bacterial restriction enzyme in oncogenesis would deepen our understanding of host-microbiome relations and impact medicine.

N. Takahashi: None. K. Hanada: None. K. Ishikawa: None. K. Yahara: None. & Venclovas: None. H. Yonezawa: None. Y. Katsura: None. H. Maki: None. I. Uchiyama: None. N. Osada: None. T. Osaki: None. C. Camargo: None. C. Rabkin: None. I. Kobayashi: None.

FIGURE 1. A hypothesis for *H. pylori*'s base-excision restriction enzyme HpPabl and stomach cancer. *H. pylori* transfers the restriction glycosylase bound to dsDNA to human cells via CagPAI Type IV secretion machinery. The glycosylase excises adenine base at its palindrome recognition sequence 5'-GTAC-3' from the human chromosome. The action of its AP lyase activity or human AP endonuclease on the resulting AP site generates double-strand breaks, which in turn lead to chromosome instability and genome rearrangements. The action of also leads to substitution mutations at A of 5'-GTAC-3'. These lead to stomach cancer.



P10.02

PIN-POINT ADAPTIVE DIFFERENTIATION UNDER FREE HOMOLOGOUS RECOMBINATION

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Objective: Why all the living forms appear well designed in structure and function has long been a mystery. In scientific terms, how does a species differentiate into groups each with distinct traits adaptive to its environment? We here address this question of *adaptation* by comparing genomes of *Helicobacter pylori*, which has high genome diversity and nearly free outcrossing homologous recombination but discrete population structure.

Materials and Methods: We divided ~1000 genome sequences, which were globally collected and accurately and completely Pacbio-decoded under *Helicobacter pylori* Genome Project, into tiny groups by sequence sharing (Principal Component Analysis) and identified their highly group-specific single nucleotide polymorphisms (SNPs).

Results: We encountered various host interaction proteins including virulence factors, outer-membrane proteins, transporters and microbiome-related proteins. To our surprise, most of these SNPs changed an amino-acid around a residue critical for their function such as active/binding sites, channel entrances, and subunit interaction sites. Most of these sites show a sign of diversifying selection. Expected tight association of a differentiation site and an adaptation site is well modeled and simulated by frequent and fine homologous recombination that shuffles nearby SNPs for selection.

Conclusions: The emerging picture of pinpoint adaptive differentiation by outcrossing homologous recombination answers the fundamental question of genetic systems, the *evolution of sex* issues. We expect it will prompt studies of protein structure/function in an adaptive/evolutionary perspective and, together with the simple method of “divide and compare many genomes”, will have a strong impact on all the fields of life sciences and their applications.

T. Sakamoto: None. N. Hiroyo: None. I. Uchiyama: None. H. Innan: None. C. Camargo: None. C. Rabkin: None. N. Osada: None.

P10.03

IDENTIFYING MACROLIDE EXPOSURE USING DRUG UTILIZATION REVIEW SYSTEM AND ITS RELATION TO CLARITHROMYCIN RESISTANCE

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Objective: We aimed to evaluate the impact of past macrolide use on antibiotic resistance profiles of *Helicobacter pylori* (*H. pylori*) using the Korean Drug Utilization Review (DUR) system.

Patients and Methods: Consecutive patients confirmed *H. pylori* infection by positive for one or more of the urea breath tests (UBT), rapid urease test (RUT), and culture between October 2021 and January 2023 were prospectively enrolled. Each patient’s prescription information was obtained using the DUR system of the Health Insurance Review and Assessment Service. The antimicrobial susceptibility tests were examined by using the serial 2-fold agar dilution method. The association between past macrolide exposure and the clarithromycin (CLR) resistance rate was evaluated.

Results: A total of 60 patients who confirmed *H. pylori* infection were finally enrolled. The median age was 59 years (interquartile range, 51-65), and 70% (42/60) were male. The positivity of UBT, RUT, and serum immunoglobulin G testing were 87.3% (48/55), 91.7% (55/60), and 100.0% (58/58), respectively. The culture showed 83.3% (50/60) positivity. The 26.7% (16/60) of patients were verified to take macrolide antibiotics for the last 5 years. As a result of antimicrobial susceptibility tests, the CLR resistance rates were significantly higher in patients with previous macrolide use than without macrolide use (57.1% vs. 8.1%, $p < 0.001$).

Conclusions: Identifying macrolide exposure using the DUR system was feasible. Previous use of macrolide significantly affected the high rate of CLR resistance. Accurate identification of previous antibiotic use and selection of appropriate regimen accordingly might be essential in increasing the *H. pylori* eradication rate.

K. Choi: None. J. Noh: None. H. Na: None. J. Ahn: None. J. Lee: None. K. Jung: None. D. Kim: None. H. Song: None. G. Lee: None. H. Jung: None.

P10.04

THE HIGH-DOSE DUAL THERAPY IS EFFECTIVE AS A FIRST-LINE TREATMENT FOR *HELICOBACTER PYLORI* IN MONGOLIA

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Objective: Mongolia has a high prevalence of *Helicobacter pylori* (*H. pylori*) infection and gastric cancer. Mongolia is localized in areas of high clarithromycin resistance (>15%) of *H. pylori*. The effectiveness of *H. pylori* treatment is decreasing due to increasing antibiotic resistance. The clarithromycin-based triple treatment rate declined to 72.7%, bismuth-based quadruple treatment rate is 90% in Mongolia. The high-dose dual therapy has fewer side effects, a high eradication rates in studies. We performed assessed the effectiveness of high-dose dual therapy for *H. pylori* infection.

Material and Methods: We recruited 85 *H. pylori*-infected patients after exclusion. All patients underwent upper gastrointestinal endoscopy and were tested with a urea breath test and *H. pylori* antigen in stool. All patients received a 14-day, high-dose dual therapy: esomeprazole (40 mg t.i.d.) and amoxicillin (1 g t.i.d.) for *H. pylori* eradication. Probiotics (Gastrus BioGaia®) are given to decrease side effects. Follow-up urea breath tests were conducted 1 month after treatment.

Results: The success rate of high dose dual therapy was 91.7% (95%, CI=89.7%-93.1%). The adverse events rate was 2.1%. Diarrhea was observed in 2 patients.

Conclusions: The 14-day esomeprazole and amoxicillin-containing high-dose dual therapy is effective in the first-line treatment of *H. pylori*.

B. Tsogt_Ochir: None. B. Namdag: None. S. Batmunkh: None. T. Bold: None.

P10.05

INHIBITORY EFFECTS OF COMMENSAL GASTROINTESTINAL BACTERIA ON *HELICOBACTER PYLORI*

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Objective: *H. pylori* is a bacterial pathogen affecting approximately 50% of the world's population. New treatment strategies are needed, as prevalence of antibiotic resistance increased dramatically during the last decade. Our previous studies showed that *H. pylori*-carriers have altered gastric bacterial communities compared to non-carriers. This suggests that non-carriers might be colonised with commensal bacteria that protect against *H. pylori* infection. Identified bacteria include *Streptococcus mitis*, *S. vestibularis*, *S. parasanguinis*, *Granulicatella adiacens* and *Gemella morbillorum*.

Materials and Methods: In order to detect an inhibition of *H. pylori* growth caused by commensal bacteria co-cultures are performed on blood agar plates and in BHI broth. Additionally, ATP-based bioluminescence tests are performed to investigate the viability of *H. pylori* cells. A potentially reduced binding ability of *H. pylori* towards eukaryotic cells is tested performing a co-culture of *H. pylori* with different gastric cancer cell lines.

Results: The first results of the co-cultures of *H. pylori* and *Streptococcus mitis* or *S. parasanguinis* on blood agar plates revealed no inhibition of *H. pylori* growth. The other identified bacteria are under investigation.

Conclusions: Those results indicate that the tested streptococci possess no potential to inhibit *H. pylori* growth *in vitro* when co-cultured on blood agar plates. Further experiments will show whether other species that were increased in non-carriers have anti-*H. pylori* activity.

J.R. Westphal: None. N. Koch: None. P. Malfertheiner: None. C. Schulz: None.

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)

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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.

D. Casas-Deza: None. J. Alcedo: None. M. Lafuente: None. J. López: None. Á. Pérez-Aísa: None. M. Pavoni: None. I.M. Saracino: None. B. Tepes: None. L. Jonaitis: None. P.S. Phull: None. D.S. Bordin: None. A. Gasbarrini: None. J. Kupcinskas: None. A. Cano-Català: None. L. Hernández: None. L. Moreira: None. O.P. Nyssen: None. F. Megraud: None. C.O. Morain: None. J.P. Gisbert: None.

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 <i>H. pylori</i> eradication therapies according to PB use, differentiated by gender. Modified intention-to-treat (mITT) analysis in the Central European geographical area.													
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	-	-
	<i>p</i>	0	-	0	-	-	0.0835	0.0685	-	-	0.0019	-	-
Triple	Coef	-0.6391	-	-0.785	-	-	-	-	-	-	-	-	-
	<i>p</i>	0.0014	-	0.0331	-	-	-	-	-	-	-	-	-
Quadruple	Coef	0	-	-	-	-	-	-	-1.0615	-	-	-	-
	<i>p</i>	1	-	-	-	-	-	-	0.0314	-	-	-	-
Sequential	Coef	-2.1224	-	-0.6749	-	-	-	-	1.1134	-	-	-	-0.3593
	<i>p</i>	0	-	0	-	-	-	-	0.0006	-	-	-	0.0366
Quadruple + B	Coef												
	<i>p</i>												
Logistic regression model for the incidence of severe AEs with <i>H. pylori</i> eradication therapies according to PB use, differentiated by gender. Modified intention-to-treat (mITT) analysis in the Central European geographical area.													
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
	<i>p</i>	0.27	0.1882	0	-	-	-	-	0.0000	-	0.0000	-	0
Triple	Coef	0.23	-	-	-	-	-	-	-2.621	-2.4203	-	-	3.6463
	<i>p</i>	0.77	-	-	-	-	-	-	0.002	0.0278	-	-	0.0105
Quadruple	Coef	-1.59	-	-0.7479	-	-	-	-	-	-	-	-	-
	<i>p</i>	0	-	0.0582	-	-	-	-	-	-	-	-	-
Sequential	Coef	-2.96	-0.0209	-	-	-	-11.5	1.1481	-	-	-	-	-
	<i>p</i>	0	0.0463	-	-	-	0.99	0.0002	-	-	-	-	-
Quadruple + B	Coef												
	<i>p</i>												

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)

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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.

D. Casas-Deza: None. J. Alcedo: None. M. Lafuente: None. J. López: None. Á. Pérez-Aísa: None. M. Pavoni: None. I.M. Saracino: None. B. Tepes: None. L. Jonaitis: None. P.S. Phull: None. D.S. Bordin: None. A. Gasbarrini: None. J. Kupcinkas: None. A. Cano-Català: None. L. Hernández: None. L. Moreira: None. O.P. Nyssen: None. F. Megraud: None. C.O. Morain: None. J.P. Gisbert: None.

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)

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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.

D. Casas-Deza: None. J. Alcedo: None. M. Lafuente: None. J. López: None. Á. Pérez-Aísa: None. M. Pavoni: None. I.M. Saracino: None. B. Tepes: None. L. Jonaitis: None. P.S. Phull: None. D.S. Bordin: None. A. Gasbarrini: None. J. Kupcinkas: None. A. Cano-Català: None. L. Hernández: None. L. Moreira: None. O.P. Nyssen: None. F. Megraud: None. C.O. Morain: None. J.P. Gisbert: None.

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)
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

P10.09

DIAGNOSTIC VALUE OF EIGHT COMMERCIAL TESTS FOR THE RAPID DETECTION OF *HELICOBACTER PYLORI* ANTIGEN IN STOOL.

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Objective: *Helicobacter pylori* Stool Antigen Test (SAT) is increasingly used for diagnosis and eradication control purposes. Various assays are currently available.

This prospective study aimed to compare eight commercial immunoassays {(ImmunoCard STAT![®]HpSA (Meridian, Bioscience), Curian[®] HpSA[®] (Meridian, Bioscience), *Helicobacter pylori* Ag Rapid Test (Selenion, CerTest), H.Pylori Ag test (Abbott), Pylori-Kset (Coris BioConcept), Pylori-strip (Coris BioConcept), RAPID[™] Hp StAR[™] Lateral Flow Kit (ThermoFisher) and STANDARD H.p. A (SD Biosensor)} which allow rapid detection of *Helicobacter pylori* antigen in stool.

Material and Methods: SAT were performed in parallel from January to September 2022, under routine conditions, in consecutive fresh stool specimens. Samples showing one or more discrepant results were additionally tested with Real Time PCR (*Helicobacter* PCR Viasure, Selenion, CerTest) and ELISA (Amplified IDEIA[™] Hp StAR[™], ThermoFisher) used as reference. Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) were measured. Moreover, applicable EASSURED criteria (Affordability, Sensitivity, Specificity, User-friendliness, Rapid and robust, Equipment-free) were used for comparison.

Results: A total of 379 stool samples have been included showing 91.2% agreement and 20.6% of positive results. Except a low PPV (83.2%) obtained for one kit, analytical performances were very good (Table 1). All the assays satisfied the ASSURE criteria, nevertheless Pylori-Kset and H.Pylori Ag test seemed to be the most cost-effective assays.

Conclusions: All the immunoassays showed good diagnostic accuracy and particularly an excellent NPV.

R. Garba: None. A. Debyttre: None. M. Stouten: None. B. Ghislain: None. M. Wautier: None. V.Y. Miendje deyi: None. H. Dahma: None.

TABLE 1. ANALYTICAL PERFORMANCES OF EIGHT IMMUNOASSAYS COMPARED TO REAL TIME PCR AND ELISA (N = 379).

IMMUNOASSAY (Manufacturer)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
ImmunoCard STAT! [®] HpSA (Meridian, Bioscience)	97.4	97.4	90.4	99.3
Curian [®] HpSA [®] (Meridian, Bioscience)	100	98.7	95.2	100
<i>Helicobacter pylori</i> Ag Rapid Test (Selenion, CerTest)	100	94.7	83.2	100
<i>H. Pylori</i> Ag test (Abbott)	97.5	99.7	98.7	99.3
Pylori-Kset (Coris BioConcept)	96.2	98	92.7	99
Pylori-strip (Coris BioConcept)	96.2	98.3	93.8	99
RAPID [™] Hp StAR [™] Lateral Flow Kit (ThermoFisher)	100	98.3	94	100
STANDARD H.p. A (SD Biosensor)	97.5	99.3	97.5	99.3

P10.10

INVESTIGATION OF PMSS1 *HELICOBACTER PYLORI* VIRULENCE FACTORS RESPONSIBLE FOR HUMAN TO MOUSE TRANSMISSION

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Objective: *Helicobacter pylori* colonizes half of the global population, causing gastric diseases including gastric cancer. *H. pylori* can be transmitted by familial (ancestral) or non-familial (non-ancestral) transmission where non-ancestral strains are more virulent. Since the mechanism of *H. pylori* transmission is not understood clearly, we investigated the transmission using *H. pylori* PMSS1.

Materials and Methods: Twenty-five single colonies were isolated from the PMSS1 strain and C57BL/6 mice were infected with the colonies for one week and categorized by the degrees of colonization ability. In the further study, mice were infected with 20 colonies re-isolated from one high group-input (HGI) colony and with three low group-output (LGO) colonies. HGI, low group-input, and LGO strains were characterized for *cag* PAI-related virulence, natural transformation efficiency, and comparative genomic analysis.

Results: Based on mouse colonization ability, four colonies belonged to high group (HG, 16%), nine to middle group (MG, 36%), and 12 to low group (LG, 48%). However, all HGI-reisolated single colonies and three LGO colonies showed CFU values like HG. Most colonies of HG and LG had high *cag* PAI-related virulence. Natural transformation competence may be required to generate a more heterogeneous population. The comparative genomic analysis between HG and LG colonies identified several mutations probably responsible for the colonization ability.

Conclusions: PMSS1 strain is heterogeneous for mouse infection abilities. Converting LG to HG happened slowly, suggesting that generating a heterogeneous population is a slow process in stomach. The comparative genomic analysis implied several genes which play a critical role in non-ancestral transmission.

M. Kim: None. S. Angulmaduwa: None. A. Ramanayake: None. M. Kim: None. J. Nam: None. D. Seo: None. J. Seo: None. Y.H. Cho: None. A.R. Kim: None. J.H. Cha: None.

IMMUNOGLOBULIN FOR CHRONIC GASTRITIS

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Objective: The aim of the work was to study the characteristics of the response of the humoral link of immunity in patients with *H. pylori*-associated diseases.

Patients and Methods: 50 patients with chronic gastritis (CG) in combination with *H. pylori* infection, 35 patients with chronic atrophic gastritis (CAG) in combination with *H. pylori* infection, and 55 practically healthy volunteers were examined. In all groups, the presence of *H. pylori* was detected by ELISA by determining the titer of specific antibodies to the CagA antigen of *H. pylori*. Antibody titers of 30 EIU or more were considered positive for *H. pylori*. Quantitative determination of IgA, IgM, IgG, IgE was carried out by enzyme immunoassay. Statistical data processing was carried out using Statistica 7.0 (StatSoft, St Tulsa, OK, USA). The significance of differences ($p < 0.05$) between the indicators of independent samples was assessed using the Mann-Whitney test.

Results: In patients with CG and CAG in combination with *H. pylori* infection, unidirectional changes in the humoral immunity were observed, an increase in IgG ($p_{1-2}=0.01$; $p_{1-3}=0.002$) and an increase in IgA ($p_{1-2}=0.03$; $p_{1-3}=0.01$) compared with the control group.

Conclusions: In CG and CAG in combination with *H. pylori* infection, immune disorders occur associated with regulatory T-cell imbalance and the development of an immune response according to Th2-mechanism with the activation of the humoral immunity link. First of all, immunoglobulins of the IgG and IgA classes begin to be actively produced against bacterial antigens.

O. Smirnova: None. A. Sinyakov: None.

P10.12

A CONSOLIDATED PIPELINE FOR GENERATING REFERENCE-QUALITY PACBIO HELICOBACTER PYLORI GENOME ASSEMBLIES AND METHYLATION PROFILES

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Objective: A high-throughput approach for generating reference-quality *H. pylori* genomes would enable a variety of downstream applications, including analysis of population structure, evolution, and phenotype-genotype associations.

Materials and Methods: As part of the *Helicobacter pylori* Genome Project (HpGP), we designed an *H. pylori* analysis pipeline aimed at generating high-quality genomes and base modification profiles of cultured isolates (i.e., single colonies) from multiple locations. The pipeline workflow consisted of assembly with the PacBio MGA/HGAP4 assembler along with independent HIFI read assembly using the hifiasm assembler with an option to polish HIFI reads by DeepConsensus. Assembled contigs were circularized using Circulator. Chromosomal contigs were annotated with known *H. pylori* genes and BUSCO score against corresponding order *Campylobacterales*. Non-chromosomal contigs that passed NCBI nucleotide database structure comparison and *in silico* replication origin sequence identification were defined as plasmid contigs. Methylation analysis and motif detection were performed on the best assembly for each isolate using PacBio's built-in base modification analysis.

Results: We sequenced and processed approximately 1,300 *H. pylori* clinical isolates, including replicates (within and between PacBio platforms). The raw read assembly coverage ranges from 130X to more than 5,000X. Complete circularized contiguous single chromosomal contigs were obtained for 99% of isolates. The BUSCO score across all genomes was greater than 95%. Among all plasmid contigs detected, 90% were completed and circularized. The final dataset includes 1,011 unique genomes.

Conclusions: Through this consolidated pipeline, we achieved reference-quality contiguous *HpGP* genomes and epigenomes. This large set of data will be publicly available to the scientific community.

W. Luo: None. K. Jones: None. D. Wang: None. C. Rabkin: None. C. Camargo: None. J. Cherry: None. J. Dekker: None.

P10.13

ASSOCIATION BETWEEN *HELICOBACTER PYLORI* INFECTION AND DIABETES MELLITUS: A CROSS-SECTIONAL STUDY IN THE CENTRAL BRAZIL REGION

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Objective: *Helicobacter pylori* is a pathogen that infects approximately half of the world's population. Several studies have shown an association between infection and metabolic syndromes, especially diabetes mellitus (DM). Inflammation associated with *H. pylori* can lead to increased insulin resistance, leading to an increased risk of DM. The aim of this study was to investigate the association between *H. pylori* infection and DM.

Material and Methods: This is a cross-sectional study carried out in Central Brazil with 117 dyspeptic patients undergoing digestive endoscopy. The study was approved by the Ethics Committee No. 2,519,032. Gastric biopsies were analyzed by histopathological and molecular techniques. A total of 45 patients were excluded from the study due to the absence of a DM diagnosis.

Results: Of the 72 dyspeptic patients (18 men and 54 women, mean age 49.1 years), 65.27% (47/72) were infected with *H. pylori* and 14.89% (7/47) were diabetic. The prevalence of *H. pylori* infection in diabetics was higher among participants with incomplete high school with 83.3% ($p=0.99$), non-smokers 63.6% ($p=0.99$) and non-alcoholic drinkers 54.5% ($p=0.24$). There was a positive relationship between coffee consumption and *H. pylori* infection in diabetics (45.3% in diabetics and 55.7% in non-diabetics). However, in the two-sample ratio test, the frequency of patients with diabetes and *H. pylori* infection was significant.

Conclusions: There was no significant association between *H. pylori* infection and DM in the studied population. The elucidation of the pathological mechanisms associated with DM can contribute to the identification of potential targets for therapeutic intervention.

D.N. Maciel: None. H.A. da Silva: None. F.A.D. Moraes: None. A.F.P.L. Ramos: None. L.D. Assunção: None. B.R. Almeida: None. L.T. Rasmussen: None. R.D. Santos: None. M.S. Barbosa: None. M.P. Curado: None.

P10.14

ASSESSING PROPHAGE IMPACT ON *HELICOBACTER PYLORI* BIOFILM FORMATIONA. SEQUEIRA¹, R. LOPES-OLIVEIRA¹, F. F. VALE^{2,1}

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Objective: Human microbial infections, usually include biofilm formation, which provides a layer of additional protection to the host immune response and antimicrobial therapy. *Helicobacter pylori* colonizes the human gastric mucosa and is associated with the several diseases such as gastritis, peptic ulcer and gastric adenocarcinoma. The ability to form biofilm of this bacterium may contribute to the long-term establishment in the human stomach. Here, we aimed to verify if the presence of prophages resulted in distinct abilities to form biofilms.

Materials and Methods: The ability to form biofilm of five strains with prophages (with a genome size larger than 20 kb) and four strains without any prophage gene was measured after 5 days of *in vitro* growth, using the liquid medium of Brucella Broth supplemented with 10% Fetal Bovine Serum, in a microaerophilic environment. The ability to form biofilm was classified as non-, weak-, or strong-producer of biofilms, according with the optical density at 595nm.

Results: We found that 80% (4/5) of the strains harboring prophages were non-producers, while one strain was classified as strong-producer of biofilm. The strains without prophages were classified as non-producers in 75% (3/4) of the cases, with one strain classified as a weak-producer.

Conclusions: No correlation has been found between the presence of complete prophages and the ability to form biofilms in the set of studied strains. The results elucidate a necessity to further study the biofilm formation of *H. pylori* strains, and the possible role of prophages in development of the biofilm.

A. Sequeira: None. R. Lopes-Oliveira: None. F.F. Vale: None.

P10.15

IN VITRO SCREENING OF NATURAL AND SMALL MOLECULES COMPOUNDS AS POTENTIAL *HELICOBACTER PYLORI* INHIBITORSA. T. Marques¹, M. U. Ferreira², F. F. Vale^{3,1}

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Objective: The Gram-negative bacteria *Helicobacter pylori* is regarded as the most prevalent bacterial pathogen in humans and the major etiological agent of peptic ulcer and gastric carcinoma. About 50 percent of the world population is infected with *H. pylori* while therapies for its eradication have failed and antibiotic resistance is increasing. Hence, the search for new treatments and safer inhibitor compounds are global priorities. In the recent drug resistance scenario, medicinal plants are suggested as repositories of novel compounds.

Material and Methods: In the present study, the efforts to identify plant-derived small molecular inhibitors of *H. pylori* J99 strain led to the screening of over than 200 compounds. *In vitro* studies of minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) were performed.

Results: The results highlighted five compounds, sharing the indole alkaloid scaffold, as potential inhibitors of *H. pylori*. These compounds showed activity against *H. pylori* with both MIC and MBC with a concentration of 20 µM. Moreover, one compound also showed a MIC and MBC at a concentration of 10 µM.

Conclusions: With our actual results, we anticipate that the search strategy based on *in vitro* techniques can identify new anti-*H. pylori* drugs and enhance the importance of the pharmacological activity studies for new alternative therapies against multidrug-resistant *H. pylori* strains.

F.F. Vale: None. A.T. Marques: None. M.U. Ferreira: None.

POSTER SESSION 11: HELICOBACTER 8

P11.01

PREVALENCE OF *HELICOBACTER PYLORI* *cagA* GENE VARIES BY RACE AMONG INDIVIDUALS UNDERGOING UPPER ENDOSCOPY

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Objective: Although overall *Helicobacter pylori* (*Hp*) infections are declining in the US, Black Americans continue to have a higher prevalence of *Hp*, as well as greater gastric cancer incidence and mortality than White Americans. In a racially diverse *Hp*+ patient population, we assessed the prevalence of the *cagA* virulence factor by race and by disease status.

Materials and Methods: From all upper endoscopies with biopsy performed at Duke University from 2015-2019, we identified 569 patients with archival tissue samples representing active *Hp* infection (n=323) or *Hp* with gastric intestinal metaplasia (GIM) (n=146). Droplet digital PCR was used to detect the *cagA* gene.

Results: *Hp*+ Black patients were significantly more likely to be *cagA*-positive than *Hp*+ White patients (82% vs. 37%, $p < 0.0001$). Evidence of *cagA* was also more common in *Hp*+ GIM than in *Hp*+ without GIM (77% vs. 56%, $p < 0.0001$). Within disease groups, the difference by race remained: among patients with *Hp*+ GIM, *cagA* was identified in 87% of Black patients vs. 50% of White patients ($p < 0.0001$); among patients with *Hp*+ without GIM, *cagA* was identified in 79% of Black patients vs. 34% of White patients ($p < 0.0001$).

