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Missing abstracts within the consecutive presentation numbers represent withdrawn papers

ELECTRONIC POSTER PRESENTATIONS

WORKSHOPS

W1 Microbiota in Health and Disease

W1.1

AGING AND SHARED HOUSEHOLD ARE THE MAIN DETERMINANT OF THE GUT MICROBIAL SIMILARITY IN TWINS

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***Objective*:** Gut microbiome plays a crucial role in health and disease. Human gut microbiome composition may be influenced by various dietary and environmental factors. Recently, genetics has been also proposed to impact microbial similarity. In this work, we systematically evaluated the impact of various factors including diet, aging, cohabitation etc. on the gut microbiome similarity in monozygotic and dizygotic twins.
Materials and Methods: Fecal samples were obtained from total 198 well-characterized twin subjects (45 monozygotic and 54 dizygotic twin pairs). Food frequency questionnaire was used for assessment. DNA was extracted and the region V1-V2 of the 16S rRNA gene was amplified and sequenced. Bray-Curtis similarity matrix was used for microbiome comparisons.
Results: Paired analyses revealed mean Bray-Curtis similarity of 11±5%. Roughly 50% of the twin pairs grouped together and showed a higher similarity (~20%) to each other than with the other twins. Mode of delivery, breast feeding and host genetics had no impact, while household-sharing and age were the major factors affecting microbial similarity. Shared *vs.* non-shared phylotypes analysis showed that in both siblings the shared phylotypes progressively diminished with aging (rho = -0.42, $p < 0.0001$), while the non-shared phylotypes increased (rho = 0.66, $p < 0.0001$).
Conclusions: Shared household and aging, but not host genetics or mode of delivery, where the main factors related to gut microbial similarity in twins irrespective of their zygotic state. The increasing shift of microbiome concordance with aging of twins suggests a dynamic adaption across the life span.

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W1.2

WHOLE METAGENOME SHOTGUN SEQUENCING AS A NEXT-GENERATION SEQUENCING APPROACH TO CHARACTERIZE THE TAXONOMY AND FUNCTIONAL RISK FACTORS OF THE GASTRIC MICROBIOME

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***Objective*:** Along with *Helicobacter pylori* (*Hp*) infection, the gastric microbiota modulates stomach cancer risk in susceptible individuals. Whole metagenome shotgun sequencing (WMS) is a next-gen-

eration sequencing approach to characterize the intestinal microbiome because of its advantageous over traditional culture and 16s rRNA sequencing including identification of bacterial and non-bacterial taxa, species/strain resolution, and functional characterization of the microbiota. In this study, we used WMS to survey the microbiome in gastric biopsy samples from Colombian patients residing in the high-risk gastric cancer town Túquerres (n=10, *Hp*-positive =7) and low-risk town of Tumaco (n=10, *Hp*-positive=6).
Materials and Methods: Extracted DNA from biopsy samples was sequenced using Illumina Novaseq. Kraken2/Braken was used for taxonomic classification and abundance. Functional gene profiles were inferred by InterProScan and KAAS analysis of assembled contigs and gene annotation.
Results: The most abundant taxa represented bacteria, non-human eukaryota, and viral genera found in skin, oral, food, and plant/soil environments including *Staphylococus*, *Streptococcus*, *Bacillus*, *Aspergillus*, and *Siphoviridae*. *Hp* was detected in all *Hp*-positive and no *Hp*-negative samples. Beta diversity was significantly different based on *Hp*-status (p=0.031), risk group (p=0.022), and sex (p=0.004). Significant differences in functional profiles were found between *Hp*-status, but not risk or sex groups. *Hp*-positive samples were significantly enriched for *Hp*-specific genes including virulence factors such as *vacA*, *cagA*, and urease, while carbohydrate and amino acid metabolism gene were enriched in *Hp*-negative samples.
Conclusions: This study shows WMS has the potential to characterize the taxonomy and function of the gastric microbiome as risk factors for stomach disease.

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W1.3

IMPLEMENTATION OF A METATRANSCRIPTOMICS STRATEGY FOR FUNCTIONAL PROFILING OF THE GASTRIC CANCER MICROBIOME

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The human microbiome contributes for homeostasis but also for the development of diseases, including cancer. Metatranscriptomics (MTX) is an emerging high-throughput sequencing approach that characterizes the active functional profile of the microbiome by analysis of the whole-community RNA. However, the application of MTX to gastric cancer tissues remains unexplored. Our aim was to implement a MTX strategy to functionally characterize the gastric cancer microbiome.
Synthetic microbiome samples were created to establish and optimize the experimental