Conclusions: In a high-risk cohort undergoing endoscopy, *Hp*+ Black patients had a higher prevalence of the established cancer risk factor *cagA* than *Hp*+ White patients, and the presence of the *cagA* gene was associated with the premalignant condition of *Hp*+ GIM. These findings suggest that the differing presence of *cagA* among *Hp*+ individuals is a key driver of the racial disparities in gastric cancer.

M. Epplein: None. S.J. McCall: None. F. Wang: None. N.R. Salama: None. K.S. Garman: None.

P11.02

STATUS OF *HELICOBACTER PYLORI* AND THE LOCATION OF GASTRIC CANCER IN A POPULATION IN THE CENTRAL BRAZIL REGION

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Objective: *Helicobacter pylori* affects more than half of the world's population and represents the most important risk factor for the development of gastric adenocarcinoma (AdG). AdG is the fifth most incident neoplasm and the fourth in mortality in the world. Gastric cancer can be classified according to cardia and non-cardia region. The aim of this study was to evaluate the association of *H. pylori* infection status and gastric cancer location.

Material and Methods: This is a cross-sectional study nested within a hospital-based case-control, carried out in the Central Brazil region, from 2019-2023. Data were collected through medical records. Patients confirmed for AdG by histology (ICD-O-3, C16) were segregated according to *H. pylori* status. Variables were compared using Pearson's chi-square test with a significance level of 5%. The study was approved by the Ethics Committee (No. 3,174,666).

Results: Of the 33 individuals with AdG, 48.2% were positive for *H. pylori* infection. Among the positive patients, 75.0% were male, 56.2% were aged less than or equal to 60 years, 68.8% were married and 56.3% were non-white. Of these patients infected with *H. pylori*, 93.7% had cancer in the non-cardia region. On the other hand, 80.0% of patients negative for *H. pylori* had cancer in the non-cardia region. Although the bacterial infection was proportionally more prevalent in patients with non-cardia AdG, there was no significant difference.

Conclusions: It is concluded that there was no difference in the status of *H. pylori* infection and the location of gastric cancer in the Brazil-Central region.

A.F.P.L. Ramos: None. D.V. Minaré: None. A.L.S. Bizinoto: None. S.B. Santiago: None. L.M. Milhomem: None. L.T. Rasmussen: None. G.A. Fernandes: None. M.P. Curado: None. M.S. Barbosa: None. G.F. Lima: None.

P11.03

GENOME-WIDE METABOLIC PATHWAYS IN *HELICOBACTER PYLORI* POPULATIONS

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Objective: *Helicobacter pylori* is the only recognized bacterial carcinogen. The gene content of *H. pylori* is variable due to a rather restricted core genome. The genomic content of an organism is linked to biochemical processes. Our study aimed to characterize the metabolic pathways of *H. pylori*.

Materials and Methods: We reconstructed genome-wide metabolic pathways of 1,011 NCBI annotated genomes with ancestral assignments from the *H. pylori* Genome Project (HpGP) using our newly curated *H. pylori* 26,695 reference genome and SRI's Pathway Tools software.

Results: We reconstructed a total of 164 genome-wide metabolic pathways. The HpGP genomes had between 131 and 150 pathways, with a median of 144. One-hundred-and-nineteen pathways were present in ≥99% of the genomes, with only 65 present in all genomes. We assessed associations (presence vs. absence) of the remaining pathways with ancestry. Notably, as compared to other major populations, hspIndigenousAmerica showed an underrepresentation of metabolic pathways related to molybdenum and thiamine biosynthesis (p -values < 0.02). Ongoing analyses are examining potential differences in disease associations.

Conclusions: Our comprehensive and large-scale analysis of metabolic pathways shows evidence of genomic decay and provides insights into the pathophysiology of *H. pylori*. Detailed data on a subset of representative HpGP genomes and visualization of predicted metabolic networks, including metabolites, enzymes, reactions, pathways, predicted operons, transport systems, and pathway-hole fillers will be available at BioCyc.

P.D. Karp: None. V. Lam: None. S. Paley: None. K. Thorell: None. R. Caspi: None. P. Subhraveti: None. D. Wang: None. R.J. Roberts: None. P. Midford: None. M. Krummenacker: None. Z.Y. Muñoz-Ramirez: None. K. Yu: None. I. Kobayashi: B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Modest; Synplogen. J. Torres: None. J.P. Dekker: None. R. Torres: None. F.F. Vale: None. W. Fischer: None. L. Marino-Ramirez: None. M.C. Camargo: None.

P11.04

A MULTICENTRE SURVEY OF *HELICOBACTER PYLORI* ANTIMICROBIAL RESISTANCE IN IRELAND

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Objective: Antibiotic resistance is one of the main reasons for *Helicobacter pylori* (*H. pylori*) treatment failure. The Maastricht VI/Florence consensus report highlighted the importance for local resistance surveys in order to guide clinicians in their choice of therapy. The aim of the study was to assess the rates of primary and secondary antibiotic resistance for *H. pylori* in Ireland.

Materials and Methods: Following ethical approval and receipt of informed consent, *H. pylori* was cultured from corpus and antral biopsy samples of patients attending Tallaght University Hospital, Letterkenny University Hospital, Mayo University Hospital and St. James's Hospital. Antibiotic susceptibility testing was performed via E-test (Biomérieux) and resistance classified according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints.

Results: In total, 126 isolates were successfully cultured and antimicrobial susceptibility assessed. 103 of these were isolates of treatment-naïve patients (50±16 years old, 59% male) and 23 were of previously treated patients (48±12 years old, 61% female). Primary resistance rates for clarithromycin, metronidazole and levofloxacin were 37.9%, 44.7% and 21.4%, respectively. Secondary resistance rates for clarithromycin, metronidazole and levofloxacin were 65.2%, 73.9% and 30.4%, respectively.

Conclusions: Antibiotic resistance rates have reached significant levels for all major classes of antibiotics for the treatment of *H. pylori* and reach nearly double the rate of resistance in the previously treated group. Of note, first-line clarithromycin triple therapy can no longer be recommended in Ireland.

T.J. Butler: None. S. Molloy: None. C. Costigan: None. K. Van der Merwe: None. V. Parihar: None. S. Semenov: None. S. Hough: None. D. Kevans: None. D. Tighe: None. D. McNamara: None. S. Smith: None.

P11.05

PROTEIN-LIGAND DOCKING AND IN VITRO SCREENING AS A TOOL TO IDENTIFY LEAD HIT COMPOUNDS TARGETING THE KEY SURVIVAL PURINE NUCLEOSIDE PHOSPHORYLASE (PNP) ENZYME OF *HELICOBACTER PYLORI*

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Objective: Resistance to many of the antibiotics used to treat *Helicobacter pylori* (HP) infection is on the rise. Indeed, the WHO has included *H. pylori* on their priority list of antibiotic-resistant bacteria to guide research and development into novel antimicrobials. To this end, protein-ligand docking of 550k+ compounds was carried out against the purine nucleoside phosphorylase enzyme (PNP), a key survival enzyme of HP. The aims of the study were: (i) to perform *in silico* docking to identify compounds with potential activity against HP *via* PNP enzyme inhibition, (ii) and to test the *in vitro* antimicrobial and cytotoxicity activity of the compounds.

Materials and Methods: The binding site of the PNP enzyme was computationally analysed and a library of compounds was virtually screened *via* protein ligand docking to identify several lead-hits to carry forward to *in vitro* screening. Lead-hits were tested for antimicrobial efficacy against reference strains (J99 and ATCC60190) and clinical isolates of HP using a broth microdilution approach. Selectivity was established using a viability assay with a stomach epithelial cell line AGS.

Results: Lead-hits were selected from protein-ligand docking results and tested *in vitro*. All compounds showed antimicrobial activity against the reference strains and both clarithromycin-sensitive and clarithromycin-resistant clinical isolates of HP (MIC 4.34-73 µg/mL). 2 compounds showed significant selectivity against human cells, having no activity on the viability of human gastric cells.

Conclusions: Protein-ligand docking provided a cost-efficient method to identify selective antimicrobial agents for *H. pylori* resulting in the identification of several lead targets that may be further developed to increase selectivity and potency.

T.J. Butler: None. S. Smith: None.

P11.06

CAGY A PROTEIN REGULATING CAG PATHOGENICITY ISLAND HAS EVOLVED TO MIRROR HUMAN POPULATIONS AND REARRANGEMENTS IN THE GENE MAY BE ASSOCIATED WITH DISEASE

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Objective: *Helicobacter pylori* (*Hp*) strains with the Cag pathogenicity island interact strongly with the gastric mucosa increasing the risk for uncontrolled inflammation. CagY is a key regulatory protein that modulates inflammation turning on/off the function of cagPAI by a still unknown mechanism. Recombination in a large, highly repetitive middle region (RMR) of *cagY* gene may be partially responsible for the switching activity. Sequencing this large repetitive region has been challenging, and the strong population structure effect makes it more difficult to identify the function-associated patterns.

Materials and Methods: We analyzed 687 *cagY* sequences identified using NCBI annotations, a subgroup of samples from the *Helicobacter pylori* genome Project sequenced by SMRT/PacBio. Several bioinformatic approaches were used to study and classify the gene, including virtual hybridization using 8mer probes (VAMPhyRE V1.3) for phylogenetic analysis, dimensional reduction algorithms and machine Learning models, (with Scikit-learn library) for genetic and structure classification.

Results: Phylogenetic analyses of the *cagY* gene and the RMR region showed a population structure that markedly followed phylogenetic results with the core-genome. Analyses of the global hybridization table with random forest and linear discrimination analyses for *cagY* gene showed a significant separation of the 13 subpopulations previously reported, whereas with RMR region Asian and African populations markedly separated from European and American subpopulations. The possible association of recombining RMR in switching cagPAI and in risk for disease is currently under study.

Conclusions: *cagY* and its RMR region have evolved to mirror human populations and the frequent recombination in RMR may be associated with disease.

J. Torres: None. M.A. Lopez-Luis: None. R. Torres-Lopez: None. A. Mendez-Tenorio: None. D. Wang: None.

P11.07

AUTOPHAGY INFLUENCES INFLAMMATION IN *HELICOBACTER PYLORI*-RELATED GASTRIC CARCINOGENESIS

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Autophagy, an intracellular degradative pathway, has dynamic roles in the host innate immune response, including inflammation and tumour suppression. Autophagy can also be directed against invasive pathogens, such as *Helicobacter pylori*, the leading cause of gastric cancer (GC). The germline mutation *ATG16L1* rs2241880 (A > G; Thr300Ala) leads to a loss of function-like phenotype, causing a defect in the physiological process of autophagy. We have previously shown rs2241880 to significantly influence the risk of gastric carcinogenesis in Han Chinese, Australian Caucasians, and Dutch.

We now aimed at identifying the underlying mechanisms by which this genetic variant impacts GC development. Using CRISPR/Cas9, knock-in *ATG16L1* rs2241880 AGS cell lines were generated (AA, AG, GG). Edited and non-edited cells were challenged with *H. pylori* GCO26 (*vacA+* *s1m1*, *cagA+*) where the inflammatory and autophagic responses were evaluated. *Ex vivo* assessment of systemic inflammatory responses associated with *ATG16L1* rs2241880, was performed using a multiplex ELISA and sera from *H. pylori*-infected functional dyspepsia patients. *ATG16L1* rs2241880 GG-carrying gastric epithelial cells demonstrated an exacerbated IL-8 inflammatory response, with a reduced TNF- α and IFN- β expression signature. Turnover of autophagy was also demonstrated to be disrupted in these cells, which was found to be further impeded by infection with *H. pylori*. Patients carrying the GG genotype demonstrated increased systemic IL-8 levels. *ATG16L1* rs2241880 GG carriage elicits an abnormal inflammatory response to *H. pylori* infection in gastric epithelial cells, coupled with a defective autophagic response, these factors could lead to persistent infection and chronic inflammation, and subsequently, GC development.

I. Simovic: None. G.L. Porras-Hurtado: None. A.R. Cobo-Alvarado: None. J.L. Cardona-Deazza: None. O. del Socorro Hincapié-Rincón: None. N.O. Kaakoush: None. N. Castano Rodriguez: None.

P11.08

THE ACCURACY OF A NEW ¹³C UREA BREATH TEST MEAL (REFEX) FOR PATIENTS WITH DYSPEPSIA AND GERD TAKING PROTON PUMP INHIBITORS

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Objective: Regular proton pump inhibitor (PPI) use decrease the sensitivity of urea breath tests (UBT) to diagnose *Helicobacter pylori*. We have performed two independent clinical studies according to requirement of EMA to determine the efficacy of a specially formulated test meal (Refex, containing a mixture of organic acids) in improving the sensitivity and specificity of the breath test in patients taking proton pump inhibitors (PPI; study 1: EudraCT-Nr.: 2008-008010-39 and study 2 EudraCT-Number: 2017-001369-25).

Patients and Methods: In first study 111 and second study 121 patients with dyspepsia and GERD were included (ITT). In first study 53 patients Hp positive and 45 Hp negative patients and in second study 54 Hp positive and 56 patients Hp negative have been analyzed by per protocol (PP). Patients were given Nexium® (AstraZeneca), 40 mg every day for 29 days. After 1-day break of PPI the new breath test was performed.

Results: The sensitivity and specificity of the ¹³C-UBT showed in the table for the PP population using a cutoff point of 2.5 ‰ and 1 day break of PPI.

Conclusions: This is the first ¹³C-UBT that can be used in patients regardless of PPI intake with high sensitivity, specificity only after 1-day break of PPI. New publication is in progress.

B. Tepes, P. Malfertheiner, S. Aygen, et.al. World Journal of Gastroenterology 23(32):5954, 2017
S. Aygen: None. B. Tepes: None. A. Canbay: None.

TABLE 1. THE SENSITIVITY AND SPECIFICITY OF NEW ¹³C-UBT TEST.

	1. study	2. study
Sensitivity	92.45 %	93.10 %
Specificity	97.96 %	98.25 %
Accuracy	95.10 %	95.65 %

P11.09

GEOGRAPHIC VARIATION IN *HELICOBACTER PYLORI* VACA SEQUENCES: AMPLIFICATION OF VACA COPY NUMBER AND LOSS OF INTACT ORFS THROUGH MULTIPLE MECHANISMS

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Objective: *Helicobacter pylori vacA* encodes a secreted protein that causes alterations in host cells. All *H. pylori* strains contain a *vacA* gene, but *vacA* is absent from most other *Helicobacter* species. In this study, we analyzed *vacA* genetic variation in a global collection of *H. pylori* isolates, and we assessed evolutionary relationships among *vacA* sequences from *H. pylori*, *H. ceterorum*, and *H. acinonychis*.

Materials and Methods: We analyzed *vacA* sequences in 1,012 strains with ancestral assignments from the *Helicobacter pylori* Genome Project, two published *H. ceterorum vacA* sequences, and three *H. acinonychis vacA* pseudogenes.

Results: Three combinations of s- and m-region genotypes were detected, and these were associated with strain ancestry. We detected disrupted *vacA* ORFs in 224 (22%) of the strains, most commonly resulting from indels (n=154) or nonsense mutations (n=50). Among the 788 samples with complete ORFs, we identified 15 (2%) strains with more than one copy of *vacA*. Notably, ten of these were strains classified as hspIndigenousAmerica, each containing three copies. Phylogenetic analyses revealed three main clades of *vacA* sequences. *H. ceterorum* and *H. acinonychis vacA* sequences clustered with *H. pylori* sequences classified as m2 and were most closely related to the duplicated hspIndigenousAmerica *vacA* alleles.

Conclusions: Disrupted *vacA* ORFs and *vacA* gene duplications are present in a higher proportion of *H. pylori* strains than previously recognized. Phylogenetic analyses reveal previously unrecognized relationships among *vacA* genes from different *Helicobacter* species.

P. Gonzalez-Hormazabal: None. S. Sandoval-Motta: None. Z. Munoz-Ramirez: None. J. Torres: None. K. Thorell: None. I. Kobayashi: B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Modest; Synplogen. C.S. Rabkin: None. D. Wang: None. M. Camargo: None. T.L. Cover: None.

P11.10

HELICOBACTER PYLORI PLASMID DETECTION AND ASSEMBLY: MAJOR CHALLENGES

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Objective: Many *Helicobacter pylori* strains carry plasmids of different size and gene content. Study of their sequence and function is essential to understanding mechanisms of genetic diversity in the *H. pylori* population. While *H. pylori* chromosomes are routinely assembled into single contigs from PacBio long-read sequence data, assembly of plasmid contigs from the same data is challenging; different assembly tools often generate different results for number and size of plasmids in the assembly. Adjusting assembly parameters to address this challenge can be a time-consuming, iterative process for each individual sample.

Material and Methods: Here, we present the results of a screening assay for detecting plasmids in *H. pylori* samples from the *Helicobacter pylori* Genome Project using exonuclease V. The assay relies on the enzyme's ability to digest linear DNA while keeping circular DNA intact. After treating genomic DNA samples, the intact circular DNAs, primarily plasmids, are assessed using capillary electrophoresis.

Results: *H. pylori* samples with plasmids can be routinely differentiated from *H. pylori* samples without plasmids using an inexpensive, high-throughput assay.

Conclusions: Exonuclease V can be used effectively to screen for the presence of plasmids in *H. pylori* samples, and determine which samples merit additional time and effort spent on genome assembly to ensure the final assembled genome reflects the DNA that was sequenced, including plasmids if they are present in the strain's DNA sample.

K. Jones: None. W. Luo: None. K. Teshome: None. D. Wang: None. J. Cherry: None.

P11.11

HELICOBACTER PYLORI INFECTION INDUCES MMP-3 AND MMP-9 EXPRESSION VIA MAPK PATHWAYS

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Helicobacter pylori-associated gastric disease involves extracellular matrix remodelling mediated by aberrant activity of matrix metalloproteinases (MMPs). We have previously reported that MMP-3 and MMP-9 are overexpressed during *in vitro* *H. pylori* infection, dependent on the phosphorylation of bacterial oncoprotein CagA. These findings were extended in an *in vivo* model of *H. pylori* infection, whereupon C57BL/6 mice were inoculated with bacterial strains HPARE, HPARE-ΔCagA and SS1. Transcriptional expression of *Mmp-3* and *Mmp-9* was evaluated via qPCR while respective protein levels in the gastric mucosa were determined immunohistochemically 6 and 9 months post-infection. We observed aberrant overexpression of MMP-3 and MMP-9 at the transcriptional and protein levels, while CagA expression was associated with MMP upregulation, during early infection. We further assessed the involvement of MAPK pathways in MMP expression during P12 *H. pylori* infection of AGS and GES-1 cell lines, in the presence of chemical inhibitors of JNK, ERK1/2 and p38 pathways. Inhibition of ERK1/2 during *H. pylori* infection abrogated MMP-3 and MMP-9 mRNA expression and halved respective protein expression in both cell lines. Upon JNK pathway inhibition in AGS cells, MMP-3 and MMP-9 mRNA

levels were found increased 5- and 3-fold respectively, possibly due to a deleterious G12D mutation in KRAS gene, resulting in constitutive ERK1/2 activation, while in GES-1 cells, mRNA and protein levels exhibited over 3-fold reduction, underlying a different response of the two cell lines. A similar, yet much less pronounced effect was observed upon p38 inhibition, possibly due to crosstalk between MAPK pathways and phospho-p38 accumulation.

I. Karayiannis: None. B. Martinez-Gonzalez: None. E. Kontizas: None. A. Voulgari Kokkota: None. K. Petraki: None. A. Mentis: None. P. Kollia: None. D.N. Sgouras: None.

P11.12

HELICOBACTER PYLORI INFECTION, PEPSINOGENS, AND SERUM GHRELIN CONCENTRATIONS FOR THE ASSESSMENT OF GASTRIC PATHOLOGY

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Objective: Gastric pathology biomarkers have been focus of research in recent years. Serum pepsinogens were associated with the topography of gastric pathology while serum ghrelin was described lower in *Helicobacter pylori* infected patients. The objective of this study was to assess serum ghrelin and pepsinogens according to *H. pylori* infection and type of gastric pathology.

Material and Methods: We included dyspeptic adults (18-70y) referred for an upper gastrointestinal endoscopy to the Hospital de Gastroenterología “Dr. Carlos Bonorino Udaondo”. Histopathology and *H. pylori* diagnosis were evaluated from gastric biopsies. Serum ghrelin concentration, pepsinogen I (PGI) and pepsinogen II (PGII) were measured by ELISA. Kruskal-Wallis and Mann-Whitney tests were applied.

Results: Thirty-five individuals (40.2±13.0y) were enrolled to date, 77.1% female. *H. pylori* prevalence was 71.4% (CI95%; 54.9-83.7%). PGI and PGII were significantly higher for *H. pylori* infected compared to uninfected volunteers (PGI: 48.1 [36.3-65.6] ng/mL vs. 25.7 [21.7-49.6] ng/mL, $p=0.014$; PGII: 4.2 [2.7-8.5] ng/mL vs. 2.0 [2.0-2.1] ng/mL, $p=0.0001$); however, PGI/PGII ratio did not differ between groups ($p=0.14$). Although serum ghrelin was not different according to *H. pylori* presence ($p=0.43$), previous results from our group in a larger population showed lower ghrelin levels in infected subjects. Serum PGII differed significantly between normal mucosa, chronic inactive and active gastritis of the antrum and corpus ($p=0.003$ and $p=0.049$), being higher in the presence of gastric pathology.

Conclusions: According to these preliminary results, *H. pylori* diagnosis, pepsinogens, and serum ghrelin concentrations might be useful as potential gastric pathology biomarkers.

P. Mantero: None. G. Cernadas: None. C. Giacomantone: None. A.M. Cabanne: None. J. Lasa: None. L. Marchesi Olid: None. M.B. Zubillaga: None. M.A. Janjetic: None. C.G. Goldman: None.

P11.13

CLINICAL COURSE AND OUTCOME OF PATIENTS WITH DRUG ALLERGY RELATED TO *HELICOBACTER PYLORI* ERADICATION

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Objective: Drug allergy is one of the most crucial adverse events that lead to discontinuation of eradication therapy. The aims of this study were to determine the clinical course and result of patients who had a history of drug allergy before *H. pylori* eradication or development of drug allergy after *H. pylori* eradication, and were referred to allergy clinic.

Patients and Methods: A total of 1,823 patients were treated for *H. pylori* infection between January 2018 and June 2022. Among them, 14 patients had a history of drug allergy before *H. pylori* eradication or developed drug allergy after *H. pylori* eradication, and were referred to allergists. All available demographic and clinical data including allergic tests were collected through review of patient files.

Results: Of 14 patients, patch test, skin test, specific IgE, and provocation test, 3 (21.4%), 8 (57.1%), 0 (0.0%), and 5(35.7%) patients were positive, respectively. Amoxicillin (28.6%) was the most common allergic drug, followed by tetracycline, clarithromycin, lansoprazole, bismuth, and probiotics. Five (35.7%) patients refused eradication; however, 9 (64.3%) patients received. One (11.1%) stopped due to drug allergy, and 8 (88.9%) were successfully eradicated based on allergic test results.

Conclusions: Although the number of patients was small, most of the patients who had undergone *H. pylori* eradication based on the results of allergic test succeeded in eradication therapy. Therefore, cooperation with the allergists may be necessary to manage adverse effects and implement successful eradication in patients who had a drug allergy history or developed drug allergy connected with *H. pylori* eradication therapy.

S. Kim: None. S. Park: None. M. Park: None. W. Moon: None. J. Kim: None. K. Jung: None. G. Choi: None.

P11.14

ISOLATION AND CHARACTERIZATION OF *HELICOBACTER* SPECIES AND IDENTIFICATION OF TWO NOVEL *HELICOBACTER SPP.* IN MARINE MAMMALS

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Objective: Gastrointestinal lesions with uncertain etiology have been widely described among marine mammals. *H. cetorum* and *H. enhydrae* have been linked to gastric diseases of dolphins, whales, sea otters as well as South American fur seals. In this study, we summarized *Helicobacter* isolation in five marine mammal species over the last 20 years and named two additional novel *Helicobacter spp.*

Materials and Methods: Tissue samples from stomachs and intestines, gastric fluid and feces were collected from Beluga whales, Atlantic white-sided dolphins and Pacific white-sided dolphins, southern sea otters, harp seals, elephant seals and California sea lions. Samples were subjected to microaerobic culture on blood agar or antibiotic-selective agar plates. *Helicobacter* isolates were subjected to biochemical characterization, 16S rRNA gene and whole genomic sequence analyses for taxonomical identification.

Results: *Helicobacter cetorum* was isolated from 1/6 Beluga whales and 13/ 60 dolphins. *Helicobacter enhydrae* was isolated from 6/23 sea otters. Two novel *Helicobacter* species were identified from the stomach and feces of harp seals and sea lions respectively by biochemical characterization and whole genome sequence analyses. *Helicobacter phocae* was isolated from 1/25 harp seals and 4/54 sea lions; it is most closely related to *H. bilis*. *Helicobacter zalophi* was isolated from 1/25 harps seal and 6/54 sea lions and is most closely related to *H. canis*.

Conclusions: *Helicobacter spp.* commonly colonize marine mammals. Characterization of novel *Helicobacter* species will assist in a more comprehensive understanding of the roles of *Helicobacter* species in the microbiota of marine mammals and their relationship to gastrointestinal diseases.

Z. Shen: None. S. Xu: None. C.G. Harper: None. J. Hurley: None. J.G. Fox: None.

P11.15

CULTURE-BASED ANTIMICROBIAL RESISTANCE OF *HELICOBACTER PYLORI* IN BUSAN, SOUTH KOREA

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Objective: *Helicobacter pylori* (*H. pylori*) eradication is important to improve public health; however, the eradication rate of *H. pylori* has declined continuously. Antimicrobial resistance is the main reason for *H. pylori* eradication failure. The aim of this study was to estimate antibiotic resistance rates of *H. pylori* based on culture and antibiotic susceptibility test.

Patients and Methods: Between April 2017 and August 2019, *H. pylori* was cultured in a total of 63 patients. A minimal inhibitory concentration test was performed for clarithromycin, metronidazole, tetracycline, levofloxacin, moxifloxacin, amoxicillin, and rifabutin using the agar dilution method. All available demographic and clinical data were collected through review of patient files.

Results: Seventeen patients (27.0%) had failed two or more *H. pylori* eradication regimens. Antibiotic resistances were 42.9% (27 out of 63) to clarithromycin; 63.5% (40/63) to metronidazole; 30.2% (19/63) to tetracycline; 71.4% (45/63) to levofloxacin; 58.1% to moxifloxacin (36/62); 25.4% (16/63) to amoxicillin; and 7.0% (4/57) to rifabutin. Multi-drug resistance rate was 87.3% (56/63). Among them, 2, 3, 4, 5, and 6 antibiotic-resistant *H. pylori* profile were 18 (28.6%), 16 (25.4%), 11 (17.5%), 9 (14.3%), and 2 (3.2%) patients, respectively.

Conclusions: Although some patients who failed eradication therapy several times were included, the antibiotic resistance rate of *H. pylori* was high, and in particular, the rate of *H. pylori* with multidrug resistance was high. Therefore, patients who have failed two or more eradication therapy may need tailored therapy through antibiotic susceptibility testing.

S. Kim: None. S. Park: None. M. Park: None. W. Moon: None. J. Kim: None. K. Jung: None. H. Bae: None.

POSTER SESSION 12: HELICOBACTER 9

P12.01

EPIDEMIOLOGICAL STUDY OF THE *HELICOBACTER PYLORI* PREVALENCE IN MOSCOW: FIRST RESULTS

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Objective: Russia is a country with the high prevalence of *H. pylori*. The data on the prevalence of infection *H. pylori* in Moscow is still limited. The aim of the study was to evaluate the prevalence of *H. pylori* infection in the population of Moscow, Russian Federation.

Materials and Methods: We enrolled 1650 residents of Moscow aged from 18 to 80, of which 465 (28%) were male, (mean age 43±15), 1185 (72%) were female (mean age 46±15). All respondents underwent ¹³C-urease breath test (UBT). We evaluated the overall prevalence of infection in the population, by age groups and by sex.

Results: The average prevalence of *H. pylori* was 38.18%. The prevalence of infection increased with age: from 18 to 25 – 25.74%, from 26 to 35 years – 30.66%, from 36 to 45 years – 42.02%, from 45 to 55 – 44.13%, 56-65 years – 43.59%, older than 65-34.34%. The maximum prevalence was noted in the age group of 45-55 years followed by a decrease in the age group older than 65 years ($\chi^2=6.635$; $p<0.01$). *H. pylori* was found in 37% of women and in 39.8% of men. Women in the age group of 45-55 years showed the highest prevalence of all age groups in women (41.15%), while men in the same age group demonstrated the infection in 53.08%. No significant gender difference was revealed in this group ($\chi^2=3.509$; $p=0.062$).

Conclusions: The prevalence of *H. pylori* in Moscow averages 38.18%. The highest prevalence was observed in men and women aged 45-55 years.

D. Bordin: B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; “Moscow Center for Innovative Technologies in Healthcare” administered by the Moscow Healthcare Department. **I. Voynovan:** B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; “Moscow Center for Innovative Technologies in Healthcare” administered by the Moscow Healthcare Department. **K. Nikolskaya:** B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; “Moscow Center for Innovative Technologies in Healthcare” administered by the Moscow Healthcare Department. **M. Chebotareva:** B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; “Moscow Center for Innovative Technologies in Healthcare” administered by the Moscow Healthcare Department. **I. Khatkov:** B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; “Moscow Center for Innovative Technologies in Healthcare” administered by the Moscow Healthcare Department

P12.02

SPECIES CLASSIFICATION OF ENTEROHEPATIC *HELICOBACTER* SPECIES ISOLATED FROM OLD WORLD NON-HUMAN PRIMATES

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Objective: Enterohepatic *Helicobacter* species (EHS) preferentially colonize the gastrointestinal and hepatobiliary system of humans and animals. *H. macacae* and *H. cinaedi* have been associated with colitis and intestinal adenocarcinoma in Old World primates (OWPs). In this study, we isolated and characterized known and novel EHS in OWPs.

Materials and Methods: Feces, intestines and liver tissues were collected from 112 OWPs including rhesus, cynomolgus and baboons. Microaerobic culture on blood agar or antibiotic-selective agar plates were performed. *Helicobacter* isolates were subjected to biochemical testing. 16S rRNA, heat shock protein 60 gene, and whole genomic sequence (WGS) analyses were conducted.

Results: Seventy-four *Helicobacter* strains were isolated from 108 rhesus representing seven *Helicobacter* species: *H. macacae*, *H. bilis*, *H. cinaedi*, novel *Helicobacter* species Monkey Taxon 2, Taxon 3, Taxon 4, and Taxon 5. *H. bilis* and *H. sp* Monkey Taxon 4 were identified in cynomolgus. *H. macacae* and *H. cinaedi* were isolated from baboon liver and intestinal sample by 16S gene analysis. WGS analysis supported that Taxons 2 and 3 were different novel species, while Taxons 4 and 5 were the same novel species. Virulence factor genes for flagella, high-temperature requirement A protein-secreted serine protease (*htrA*), neutrophil activating protein (*napA*), and putative fibronectin domain-containing lipoprotein (*flpA*) were present in each novel taxon. Taxon 4 and 5 harbored genes for *Campylobacter* invasion antigen B (*ciaB*) and cytolethal distending toxin subunits (*cdtABC*).

Conclusions: Multiple *Helicobacter* spp. colonize the gastrointestinal tract and liver of OWPs. Identification and classification of novel EHS in non-human primates will provide further understanding of *Helicobacter* spp. involvement in gastrointestinal diseases.

Z. Shen: None. **S. Xu:** None. **A. Mannion:** None. **R.P. Marini:** None. **J.G. Fox:** None.

P12.03

ENTEROHEPATIC *HELICOBACTER* SPECIES ISOLATED FROM NEW WORLD NON-HUMAN PRIMATES AND LEMURS

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Objective: New World primates (NWP) and lemurs have been widely used in biomedical research. Gastrointestinal diseases have been reported in NWP. Enterohepatic *Helicobacter* species (EHS) have been linked to inflammatory bowel diseases and cholecystitis in tamarins and marmosets. In this study, we screened for *Helicobacter* species in NWP and lemurs in order to identify and classify novel *Helicobacter* species in this population.

Materials and Methods: Feces, intestines and liver tissues collected from cotton-top tamarins, gold lion tamarin, common marmosets, Goeldi's marmosets, squirrel monkeys, spider monkeys and feces from lemurs were subjected to microaerobic culture. *Helicobacter* isolates were subjected to biochemical testing; 16S rRNA, heat shock protein 60 and *rpoB* genes were used for sequence analyses and taxonomical identification.

Results: *H.saguini* was isolated from 19/91 cotton-top tamarin. *H.jaachi* was isolated from 22/82 common marmosets, *H.cinaedi* was isolated from 4/4 spider monkeys; *H.sp* closely related to *H.saguini* was isolated from 1/4 Goeldi marmosets; novel *H.sp* closely related to *H.didelphidarum* was isolated from one squirrel monkey; novel *H.sp* closely related to *H.canadensis* was isolated from one gold lion tamarin. Eight strains belong to three *Helicobacter* species were isolated from different species of lemurs including 5 strains of *H.sp* monkey Taxon 5; 2 strains of *H.sp* monkey taxon 2 and a novel *H.sp* were closely related to *H.pullorum*.

Conclusions: EHS are commonly present in the gastric intestinal tracts of NWP and lemurs, Further identification and classification of novel EHS isolated from non-human primates will provide better understanding of the taxonomy and epidemiology of *Helicobacter*.

Z. Shen: None. S. Xu: None. J. Cullen: None. J.G. Fox: None.

P12.04

AZOBENZENESULFONAMIDES AS SELECTIVE CARBONIC ANHYDRASE INHIBITORS: AN INNOVATIVE STRATEGY AGAINST *H. PYLORI* INFECTION

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Objective: *Helicobacter pylori* has been indicated by the World Health Organization as a high priority pathogen due to the decrease of efficacious strategies available for its eradication. The failure of antimicrobial therapies can be related to both its genetic variability and the ability to develop biofilm, therefore, the identification of novel anti-*H. pylori* strategies is essential. In this study twenty new azobenzenesulfonamides were synthesized to inhibit *H. pylori* growth by interacting with innovative targets such as carbonic anhydrases. The in vitro enzyme inhibitory activity of such molecules was in the nanomolar range.

Materials and Methods: The Minimum Inhibitory Concentration was determined via the broth microdilution method and confirmed through alamarBlue assay. The Minimum Bactericidal Concentration was determined via the Colony Forming Units count. The most active compounds were then chosen to evaluate their toxicity using an *in vivo* animal model such as *Galleria mellonella*. Each larva received 10 µL of the tested compound and was monitored for 4 days to score mortality.

Results: The tested compounds showed a different activity profile with MIC values ranging from 4 to 64 µg/mL. Four compounds showed good activity with a MIC and MBC ranging between 4-8 µg/mL and 4-16 µg/mL respectively. The *in vivo* toxicity assay demonstrated that the molecules are non-toxic.

Conclusions: The data obtained in this study proved that these compounds can represent a novel approach to counteract *H. pylori* infections. However, further studies concerning pharmacokinetics and pharmacodynamics will be needed for a possible future application in the medical field.

B. Marinacci: None. F. Melfi: None. S. Francati: None. R. Grande: None. L. Giampietro: None.

P12.05

GENOMIC DETERMINANTS OF ANTIBIOTIC RESISTANCE IN *HELICOBACTER PYLORI* TREATMENT AND SURVEILLANCE

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Objective: 20-30% of *Helicobacter pylori*-positive patients fail in eradication therapy due to *de novo* acquisition of drug resistance during treatment and increased prevalence of drug-resistant strains. Genomic-based susceptibility testing allows the identification of drug resistance-associated mutations, complementing conventional diagnostics and advancing towards pathogen-based personalized treatments.

Materials and Methods: We built a curated catalogue of mutations conferring resistance to levofloxacin (*gyrA* N87K/I, A88V/P, D91G/N/Y and N97K) and clarithromycin (23S*rDNA* A2142G/C and A2143G) from the literature and applied it to 1,011 samples from the *Helicobacter pylori* Genome Project (*HpGP*). We phenotyped a subset of *HpGP* strains for clarithromycin (n=328) and levofloxacin (n=333) in a centralized laboratory using E-test and assessed genotype-phenotype concordance. We performed a genome-wide association study (GWAS) based on 20-mers and unitigs to identify novel antibiotic resistance-associated regions. We also calculated region-specific prevalence estimates of resistance by combining *HpGP* genomes with 810 NCBI publicly available whole-genome sequences.

Results: All clarithromycin and levofloxacin-resistant *HpGP* samples were predicted with 100% sensitivity and specificity. In agreement, the GWAS did not find novel regions associated with antimicrobial resistance. Our combined analysis (n=1,821) found a high clarithromycin resistance in the Western Pacific (61%) and the European (21%) regions, and a high levofloxacin resistance in the Americas (34%) and the Western Pacific regions (32%).

Conclusions: Point mutations accurately predict resistance to clarithromycin and levofloxacin. This information is relevant for assay development and molecular surveillance. Our findings suggest that the empirical use of clarithromycin and levofloxacin without susceptibility testing may not be appropriate in some geographic regions.

F.J. Martínez-Martínez: None. Á. Chiner-Oms: None. V. Furió: None. Y. Yamaoka: None. J.P. Dekker: None. F. Mégraud: None. M.C. Camargo: None. I. Comas: None. P. Lehours: None.

P12.06

A WHOLE GENOME SEQUENCING FOR SEARCHING GENETIC DETERMINANTS OF CLARITHROMYCIN RESISTANCE IN RUSSIAN *HELICOBACTER PYLORI* CLINICAL ISOLATES

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It is generally accepted that clarithromycin resistance in *H. pylori* is associated with point mutations A2146G/C and A2147G in the 23S*rRNA* gene. The efflux pump clusters are also may be involved in the development of resistance to clarithromycin. In this study, we aimed to detect point mutations in the 23S*rRNA* gene and four efflux pump clusters hp0605-hp0607, hp0971-hp0969, hp1327-hp1329, hp1489-hp1487 in *H. pylori* clinical isolates and assess the correlation with phenotypic drug susceptibility testing (pDST). The total genomic DNA of 44 *H. pylori* strains was extracted using the QIAamp DNA (QIAGEN, Germany) and WGS performed using the

DNBSEQ-G50 (MGI,China). pDST to clarithromycin of the *H. pylori* cultures was assessed by using conventional disc diffusion method according to CLSI. The filtered reads (quality of bases >Q30) were aligned to the reference genome of *H. pylori* 26695 (NC_000915). Of the 44 *H. pylori* strains, 23 showed clarithromycin-susceptible (CLR-S) and 21 – clarithromycin-resistant (CLR-R) phenotypes. Totally, 37 single nucleotide polymorphisms (SNPs) in the full-length 23SrRNA gene were revealed, however, only one mutation – A2147G – was significantly associated with pDST ($p=0.0001$). Of the 21 CLR-R strains, 14.3% (3/21) and 57.1% (12/21) carried the 2146G and 2147G variants. All CLR-S strains (23/23, 100%) possessed the A2146 allele, 95.7% (22/23) had the A2147 allele. All 2147G strains possessed A2146 allele, while all 2146G strains possessed A2147 allele. Among four efflux pump clusters we detected five non-synonymous SNPs – A2524G (hp0607) ($p>0.05$), C2060T (hp0969) ($p=0.04$), C745T/A746T (hp1328) ($p>0.05$), A2295T (hp1329) ($p>0.05$) presented only in CLR-R strains.

D. Starkova: None. D. Polev: None. N. Gladyshev: None. A. Svarval: None.

P12.07

THE PREVALENCE OF *HELICOBACTER PYLORI* INFECTION IN THE SLOVENIAN SOUTHEAST REGION USING TWO STOOL ANTIGEN TESTS

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Objective: Stool antigen testing (SAT) is one of the most important noninvasive methods for the diagnosis of *Helicobacter pylori* infection. The aim of this study was to determine the prevalence of infection in adults from the Slovenian Southeast region using two monoclonal SAT.

Materials and Methods: $n=47$ nonselected, treatment-naive subjects [mean age 44 years (27-62), 64% ($n=28$) women], 30% ($n=14$) with dyspeptic symptoms, 4% ($n=2$) had received proton pump inhibitors before testing. Automated LIAISON Meridian *H. pylori* SA chemiluminescence immunoassay Chemiluminescence Immunoassay (CLIA) (DiaSorin, Italy) and manual immunochromatographic *H. pylori* Antigen Rapid Test Cassette Beright (ICT) (Hanzho Alltest Biotech, China) were used. Serology (VIDAS *H. pylori* IgG, bioMérieux, France) was performed for discrepant results.

Results: The prevalence determined by CLIA and ICT SAT was 43% (95%CI: 28-58%) and 32% (19-47%), respectively. 5 subjects had discordant results (11%), all positive by CLIA, 4 weakly positive (index < 2.5; 1.33, 1.47, 2.37, 2.42), and 1 strongly positive (index > 45; 45.8). On serology (reference), 3/5 of them were confirmed positive. The sensitivity/specificity of CLIA and ICT SAT were 100%/93% and 83%/100%, respectively. The prevalence was estimated to be 38% (25-54%).

Conclusions: The high prevalence of *H. pylori* infection was detected in the Slovenian Southeast region using two different SATs. The CLIA had higher sensitivity (100%) than the ICT (83%). Caution is warranted when the test-and-treat strategy is based only on the SAT result. Continuous validation and quality assurance of diagnostic methods is warranted. This is particularly important in the case of manual ICT SAT.

B. Sodec: None. T. Grubar Kovačič: None. A. Slobodnik Kavčič: None. B. Radovan: None. N. Klobučar: None. A. Simonič: None. A. Retelj: None. N. Omahen: None. S. Jeverica: None.

P12.08

CLARITHROMYCIN PRIMARY RESISTANCE IN THE SLOVENIAN COASTAL REGION DETERMINED BY PCR AND CULTURE-BASED METHODS, 2022-2023

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Objective: Maastricht VI guidelines recommend clarithromycin susceptibility-guided therapy using molecular or culture-based methods if available. In Slovenia, this approach is rare in adults due to the fact that local guidelines mandate susceptibility testing after the second treatment failure. In 2009 and 2018, primary resistance to clarithromycin in Slovenia was 20% and 16%, respectively. Here, we aimed to test primary resistance to clarithromycin in a Slovenian coastal region.

Materials and Methods: Consecutive treatment-naïve patients were included between September 2022 and March 2023. Two gastric biopsies (antrum and corpus) were collected for PCR and culture. The Allplex H. pylori & ClariR assay (Seegene, South Korea), which detects *H. pylori* and the three major mutations A2142G, A2143G, and A2142C, was used for PCR and Etest (bioMérieux) for clarithromycin MIC.

Results: n=42 patients, mean age 58 years (33-82 years), 50% (n=21) women, tested positive for *H. pylori* by either PCR or culture and were used for primary resistance determination. Clarithromycin resistance was detected in 5 patients (12%, 95% CI 4-26%), in 4 by PCR (3x A2143G and 1x A2142G) and in 1 by culture [clarithromycin MIC of 8 mg/L (=resistant), no mutations detected by PCR].

Conclusions: Lower than expected primary clarithromycin resistance (12%) was detected in a Slovenian Coastal region, but with a wide confidence interval (4-26%). PCR from gastric biopsy accurately detected infection and clarithromycin resistance and can be used for systematic monitoring of primary resistance. Additional resistance determinants should be included in molecular tests to cover more treatment options in case of clarithromycin-resistant infection.

T. Grubar Kovačič: None. A. Slobodnik Kavčič: None. B. Radovan: None. N. Klobučar: None. N. Omahen: None. T. Marušič: None. M. Grbec: None. D. Najdenoski: None. B. Luštrek: None. B. Berger: None. S. Jezeršek: None. S. Jeverica: None.

P12.09

LOW ACCURACY AND LIMITED DIAGNOSTIC INFORMATION OF UREASE TEST FROM GASTRIC BIOPSIES LIMIT ITS UTILITY FOR RAPID EXCLUSION OF HELICOBACTER PYLORI INFECTION DURING ENDOSCOPY

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Objective: In Slovenia, urease test and empiric therapy are still regularly used in endoscopy setting. Our aim was to re-evaluate the clinical characteristics of commonly used invasive diagnostic tests for the detection of *Helicobacter pylori*: urease test, histology, culture and PCR.

Materials and Methods: Consecutive, treatment-naïve patients were included in the study. 2 biopsies (corpus and antrum) were obtained for urease testing, histology, and microbiology (culture and PCR). Sensitivity, specificity, positive and negative predictive values were calculated. The intake of proton pump inhibitors (PPI) 2 weeks and antibiotics 4 weeks before gastroscopy was recorded and the diagnostic impact was calculated.

Results: n=114 patients [mean age 52 years (25-82), 50% (n=57) female] were included, 40% (n=46) received PPIs and 4% (n=5) received antibiotics prior testing. Concomitant PCR and histology detection was considered the gold standard. 37% (n=42; 95% CI 28-46%) of patients were positive. The diagnostic performances are shown in Table 1.

Conclusions: The low sensitivity, low negative predictive value, need for additional reading at 24 hours, and limited diagnostic information with respect to treatment selection severely limit the utility of the urease test for detecting *H. pylori* infection from biopsy specimens. Both histology and PCR reliably detect *H. pylori* infection, and PCR can also be used to guide clarithromycin-based therapy.

S. Jeverica: None. T. Marušič: None. M. Grbec: None. D. Najdenoski: None. B. Luštrek: None. B. Berger: None. T. Grubar Kovačič: None. A. Slobodnik Kavčič: None. B. Radovan: None. N. Klobučar: None. N. Omahen: None. S. Jezeršek: None.

TABLE 1. DIAGNOSTIC CHARACTERISTICS OF INVASIVE DIAGNOSTIC TESTS.

Diagnostic test	Sensitivity	Specificity	PPV	NPV	PPI (<2 weeks)	Antibiotics (<4 weeks)		
						OR	p-value	OR
Urease test (30 min)	0.55	0.97	0.92	0.79	2.38	0.09	0.77	0.82
Urease test (24 h)	0.76	1	1	0.88	6.72	0.02	<0.01	0.99
Culture	0.80	1	1	0.89	4.92	0.06	<0.01	0.99
Histology	1	1	1	1	1	1	1	1
PCR	1	1	1	1	1	1	1	1

P12.10

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

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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 demography, 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-metronidazole (33%), with differences between regions. The overall first-line effectiveness was 86.7% but ranged from 78% in Aragón 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.

L. Hernández: None. B.J. Gómez Rodríguez: None. S.J. Martínez-Domínguez: None. R. Pajares Villaroya: None. J. Tejedor-Tejada: None. P. Pazo Mejide: None. M. Sánchez Alonso: None. N. Alcaide: None. J.M. Huguet: None. P. Mata-Romero: None. J. Llach: None. A. Cuadrado: None. E. Ivo: None. E. Albéniz: None. A. Cano-Català: None. L. Moreira: None. P. Parra: None. O.P. Nyssen: None. J.P. Gisbert: None.

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

P12.11

DETERMINANTS OF VIRULENCE OF *HELICOBACTER PYLORI* CLINICAL ISOLATES IN RUSSIA

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Objective: *Helicobacter pylori* was proved to be the principal causative agent of gastroduodenal disorders in human. Currently there is a very limited number of studies evaluating *H. pylori* genotypes in Russia.

The aim of the study is to determine *H. pylori* genotypes associated with the clinical outcomes in patients with *H. pylori* infection.

Materials and Methods: Using standard PCR method for detection of genetic determinants of virulence (*cagA*, *vacA*, *oipA*, *iceA* и *babA2*), we analyzed 56 *H. pylori* strains isolated from biopsies collected during endoscopy of patients with chronic gastritis (G, n=36) and duodenal ulcer (DU, n=20).

Results: As a result, *cagA* and *oipA* genes was found in 64.3% and 60.7% *H. pylori* strains respectively, without significant difference between clinical manifestations. The *vacA s1* allele was significantly dominant in patients with DU – 95% vs. 63.9% in G ($p=0.01$). No significant difference in *vacA m1/m2* and *i1/i2* alleles was found in *H. pylori* from different groups of patients. All *cagA+* strains possessed *vacA s1* allele. The *cagA+/vacA s1* genotype reached 80.0% in patients with DU, whereas in patients with G – 50.0%. 11 out of 12 of the *cagA-/vacA s2* genotype were isolated from patients with G. The *iceA1* allele of *H. pylori* was detected in 45.0% of patients with DU and 33.3% of patients with G. Detection of *babA2* was observed in 51.8% cases, however, the presence of *babA2* was not significantly associated with DU nor G.

Conclusions: The significant association between the *vacAs1* genotype and clinical manifestations of *H. pylori* infection has been established.

N.S. Gladyshev: None. A. Svarval: None. S. Daria: None.

P12.12

BIOINFORMATIC ANALYSIS REVEALS COMPLETED PROPHAGE GENOMES WITHIN ADMIXED *HELICOBACTER PYLORI* POPULATIONS ORIGINATING FROM CABO VERDE

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Objective: *Helicobacter pylori* is a gut bacterium that has coevolved with humans for over 100,000 years and presently infects approximately half of the global population. The population of Cabo Verde is unique because the people have combined African and European ancestry. *H. pylori* from these hosts previously underwent population genetic analysis which revealed four distinctive admixed sub-populations. This study aims to determine the presence of prophages, from lysogenic bacteriophages, in admixed *H. pylori* and if there are different quantities of prophage identified between sub-populations.

Materials and Methods: 538 *H. pylori* isolates were assembled from 178 asymptomatic Cabo Verdean hosts. PhageBoost was used to identify prophages and CheckV was used to filter prophage genomes with a completeness of > 80%, as well as perform clustering.

Results: 9 prophage genomes were identified among 9 isolates, with an average length of 47,169 bp (range: 31,998 bp-69,561 bp) and average number of genes of 41 (range: 33-62). Integrase and holin genes are potential markers of complete prophage genomes, 2 prophage genomes contained both these genes, 3 only contain integrase genes and 4 did not contain either gene. When differences in the number of *H. pylori* isolates per Cabo Verdean sub-population have been taken into account, there is no significant difference ($p = 0.14$) in the number of prophages identified between sub-populations.

Conclusions: Our results reveal 1.7 % of the Cabo Verde *H. pylori* isolates contain complete prophages, where the assigned sub-population of the isolates and the presence of complete prophages are independent.

E. Cave: None. S. Beleza: None.

P12.13

EFFICACY OF *HELICOBACTER PYLORI* ERADICATION TREATMENT IN OBESE PATIENTS UNDERGOING BARIATRIC SURGERY

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Objective: Several factors could influence the efficacy of *Helicobacter pylori* eradication treatment, which may be impaired in obese patients due to not fully elucidated mechanisms. We previously demonstrated a lower eradication rate in obese patients compared to normal weight adults. This study was aimed to evaluate *H. pylori* eradication rates according to obesity categories of patients undergoing bariatric surgery.

Material and Methods: We included *H. pylori* infected adults who undergone bariatric surgery. Obesity was categorized according to Body Mass Index (BMI) into Class 2 (BMI 35.0-39.9), Class 3 (BMI 40.0-49.9), and Class 4 (BMI ≥ 50.0). *H. pylori* infection was diagnosed by histological assessment of gastric biopsies. Quadruple concomitant *H. pylori* eradication treatment (PPI, clarithromycin, amoxicillin, and metronidazole) was administered for 14 d, and a 6-8 wk post-treatment control was performed by the ¹³C-Urea Breath Test. Multiple logistic regression was used for statistical analysis.

Results: A population of 129 consecutive naïve *H. pylori* positive patients was analyzed. Age, gender, smoking habits and adverse events did not differ according to obesity categories. Successful *H. pylori* eradication was obtained in 77.8% (42/54; 95%CI, 65.1-86.8) of Class 2, 67.4% (31/46; 95%CI, 53.0-79.1) of Class 3, and 51.7% (15/29; 95%CI, 34.4-68.6) of Class 4 obese patients, which was significantly different among the three groups ($p < 0.05$).

Conclusions: Obesity category affects the efficacy of *H. pylori* eradication treatment in adults undergoing bariatric surgery. New strategies of eradication are needed, mainly in morbid obese patients.

O. Laudanno: None. A. Riquelme: None. G. Ahumarán: None. M. Thome: None. P. Gollo: None. P. Gonzalez: None. P. Mantero: None. C.G. Goldman: None.

P12.14

DECIPHERING GASTRIC CANCER SUSCEPTIBILITY THROUGH MULTI-POPULATION GENOME-WIDE ASSOCIATION ANALYSIS WITHIN THE *HELICOBACTER PYLORI* GENOME PROJECT

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Objective: *Helicobacter pylori* is a cause of gastric cancer. However, our understanding of genetic variants responsible for carcinogenesis remains incomplete. Most microbial genome-wide association studies (GWAS) have addressed traits under strong selection (e.g., drug resistance).

Materials and Methods: Using *Helicobacter pylori* Genome Project (HpGP) genomes from 17 ancestral populations, we conducted GWAS of gastric cancer (n=233) and advanced intestinal metaplasia (n=172), versus non-atrophic gastritis controls (n=606). We performed a linear mixed model approach in pySEER to test for disease associations with unitigs, single nucleotide polymorphisms, insertion/deletions in coding/non-coding regions, and gene presence/absence. We used three reference *H. pylori* genomes (hpEurope 26695, ELS37 and hpEAsia F57) to ensure that variants are called in the same coordination for all genomes and for comparison with previous population-specific GWAS in European and Asian *H. pylori* strains.

Results: Our genome-wide analyses with the gene presence/absence and unitigs confirmed the previously recognized disease associations with the *cag* pathogenicity island (PAI) encoding the *cagA* virulence factor and other *cag* PAI proteins. In addition, there were suggestive associations with features of genes encoding outer membrane and transmembrane proteins. Ongoing analyses are examining potential differences in associations with *H. pylori* strains from malignant vs. premalignant lesions.

Conclusions: Our analysis provides insights into gastric carcinogenesis. Some identified genetic variants require functional validation.

D. Wang: None. K. Yu: None. C. Rabkin: None. M.C. Camargo: None. K. Yahara: None. R. Torres: None. D. Falush: None.

P12.15

ROLE OF FAMILY MEMBERS AND SOURCE OF WATER IN TRANSMISSION OF *HELICOBACTER PYLORI* INFECTION IN A LIBYAN RURAL REGION

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Objective: It is reported that family members & source of drinking water as potential route of transmission of *Helicobacter. pylori*. No data available in Libyan families' residents in a rural region. Thus, the aim to determine the prevalence of *H. pylori* among healthy families.

Materials and Methods: The study involved 119 healthy members of 30 family living in Sabratha city. A blood sample of 119 family members (61 Males, 58 Females, median age 35years), using ELISA to detect anti-*H. pylori* IgG, a questionnaire were completed by interview. In addition, a total of 30 water samples were collected from the upper well level of the wells, *H. pylori* specific DNA was examined using PCR.

Results: Overall seroprevalence *H. pylori* was (47.45%), less in female than male participants 45%, 55% respectively, a gradual increase with age, with highest age group of 30-35 years. It found eleven family (37%) have more than one member infected. *H. pylori* DNA was not found in well water samples with negative PCR results.

Conclusions: Prevalence of *H. pylori* infection among asymptomatic population in Sabratha city is high. The PCR is accurate, reliable method to identify *H. pylori*- DNA. The well water in the natural environment in rural region of Sabratha could not be a risk factor for *H. pylori* transmission, and infected family member could be a role of transmission of *H. pylori* in a Sabratha. However, further community -based research in other regions is necessary to identify risk factors associated *H. pylori* infections.

A.T. Nami: None. M. Drah: None. S. Othman: None. R. Lahmer: None. S. Nami: None.

POSTER SESSION 13: HELICOBACTER 10

P13.01

SEMI-QUANTITATIVE ASSESSMENT OF *HELICOBACTER PYLORI* BY RAPID UREASE TESTS IN PEDIATRICS

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Objective: In pediatrics, a semi-quantitative assessment of *Helicobacter pylori* urease activity is a desirable testing parameter.

Material and Methods: The study involved 56 children (14.5±3.1 y.o.) with recurrent abdominal pain. The semi-quantitative assessment of urease activity of two RUTs was compared: the ProntoDry® (GASTREX, France) and the AMA RUT Expert M® (AMA LLC, Russia) with the data obtained by histological and PCR analyses.

Results: Analysis of the urease activity based on ProntoDry® and Expert® revealed a very high correlation between them ($r = 0.914$, $p < 0.05$). The results of the Expert® coincided with the histological data of all patients. The complete agreement between the negative results of both RUTs and histological analysis of biopsy specimens was found in 95 % of cases. Based on histology, a marked correlation was found between the overall *H. pylori* infection profile and the semi-quantitative Expert® ($r = 0.523$, $p < 0.05$) and ProntoDry® ($r = 0.451$, $p < 0.05$) indicators. The analysis showed a high correlation between the PCR test and the semi-quantitative indicators of the ProntoDry® ($r = 0.721$, $p < 0.05$) and a noticeable correlation with the Expert® indicators ($r = 0.632$, $p < 0.05$).

Conclusions: A high correlation of the semi-quantitative indicators obtained using the ProntoDry® and AMA RUT Expert M® tests was found; a noticeable correlation of the urease activity with the PCR test was revealed. Resulting of the histological assessment of *H. Pylori* contamination and localization, a significant correlation with the level of the urease activity was determined.

Y. Gaykova: None. E. Kolomina: None. N. Parolova: None. S. Ermakov: None. U. Babaeva: None.

P13.02

PREVALENCE AND ANTIBIOTIC SUSCEPTIBILITY OF CAMPYLOBACTER IN ETHIOPIAN CHILDREN WITH DIARRHOEA AND DOMESTIC ANIMALS

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Objective: *Campylobacter* infects multiple hosts, and rising resistance to ciprofloxacin is alarming. This study investigated the prevalence of *Campylobacter* and its antibiotic resistance in Ethiopian children with diarrhoea and domestic animals.

Material and Methods: Upon parental informed consent, faecal samples from 303 children, and 711 from animals were collected. *Campylobacter*s were isolated using standard bacteriological methods. Typical isolates were identified with MALDI-TOF MS and m-PCR. Antibiotic susceptibility was determined using gradient strip diffusion test.

Results: *Campylobacter* was present in 21% (n=216) of the 1014 samples, with 19% in children (n=59). Of the 216 strains, 82% were *C. jejuni* (n=178), 8% *C. coli* (n=18), and 1% *C. fetus* (n=2). Co-infection with both *C. jejuni* and *C. coli* was observed in 7% of the samples (n=16). Simultaneous infections in children and animals were observed in 23 of 245 households, with concordant species in twenty-two households. *C. coli* had higher ciprofloxacin resistance (50%) (n=12) than *C. jejuni* (14%) (n=14). Co-resistance to ciprofloxacin and doxycycline was found in ten strains. MICs of azithromycin and erythromycin were comparable for the two species, but MIC of 256 µg/ml for azithromycin and 48 µg/ml for erythromycin was revealed in one *C. jejuni* from children, and another *C. jejuni* from poultry, respectively. Ciprofloxacin's and doxycycline's mean MIC values were much higher among strains from poultry (7.23 and 12.19 µg/ml, respectively) compared to children (2.68 and 0.41 µg/ml, respectively).

Conclusions: Possible household-level transmission of *Campylobacter*, and mono and combined resistance to ciprofloxacin and doxycycline is a concern.

W. Mulu: None. M. Joossens: None. M. Kibret: None. K. Houf: None.

P13.03

ASSESSING THE VALIDITY OF *HELICOBACTER PYLORI* DETECTION METHODS IN COMMUNITY-DRIVEN RESEARCH

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Objective: Indigenous communities in Northern Canada have higher *Helicobacter pylori* (*Hp*) prevalence than the Canadian average. The Canadian North *Hp* (CANHelp) Working Group links academic researchers with community leaders and healthcare providers to address community concerns about *Hp*-associated health risks. This study aimed to evaluate the validity of three *Hp* detection methods used to assess participants in community-driven projects from 2008 through 2017: the ¹³C-urea breath test (UBT) along with histology and culture of gastric biopsies.

Materials and Methods: We describe *Hp* infection prevalence by detection method and agreement between methods (percent with concordant results of participants tested). We estimated sensitivity and specificity of each method against alternating gold standard definitions.

Results: *Hp* prevalence was 53% in 1,291 participants with UBT results, 71% in 407 participants with histology results, and 67% in 401 participants with culture results. A subset of participants had gastroscopy after receiving UBT results; *Hp*-positive participants were more motivated to consent to gastroscopy. Of 357 participants with results from 3 tests, 82% [95% confidence interval (CI):77-85%] were concordant on all 3. Estimated agreement was 94% (95%CI: 91.96%) for UBT and histology, 83 (95%CI: 78.86%) for UBT and culture, and 86% (95%CI: 83-90%) for histology and culture. Estimated sensitivity and specificity against each of the other methods were similar for histology and UBT and substantially lower for culture.

Conclusions: This study provides evidence of good accuracy of methods used to classify *Hp* status in CANHelp community projects. It suggests excellent accuracy of histopathology and UBT results.

H. Dang: None. T. Cromarty: None. S.V. Zanten: None. S. Girgis: None.

P13.04

THE CONTRIBUTION OF *HELICOBACTER PYLORI* INFECTION TO THE FORMATION COMORBID IBS PHENOTYPE

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Objective: The comorbidity of irritable bowel syndrome (IBS) and functional dyspepsia (FD) is widespread in clinical practice. The association of *Helicobacter pylori* (*Hp*) with FD is well known, but data on the effect of *Hp* on the comorbid course of IBS and FD are limited. The aim of the study was to evaluate the contribution of *Hp* infection to the formation of the comorbid phenotype of IBS.

Materials and Methods: the study included 263 patients with IBS, among which 98 (37.3%) had IBS and FD overlap. All participants were surveyed according to the questionnaires GSRS, HADS, the level of zonulin in the feces was studied.

Results: According to our data, *Hp* does not affect the incidence of IBS and FD comorbidity (Table 1). However, in individuals with overlap syndrome, the presence of *Hp* infection is a negative prognostic factor that determines the severity of IBS. In this subgroup of individuals, more pronounced abdominal pain, dyspepsia, diarrhea was revealed, they more often had signs of clinically pronounced anxiety and depression, and a maximum increase in the content of zonulin in the feces was detected as reflection of the epithelial permeability syndrome.

Conclusions: A history of *Hp* infection in patients with overlapping IBS and FD is associated with a more severe course of the disease. It is necessary to assess the course of comorbidity of IBS and FD in dynamics after eradication therapy.

M. Livzan: None. O. Gaus: None. D. Popello: None.

TABLE 1. COMPARATIVE CHARACTERISTICS OF STUDY PARTICIPANTS ACCORDING TO THE STUDY PARAMETERS.

Index	Main group (IBS+FD+), n=98		Comparison group (IBS+FD-), n=165		Statistical significance of differences
	Subgroup 1 (Hp+), n=59	Subgroup 2 (Hp-), n=39	Subgroup 3 (Hp+), n=87	Subgroup 4 (Hp-), n=78	
Sex					
Male	8 (13.6)	5 (12.8)	10 (11.5)	11 (14.1)	$\chi^2=0.25, =0.876$
Female	51 (86.4)	34 (87.2)	77 (88.5)	67 (85.9)	
Average age	28 [24.8; 33]	27.5 [25; 31]	28 [24; 34]	27 [25; 34.5]	$\chi^2=0.09, =0.963$
<i>The severity of gastrointestinal symptoms according to the GSRS scale, score</i>					
Abdominal pain*	4.5 [3.5; 5.5]	3.0 [2.5; 4.5]	2.7 [1.5; 3.5]	2.3 [1.3; 3.5]	$\chi^2=19.65, p=0.002$
Constipation	2.8 [1.0; 4.3]	2.6 [1.0; 4.2]	2.7 [2.0; 3.0]	2.7 [1.5; 3.8]	$\chi^2=0.39, p=0.705$
Diarrhea*	3.8 [2.3; 5.0]	2.9 [2.0; 4.3]	2.5 [1.0; 3.7]	2.7 [2.0; 3.0]	$\chi^2=14.11, p=0.004$
Dyspepsia*	4.0 [3.5; 4.5]	3.0 [2.0; 4.0]	1.0 [1.0; 1.5]	1.0 [1.0; 1.0]	$\chi^2=15.72, p=0.003$
<i>Prevalence of anxiety on the HADS* scale, abs (%)</i>					
clinically expressed	27 (45.8)	12 (30.8)	11 (12.6)	3 (3.9)	$\chi^2=18.55, p<0.001$
subclinical	29 (49.2)	16 (41.0)	30 (34.5)	27 (34.6)	
Absence	3 (5.0)	11 (28.2)	46 (52.9)	48 (61.5)	
<i>Prevalence of depression according to the HADS* scale, abs (%)</i>					
clinically expressed	20 (33.9)	8 (20.5)	13 (14.9)	12 (15.4)	$\chi^2=17.05, p=0.001$
subclinical	19 (32.2)	13 (33.3)	18 (20.7)	20 (25.6)	
Absence	20 (33.9)	18 (46.2)	56 (64.4)	46 (59.0)	
<i>The content of the marker of intestinal permeability, ng/ml</i>					
Zonulin in feces*	202.5 [120.0; 280.4]	163.0 [105.8; 240.5]	135.0 [100.1; 165.3]	117.8 [95.0; 149.5]	$\chi^2=20.17, p<0.001$

Note: * - statistically significant differences

P13.05

HELICOBACTER PYLORI INFECTION IN PATIENTS WITH AUTOIMMUNE GASTRITIS: INCIDENCE AND PATHOMORPHISM OF THE DISEASE

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Objective: Autoimmune inflammation and HP infection are the leading causes of chronic gastritis, and therefore the assessment of the course of the disease with the combined influence of two etiological factors seems to be an urgent task. The aim of the study was to identify the incidence of HP infection in patients with autoimmune gastritis (AIG) and to evaluate the course of the disease with mixed etiology.

Materials and Methods: The main group – 24 patients with AIG and HP infection, comparison group – 23 patients with AIG only. There were no differences between groups in terms of sex and age of patients. All underwent a general clinical study, a laboratory study, endoscopy with the NBI close focus function with biopsy sampling using the OLGA system.

Results: Patients of the main group often complained of dyspepsia and significantly more often had a combination of anemia and sideropenia syndromes, while patients of the comparison group showed a predominance of manifestations of anemic syndrome associated with vitamin B12 deficiency. Patients of the main group showed pangastritis and 3 times more often had erosions of the gastric mucosa compared to patients in the comparison group, and also had a significantly higher degree of gastritis, while the stage of the disease in both groups was comparable. We also noted no differences in the frequency of detection of hyperplasia enterochromaffin cells during immunohistochemical studies.

Conclusions: The combination of the two leading etiological factors of gastritis leads to the formation of gastritis with characteristic clinical and histological stigmas of the disease.

M. Livzan: None. A. Gubanov: None. S. Mozgovoi: None. O. Gaus: None.

P13.06

NOD1 REGULATES GASTRIC ACIDITY AND FAVOURS BACTERIAL PERSISTENCE DURING CHRONIC *HELICOBACTER PYLORI* INFECTION IN MICE

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The innate immune protein NOD1 restricts bacterial colonisation during acute *Helicobacter pylori* infection in mice. The aim of this study was to determine the role of NOD1 in chronic infection.

In contrast to acute infection models, we found that *Nod1*^{-/-} mice at 8 weeks post-infection had reduced bacterial loads, when compared with *Nod1*^{+/+} animals ($p = 0.073$). *H. pylori*-infected *Nod1*^{-/-} mice had decreased gastric inflammation ($p = 0.057$) and immune cell infiltration (CD45⁺ cells, macrophages; $p < 0.0005$) but increased levels of epithelial cell hyperplasia ($p < 0.0005$). *Nod1*^{-/-} mice also had increased apoptosis ($p < 0.0005$), suggesting that NOD1 prevents cell death induced by *H. pylori* *in vivo*. To further understand the role of NOD1 in chronic *H. pylori* infection, we performed microarray analyses on gastric tissues from *H. pylori*-infected *Nod1*^{+/+} and *Nod1*^{-/-} mice. One of the most downregulated genes in *Nod1*^{-/-} mice was *Adcyap1r1* ($p < 0.0005$), encoding Pituitary adenylate cyclase-activating polypeptide receptor type 1. This receptor, located on enterochromaffin-like cells, binds Pituitary adenylate cyclase-activating polypeptide to induce histamine release and promote gastric acid secretion by parietal cells. Consistent with the reduced levels of gastric *Adcyap1r1* expression, *H. pylori*-infected *Nod1*^{-/-} mice had significantly decreased serum gastrin levels ($p < 0.002$) and increased gastric pH ($p < 0.015$), when compared with *Nod1*^{+/+} animals. In conclusion, we have identified a new role for NOD1 in gastric acid regulation and propose that this promotes a favourable environmental niche for *H. pylori* persistence in the stomach.

R.L. Ferrero: None. K. D'Costa: None. L. Tran: None. L.H. Le: None.

P13.07

HELICOBACTER PYLORI INDUCES STRAIN-SPECIFIC PATHOLOGICAL ALTERATIONS IN INFECTED HEPATOCYTES

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Objective: *Helicobacter pylori* (Hp) is a human pathogen leading to peptic ulcer disease, atrophic gastritis and gastric cancer. Additionally, Hp has been associated with many extra-gastric diseases including aggravation of liver damages that predispose to hepatocellular carcinoma. Here, we report the potential mechanisms behind Hp-induced alterations in liver cells and verify the pathophysiological changes in livers of infected mice.

Material and Methods: Different Hp strains were used to infect liver cells to analyze the morphological and inflammatory changes as well as changes in transcriptome level. Female 129/B1/6 mice were infected with different Hp strains in agreement with the local Ethics committee and the liver sections were submitted for immunohistopathological analysis.

Results: CagA-positive Hp strains remodel actin cytoskeleton of infected hepatocytes by inducing podosomes. Overexpressed CagA is phosphorylated in Huh7 cells and pCagA is sufficient to trigger the formation of podosomes. These invasive micro-domains mediate extracellular matrix degradation and are related to increased release of inflammatory cytokines. Importantly, we show a direct correlation between strain-specific NF- κ B pathway activation and podosome formation through selective inhibition by BAY 11-7082. The transcriptome analysis indicated cell type and strain-specific changes upon infection. Immuno-histopathological study of liver sections confirmed the presence of Hp in infected livers, increase of inflammatory factors, accumulation of collagen I as well as various liver pathologies.

Conclusions: Our data indicates that Hp infection contributes to liver pathologies and CagA phosphorylation-dependent mechanism through the activation of NF- κ B pathway might be one of determinative factors for the progression of the liver diseases.

P. Spuul: None. O. Smirnova: None. S. Khalid: None. K. Roots: None. J.K. Tamm: None. C. Varon: None.

P13.08

ELUCIDATING THE REASONS FOR *HELICOBACTER PYLORI* ERADICATION FAILURE – ANTIBIOTIC RESISTANCE AND COEXISTENCE OF *H. PYLORI* WITH *CANDIDA* SPECIES

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Objective: The failure in successful *Helicobacter pylori* (*H. pylori*) eradication has been primarily associated with antibiotic resistance, however, other factors may contribute. This study aimed to assess the frequency of *H. pylori* and *Candida* spp. co-infection in gastric samples of *H. pylori*-positive patients, as yeasts were proposed to be endosymbiotic hosts to *H. pylori*.

Materials and Methods: *H. pylori* was detected in gastric biopsy samples using staining and molecular methods in 110 patients with gastrointestinal diseases. Detection of *H. pylori* mutations associated with antibiotic resistance, and *Candida* spp. detection and identification were performed by using the real-time PCR method. The presence of any relationship between *Candida* colonization, *H. pylori* mutations, demographic characteristics, and histopathological categories was assessed and statistically evaluated.

Results: *Candida* spp. were detected in 8% (n=9) patients and *Candida* colonization was associated with older age, with a significantly higher median age (65 years) in the *Candida*-positive compared to the *Candida*-negative group (54 years) ($p < 0.05$). In 52% and 47% of participants, mutations associated with clarithromycin and fluoroquinolone resistance were detected, respectively. Dual resistance was 30%. Antibiotic resistance rates were higher in females, participants with previous eradication attempts, and higher atrophy scores ($p < 0.05$).

Conclusions: Alarming high antibiotic resistance was observed, indicating the necessity for more effective *H. pylori* treatments. Due to the scarcity of *Candida* presence, the co-occurrence of *H. pylori* and *Candida* is not a major factor contributing to the eradication failure. The older age favored *Candida* colonization, suggesting that age-related changes could contribute to dysbiosis and gastric pathologies.

A. Bačić: None. I. Petković: None. M. Rajilić-Stojanović: None. V. Milivojević: None. D. Kekić: None.

P13.09

PREVALENCE CHANGES OF *HELICOBACTER PYLORI* INFECTION IN DYSPEPTIC PATIENTS IN ROMANIA

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Objective: *Helicobacter pylori* (HP) is one of the most important risk factors in upper gastrointestinal tract diseases. Recent data describes a fall in *Helicobacter pylori* prevalence rate in Romania in the last 30 years, although it is still one of the most common infections among patients. Our study aims to provide updated clinical and epidemiological data on the current status of HP infection among dyspeptic patients in north-western Romania.

Materials and Methods: We conducted a retrospective study using our tertiary care center's database in the Second Department of Internal Medicine, Emergency Clinical County Hospital, Cluj-Napoca, Romania in three years interval. We selected only cases referred for dyspepsia. HP status for active HP infection was assessed by rapid urease test and histopathology.

Results: We surveyed 715 patients who met the inclusion criteria. The patients were aged between 18 and 90 years and the male to female ratio was 1:1.43. Active HP infection was identified in 194 patients (27.13%). HP prevalence in men was 24.14% and 29.21% in women. The mean age at admission was 58.5±15.6 years old.

Conclusions: We confirmed the recent data that suggested HP prevalence in Romania as being lower compared to 30 years ago and also found lower rates of infection compared to those previously described in recent years, which approximated the HP prevalence in Romania at 40.8%. The infection rates described by our study are comparable to data shown by other studies in Western Europe.

R.A. Farcas: None. S. Grad: None. C. Grad: None. D.L. Dumitrascu: None.

P13.10

BACILLARY-COCCOID TRANSFORMATION ACTIVITY OF *HELICOBACTER PYLORI* IN THE ANTRUM AND BODY OF THE STOMACH

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Objective: The study of the mechanisms of resistance of *Helicobacter pylori* to eradication therapy contributes to the search for new strategies for the diagnosis and treatment of *H. pylori*. One of the resistance mechanisms is bacillary-cocoid transformation (BCT). The objective of the study was to compare the activity of BCT in the antrum and body of the stomach among themselves in patients with chronic gastritis and to develop a scale for assessing the degree of its activity.

Materials and Methods: BCT in the body and antrum of the stomach and development of the scale were performed based on 72 and 220 biopsy smears, respectively. The form of *H. pylori* was identified using immunocytochemical method (ICH) research. BCT activity was assessed by counting the number of coccoïd forms per 100 *H. pylori* cells.

Results: A high correlation of BCT activity in the antrum and gastric body was revealed. Based on the cluster analysis of ICH results, a BCT activity scale was developed, since which patients were divided into 3 classes with coccoïdal contamination (%) according to this parameter: A [10:11]; B [12:19]; C [20:100]. Class A (absent) included about 73% of patients, B (bacillary) included 20% of patients, and C (coccoïd) included 7% of patients.

Conclusions: A scale for assessing the activity of BCT has been developed, which will allow a semi-quantitative assessment of the content of coccoïd forms to refine the strategy of therapeutic intervention. To use this scale, a single biopsy from the gastric antral region is required.

N.S. Gladyshev: None. R.V. Deev: None. V.Y. Kravtsov: None.

P13.11

MYCOBACTERIUM BOVIS BCG INCREASE THE SELECTED DETERMINANTS OF MACROPHAGE ACTIVITY, WHICH WERE DIMINISHED IN RESPONSE TO GASTRIC PATHOGEN *HELICOBACTER PYLORI***W. GONCIARZ, W. ORŁOWSKA, A. DOMAŃSKA, P. PŁOSZAJ, M. CHMIELA**

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Objective: High antibiotic resistance of gastric pathogen *Helicobacter pylori* (HP) and the ability to escape the host immune response prompt searching for therapeutic immunomodulators. Bacillus Calmette- Guerin (BCG) vaccine with *Mycobacterium bovis* (Mb) is a candidate for modulation the activity of immunocompetent cells, and onco-BCG formulation was successfully used in immunotherapy of bladder cancer.

The aim of the study was to determine the influence of onco-BCG on the phagocytic capacity of human THP-1 macrophage cells, using the model of *Escherichia coli* bioparticles and HP fluorescently labeled.

Materials and Methods: Deposition of cell integrins CD11b, CD11d, CD18, membrane/soluble lipopolysaccharide (LPS) receptors, CD14 and sCD14, respectively, and the production of macrophage chemotactic protein (MCP)-1 were determined. Furthermore, a global DNA methylation, was also assessed. Human THP-1 macrophages (TIB 202) primed or primed and restimulated with onco-BCG or Hp, were used for assessment of phagocytosis towards *E. coli* or HP surface (immunostaining) or soluble activity determinants, and global DNA methylation (ELISA).

Results: THP-1 macrophages primed/ restimulated with BCG showed increased phagocytosis capacity towards *E. coli* fluorescent particles, elevated expression of CD11b, CD11d, CD18, CD14, sCD14, increased MCP-1 secretion and DNA methylation.

Conclusions: Preliminary results indicate that BCG mycobacteria may also induce the phagocytosis of HP by THP-1 monocytes. Priming or priming and restimulation of macrophages with BCG resulted in an increased activity of these cells, which was negatively modulated by HP.

Funding: This research was financially supported by University of Lodz, Grant Number 15/GNZPA/2022 (B2111001000027.07).

W. Gonciarz: None. W. Orłowska: None. A. Domańska: None. P. Płoszaj: None. M. Chmiela: None.

P13.12

SALVIA CADMICA BOISS. EXTRACTS MODULATE ACTIVITY OF MACROPHAGES PRIMED WITH LIPOPOLYSACCHARIDE OF GASTRIC PATHOGEN *HELICOBACTER PYLORI***W. GONCIARZ¹, P. PŁOSZAJ¹, A. DOMAŃSKA¹, W. ORŁOWSKA¹, E. PIĄTCZAK², M. CHMIELA¹**

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Objective: *Salvia cadmica* Boiss. root and aerial part extracts enriched with polyphenols are bactericidal towards gastric pathogen *Helicobacter pylori* (Hp) and diminish deleterious effects induced by Hp lipopolysaccharide (LPS) towards gastric epithelial cells.

The aim of this study was to examine the influence of *S. cadmica* extracts on the M1/M2 polarization of macrophages primed with Hp LPS vs standard LPS *Escherichia coli* (Ec), and the macrophage cytokine as well as phagocytic activity, which are affected during Hp infection.

Material and Methods: Macrophages derived from THP-1 human monocytes primed with LPS Hp/Ec and/or *S. cadmica* extracts, were examined for the biomarkers of activation (surface, cytoplasmic or soluble), and phagocytic capacity. The bone marrow macrophages of *Caviae porcellus* were used to determine the engulfment of Hp.

Results: Priming of THP-1 cells (24h) with LPS Hp/Ec resulted in polarization of M1 macrophages, activation of nuclear factor kappa B, secretion of tumor necrosis factor (TNF)- α , interleukin (IL)-1 beta, macrophage chemotactic protein (MCP)-1, immunoregulatory IL-10, and production of reactive oxygen species. These effects were diminished after restimulation of cells with *S. cadmica* extracts. THP-1 macrophages exposed to studied extracts showed an increased phagocytic capacity, in conjunction with elevated CD11b/CD11d expression and enhanced production of inducible nitric oxide synthase. They also increased Hp engulfment by bone marrow macrophages. These effects were not related to a global DNA methylation.

Conclusions: *S. cadmica* extracts possess an immunomodulating activity, which might be useful in control of *H. pylori* LPS driven activity of macrophages.

W. Gonciarz: None. P. Płoszaj: None. A. Domańska: None. W. Orłowska: None. E. Piątczak: None. M. Chmiela: None.

P13.13

STEREOCOMPLEXED MICROPARTICLES LOADED WITH SALVIA CADMICA BOISS. EXTRACTS FOR ENHANCEMENT OF IMMUNE RESPONSE TOWARDS *HELICOBACTER PYLORI*

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Objective: Controlled delivery of therapeutic substance gives numerous advantages (prevents degradation, improves uptake, sustains concentration, lowers side effects).

The aim of the study was to encapsulate *Salvia cadmica* extracts (root or aerial part), enriched with polyphenols with immunomodulatory activity, in stereocomplexed microparticles (sc-PLA), for using them to enhance the immune response towards gastric pathogen *Helicobacter pylori*.

Material and Methods: Microparticles were made of biodegradable poly (lactic acid) (PLA) and poly(D-lactic acid) (PDLA). Their stereocomplexation was used to form microspheres and enhance the stability of the obtained particles in acidic/basic pH. The release of *Salvia cadmica* extracts was done in different pH (5.5, 7.4 and 8.0)

Results: The obtained polymers are safe *in vitro* and *in vivo* (guinea pig model). The sc-PLA microparticles release of *S. cadmica* extracts in pH 5.5, 7.4, and 8.0. *S. cadmica* extracts enhanced the phagocytic activity of guinea pig bone marrow-derived macrophages, which was diminished by *H. pylori*, and neutralized *H. pylori* driven enhanced production of tumor necrosis factor (TNF)- α and interleukin (IL)-10.

Conclusions: The sc-PLA encapsulated *S. cadmica* extracts can be recommended for further *in vivo* study in guinea pigs infected with *H. pylori* to confirm their ability to improve an immune response towards this pathogen.

W. Gonciarz: None. M. Chmiela: None. B. Kost: None. E. Piątczak: None. W. Orłowska: None. A. Domańska: None. P. Płoszaj: None. M. Brzeźiński: None.

P13.14

COMPARATIVE ANALYSIS OF *HELICOBACTER PYLORI* STRAINS ISOLATED FROM ESTONIA IN 2020-2022**L. TRUU¹, K. ROOTS¹, K. SUURMAA², A. RÜÜTMANN³, I. SARAND¹, P. SPUUL¹**¹Tallinn University of Technology, Department of Chemistry and Biotechnology, Tallinn, Estonia; ²West Tallinn Central Hospital, Department of Endoscopy, Tallinn, Estonia; ³University of Tartu, Faculty of Medicine, Tartu, Estonia

Objective: *Helicobacter pylori* (HP) infection is highly common in Estonia, which results in high incidence of gastric cancer. Here, we use PCR and whole genome sequencing (WGS) to describe the pathogenicity and antibiotic resistance of HP strains circulating in Estonia.

Patients and Methods: 23 patients with different gastric problems were enrolled in the study. Written informed consent was obtained from all patients before endoscopy. Gastric biopsies were obtained from antrum and corpus. From each HP-positive biopsy, several colonies were picked for DNA extraction and downstream PCR genotyping or whole genome sequencing. In addition to that, antibiotic susceptibility testing (AST) from one colony of each biopsy was done.

Results: Out of 23 patients enrolled in the study, 16 (70%) were infected with HP. Different HP subpopulations were detected in 70% of the samples. CagA oncogene was found in 7 (44%) cases and the highly pathogenic VacA s1 allele was present in 13 (81%) patients. Antibiotic resistance turned out to be a major problem, as the HP strains of only 6 patients (38%) were susceptible to all antibiotics tested. WGS was used to pinpoint the exact mutations causing antibiotic resistance.

Conclusions: Using the combination of PCR and WGS, we show that the HP strains circulating in Estonia are highly virulent and contain multiple mutations resulting in elevated antibiotic resistance rate.

L. Truu: None. K. Roots: None. K. Suurmaa: None. A. Rütümann: None. I. Sarand: None. P. Spuul: None.

POSTER SESSION 14: HELICOBACTER 11

P14.01

ANTI-CAGA IN *HELICOBACTER PYLORI*-INFECTED PATIENTS WITH DYSPEPSIA IN SOUTH OF LIBYA**A. T. NAMI¹, A. SHAHLOL², A. ALAJWAD², S. NAMI³, A. FITOURI**¹School of Medical Sciences, Libyan Academy, Tripoli, Libyan Arab Jamahiriya; ²Department of Medical Laboratories, College of Medical Technology, Wadi Al Shati University, Wadi Al Shati,, Libyan Arab Jamahiriya; ³Faculty of Medicine, Azzaytuna university, Tarhuna, Libyan Arab Jamahiriya; ⁴Department of Medicine, Tripoli Central Hospital, Tripoli, Libyan Arab Jamahiriya

Objective: *Helicobacter pylori* (*H. pylori*) infection is common and still one of the most frequent bacterial infections in developing countries. Recent studies reported that prevalence of *cagA* positive *H. pylori* infections varies according to geographical area and age of the patients. No data available regarding the prevalence of *H. pylori* and its pathogenicity marker CagA. Therefore, the aim to determine CagA seroprevalence in *H. pylori*-positive dyspeptic patients in south of Libya.

Materials and Methods: One Hundred dyspeptic patients attending Al-Barrak General Hospital (23 male, 77 female mean age 40 years) were invited to participate and donate a blood sample. Presence of *H. pylori* infection and (anti-IgG CagA) was assessed using ELISA method, a questionnaire covering sociodemographic variables were completed by interview.

Results: The overall (73.0%) patients were *H. pylori*-positive, were more prevalent in females' patients (56%). There was no increase with age, However, (61.6%) patients carried anti-CagA antibodies and there was no difference between gender or age group.

Conclusions: In Brack alshati region, prevalence of *H. pylori* infection was found in high rate among the adult dyspeptic participants, which might be related to socioeconomic status and environmental living condition as a major risk factor associated gastric pathogen infection. This finding highlighted the importance of screening of asymptomatic subjects in families with *H. pylori* infected member in Libyan south. However, further studies in large group of dyspeptic patients in other south regions should be conducted to confirm the study findings.

A.T. Nami: None. A. Shahlol: None. A. Alajwad: None. S. Nami: None. A. Fitouri: None.

P14.02

FIRST DESCRIPTION OF THE DATA FROM THE LATIN AMERICAN REGISTRY ON THE MANAGEMENT OF *HELICOBACTER PYLORI* INFECTION (Hp-LATAMReg)

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Objective: There is limited information regarding the best approach for *Helicobacter pylori* management in Latin America. Our aim was to describe the main characteristics of the *H. pylori* eradication treatment in Latin America.

Materials and Methods: A multicenter, prospective, international registry (Hp-LATAMReg) was conducted. Information about therapies used by gastroenterologists in five countries (Chile, Argentina, Mexico, Peru, and Colombia) from 2015 to 2023 was registered in an e-CRF AEG-REDCap database. The modified intention-to-treat (mITT) effectiveness, safety, and adherence was analyzed for the first-line regimens. Data were quality reviewed.

Results: We registered 681 patients, of which 599 (88%) were treatment-naïve. The most frequent indication for treatment was dyspepsia (n=443, 65%). The most commonly prescribed first-line therapies were: proton pump inhibitor (PPI)-amoxicillin (A)-clarithromycin (C), PPI-C-A-Metronidazole (M), PPI-A, PPI-C-A-Bismuth (B) and PPI-A-Levofloxacin (L). Most of the regimes were 14-day long (n=546,

93%), and administered low-dose PPIs (n=282, 47%). The first-line mITT overall effectiveness ranged from 80% to 91%, and PPI+C+A+M was the only regimen that achieved over 90% eradication (Table). The incidence of at least one adverse event was 35%, the most common being abdominal pain (17%). Acceptable adherence, defined as >90% of drug intake, was observed in 97%.

Conclusions: In Latin America, optimal (>90%) effectiveness was only obtained with 14-day concomitant non-bismuth quadruple therapy (PPI-C-A-M). Triple therapies and low-dose PPIs are still commonly prescribed, leaving room for improvement.

D. Reyes Placencia: None. J. Remes-Troche: None. O. Laudanno: None. A. Piscoya: None. J. Ramírez García: None. G. Otoyá: None. G. Latorre: None. J. Chahuan: None. A. Arenas: None. M. Pizarro: None. F. Martínez: None. M. Binder: None. P. Medel: None. E. Fuentes-Lopez: None. A. Cano-Català: None. L. Moreira: None. O. P. Nyssen: None. J. P. Gisbert: None. A. Riquelme: None.

TABLE 1. MOST COMMONLY USED FIRST-LINE ERADICATION THERAPIES FOR H. PYLORI INFECTION IN LATIN AMERICA, BY LENGTH OF TREATMENT AND PROTON PUMP INHIBITOR DOSE.

Prescriptions, n (%)	PPI-C-A272 (46%)	PPI-C-A-M107 (18%)	PPI-A44 (7%)	PPI-C-A-B36 (6%)	PPI-A-L33 (6%)
Length of treatment					
7 days	6 (2.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
10 days	17 (6.3%)	1 (0.9%)	1 (2.3%)	0 (0%)	5 (15.2%)
14 days	246 (91.4%)	106 (99.1%)	43 (97.7%)	36 (100%)	28 (84.8%)
PPI dose*					
Low	167 (61.6%)	42 (39.3%)	1 (2.3%)	13 (36.1%)	14 (45.2%)
Standard	34 (12.5%)	10 (9.3%)	3 (6.8%)	9 (25%)	1 (3.2%)
High	70 (25.8%)	55 (51.4%)	40 (90.9%)	14 (38.9%)	16 (51.6%)
mITT effectiveness	79.8% of 272	90.7% of 107	86.4% of 44	80.6% of 36	72.7% of 33

A: amoxicillin; B: bismuth; C: clarithromycin; L: levofloxacin, M: metronidazole; PPI: proton pump inhibitor; * 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.

P14.03

COMMUNITY-DRIVEN BACTERIAL GENOMICS RESEARCH: ANTIMICROBIAL RESISTANCE AND VIRULENCE OF *HELICOBACTER PYLORI* STRAINS FROM ARCTIC INDIGENOUS COMMUNITIES IN CANADA

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Objective: The risk of gastric cancer mortality is elevated in Indigenous populations globally. Effective treatment of *Hp* infection requires burdensome antibiotic regimens. Treatment failure is common, increasing the frequency of antibiotic-resistant *Hp* infection. Evidence suggests associations of *Hp* antibiotic resistance with genetic mutations and virulence genotypes. We aimed to investigate genomic patterns relevant to antibiotic resistance and virulence in *Hp* strains isolated from residents of 7 Indigenous communities in the Northwest Territories and Yukon, Canada.

Materials and Methods: Participants in community-driven projects had gastric biopsies taken for tissue culture during 2008-2017. We identified virulence genes by PCR genotyping and, in some cases, whole-genome sequencing. We used ETESTs™ to assess resistance to 7 antibiotics, classifying outcomes as resistant to 1+ antibiotic(s) or 2+ antibiotics. We report prevalence of resistance outcomes and virulence genes; because gastric cancer is more common in men, we stratified results by sex.

Results: Of 203 *Hp* isolates cultured from 400+ participants and tested for resistance, 43% [95%CI 38.50%] were resistant to 1+ antibiotics (49% [95%CI, 39.58%] among women and 37% [95%CI, 27.47] among men), and 12% [95%CI 8.18%] were resistant to 2+ antibiotics (17% [95%CI 10.25] among women and 6% [95%CI 2.14] among men) to 2+ antibiotics); >50% of 203 isolates examined for virulence genes had *cagA*, *sabA*, *oipA*, and *dupA*.

Conclusions: Our community-driven projects engage underrepresented Indigenous populations in *Hp* genomics research, revealing higher prevalence of resistant infection in women relative to men. We will estimate associations of resistant *Hp* infection with virulence genes.

L.A. Lindsey: None. D. Quilty: None. S.V. van Zanten: None. N. Knox: None. K. Thorell: None. A. Assi: None. K.J. Goodman: None.

P14.04

TRENDS IN MACROLIDE USE AND PREVALENCE OF *HELICOBACTER PYLORI* CLARITHROMYCIN RESISTANCE IN HUNGARY

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Objective: Clarithromycin (Cla), a member of the macrolide family of antibiotics, is one of the most important agents for the eradication of *Helicobacter pylori* infections, and the development of resistance to it may contribute to the increasing rate of unsuccessful eradication attempts. Trends in macrolide use have a fundamental impact on the population level of resistance to clarithromycin.

Materials and Methods: Gastric biopsy specimens from 7995 *Helicobacter pylori* infected patients from Central Hungary were tested in our molecular pathology laboratory by rRNA-targeted Cla-resistance Fluorescence In Situ Hybridization as a reflex Cla-susceptibility test for *Helicobacter pylori*-positive gastric biopsies. Annual prevalence rates of Cla-resistance were analysed for the period 2005-2022 using our previously published mathematical model and macrolide consumption trends in Hungary.

Results: Our mathematical model predicted an increase in Cla-resistance prevalence from 18.02% to 19.34% for the period 2005-2022 with constant macrolide consumption, but our data show an increase from 18.02% to 20.36%. Since 2000, the overall macrolide consumption has been slightly decreasing, but within this there has been a sharp decline in the use of short-acting macrolides (e.g., erythromycin), a steady decline in the use of intermediate-acting ones (such as clarithromycin), but in parallel a large increase in the use of long-acting macrolides (such as azithromycin).

Conclusions: The increasing trend in the prevalence of clarithromycin resistance among *Helicobacter pylori* infections, higher than predicted by the mathematical model, suggests that previously unassumed factors may influence this, including shifts in macrolide consumption portfolio, a marked increase in consumption of long-acting macrolides.

Á. Jakab: None. É. Kocsmár: None. G. Buzás: None. M. Matuz: None. R. Benkő: None. V. Papp: None. A. Szijártó: None. G. Röst: None. G. Lotz: None. I. Szirtes: None.

P14.05

EFFICACY OF STANDARD TRIPLE THERAPY FOR *HELICOBACTER PYLORI* ERADICATION IN LIBYAN DYSPEPTIC PATIENTS: MULTICENTER EXPERIENCE STUDY**A. T. NAMI¹, A. TUMI², M. ALSARI², I. ALAMAR², A. FITOURI²**¹School of Medical Sciences, Libyan Academy, Tripoli, Libyan Arab Jamahiriya; ²Department of Medicine, Tripoli Central Hospital, Tripoli, Libyan Arab Jamahiriya**Objective:** The recommended treatment in Libya for eradication *H. pylori* is standard triple therapy. The purpose was to evaluate the efficacy of STT in Dyspeptic adult in Tripoli, Libya.**Patients and Methods:** A 140 dyspeptic Adult, already diagnosed with *H. pylori* infection based on gastric histopathological examination. Patients were divided into two groups group (70 patients) received STT for 10 days & was compared with the same antibiotic regime over 14 days (70 patients). The successful *H. pylori* eradication evaluated by negative UBT four weeks after treatment.**Results:** 140 eligible patients (52% Females, 48% Males, median age 32.5 years). Eradication rate after first-line therapy for group 1 was 58.0%, group 2 was 64.0%. Eradication rate was similar for both groups independently of degree of *H. pylori* infection, differences in place of residence (urban or rural), age, gender were not found.**Conclusions:** Symptomatic *H. pylori* infection in dyspeptic patients should always be treated. The UBT is accurate, reliable method to identify *H. pylori*-positive patients, to determine response to treatment. The Standard Triple-agent therapy for either 10 or 14 days is insufficient for eradicating *H. pylori* infection and both duration therapies show suboptimal eradication rates and poor clinical response. The level of *H. pylori* antibiotic resistance is high in our region. The necessity of implementation of registry data into the guidelines for management of *H. pylori* infection in Libya should be welcomed. Future randomized controlled trails are required in Libya to measure the effectiveness of a new intervention or treatment for *H. pylori* infections.**A.T. Nami: None. A. Tumi: None. M. Alsari: None. I. Alamar: None. A. Fitouri: None.**

P14.06

ASSOCIATIONS OF NSAID USE WITH *HELICOBACTER PYLORI* DENSITY AND DYSPEPSIA SYMPTOMS IN CANADIAN ARCTIC INDIGENOUS COMMUNITIES**R. SHAHID, O. CHINBAATAR, L. A. LINDSEY, K. J. GOODMAN, C. (CANHELP) WORKING GROUP**

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Our community-driven projects address concerns of Arctic Indigenous communities in Canada about health risks from *Helicobacter pylori* (*Hp*) infection. Common nonsteroidal anti-inflammatory drugs (NSAID) can cause gastroduodenal mucosal damage similar to that caused by *Hp*. Studies of interaction between *Hp* infection and NSAID use report conflicting results. Because chronic dyspepsia sometimes occurs with mucosal injury, we aimed to investigate associations of NSAID use and *Hp* density with chronic dyspepsia symptoms in project participants.CANHelp staff conducted *Hp* infection screening and questionnaire-based interviews in 9 northern Canadian communities during 2008-2017. A subset of participants underwent gastroscopy, with *Hp* density graded by a pathologist. We will describe the frequency of chronic dyspepsia symptoms within categories of NSAID use, *Hp* infection status, and *Hp* density (to be added in). We will use multivariable logistic regression to estimate the association with dyspepsia symptoms of NSAID use *Hp* status and *Hp* density, and examine interactions between these variables.Table 1 shows population demographic variable distributions and prevalence of symptoms. Of 365 participants with *Hp* density classified as mild, moderate or marked, 45%(95%CI:33,57%), 53%(95%CI:44,63%) and 36%(95%CI:25,48%) used NSAIDS, respectively. Further analysis is underway.Our projects provide abundant data for examining interactions between NSAID use and *Hp* infection in chronic digestive disease in Arctic Indigenous populations.**R. Shahid: None. O. Chinbaatar: None. L.A. Lindsey: None. K.J. Goodman: None. C. (CANHelp) Working Group: None.**

TABLE 1. DEMOGRAPHIC CHARACTERISTICS AND PREVALENCE SYMPTOMS BY NSAID USE AND HP STATUS.

Study Population (n = 1,179)	NSAID Use				Hp Status			
	NSAID User		NSAID Non-user		Hp Positive		Hp Negative	
	n	%	n	%	n	%	n	%
Sex								
Male	247	38.3	250	46.7	275	44.3	222	39.8
Female	397	61.7	285	53.3	346	55.7	336	60.2
Age Group								
0-9	9	1.40	46	8.60	24	3.86	31	5.56
10-19	58	9.01	80	15.0	58	9.3	80	14.3
20-29	78	12.1	77	14.4	106	17.1	49	8.78
30-39	113	17.6	66	12.3	91	14.7	88	15.8
40-49	134	20.8	73	13.6	115	18.5	92	16.5
50-59	132	20.5	95	17.8	117	18.8	110	19.7
60-69	78	12.1	63	11.8	67	10.8	74	13.3
70-96	42	6.52	35	6.5	43	6.92	34	6.09
Ethnicity								
Non-Indigenous	126	19.6	70	13.1	29	4.67	167	29.9
Indigenous	518	80.4	465	86.9	592	95.3	391	70.1
Community								
Aklavik, NT	72	11.2	258	48.2	203	32.7	127	22.8
Old Crow, YT	89	13.8	44	8.22	88	14.2	45	8.06
Fort McPherson, NT	115	17.9	59	11.0	105	16.9	69	12.4
Tuktoyaktuk, NT	56	8.70	29	5.42	46	7.41	39	6.99
Ross River, YT	61	8.47	41	7.66	46	7.41	56	10.0
Teslin, YT	85	13.2	32	5.98	45	7.25	72	12.09
Inuvik, NT	86	13.4	37	6.92	33	5.31	90	16.1
Pelly Crossing, YT	36	5.59	19	3.55	28	4.51	27	4.84
Carmacks, YT	44	6.83	16	2.99	27	4.35	33	5.91
Symptoms								
	Prevalence	95% CI	Prevalence	95% CI	Prevalence	95% CI	Prevalence	95% CI
Sex								
Epigastric pain	21.4	18.3, 24.8	17.0	13.9, 20.5	17.4	14.5, 20.6	21.7	18.3, 25.3
Epigastric discomfort	20.8	17.7, 24.2	13.9	11.0, 17.1	15.0	12.3, 18.1	20.6	17.3, 24.2
Nausea	22.0	18.9, 25.5	15.5	12.6, 18.9	16.6	13.7, 19.7	21.9	18.5, 25.5
Postprandial fullness	24.8	21.6, 28.4	18.1	15.0, 21.7	19.6	16.6, 23.0	24.2	20.7, 28.0
Excessive belching	19.9	16.9, 23.2	15.7	12.7, 19.1	17.7	14.8, 20.9	18.3	15.2, 21.7
Upper abdominal bloating	33.2	29.6, 37.0	19.8	16.5, 23.4	24.3	21.0, 27.9	30.3	26.5, 34.3
Early satiety	26.4	23.0, 30.0	23.8	20.2, 27.6	23.8	20.5, 27.4	26.7	23.1, 30.6

P14.07**EFFICACY OF STANDARD TRIPLE THERAPY IN *HELICOBACTER PYLORI* INFECTION: A SINGLE CENTRE IRISH EXPERIENCE****H. SHAH, A. QASIM, A. HAFEEZ**

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Objective: There have been recent concerns regarding increasing antibiotic resistance and poor *Helicobacter* eradication rates with standard regimens. This has led to changes in suggested therapy regimens for areas with increasing bacterial resistance. The aim of this retrospective therapy was to assess *H. pylori* eradication among treatment naive patients who received standard triple therapy following positive urease test.

Patients and Methods: All included individuals attended our endoscopy services between January 2022 to March 2023. Patient age, gender, endoscopy indication, duration and constituents of used therapy, use of concomitant medications, therapy outcomes, complication and any drug allergies were recorded. Therapy outcomes were determined using urea breath test performed at least 6 weeks following therapy completion.

Results: A total of 241 (male= 120) individuals were included in final analysis. Median age was 52 years with range 18-83 years. Indication for endoscopy in majority (90%) was non-ulcer dyspepsia (n=219). Standard triple therapy consisted of standard dose proton pump inhibitor (PPI), with amoxicillin 1-gram and clarithromycin 500 milligram twice daily (n=230) and metronidazole 400 milligram was substituted in penicillin allergic (n=11). Esomeprazole was most commonly used PPI (n=201). Therapy failure rate was 15.7% (n=38) and eradication failures in male and female were similar, 16.7% and 14.8% respectively. Therapy failure for age group 40-50 years was 21.4%.

Conclusions: In our limited experience triple therapy outcomes were within acceptable range. Higher antibacterial resistance was not observed in our selected group. Further publication of wider scale multicentre experience will be helpful in determining antibiotic resistance in wider community levels.

H. Shah: None. A. Qasim: None. A. Hafeez: None.

P14.08

THE FREQUENCY OF DETECTION OF SEROLOGICAL MARKERS OF ATROPHY IN RESPONDENTS FROM AN EPIDEMIOLOGICAL STUDY OF THE PREVALENCE OF *HELICOBACTER PYLORI* INFECTION IN MOSCOW: FIRST RESULTS

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Objective: *H. pylori* causing atrophic gastritis, which is associated with gastric cancer.

The aim of the study was to assess the gastric mucosa atrophy serological markers (serum pepsinogen I (PG I) and pepsinogen II (PG II) concentration) and their correlation with the results of a gastric mucosa morphological assessment.

Materials and Methods: We enrolled 1650 residents of Moscow aged from 18 to 80, 28% male, (mean age 43±15), 72% female (mean age 46±15). All respondents underwent ¹³C-UBT and the serum PG I and PG II concentrations were tested. Serological atrophic gastritis was diagnosed if a serum PG I/II ratio of < 3.0 and a serum PG I level of < 30 µg/l. Upper GI endoscopy with OLGA system was performed in 43 respondents.

Results: The average prevalence of *H. pylori* was 38.18%. The highest rates of low serum PG I were found in the group older than 65 years old (26.76%). PG I/II ratio lower than 3.0 was tested in 15.2% of participants, while in the group of older than 65 years low ration was seen in 31.81% of participants. The low PG I and PG I/II ratio were found to have a correlation with atrophic gastritis according to OLGA -0.09 ($p<0.01$) and -0.18 ($p<0.01$), respectively. Low PG I and PG I/II ratio were also correlated with the stage of gastritis according to OLGA, -0.09, ($p<0.01$) and -0.17 ($p<0.01$).

Conclusions: The serological atrophic gastritis was confirmed in 15% of analyzed cohort. In the older age group (65 years and older) it exceeds 25%.

D. Bordin: B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; "Moscow Center for Innovative Technologies in Healthcare" administered by the Moscow Healthcare Department. K. Nikolskaya: B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; "Moscow Center for Innovative Technologies in Healthcare" administered by the Moscow Healthcare Department. I. Voynovan: B. Research Grant (principal investigator, collaborator or

consultant and pending grants as well as grants already received); Significant; “Moscow Center for Innovative Technologies in Healthcare” administered by the Moscow Healthcare Department. A. Dorofeev: B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; “Moscow Center for Innovative Technologies in Healthcare” administered by the Moscow Healthcare Department. S. Khomeriki: B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; “Moscow Center for Innovative Technologies in Healthcare” administered by the Moscow Healthcare Department.

P14.09

COMMUNITY-DRIVEN INVESTIGATION OF ENVIRONMENTAL SOURCES OF *H. PYLORI* INFECTION IN INDIGENOUS COMMUNITIES IN NORTHERN CANADA

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Objective: The Canadian North *Helicobacter pylori* (CANHelp) Working Group conducts community-driven projects to address the high frequency of *H. pylori* (*Hp*) infection and gastric cancer in Indigenous communities in Northern Canada. Community members were particularly worried about whether *Hp* spreads through contaminated drinking water. While evidence suggests that *Hp* spreads mainly through direct person-to-person contact, the contribution of environmental sources of infection remains unclear. This study examines the association between environmental exposures and *Hp* prevalence in 9 communities in the Northwest Territories and Yukon, Canada.

Patients and Methods: This cross-sectional study uses CANHelp project data collected during 2008-2017. Of 1,422 participants, household exposures were available for 1,146, individual exposures for 927, and *Hp* status for 1,378; 407 had data on all study variables. We report *Hp* prevalence and 95% confidence intervals (CI) by exposure. We will use multivariable logistic regression to estimate associations (to be added).

Results: Of 407 participants (male=43%, Indigenous=86%), 55% (225/407) were *Hp*-positive. Among *Hp*-positive participants, 97% (218/225) were Indigenous (*Hp* prevalence=62%, 95%CI: 57, 68) and 3% (7/225) were non-Indigenous (*Hp* prevalence=12%, 95%CI: 5, 24). Compared to unexposed participants, *Hp* prevalence was similar for those who reported drinking untreated water in the preceding 12 months (56%, 95%CI: 47, 64), ever drinking untreated water (55%, 95% CI: 50, 60), problems with sewage (59%, 95%CI: 43, 74), mouse droppings in the house (59%, 95%CI: 43, 74), or handling animal innards (57%, 95%CI: 52, 62).

Conclusions: This lays the groundwork for multivariable analysis to estimate associations adjusted for confounding.

L. Baquiran: None. E. Walker: None. T. Cromarty: None. K.J. Goodman: None.

P14.10

REAL-TIME ASSESSMENT OF PH BY ENDOFASTER, ANY ADVANTAGES TO THE CLINICAL PRACTICE?

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Objective: The use of Proton Pump Inhibitors (PPIs), theoretically decreases the bacterial load of *Helicobacter pylori* (Hp), compromising the acuity of diagnostic methods. Endofaster measures real-time concentration of ammonia (NH₃) and pH in gastric juice, allowing *Helicobacter pylori* (Hp) detection during upper gastrointestinal endoscopy (EGD). We thus aim to evaluate if higher gastric pH has a correlation with symptoms and if it decreases the acuity of the detection of Hp by histology, stool antigen test and Endofaster.

Patients and Methods: Prospective single center cohort study. All the consecutive patients that underwent upper endoscopy with indication for Hp testing. Patients with prior evidence of no Hp infection or with insufficient gastric juice were excluded. PPIs intake was considered in case they had been taken in the two previous weeks.

Results: Inclusion of 99 patients (46.7% male; median age-60years, IQR 46-68). PPI was taken in 45 cases. Median pH 2.1 (IQR 1.6-4.5). A statistically significant difference was found between patients under PPI (3.1 (IQR3.1-4.5) and patients not taking these drugs 1.7 (IQR1.4-2.1); $p < 0.001$). The univariate analysis revealed that dyspeptic or gastroesophageal reflux symptoms were not associated with gastric pH ($p = 0.581$). The multivariate analysis revealed that PPIs did not compromise the evaluation of Hp by histology, stool antigen test and Endofaster, despite the fact that in the latter, p -value was almost statistically significant ($p = 0.084$).

Conclusions: Higher gastric pH (assessed by Endofaster) does not seem to be associated with symptoms. Nevertheless, Higher gastric pH, associated with PPIs may compromise the detection of Hp by Endofaster.

M. Temido: None. A. Trigo: None. N. Almeida: None. E. Gravito-Soares: None. M. Gravito-Soares: None. L. Santos: None. C. Chaves: None. D. Feijó: None. M. Viegas: None. M. Donato: None. A. Carmo: None. C. Chaves: None. F. Rodrigues: None. M. Cipriano: None. P. Figueiredo: None.

P14.11

TACKLING ANTIBIOTIC RESISTANCE OF *HELICOBACTER PYLORI*: A MULTILAYERED PROBLEM

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Objective: Antibiotic resistance is a global health problem and one of the main reasons for *Helicobacter pylori* (*H. pylori*) infection eradication failure. Pretreatment susceptibility testing has been proposed as the key in overcoming antibiotic resistance. However, the complexity of *H. pylori* genotype has made this task more challenging. The aim of this study was to assess the prevalence of *H. pylori* resistance to most commonly prescribed antibiotics.

Material and Methods: A retrospective interventional study including 180 *H. pylori* isolates from *H. pylori*-positive patients was conducted. Resistance to clarithromycin (CLA-R) and fluoroquinolones (FLQ-R) was assessed using the real time-PCR molecular test.

Results: Antibiotic resistance was detected in 67.2% of patients; the overall CLA-R was 55.6%, FLQ-R was 50%, while dual resistance was 33.8%. CLA-R in the treatment-naïve patients was 42.8%, FLQ-R was 32.1% and dual resistance was 28.6%. In the previously treated patient-group, CLA-R was 61.3%; FLQ-R 58% while dual resistance was 42.7%. Interestingly, 2.1% samples of the total population simultaneously displayed a completely sensitive and resistant genotype to FLQ, suggesting the potential presence of at least two *H. pylori* isolates in the biopsy sample.

Conclusions: An alarmingly high antibiotic resistance was noted across all patient-groups, regardless if previously treated or not. This suggests the need for a more in-depth assessment of this problem and, considering discrepancies between *in vitro* and *in vivo* antibiotic resistance, being mindful of the possibility of a simultaneous presence of more *H. pylori* strains as possible reason for treatment failure.

V. Milivojevic: None. D. Kekic: None. L. Ranin: None. T. Milosavljevic: None.

P14.12

THE EFFICACY AND SAFETY OF VONOPRAZAN IN DUAL/TRIPLE/QUADRUPLE REGIMENS BOTH IN FIRST-LINE AND RESCUE THERAPY FOR *HELICOBACTER PYLORI* ERADICATION: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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Objective: The efficacy of *H. pylori* eradication therapies containing a proton pump inhibitor (PPI) has lately decreased. Vonoprazan (VPZ), a potassium-competitive acid blocker, provides higher gastric acid suppression than PPIs. We performed a meta-analysis evaluating the efficacy and safety of VPZ for *H. pylori* eradication.

Materials and Methods: Studies were searched in PubMed, Embase and the Cochrane Library. The efficacy was evaluated by intention-to-treat analysis. Data were combined by meta-analysing risk differences (RD), and heterogeneity was evaluated by subgrouping.

Results: Overall, 75 studies evaluated 44,992 patients (22,264 receiving VPZ and 22,658 PPIs). The overall VPZ efficacy was 88% (95%CI=87-90%): 85%, 88% and 95% with dual/triple/quadruple-VPZ-containing therapies. No significant differences were found between dual vs. triple regimens. The first-line VPZ efficacy was 87% (95%CI=86-89%) whereas it was 90% (95%CI=87-93%) in rescue therapy. VPZ performed better than PPIs in treatment-naïve patients (87% vs. 70% respectively; RD=0.12, 95%CI=0.10-0.14, $p<0.00001$, $I^2=83%$); however, no significant differences were shown in rescue therapy (further details in Table 1). VPZ adverse events rate was 18% (95%CI=15-20%) and did not differ from PPIs-based regimens.

Conclusions: The efficacy of VPZ-based regimens was over 85% in all treatments. The advantage of triple over dual VPZ-based regimens could not be demonstrated. In treatment-naïve and clarithromycin-resistant patients, VPZ performed better than PPIs; however, in rescue therapy and in clarithromycin-susceptible patients, this advantage was not confirmed. Tolerability was similar with both regimens.

B. Martínez: None. **O.P. Nyssen:** B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; Mayoly and Allergan. **F. Consultant/Advisory Board;** Significant; Mayoly and Allergan. **J.P. Gisbert:** B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; Mayoly, Allergan, Diasorin, Gebro Pharma, and Richen. **D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness);** Significant; Mayoly, Allergan, Diasorin, Gebro Pharma, and Richen. **F. Consultant/Advisory Board;** Significant; Mayoly, Allergan, Diasorin, Gebro Pharma, and Richen.

TABLE 1. COMPARISONS OF VONOPRAZAN-BASED VS. PPI-BASED THERAPY FOR *H. PYLORI* ERADICATION.

SUBGROUP ANALYSES	RD [95%CI]	NUMBER OF STUDIES	NUMBER OF PARTICIPANTS
First-line therapy	0.12 [0.10, 0.14]*	41	31,229
First line therapy (only RCTs)	0.08 [0.04, 0.11]*	16	4,763
Rescue therapy	0.03 [-0.01, 0.06]	14	6,675
Rescue therapy (only RCTs)	0.07 [-0.24, 0.38]	2	109
Patients with clarithromycin-sensible strains	0.05 [0.01, 0.09]	8	2,125
Patients with clarithromycin-susceptible strains (only RCTs)	0.02 [-0.01, 0.05]	5	1,689
Patients with clarithromycin-resistant strains	0.35 [0.27, 0.42]*	7	797
Patients with clarithromycin-resistant strains (only RCTs)	0.32 [0.19, 0.46]*	4	519

RD-risk difference; CI-confidence interval; RCT: ransomised clinical trial; *Statistically significant

P14.13

EFFECTIVENESS & SAFETY OF HIGH DOSE DUAL THERAPY: A SINGLE CENTRE EXPERIENCE

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Objective: In recent years, *H. pylori* eradication rates have fallen, likely due to increasing antibiotic resistance. Previously our team showed Clarithromycin Triple Therapy (CTT) failure in 123/482 (26%) of people-suggesting high prevalence of clarithromycin-resistant *H. pylori* in Ireland. There are few therapeutic options available in Ireland. Maastricht VI guidelines recommends High Dose Amoxicillin (HDA) can be considered in areas of high clarithromycin-resistance, subject to local evidence.

Materials and Methods: We aimed to assess efficacy of HDA therapy for *H. pylori*. All patients testing positive for *H. pylori* in a Tertiary Centre were treated with HAD (Amoxicillin 1g TDS & Esomeprazole 40mg BD x2/52). Eradication was confirmed with UBT 4/52 post-therapy. A delta-over-baseline >4 was considered positive. Demographics & CTT eradication rates between 2019-2022 were reviewed from the EPR.

Results: To date, 111 patients were identified. 7 were excluded due to penicillin allergy. 17 declined/DNA follow-up testing (N=87). No patients had *H. pylori* C&S available. 53 (61%) were female, mean age 46. 53 patients (61%) were treatment-naïve (57%Female, mean age 45). Eradication was achieved in 53 (61%) cases overall, 37 (70%) in the naïve group. Age & Gender were not predictors of eradication. There was no significant difference in eradication between HDA & CTT groups ($p=0.5093$).

Conclusions: Eradication rates were disappointingly low 17 (15%) patients declined post-eradication UBT. This represents a re-testing bias towards those with symptoms/persistent infection. While not a direct comparison with our previous standard-of-care, HDA appears non-inferior to CTT as first line therapy for *H. pylori* for our cohort. It is cheaper, has a better side effect profile & fewer drug interactions and could be considered as first line therapy for *H. pylori* when quadruple therapy is unavailable.

C. Costigan: None. T.J. Butler: None. F. O'Hara: None. J. O'Connell: None. S. Smith: None. D. McNamara: None.

P14.14

ASSOCIATION BETWEEN ALCOHOL, TOBACCO AND CAGA AND VACA POSITIVE HELICOBACTER PYLORI INFECTION IN INDIVIDUALS WITH GASTROPATHIES IN BRAZIL

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Objective: *Helicobacter pylori* is associated with several gastropathies, including gastric cancer. The diversity in the severity is due to the imbalance of the parasite-host relationship. The gene *cagA* and the *vacA* gene are virulence factors associated with severe gastropathies. Alcohol and tobacco consumption are risk factors for *H. pylori* infection. The study aimed to verify the association of the *H. pylori* *cagA* and *vacA* virulence genes isolated from dyspeptic patients with tobacco and alcohol consumption and the severity of the infection.

Material and Methods: A total of 117 samples of dyspeptics were collected. Samples were subjected to 16S rRNA extraction and amplification. Positive samples were used for *cagA* and *vacA* virulence gene screening. The amplicons were sequenced for confirmation. The study was approved by the Ethics Committee nº 2,519,032.

Results: The prevalence of *H. pylori* was 68.37% (80/117), of these samples 75% (60/80) were positive for the *cagA* gene and 52.50% (47/80) positive for the *vacA* gene. No statistically significant associations were found between *cagA* and alcohol ($p=0.68$) and tobacco ($p=0.57$). Regarding the *vacA* gene, no association was observed with alcohol ($p=0.18$) or tobacco ($p=0.85$). The frequency of severe and non-severe diseases was higher in *cagA* and *vacA* positive patients, but there was no relationship between alcohol and tobacco consumption.

Conclusions: The prevalence of *H. pylori* was high in patients undergoing upper digestive endoscopy. Tobacco and alcohol were not risk factors for serious and non-severe diseases in patients infected with *H. pylori*, *cagA* and *vacA* positive strains.

M.S. Barbosa: None. D.P. Garcia: None. R.D. Santos: None. L.D. Assunção: None. F.D. Moraes: None. L.T. Rasmussen: None. A.F.P.L. Ramos: None. M.P. Curado: None.

P14.15

PREVALENCE OF RESISTANCE *HELICOBACTER PYLORI* TO CLARITHROMYCIN IN PATIENTS WITH RHEUMATOID ARTHRITIS AFTER COVID-2019

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Objective: To assessment the prevalence of clarithromycin-resistant strains of *Helicobacter pylori* (*H. pylori*) in rheumatoid arthritis patients with nonsteroidal anti-inflammatory drug gastropathy after COVID-2019.

Patients and Methods: We studied 60 rheumatoid arthritis patients after COVID-2019 (mean age 36.9 years) with NSAID-gastropathy. *H. pylori* infection detected by rapid urease test (RUT), 13C-urea breath test (13C-UBT) and ELISA (antibodies to *H. pylori* in the serum). *H. pylori* resistance to clarithromycin determined by multiplex PCR for determination of A2142G and A2143G mutations.

Results: *H. pylori* infection prevalence according to RUT was 65.0% (39 patients), 13C-UBT and ELISA were positive in 68.3% (41 patients) and 63.3% (38 patients), $p=0.03$. DNA *H. pylori* from the gastric mucosa biopsies obtained at 66.7% (40 patients). The clarithromycin-resistant level in the study group was 17.5% (7 patients). Isolated mutations of A2143G and A2142G determined in 1 (14.3%) and 2 (28.6%) mucosa samples, and the combination of mutations A2143G and A2142G detected in 4 (57.1%) patients.

Conclusions: *H. pylori* clarithromycin- resistance level among rheumatoid arthritis patients after COVID-2019 does not have a significant effect on the choice of the eradication therapy regime in our region.

V. Kryvy: None. I. Iskova: None. I. Klyarytska: None. T. Tsapyak: None.

P14.16

TIMING OF HELICOBACTER ERADICATION IN PATIENTS WITH PEPTIC ULCER DOES NOT AFFECT SUCCESS RATE

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Objective: *Helicobacter pylori* (HP) eradication is essential in patients with peptic ulcer to reduce peptic ulcer recurrence. Proton pump inhibitor (PPI) for 4 to 8 weeks is treatment of choice for peptic ulcer disease. To date, it has not been established when HP eradication therapy should be initiated in patients with peptic ulcer disease (PUD). We aimed to evaluate whether initiation time of HP eradication after diagnosis of PUD affects success rate.

Patients and Methods: We retrospectively reviewed 2,427 patients underwent esophagogastroduodenoscopy (EGD) and HP status by rapid urease test, urea breath test or *Helicobacter pylori* PCR from Jan 2018 to Dec 2021 in a single center. Data were collected including EGD results, underlying disease, PPI treatment period from diagnosis of PUD to HP eradication, presence or absence of PUD hemorrhage, HP eradication regimen and success or failure of HP eradication.

Results: EGD revealed 1,484 PUD, 109 early gastric cancer, 4 MALT lymphoma, and 46 lymphofollicular gastritis. Of the 1,484 PUD patients, HP was positive in 691 patients (41.7%). PPI treatment period from PUD diagnosis to initiation of HP eradication ranged from 0 to 180 days. Comparing patients with PPI treatment period less than 4 weeks with those over 4 weeks success rate of HP eradication did not differ significantly. (success rate 89.4% and 86.2%, respectively, $p=0.509$).

Conclusions: Timing of HP eradication after diagnosis of PUD did not affect HP eradication success rate.

Y. Kim: None. C. Oh: None. J. Kim: None. J. Park: None.

POSTER SESSION 15: MICROBIOTA 1

P15.01

STANDARDISATION OF MICROBIOME RESEARCH WITH THE NFDI4MICROBIOTA

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There are as many microbiomes as there are methods to study them - however as re-using previous research data is becoming more and more important so does the standardisation of methodology reaching from sample collection to wetlab work to computational analysis. All of these aspects of the research process can have an impact on the scientific conclusions drawn at the end. The NFDI4Microbiota is a German consortium aiming to support the national and international microbiome community with data access, analysis services, (meta)data standards and training. For the metadata standardisation not only creating tools to check for data and metadata quality but also to make it as easy as possible for users to submit metadata - as few as needed and as many as possible. This is supported by setting standards for experimental protocols as well as computational workflows which are tested for their practicality through our community-submitted use-cases. The NFDI4Microbiota will support scientists at every step of the research process, will help to make microbiome data comply with the FAIR principles (findable, accessible, interoperable and re-useable) and provide a valuable, community drive resource for microbiome research.

S. Schulz: None. M. Kuhn: None. P. Bork: None.

P15.02

ALTERATION OF GUT MICROBIOTA IN ULCERATIVE COLITIS

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Objective: Ulcerative colitis (UC) is a chronic, relapsing inflammatory bowel disease with a multifactorial etiology. Besides other factors, associations of intestinal bacteria and the onset and course of UC have also been reported. The aim of our study was to identify changes in the different taxonomic levels of gut microbiota during active and quiescent UC.

Materials and Methods: Study included three age- and sex-matched patient groups: control (CON, n=25), active UC (aUC, n=27) and quiescent UC (qUC, n=20). Stool DNA was subjected to the 16S rRNA-coding gene V1-V2 hypervariable region next generation sequencing on MiSeq (Illumina) platform. Further, bioinformatics and statistical analysis were performed.

Results: CON patients had the highest α -diversity compared to aUC or qUC patients, but there were no significant differences between UC activity states. Significant microbial community clusters were identi-

fied between CON subjects and patients with aUC or qUC. However, no significant differences in β -diversity were found between two disease states. Samples from CON subjects had higher in-between sample similarity (mean 0.542 ± 0.117) than patients with aUC (mean 0.638 ± 0.161) and qUC (0.6 ± 0.145). In addition, 16, 13 and 27 core taxa were identified in aUC, qUC and CON group, respectively. Differential abundance of *Paraprevotella* and *Cuneatibacter* genera was detected when comparing CON vs. aUC, *Faecalibacterium*, *Prevotellamassilia*, *Mediterraneibacter* and *Cuneatibacter* genera – CON vs. qUC.

Conclusions: our study revealed the association of both qualitative and quantitative gut microbiota changes with UC. Study was funded by the Research Council of Lithuania (Grant No. S-MIP-20-56).

R. Inciuraite: None. R. Gedgudas: None. R. Lukosevicius: None. S. Juzenas: None. G. Kiudelis: None. L.V. Jonaitis: None. J. Kupcinskis: None. J. Skieceviciene: None.

P15.03

EFFECT OF ORAL *BIFIDOBACTERIUM BREVE* ON FACIAL SKIN: A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED STUDY

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Objective: Recently, anti-inflammatory and/or photoprotective effects of *Bifidobacterium* are increasingly studied in both mice and humans, yet the full effects are still unknown. In this study, we aim to investigate the effect of oral *B. breve* M-16V on the facial skin in human.

Material and Methods: In a randomized double-blind placebo-controlled trial, adult women with no undergoing clinical treatment on face received *Bifidobacterium breve* M-16V (1×10^{10} CFU) or placebo twice daily for 12 weeks. Facial skin condition was evaluated both objectively and subjectively by dermatologist, Canfield VISIA[®] evolution and participants, at baseline, 4, 8 and 12 weeks. The primary outcome was the total VISIA[®] score at each check point. All the other skin scores were also analysed.

Results: The data of 120 participants (59 probiotic, 61 placebo) were collected. The mean total VISIA[®] score was tended small in probiotic group at week12 but did not show statistical difference ($p=0.38$). The count of brown spots decreased at week4 in probiotic group ($p=0.011$) while it worsened in placebo at week12 ($p=0.001$). The adjusted score of brown spots improved in probiotic group at week4 ($p=0.001$) and week8 ($p=0.05$). The subjective evaluation of skin moisture, wrinkles and bowel movement improved in probiotic group at week12. Adverse events were seen in 37.3%, and its frequency was not statistically different between both groups. There were no serious adverse events during the trial.

Conclusions: Oral intake of *B. breve* M-16V appears to benefit skin condition by improving brown spots, facial wrinkles, moisture and bowel movement.

Y. Nishikawa: None. T. Ohkusa: None. N. Sato: None.

P15.04

MUCIN-MICROBIOME SIGNATURES SHAPE THE TUMOR MICROENVIRONMENT IN GASTRIC CANCER

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Objective: We aimed to identify mucin-microbiome signatures shaping the tumor microenvironment in gastric adenocarcinomas and clinical outcomes.

Patients and Methods: We performed high-throughput profiling of the mucin phenotypes present in 108 gastric adenocarcinomas and 20 functional dyspepsia cases using validated mucin-based RT-qPCR with subsequent immunohistochemistry validation and correlated the data with clinical outcome parameters. The gastric microbiota was assessed by 16S rRNA gene sequencing, taxonomy, and community composition determined, microbial networks analyzed, and the metagenome inferred in association with mucin phenotypes and expression.

Results: Gastric adenocarcinomas with an intestinal mucin environment or high-level MUC13 expression are associated with poor survival. On the contrary, gastric MUC5AC or MUC6 abundance was associated with a more favorable outcome. The oral taxa *Neisseria*, *Prevotella*, and *Veillonella* had centralities in tumors with intestinal and mixed phenotypes and were associated with MUC13 overexpression, highlighting their role as potential drivers in MUC13 signaling in GC. Furthermore, dense bacterial networks were observed in intestinal and mixed mucin phenotype tumors whereas the lowest community complexity was shown in null mucin phenotype tumors due to higher *Helicobacter* abundance resulting in a more decreased diversity. Enrichment of oral or intestinal microbes was mucin phenotype dependent. More specifically, intestinal mucin phenotype tumors favored the establishment of pro-inflammatory oral taxa forming strong co-occurrence networks.

Conclusions: Our results emphasize key roles for mucins in gastric cancer prognosis and shaping microbial networks in the tumor microenvironment. Specifically, the enriched oral taxa associated with aberrant MUC13 expression can be potential biomarkers in predicting disease outcomes.

B. Oosterlinck: None. W. Arras: None. H. Ceuleers: None. J.G. De Man: None. K. Geboes: None. H. De Schepper: None. M. Peeters: None. S. Lebeer: None. J. Skieceviciene: None. G.L. Hold: None. J. Kupčinskas: None. A. Link: None. B.Y. De Winter: None. A. Smet: None.

P15.05

FAECAL TRANSPLANTATION FOR IRRITABLE BOWEL SYNDROME PATIENTS: INCREASING THE DOSE OF THE TRANSPLANT IMPROVES THE RESPONSE OF MALES AND PATIENTS WITH MODERATE SYMPTOMS

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Objective: Females IBS patients and patients with severe IBS respond better to faecal microbiota transplantation than males and those with moderate IBS.

Patients and Methods: The study included 186 IBS patients (131 females and 55 males and 143 with severe and 43 with moderate IBS). They were randomized 1:1:1 into 90 g transplant administered to the colon, to the duodenum, or to the duodenum twice with a week interval. The patients provided a faecal sample and were asked to complete questionnaires at the baseline, and at 3 months, 6 months, 1 year and 2 years after FMT. The faecal bacteria were analysed using 16S rRNA gene PCR DNA amplification/probe hybridization covering the V3-V9 regions.

Results: The response rates in females were 82%, 78%, 71% and 70% at 3 months, 6 months, 1 year and 2 years after FMT, respectively. The corresponding figures for males were 72%, 67%, 67% and 60%. There was no difference between females and males regarding the response rates to FMT at all observation times. In IBS patients with severe IBS, the response rates were 75%, 73%, 65% and 69% at 3 months, 6 months, 1 year and 2 years after FMT, respectively. The corresponding values for IBS patients with moderate IBS were 80%, 61%, 69% and 62%. The response rates did not differ between IBS patients with severe and moderate IBS at all observation intervals.

Conclusions: Increasing the transplant dose to 90 g improved responses to FMT of the male IBS patients and patients with moderate IBS.

M. El-Salhy: None. O. Gilja: None. J. Hatlebakk: None.

P15.06

THE IMPACT OF H. PYLORI ERADICATION REGIMENS ON GUT MICROBIOME TAXONOMIC DISTRIBUTION AND RESISTOME

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Objective: The administration of antibacterial therapies aimed at eradicating *Helicobacter pylori* (*H. pylori*) may amplify the reservoir of resistant bacteria within the gastrointestinal tract. In this study, we examined the diversity of the gut microbiome and resistome within a six-month interval after eradication in two eradication cohorts.

Materials and Methods: The current randomized controlled clinical trial is a part of the GISTAR study in Latvia. Asymptomatic individuals with *H. pylori* infection were enrolled and randomly assigned to receive either 14-day standard clarithromycin-based triple therapy (clarithromycin 500 mg, amoxicillin 1000 mg, esomeprazole 40 mg, BID, further AMX/CLARI) or high-dose amoxicillin/bismuth therapy (bismuth-subcitrate 240 mg given BID, amoxicillin 1000 mg TID, esomeprazole 40 mg BID, further AMX/BI). A control group with comparable characteristics and unknown *H. pylori* status was also included. Stool samples were collected before and six months post-treatment. Shotgun metagenomic sequencing was conducted to analyze the gut microbiota composition.

Results: In total, 27 patients received AMX/BI and 31 – AMX/CLARI therapy, 50 patients were designated as controls. We did not reveal a noticeable shift pattern of the 150 most abundant genera among the therapy groups. Alpha and beta diversities almost restored at follow-up. However, a significant difference ($p=0.05$) was observed in antimicrobial resistance gene counts in the AMX/CLARI group.

Conclusions: Clarithromycin-based triple therapy induced a broad range of significant changes in resistance mechanisms for at least a 6-month period. That suggests limiting such treatments even in the areas with low *H. pylori* resistance to clarithromycin.

O. Sjomina: None. R. Vangravs: None. E. Leonova: None. I. Polaka: None. D. Pupola: None. K. Civkulis: None. A. Jenicka: None. S. Parsutins: None. I. Stonans: None. J.Y. Park: None. L. Engstrand: None. M. Leja: None.

P15.07

INCREASING CORRELATION IN THE MICROBIOTA COMPOSITIONS OF SALIVA, GASTRIC JUICE, AND GASTRIC TISSUE DURING GASTRIC CARCINOGENESIS

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Objective: Although gastric microbiome is suspected to play a role in gastric cancer development, few studies have examined its association with oral microbiome. We aimed to investigate the relationship between the oral and gastric microbiomes at different stages of gastric carcinogenesis.

Materials and Methods: We collected saliva, gastric juice, gastric tissue, serum, urine, and feces samples from 9 healthy adults, 46 low-grade dysplasia (LGD), 25 high-grade dysplasia (HGD), and 27 gastric cancer (GC) patients. We extracted bacteria and bacteria-derived vesicles from these samples and performed metagenome analysis using NGS analysis with the 16S rRNA gene. We then used Spearman's rank correlation to analyze the similarity of microbial composition between each sample at each stage of disease progression.

Results: Our analysis using bacteria showed that the similarity of microbial composition between saliva and gastric juice increased from 0.18 in the normal group to 0.58, 0.60, and 0.58 in LGD, HGD, and GC groups, respectively. We found similar trends in the similarity of microbial composition between gastric juice and gastric tissue, as well as between saliva and gastric tissue, with a stronger association in

the patient groups compared to the normal group. However, this trend of increasing similarity was less pronounced in the analyses using bacteria-derived vesicles.

Conclusions: The similarity of microbiome composition between saliva, gastric juice, and gastric tissue increased along the cascade of gastric carcinogenesis. This suggests that oral commensals may play a role in the development of gastric cancer through their interaction with the gastric microbiome.

H. You: None. H. Seo: None. J. Park: None. B. Kim: None. J. Kim: None.

P15.08

COLORECTAL SURGERY AND ANASTOMOTIC INSUFFICIENCY ARE ASSOCIATED WITH MUCOSAL MICROBIOME ALTERATIONS

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Changes in the mucosal microbiome after colorectal surgery may be associated with postoperative complications. In particular, anastomotic leakage (AL) may depend on microbial factors that could lead to an adverse outcome. The aim of this study was to evaluate the dynamics of microbiome changes in CRC patients before, during and after surgery in relation to AL. We systematically analysed sequential samples from patients before, during and after surgery. Biopsies were taken from 3 peritumoral sites (proximal to tumour, extra-tumour, distal to tumour). All patients received standardised preoperative intraluminal bowel decontamination and a single short course of periinterventional systemic antibiotics. DNA extraction was followed by amplification of the V1-V2 region of the 16S rRNA gene and Illumina sequencing. 259 different genera were found in the cohort, with Phocaeicola, Prevotella and Enterococcus showing the highest abundance. Hierarchical clustering showed that samples from the same patient at the same time point generally had high similarity (66%), and in 6 cases all samples formed a cluster at more than one time point. Periinterventional measures were associated with a significant decrease in diversity in samples taken during or after surgery. Samples with AL had a different microbial structure at all time points, with Prevotella being more abundant in the AL-group ($p < 0.0001$), while Phocaeicola showed greater abundance in the sufficient anastomosis group ($p = 0.04$). Colorectal surgery is associated with changes in the mucosal microbiota. Patients with AL have an altered microbiome. Further studies are needed to decipher the functional interactions between the microbiota and mucosal tissue.

K. Lehr: None. N.M. Hipler: None. D. Schanze: None. M. Zenker: None. A. Link: None. U.G. Lange: None. A. Hoffmeister: None. J. Feisthommel: None. D. Buchloh: None. B. Jansen-Winkeln: None.

P15.09

ASSESSMENT OF THE MICROBIOME OF BILIARY STENTS IN PATIENTS WITH OBSTRUCTIVE BILIARY DISEASE

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The microbiome is one of the key mediators of GI diseases, including chronic inflammatory conditions and cancer. Alterations in the biliary microbiome have been reported in patients with biliary diseases such as cholangiocarcinoma. The most previous studies have focused on either the faecal microbiome or the biliary microbiome. In this proof-of-principle study, we aimed to evaluate biliary stents as a novel biological specimens' source for microbiome analysis in patients with biliary tract disease.

A total of 123 patients with a total of 245 stents and 17 bile samples were included in this study: n=53 with malignant disease, n=70 with non-malignant disease including patients with post-operative stenosis. DNA was extracted from the stents and the V1-V2 region of the 16S rRNA gene was amplified by PCR and barcoded for high-throughput sequencing using the Illumina platform.

We detected 321 genera in the stents. The most abundant genera are Enterococcus, Lactobacillus and Escherichia/Shigella. When comparing bile with the stent microbiome, we found a high Bray-Curtis similarity, confirming that stents can be used instead of bile to analyse the bile duct microbiome. Three microbial clusters were identified that differed significantly clinically in terms of their underlying diseases, but also in terms of laboratory values such as CRP and AP ($p=0.0064$, $p=0.0021$, respectively). We have established an innovative biomarker tool for the analysis of the biliary microbiome. The stent microbiome was clustered into three distinct microbial types that were associated with different clinical phenotypes and may have clinical implications.

K. Lehr: None. N.M. Hipler: None. C. Thon: None. D. Schanze: None. M. Zenker: None. D. Bruder: None. M. Müssen: None. W. Obst: None. V. Keitel-Anselmino: None. J. Weigt: None. A. Link: None.

P15.10

THE INFLUENCE OF HEALING EARTH ON THE GASTROINTESTINAL MICROBIOME OF IBS-PATIENTS

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Objective: Irritable bowel disease (IBS) is the most prevalent functional gastrointestinal disorder affecting about 3-10% of the world's population. Luvos® healing earth is an over-the-counter medical product with the potential to alleviate IBS symptoms. Altered fecal microbiota profiles were found in patients suffering from IBS. Our study aimed to characterize the bacterial composition in fecal samples from IBS patients before, during and after treatment with healing earth.

Material and Methods: Fecal samples from twelve healthy individuals (six women, 25.5 ± 3.9 years) and nine patients with Diarrhea-predominant IBS (IBS-D) (six women, 26.7 ± 8.1 years) were collected at six different timepoints before, during and after six weeks healing earth treatment (6.2 g) twice a day. The quality of life was assessed at each time point using the IBS-QoL questionnaire. Bacterial DNA was extracted and the V1-V2-region of the 16S rRNA gene was sequenced by Illumina MiSeq.

Results: The bacterial composition was compared longitudinally for each subject as well as at each time point between the two groups. Bacterial communities show no significant changes over time in case of healing earth intake. Additionally, no significant changes in the quality of life were observed during the intake period.

Conclusions: In our study setup, the intake of healing earth did not result in significant changes in the bacterial communities of the study participants. Also considering the lack of improvement in the quality of life, our findings suggest that healing earth does not provide a therapeutic benefit in the treatment of IBS.

S. Krikonas: None. R. Vasapoli: C. Other Research Support (supplies, equipment, receipt of drugs or other in-kind support); Significant; © Heilderde-Gesellschaft Luvos Just GmbH & Co. KG. N. Koch: None. P. Malferttheiner: None. C. Schulz: None.

POSTER SESSION 16: MICROBIOTA 2

P16.02

MICROBIOME PROFILE OF COLORECTAL CANCER PATIENTS' GUT MUCOSA AND BLOOD PLASMA SAMPLES

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Objective: Colorectal cancer (CRC) is one of the most common cancer types worldwide and the second leading cause of cancer-related mortality. The gut microbiome takes an important part in cancerogenesis. Moreover, bacterial sequences are found in the human bloodstream and might be of clinical significance. Thereby, the aim of this study was to identify microbiome profile of CRC patients using gut mucosa biopsy and blood plasma samples and find presumable biomarkers for CRC diagnostic.

Material and Methods: In total, 313 people, including CRC patients, adenomatous polyps (AP) patients, and control individuals were recruited in this study. Blood and gut mucosa biopsies samples were collected and from all samples were extracted DNA. V1-V2 region of bacterial 16S rRNA gene were amplified and sequenced. Bioinformatical and statistical analysis were performed to reveal bacterial profile of each study group.

Results: The global structures were significantly different between control, CRC, and AP groups both in biopsy and blood samples. Analysis revealed list of bacteria the number of which was significantly different between the groups. Tissues' microbiome was 20 times richer than blood microbiome. In CRC patients' samples bacterial richness and diversity decreased in tissue and increased in blood samples. Model of 8 bacterial DNA signatures in blood showed high sensitivity and specificity (AUC: 0.801).

Conclusions: Based on tissue and blood microbial profile it was possible to distinguish healthy state from CRC or AP. Distinct bacterial DNA signatures in blood could presumably be used as biomarkers for CRC.

D. Nikitina: None. R. Lukosevicius: None. J. Kupcinkas: None. J. Skieceviene: None.

P16.03

IS GUT MICROBIOTA CHARACTERIZATION AN EFFECTIVE TOOL IN IBD DIAGNOSTICS?

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Objective: IBD has no known cure, and the treatment regimens vary based on the type, extend and severity. The composition of gut microbiota holds significant potential in assessing the disease severity and treatment outcomes. In a project funded by the Norwegian Research Council, Genetic Analysis (GA) aims to develop a gut bacteria IBD test. Results from our pilot study is presented.

Material and Methods: Fecal bacterial DNA samples from newly diagnosed treatment naïve IBD patients, and from healthy donors, were analyzed using the multiplex GA-map[®] Discovery panel on the proprietary GA-map[®] Platform technology (1) to target the 16s rRNA gene variable regions (V3 to V9). Statistical analysis was performed to compare differences between groups, and the p values were adjusted using Bonferroni's correction.

Results: Samples from 89 UC and 73 CD patients, and 64 healthy donors were analysed. In total, 40 bacteria markers showed a significant difference in abundance between healthy and CD/UC. In UC patients, *Blautia* was significantly higher in abundance while *Fusobacteria* was significantly lower in abundance when compared to healthy. In CD patients, *Akkermansia* and Lachnospiraceae was significantly lower in abundance than in healthy. *Faecalibacterium prausnitzii*, *Roseburia hominis*, and *Bacteroides* was much less abundant, while *Escherichia* and *Shigella* were more abundant in both UC and CD compared to healthy.

Conclusions: The results from the multiplex gut bacteria panel shows great opportunity for identification of distinct microbiota signatures in different disease groups and encourage the further development of a targeted microbiota tools in IBD diagnostics.

C. Casén: A. Employment (full or part-time); Significant; Genetic Analysis AS. B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; Norwegian research council. E. Ownership Interest (stock, stock options, patent or other intellectual property); Modest; CC own stocks in Genetic Analysis. T.G. Kirubakaran: A. Employment (full or part-time); Significant; Genetic Analysis AS.

P16.04

GASTRIC CANDIDA INFECTION

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The study investigated the role of Candida in the pathogenesis of gastritis infection in 35 subjects, including 17 males (49%) and 18 females (51%), who had undergone gastroscopy and had a report of macroscopic Candida plaques. The gastric fluid was analyzed for Candida culture (CHROMagar Candida plus) and UBT 13 C *Helicobacter pylori* Breath Test was performed. Results showed that 34 (98%) subjects were positive for *Candida spp.*, with 31 (91%) identified as *Candida albicans*, and three (9%) as *Candida glabrata*, while only one of all (2%) was negative. Furthermore, eleven subjects tested positive with the *Helicobacter pylori* Breath Test.

A. Barrios: None.

P16.05

USE OF THE INVERTEBRATE MODEL GALLERIA MELLONELLA LARVAE FOR HELICOBACTER PYLORI INFECTION: IMPACT ON LARVAE MICROBIOTA

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Objective: The use of animal models is important to study *Helicobacter pylori* infection, host-pathogen interactions, or the activity of a new antibacterial drug. Here, we present an assessment of the suitability of greater wax moth *Galleria mellonella* to study *H. pylori* infection, evaluating the impact of infection of *G. mellonella* microbiota.

Material and Methods: Sets of 10-18 larvae were infected with *H. pylori* reference strain J99 or with the clinical strain *H. pylori* 10222A, with bacterial concentrations between 10E5 and 10E8 CFU/mL. Control sets were created by injecting 10-18 larvae with PBS. Survival rates were determined by comparing infected larvae with control, up to 120h post-infection. Surviving larvae from infected and control sets were sacrificed, macerated, and submitted to 16S rRNA metagenomics.

Results: Initial results show that *G. mellonella* is susceptible to *H. pylori*, with survival rates being reduced by the infection with clinical strain after 24h, when compared to the reference strain. Optimal bacterial concentrations also vary with the strain used, as 10222A showed higher lethality than J99, even at lower bacterial load. Analysis of 16S data of *H. pylori* infected larvae reveals its presence among the larvae microbiome, with an average of 5.57% (\pm 5.34%) of relative abundance.

Conclusions: *G. mellonella* is susceptible to infection by *H. pylori*, establishing among the bacterial community of the larvae. Optimal bacterial concentrations must be optimized and used to assess the virulence of several clinical *H. pylori* strains in *G. mellonella* model, combining the results with data generated by 16S rRNA metagenomics.

F.F. Vale: None. J.S. Vital: None. R. Lopes-Oliveira: None. A.T. Marques: None. L. Tanoiro: None.

P16.06

GUT MICROBIOTA AND LIVER CIRRHOSIS

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Objective: Intestinal dysfunction, dysbiosis and endotoxin produced by Gram-negative bacteria are key factors in bacterial translocation in patients with liver cirrhosis and are the cause of inflammatory reactions with subsequent infections and impairment of portal and systemic circulation, thus favoring the progression and complication of liver cirrhosis.

Material and Methods: The study enrolled 15 patients with liver cirrhosis (LC) with alcohol etiology and 5 healthy controls. The severity of liver cirrhosis was assessed by MELD and Child-Pugh classification. 5 patients were with Child-Pugh score A, 5 patients were with Child-Pugh score B, and 5 patients were with Child-Pugh score C. Gut microbiota was evaluated in fecal samples using the next-generation 16S rRNA sequencing, Ion 16TM Metagenomics Solution for Personal Genome Machine.

Results: We observed differences in gut microbiota between patients with LC and the control group. In patients, we found significantly reduced *Eubacterium*, *Bacteroides*, *Ruminococcaceae*, *Faecalibacterium*, and *Bifidobacterium* and increased *Clostridium*, *Streptococcus*, *Streptococcaceae*, *Enterobacteriaceae*, *Enterococcus faecalis*. A significant reduction of *Bacteroides*, *Faecalibacterium*, and *Bifidobacterium* was observed with advancing age. Alcohol use and smoking are associated with an increase in *Clostridium*, *Streptococcus*, and *Enterobacteriaceae*. We found significantly lower levels of *Bacteroides*, *Ruminococcaceae*, *Faecalibacterium*, and *Bifidobacterium* and an increase in *Clostridium*, *Streptococcus*, *Streptococcaceae*, *Enterobacteriaceae* in patients with decompensated cirrhosis (Child-Pugh B or C).

Conclusions: Correction of impaired intestinal bacterial flora and its metabolic function might lead to the effective pathogenetic treatment of liver cirrhosis, its complications, or progression.

M. Kovacheva-Slavova: None. H. Valkov: None. T. Angelov: None. V. Petkova: None. R. Dodova: None. R. Kaneva: None. B. Vladimirov: None.

P16.07

CHARACTERIZATION OF THE MICROBIOME IN LOW MICROBIAL BIOMASS SAMPLES WITH METATRANSCRIPTOMICS

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Objective: Metatranscriptomics is a high-throughput sequencing technique to investigate the functional profile of the microbiome by examining the RNA of the entire community. However, its potential application in low microbial biomass samples has yet to be explored. Our goal was to develop a metatranscriptomics approach that can efficiently profile the microbiome in low microbial biomass samples.

Material and Methods: To establish the computational workflow of our experiment, we prepared four synthetic samples by spiking a mock microbial community of well-defined composition with a human cell line, and gradually increased the host:bacteria ratio to 10%, 70%, 90%, and 97% host cells. RNA was isolated, treated with DNase, and depleted from ribosomal RNA. Sequencing was performed on the Illumina NovaSeq 6000 with 15 Gbp/sample. Taxonomic profiling was performed using different classifiers, and the microbial profiles from each classifier were integrated into HUMAnN3 for functional analysis.

Results: After evaluating the effectiveness of different taxonomic classifiers, we found that Kraken2/Bracken with optimized settings generated the most accurate taxonomic profile (highest precision and recall) of the synthetic sample with 97% host and low microbial biomass (SS97). Notably, the use of this Kraken2/Bracken taxonomic profile greatly enhanced HUMAnN3 functional analysis of SS97, leading to the identification of a higher number of microbial functions in comparison to other classifiers.

Conclusions: We implemented an optimized metatranscriptomics strategy for profiling the microbiome in low biomass samples, which can now be effectively employed to evaluate the functional activity of the microbiome in human tissue specimens.

Acknowledgements: FCT – 2022.02141.PTDC.

C. Figueiredo: None. J. Pereira-Marques: None. R.M. Ferreira: None.

P16.08

GASTRIC CANCER METABOLITE PROFILING REVEALS THE PRESENCE OF COMPOUNDS WITH CARCINOGENIC POTENTIAL

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Objective: Gastric cancer is one of the world's most incident and deadliest cancers. The development of this malignancy is influenced by the gastric microbiome. We hypothesize that the gastric microbiome has a unique metabolic program, which generates genotoxic metabolites that promote neoplastic transformation and facilitate tumor progression. Our main aim is to identify microbiome-derived metabolites that contribute to gastric cancer.

Materials and Methods: A total of 60 samples comprising 30 gastric cancer tissues and 30 paired-normal tissues were included. Untargeted metabolomics with a semi-polar strategy was used to characterize these samples. Compounds were annotated based on confidence degree of accurate mass, known retention time and tandem mass spectra. Data was analysed using MetaDiff R Package. The carcinogenic potential of the metabolites was assessed by comprehensive searches in the literature and in multiple chemical databases.

Results: We detected a total of 873 valid metabolites in the 60 tissue samples. Using principal component analysis, a clear separation of the metabolite profiles was observed between cancer and non-cancerous tissue samples. Analysis of the differentially abundant metabolites revealed an enrichment of 41 metabolites in gastric cancer tissues. By combining the information regarding their association with cancer, toxicity, and microbial enzymatic reactions, we identified several microbial-derived metabolites with carcinogenic potential.

Conclusions: The metabolite profile of gastric cancer harbour compounds with carcinogenic potential. Further studies are needed to ascertain the contribution of the gastric microbiome to the production of these metabolites.

2022.02141.PTDC

R.M. Ferreira: None. I. Castro: None. M. Mendes-Rocha: None. J. Pereira-Marques: None. C. Figueiredo: None.

P16.09

GUT MICROBIOTA PROFILE OF PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Objective: There is increasing evidence that gut microbiota dysbiosis can play a role in the development of the type 2 diabetes mellitus (T2D).

Patients and Methods: The aim of this study was to investigate gut microbiota taxonomic composition in patients with T2D compared to healthy adults. Gut microbiota composition was analyzed in fresh stool samples from 36 patients with T2D and 42 healthy subjects (control group) using 16SrRNA sequencing (IlluminaMiSeq-platform). Relative abundance of bacterial phylum and genera were evaluated; $p < 0.05$ was considered statistically significant.

Results: Two phyla were the most predominant in the gut of the T2D and control group: Firmicutes ($77.2 \pm 12.2\%$ and $76.9 \pm 13.8\%$, $p = 0.9$) and Bacteroidetes ($13.6 \pm 10.1\%$ and $15.0 \pm 13.4\%$, $p = 0.8$), without significant differences between both groups. Proteobacteria phyla were the next predominant phyla ($3.5 \pm 4.9\%$) in T2D group compared to controls ($1.6 \pm 2.9\%$, $p = 0.001$). While Actinobacteria was the third prevalent phyla in the control group ($5.0 \pm 6.7\%$), it tended to be depleted in T2D ($1.9 \pm 1.3\%$, $p = 0.06$). The most pronounced differences were found in the relative abundance of the following bacterial genera between two groups: Bifidobacterium ($0.8 \pm 0.9\%$ and $4.0 \pm 6.0\%$ in controls, $p = 0.009$), Bacteroides ($7.1 \pm 6.5\%$ and $4.5 \pm 4.9\%$, $p = 0.03$), Coprococcus ($5.9 \pm 4.0\%$ and $3.6 \pm 1.8\%$, $p = 0.008$), Ruminococcus ($2.2 \pm 2.3\%$ and $1.1 \pm 0.9\%$, $p = 0.04$), Faecalibacterium ($9.5 \pm 6.0\%$ and $14.8 \pm 8.4\%$, $p = 0.007$), Megamonas ($1.2 \pm 5.7\%$ and $0.0002 \pm 0.001\%$, $p = 0.01$), Enterobacteriaceae ($2.8 \pm 4.5\%$ and $1.1 \pm 2.5\%$, $p = 0.0060$), respectively.

Conclusions: The gut microbiota profile of patients with T2D was characterized by the predominance of potentially pathogenic bacteria, which could have a negative effect on the human health and depleted abundance of potentially beneficial bacteria such as butyrate producing bacteria.

D. Safina: None. L. Gaysina: None. A. Abakumova: None.

POSTER SESSION 17: MICROBIOTA 3

P17.01

PREVALENCE OF TORCH INFECTIONS IN INFANTS WITH CHOLESTATIC JAUNDICE ADMITTED TO A CHILDREN'S HOSPITAL IN SOUTHERN VIET NAM

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Objective: TORCH infections complex including Toxoplasmosis, others (Syphilis, Hepatitis B, Varicella-zoster virus, Parvovirus B19), Rubella virus, Cytomegalovirus, Herpes simplex virus. Initial evidence of TORCH infections can appear very early in pregnancy or in the perinatal period. Infections including TORCH infections and sepsis are among the important causes of infantile cholestatic jaundice.

Patients and Methods: A retrospective record-based study was performed at Children's Hospital 2, Vietnam. We collected TORCH infections complex data from the records of all infants with cholestatic jaundice admitted between October 2021 and April 2023. We confirmed the diagnosis using chemiluminescence to quantify seroprevalence for IgG and IgM.

Results: A total of 397 patients under 1 year of age with cholestatic jaundice were treated in our facility during the study period. The mean age of patients at the time of TORCH testing was 56.45 ± 35.33 days. The overall rate of TORCH infections was 40.8% (162/397). Serum IgM was positive for CMV 34.5% (137/397), HSV 9.06% (36/397), EBV 5.8% (21/358), Siphilis 2.9% (9/310), HBV 2.7% (10/365), Rubella 0.7% (3/396), Toxoplasma 0.5% (2/397).

Conclusions: The rate of seropositivity for IgM antibodies correlated with TORCH infections is very high in infants with cholestatic jaundice in developing regions such as Vietnam. We recognize that syphilis is still a matter of concern today.

T. Duong Thi: None.

TABLE 1. PREVALENCE OF TORCH INFECTIONS IN INFANTS WITH CHOLESTATIC JAUNDICE.

TORCH infections	N (%)	Days of age, Mean \pm sd	95%CI
Negative for all agent	169 (42.57)	40.97 \pm 29.67	36.46-45.48
Positive for any agent	228 (57.43)	67.92 \pm 34.86	63.37-72.47
Combined	397 (100)	56.45 \pm 35.33	52.96-59.93
diff (t-test) $p < 0.001$		-26.94	(-33.33)-(-20.56)

TABLE 2. PREVALENCE OF TORCH INFECTIONS BETWEEN NEONATES AND OLDER INFANTS WITH CHOLESTATIC JAUNDICE.

TORCH infections	≤ 28 days, N (%)	> 28 days, N (%)	Total, N (%)
Positive for any agent	23/90 (25.56)	205/307 (66.78)	OR = 0.17, $p < 0.001$, 95%CI (0.1-0.29)
Cytomegalo virus IgM	3/90 (3.33)	134/307 (43.64)	137/397 (34.50)
Cytomegalo virus IgG	72/74 (97.29)	241/251 (96.01)	313/325 (96.30)
<i>Treponema pallidum</i>	6/68 (8.82)	3/242 (1.23)	9/310 (2.90)
<i>Toxoplasma gondii</i> IgM	0/90 (0)	2/307 (0.65)	2/397 (0.50)
<i>Toxoplasma gondii</i> IgG	1/72 (1.38)	24/260 (9.23)	25/332 (7.53)
Rubella virus IgM	0/90 (0)	3/306 (0.98)	3/396 (0.75)
Rubella virus IgG	56/74 (75.67)	151/259 (58.3)	207/333 (62.16)
Herpes Simplex virus IgM	6/90 (6.66)	30/307 (9.77)	36/397 (9.06)
Herpes Simplex virus IgG	68/72 (94.44)	224/260 (86.15)	292/332 (87.95)
Epstein Barr virus IgM	2/77 (2.59)	19/281 (6.76)	21/358 (5.86)
Epstein Barr virus IgG	58/65 (89.23)	142/226 (62.83)	200/291 (68.72)
HBsAg	2/70 (2.85)	8/295 (2.71)	10/365 (2.73)
Anti HBs	9/25 (36)	120/270 (44.44)	129/295 (43.72)

P17.02

MUTUAL INTERPLAY OF THE GUT MICROBIOTA COMPOSITION AND DIET

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Objective: While it is known that diet is responsible for the gut microbiota composition, many questions remain unclear.

Materials and Methods: The aim of the study was to evaluate the association between the gut microbiota taxonomic composition and food intake of the healthy subjects. Stool samples were analyzed from 66 healthy subjects using shotgun metagenomic sequencing technology (SOLiD 5500 Wildfire-platform), and a food questionnaire was utilized. Correlations between food groups and the microbiota composition were analyzed, p -value <0.05 was considered significant.

Results: The results revealed the presence of only mild and moderate ($0 < r < 0.5$ or $-0.5 < r < 0$) correlations. The following positive correlations were identified: dairy and bakery intake correlated with relative abundance of *Firmicutes* ($r=0.33$ and $r=0.27$, respectively), meat/high-proteins-with *Spirochaetes*

($r=0.27$) phylum; negative – between milk product and *Bacteroidetes* ($r=-0.34$). Several correlations were observed between food consumption and abundance of bacterial genera: bakery intake positively correlated with *Methanosphaera* ($r=0.33$), *Clostridium* ($r=0.37$), *Megasphaera* ($r=0.3$); negatively – with *Bacteroides* ($r=-0.33$), *Barnesiella* ($r=-0.25$), *Coprobacter* ($r=-0.29$), *Oscillibacter* ($r=-0.27$), *Sutterella* ($r=-0.36$). Positive correlations were revealed between vegetables/fruits intake and abundance of *Weissella* ($r=0.28$), *Butyrivibrio* ($r=0.24$), *Haemophilus* ($r=0.28$), *Methanosphaera* ($r=0.32$); negative – with *Alistipes* ($r=-0.37$), *Sutterella* ($r=-0.24$). Dairy positively correlated with *Lactobacillus* ($r=0.255$), *Lactococcus* ($r=0.27$); negatively – with *Bacteroides* ($r=-0.29$). Fatty food intake positively correlated with *Clostridium* ($r=0.27$), *Peptostreptococcaceae* ($r=0.25$), *Mitsuokella* ($r=0.29$), *Methanosphaera* ($r=0.35$), P22likevirus ($r=0.31$); negatively- with *Barnesiella* ($r=-0.33$), *Roseburia* ($r=-0.26$), *Sutterella* ($r=-0.33$). Positive correlations were identified between meat/high-proteins and abundance of *Prevotella* ($r=0.38$), *Dorea* ($r=0.32$), *Enterobacter* ($r=0.26$), *Haemophilus* ($r=0.36$), and between sugars and abundance of *Haemophilus* ($r=0.25$); negative – with *Blautia* ($r=-0.34$), *Holdemania* ($r=-0.33$).

Conclusions: Some correlations between the gut microbiota composition and food consumption were confirmed, potentially, this knowledge could be used to develop personalized strategies to modify microbiome composition.

D. Safina: None. M. Markelova: None. S. Abdulkhakov: None. T. Grigoryeva: None. M. Siniagina: None. D. Kamaldinova: None. G. Synbulatova: None. R. Abdulkhakov: None.

P17.03

POSTBIOTIC METABOLITES AS INTESTINAL BARRIER PROTECTORS DURING HELICOBACTER PYLORI ERADICATION THERAPY

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Objective: *Helicobacter pylori* eradication therapy, including antibiotic use, often leads to gut microbiota dysbiosis and intestinal barrier damage. Probiotics are often used to restore altered gut microbiota during and after eradication. We hypothesized that postbiotics, especially bacterial metabolites, could be used to prevent the intestinal barrier damage and protect the liver during eradication therapy.

Materials and Methods: The intestinal cell line Caco-2 was exposed to dextran sodium sulfate (DSS) and lipopolysaccharide (LPS). HepG2 hepatocarcinoma cells were exposed to free fatty acids. In these models we study the effects of bacterial metabolites on cell viability (XTT test), secretion of pro-inflammatory cytokine IL-8 (ELISA), permeability of the cell monolayer (FITC-dextran transport), triglyceride accumulation (GPO-PAP method), IL-8 and ZO-1 mRNA expression (RT-PCR).

Results: DSS reduced the viability of CaCo-2 cells by 25%, while valeric acid increased cell viability by 9%. LPS increased the permeability of Caco-2 cell monolayer by 36%, while indole-3-propionic acid reduced the permeability by 31%. LPS induced a 4-fold increase in IL-8 mRNA expression, and reduced ZO-1 mRNA expression by 52%. Butyric acid reduced IL-8 mRNA expression by 58%; indole-3-propionic acid increased ZO-1 mRNA expression by 91%. Indole-3-propionic acid reduced triglyceride accumulation by 20%.

Conclusions: Bacterial metabolites positively affected cell viability and barrier function, suppressed inflammation, and reduced liver triglyceride accumulation. Postbiotic metabolites can be considered as potential protective agents for the intestinal barrier and liver during *Helicobacter pylori* eradication therapy. Supported by RSF, No. 20-65-47026. T. Sall: None. S. Sitkin: None. L. Lazebnik: None. T. Vakhitov: None.

T. Sall: None. S. Sitkin: None. L. Lazebnik: None. T. Vakhitov: None.

P17.04

METAGENOMIC ANALYSIS OF THE CHANGES OF INFANT FAECAL MICROBIOTA AFTER INTRODUCTION OF DIFFERENT FOOD ITEMS

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Objective: Infant gut microbiome experience profound changes during the first year of life, especially after introduction of different food products. Metagenomic sequencing allows identification of various minor changes of gut microbiome profile. The aim of the study was to analyse the composition of the infant faecal microbiome in relation to introduction of different food products.

Materials and Methods: A study was performed at primary healthcare centers. The parents of children filled out a questionnaire and brought the child's faecal samples. The metagenomic sequencing was performed to identify the microorganism population structure in faecal samples. Median relative abundance (MRA) of various genera was compared among children who had/had not received different food items (gluten, eggs, fish, cow milk). Statistical analyses: Mann-Whitney test (statistical program MedCalc).

Results: In total, 92 children were included in the study; M/F ratio 57/34 (57=62.6%;34=37.4%); mean age 8.46 (±SD 4.87); range 0.5-15 months. Majority were delivered vaginally (79%; 72/92). The MRA of the following genera differed significantly in children after introduction of several food items: *Halomicroarcula*, *Halobacterium*, *Sulfurospirillum*, *Haladaptatus*, *Haloglomerus*, *Parasaccharibacter*, *Aminobacter*, *Halococcus* – after introduction of gluten; *Sulfurospirillum* *Haloglomerus* *Haladaptatus* *Halococcus* *Tequintavirus* – after introduction of fish; *Sulfitobacter* *Sulfurospirillum* *Alcanivorax* *Dhakavirus* *Mosigvirus* – after introduction of cow milks; *Halobacterium* *Sulfurospirillum* *Haladaptatus* *Haloglomerus* *Acaryochloris marina* – after introduction of eggs in the infants diet.

Conclusions: Significantly higher abundance of *Sulfurospirillum* in all studied groups suggest increase of hydrogen producers after introduction of solid food, while higher abundance of *Halobacterium* could indicate increase of organisms that require salt for growth. However, the relationship among microorganisms should be studied further.

M. Runge: None. E. Zelca: None. D. Fridmanis: None. L. Zaharova: None. I. Daugule: None.

P17.05

ALTERED GASTROINTESTINAL HOMEOSTASIS AND MICROBIOTA COMPOSITION IN A MOUSE MODEL FOR PSYCHIATRIC DISORDERS.

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Objective: Psychiatric disorders often coincide with gastrointestinal (GI) dysfunction. However, the mechanisms underlying GI symptom generation in diseases that primarily strike the brain remain obscure. Aberrant expression of Disrupted-in-Schizophrenia-1 (DISC1), a hub and scaffold protein that plays an essential role in neural connectivity, is an important risk factor associated with the onset of mental illness. We aim to understand whether DISC1 perturbation affects GI homeostasis, ENS function, and intestinal microbiota.

Materials and Methods: To investigate the effects of DISC1 disruption, we compared DISC1 locus impaired (LI) with wild-type littermates by mRNA and protein expression studies, histology and *in vivo* gut function assays. Microbiome analyses were performed using 16S rDNA amplicon profiling.

Results: Whole gut transit time measurements revealed that DISC1 LI mice present with faster GI transit. However, the bead expulsion assay did not reveal differences in distal colonic motility. Mutant mice showed a reduced wet weight per stool, while no changes were found in stool water content or intestinal permeability. Histopathological alterations were not observed. DISC1 LI mice have increased myenteric neuron numbers, accompanied by reduced gene expression levels of neuronal subtype markers. Linear discriminant analysis scoring revealed enrichment of *Bacteroides* and reduced levels of *Muribaculaceae* and *Clostridia* in mutants.

Conclusions: We demonstrate that disruption of DISC1 alters GI motility without inducing mucosal dysfunction or changes in intestinal cyto-architecture. Mutant mice present with changes in ENS composition and intestinal dysbiosis. Our current experiments focus on understanding how altered host-microbiota interactions in DISC1 mutants contribute to changes in gut function.

K. Tasnády: None. A. Cardilli: None. I. Hamad: None. N. Vaes: None. M. Gijbels: None. M. Kleinewietfeld: None. A. Sawa: None. B. Brône: None. V. Melotte: None. W. Boesmans: None.

P17.06

UNRAVELING THE MICROBIAL ODYSSEY: NAVIGATING THE MICROBIOTA-GUT-VAGINA AXIS IN WOMEN WITH ENDOMETRIOSIS IN THE ISALA PROJECT

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Both the gut and vaginal microbiome are essential for shaping women's health. However, compared to the gut, the vaginal microbiome remains understudied, hampering much-needed innovations in diagnostics and therapeutics. Therefore, we launched Isala (<https://isala.be/en/>), a large-scale citizen science project on the female microbiome and women's health with a focus on vaginal lactobacilli (<https://isala.be/en/>). In this study, we aim to come to a better understanding of the vaginal microbiome in women with endometriosis, an inflammatory disease characterized by endometrium-like tissue outside the uterus potentially causing pelvic pain and/or infertility. In a first phase, the vaginal microbiome profiles of 71 endometriosis patients were compared to the data of the 3,265 healthy controls from the Isala cohort. Associations between endometriosis and self-reported health indicators were studied. Lactobacillus taxa, most notably *L. crispatus* and *L. iners* were the most dominant taxa in endometriosis patients, similar as for the overall Isala population. The sequencing data was complemented by qPCR analysis to compare the absolute abundances of several Lactobacillus species between women with endometriosis and the control group. Finally, higher comorbidities were reported by endometriosis patients than by the healthy controls. In particular, the occurrence of irritable bowel syndrome was found to be almost three times higher among endometriosis patients compared to the control group. This data suggests that there is a potential gut-vagina axis and that the gut's physiology, function, and microbiome may contribute to the development of endometriosis.

I. Rahou: None. S. Ahannach: None. C.N. Allonsius: None. S. Condori: None. S. Wittouck: None. S. Lebeer: None.

P17.07

FINE-SCALE MAPPING OF THE VAGINAL MICROBIOME AND ITS INFLUENCING FACTORS

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Vaginal microorganisms are key for our reproduction and health, but a deeper understanding of the composition and function of the vaginal microbiome is needed in healthy women to design better diagnostics and therapeutics. Here, we used a citizen-science approach and actively motivated women to self-sample and co-create dynamic research on how health, life course and lifestyle are associated with the vaginal microbiome. We found that *Lactobacillus* taxa were dominant in 78% of the 3,345 healthy women who donated a vaginal swab, most notably *Lactobacillus crispatus* and *Lactobacillus iners*. In 15% of the women, these species co-occurred in similar amounts demonstrating a continuum in the vaginal microbiome and arguing against previously described suggestions of discrete community state types. We further found that most vaginal taxa show small to moderate positive or negative abundance correlations with each other, and that positively interacting vaginal taxa can be summarized by grouping them into four modules (*L. crispatus*-, *Gardnerella*-, *Prevotella*-, and *Bacteroides*-modules). Interestingly, we found that the *Limosilactobacillus* genus was prevalent in almost 50% of the vaginal samples and positively correlated with *L. crispatus* and *L. jensenii*. Besides age, having children and stage of the menstrual cycle were most strongly associated with different parameters of the vaginal microbiome. Menstrual hygiene, contraceptive use, sexual intercourse, intimate partnership, diet and other factors showed finer-scale associations with the microbiome composition (explained variance 10.2%). This high-resolution mapping of the vaginal microbiome and its metadata in health provides a unique reference for follow-up case-control and intervention studies.

S. Ahannach: A. Employment (full or part-time); Significant; University of Antwerp. B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; ERC, FWO. T. Gehrman: None. S. Wittouck: None. T. Eilers: None. E. Oerlemans: None. S. Condori: None. J. Dillen: None. I. Spacova: None. L. Vander Donck: None. C. Masquillier: None. C. Allonsius: None. P. Bron: None. W. Van Beeck: None. C. De Backer: None. G. Donders: None. V. Verhoeven: None. S. Lebeer: None.

P17.08

FEATURES OF THE SMALL INTESTINAL BACTERIAL OVERGROWTH PREVALENCE AGAINST THE BACKGROUND OF LACTASE DEFICIENCY

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Objective: Clinical manifestations of lactase deficiency (LD) in the gastrointestinal tract have much in common with the syndrome of excessive bacterial growth in the small intestine (SIBO). We assessed the prevalence of SIBO in patients with gastrointestinal symptoms following ingestion of dairy products and the relationship between LD and SIBO.

Patients and Methods: The study included patients with functional intestinal symptoms that occur after ingestion of dairy products. The severity of complaints was assessed according to a questionnaire of gastrointestinal symptoms, hydrogen-methane-lactulose breath test (LBT) was used to diagnose SIBO, LD was determined by polymorphism analysis MCM6 gene, lactose intolerance (LI) was diagnosed with hydrogen-methane-lactose breath test (LacBT).

Results: A 103 patients were included, 31(30.1%) with severe LD, 52(50.5%) with mild LD, 24 (23.3%) were positive for LBT. C/C polymorphism in combination with lactose intolerance according to LBT showed a higher positive reaction to LBT or LBT(H2) than in the control group (31.8% vs. 8.4%, $p=0.029$). There was no significant difference in symptom scores depending on the presence of LD or SIBO. The LBT(H2)-positive group had more patients with LQT than the other groups (30.9% vs. 9.3%, $p=0.036$). Only LBT(H2)-positivity was significantly associated with a higher risk of LQT in multivariate analysis (OR 5.27; $p=0.016$).

Conclusions: H2-producing SIBO is common in patients with severe LD when lactose intolerance is suspected. SIBO should be considered in the treatment of intestinal symptoms in patients with lactose intolerance.

V. Kryvy: None. I. Klyarytska: None. I. Iskova: None. T. Tsapyak: None.

P17.09

UNDERSTANDING THE INFLUENCE OF DONOR LIVER MICROBIOME ON RECIPIENT OUTCOMES IN LIVER TRANSPLANTATION: A STUDY ON THE ROLE OF THE BILIARY MICROBIOME

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Objective: The only promising therapy for patients with terminal liver diseases is orthotopic liver transplantation. However, acute perioperative and chronic risks such as infections and biliary complications are a common complication. The biliary system plays a crucial role in mechanisms of liver tissue regeneration and immune defense. The biliary system was previously considered sterile, but recent studies show that bile fluids contain several different bacterial phyla. The impact of the donor's liver microbiome on the recipient after liver transplantation is not yet clear. The objective is to examine the biliary microbiome of liver transplant recipients at different stages to identify potential bacterial factors that may affect post-operative complications. The aim is to assess the effect of changes in the biliary microbiome on the development of biliary complications and how it affects the development of biliary complications after transplantation.

Material and Methods: Samples of tissue from the bile ducts and bile were collected from both the donor's liver before and after transplantation, as well as from the recipient's liver before the transplant procedure, involving 100 patients. RNA was extracted and a sequence-based analysis of the bacterial community will be carried out using libraries generated from reverse transcripts of RNA. This will identify the active bacterial community.

Results: The results of this study will provide insight into the changes in the biliary microbiome after liver transplantation and its potential impact on the development of biliary complications.

Conclusions: These findings may have important implications for the development of new strategies to prevent and manage biliary complications after liver transplantation.

A. Tomasevic: None. N. Koch: None. U. Wirth: None. C. Schulz: None.

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Public Price: 76,35€*

PYLERA®**

140mg/125mg/125 mg capsules

Bismuth subcitrate potassium
Metronidazole
Tetracycline hydrochloride

A 3-in-1 technology to eradicate *Helicobacter pylori*¹

Therapeutic indications¹

In combination with omeprazole, Pylera® is indicated for the eradication of *Helicobacter pylori* and prevention of relapse of peptic ulcers in patients with active or a history of *H. pylori* associated ulcers.

*Public price applicable in Belgium. ** In Belgium, this medicinal product is authorised under the name TRYPLERA.

LEGAL INFORMATION

NAME OF THE MEDICINAL PRODUCT: Pylera 140 mg/125 mg/125 mg capsules. **QUALITATIVE AND QUANTITATIVE COMPOSITION:** Each capsule contains 140 mg of bismuth subcitrate potassium (equivalent to 40 mg bismuth oxide), 125 mg of metronidazole and 125 mg of tetracycline hydrochloride. Excipients with known effect: Each capsule contains 61 mg of lactose monohydrate and 32 mg of potassium. For a full list of excipients, see section List of excipients **PHARMACEUTICAL FORM:** Capsule, hard (Capsule). Elongated, white, opaque capsule with Aptalis Pharma logo printed on the body and 'BMT' printed on the cap in red ink. It contains a white powder plus a smaller white opaque capsule containing a yellow powder. **CLINICAL PARTICULARS: Therapeutic indications:** In combination with omeprazole, Pylera is indicated for the eradication of *Helicobacter pylori* and prevention of relapse of peptic ulcers in patients with active or a history of *H. pylori* associated ulcers. **Posology and method of administration: Posology:** Each dose of Pylera includes 3 identical hard capsules. Each dose should be taken 4 times a day, 3 capsules after breakfast, 3 capsules after lunch, 3 capsules after the evening meal and 3 capsules at bedtime (preferably after a snack) for a total of 12 capsules per day over a period of 10 days. One omeprazole 20 mg capsule/tablet should be taken twice a day, at the same time as the morning meal and evening meal doses of Pylera for the full 10 days of therapy. Daily dosing schedule for Pylera:

Time of dose	Number of capsules of Pylera	Number of capsules/tablets of omeprazole
After breakfast	3	1
After lunch	3	0
After evening meal	3	1
At bedtime (preferably after a snack)	3	0

Missed doses can be made up by extending the normal dosing schedule beyond 10 days until all the medicinal product has been consumed. Patients should not take two doses at one time. If more than 4 consecutive doses (1 day) are missed, the prescribing physician should be contacted. Patients with hepatic or renal impairment: Pylera is contraindicated in patients with renal or hepatic impairment (see sections Contraindications and Special warnings and precautions for use). The safety and effectiveness of Pylera in hepatic or renal impaired patients has not been evaluated. Older people: Experience in older people is limited. In general, the greater prevalence of decreased hepatic, renal, or cardiac function, as well as the presence of concomitant diseases and multiple concomitant medicinal therapies should be considered when prescribing Pylera for this patient population. Paediatric population: Pylera is contraindicated in children less than 12 years of age (see section Contraindications) and not recommended in children 12 to 18 years of age. **Contraindications:** Pregnancy and breast-feeding, Paediatric population (up to 12 years of age), Renal or hepatic impairment, Hypersensitivity to the active substances, other nitroimidazole derivatives, or to any of the excipients listed in section List of excipients, Patients with Cocaine syndrome (see section Undesirable effects). **Undesirable effects: Summary of the safety profile:** The adverse reactions reported with Pylera in combination with omeprazole during controlled clinical trials were consistent with the known safety profile of bismuth subcitrate potassium, metronidazole and tetracycline hydrochloride when given as separate products. The most commonly reported adverse reactions (very common) during treatment with Pylera are, in decreasing order of frequency: abnormal faeces, diarrhoea, nausea, and dysgeusia (including metallic taste). Severe cutaneous adverse reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell syndrome; potentially fatal) have been reported with the use of Pylera and the individual components, metronidazole and tetracycline. The occurrence of severe cutaneous adverse reactions require immediate discontinuation of Pylera. Pseudomembranous colitis (Clostridium difficile colitis) and peripheral neuropathy have been reported with the use of Pylera (see section 4.4). **Tabulated list of adverse reactions:** Adverse reactions are presented from pooled data of three phase III controlled clinical trials (540 patients exposed to Pylera) and post-marketing experience (including spontaneous, regulatory and literature reports). Adverse reactions are ranked under headings of frequency, using the following categories: very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$); not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

System Organ Class Preferred Term	Very common ($\geq 1/10$)	Common ($\geq 1/100$ to $< 1/10$)	Uncommon ($\geq 1/1,000$ to $< 1/100$)	Not known
Infections and infestations		Vaginal infection	Candidiasis, oral candidiasis, vaginal candidiasis	Pseudomembranous colitis
Immune system disorders			Drug hypersensitivity	
Metabolism and nutrition disorders		Anorexia, decreased appetite		
Psychiatric disorders			Anxiety, depression, insomnia	
Nervous system disorders	Dysgeusia (including metallic taste*)	Headache, dizziness, somnolence	Hypoesthesia, paraesthesia, amnesia, tremor	Peripheral neuropathy, aseptic meningitis
Eye disorders			Blurred vision	
Ear and labyrinth disorders			Vertigo	
Gastrointestinal disorders	Diarrhoea, nausea, abnormal faeces (including black stools*)	Vomiting, abdominal pain (including abdominal pain upper), dyspepsia, constipation, dry mouth, flatulence	Tongue oedema, mouth ulceration, stomatitis, abdominal distension, eructation, tongue discoloration	
Hepatobiliary disorders		Alanine aminotransferase increased, aspartate aminotransferase increased		
Skin and subcutaneous tissue disorders		Rash (including rash maculo-papular, rash pruritic)	Urticaria, pruritus	Blister, Skin exfoliation, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell syndrome), DRESS syndrome (Drug Reaction with Eosinophilia and Systemic Symptoms)
Renal and urinary disorders		Chromaturia		
General disorders and administration site conditions		Asthenic conditions**	Chest pain, chest discomfort	

* Lowest Level Term (LLT); ** High-Level Term (HLT); MedDRA Version 11.0

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1. Pylera®. Summary of product characteristics. (DCP common text).



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- Compact 2-channel cubic system (1 patients)
- Management system through simple software
- self check, calibration, patient archive, daily work list
- Auto check for voltage evaluation on 12c / 13c
- Response within 3 minutes
- Report with DOB + outcome (positive / negative)
- Does not require dedicated personnel
- No limit of daily test execution
- Automatic air circuit cleaning with each test
- Reading through aluminum bags
- Latest generation infrared reading system (NDIR)

Specialists in diagnosis of Helicobacter Pylori infection



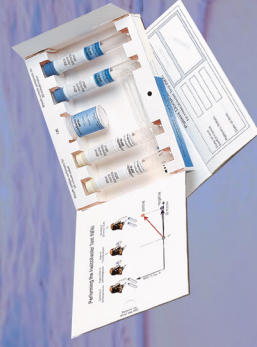
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- Compact 10-channel cubic system (5 patients)
- Management system through simple and intuitive software
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- self check, calibration, patient archive, daily work list
- output for PC connection
- Auto check for voltage evaluation on 12c / 13c
- Response within 3 minutes
- Report with DOB + outcome (positive / negative)
- Report in A4 format
- Does not require dedicated personnel
- No limit of daily test execution
- Automatic air circuit cleaning with each test
- Reading through aluminum bags
- Latest generation infrared reading system (NDIR)

instruments designed to measure the 13C change in exhaled respiratory CO₂ gas by infrared spectroscopy analysis to determine infection of Helicobacter pylori.

Helicobacter Test INFAI®

One of the most used
¹³C-urea breath tests for the diagnosis
of Hp-infections worldwide



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- Serialization according to the EU's Falsified Medicines Directive
- More than 7.0 million Hp Test INFAI performed worldwide
- Registered in more than 40 countries worldwide
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- Modified Hp test for patients taking PPIs (REFEX)
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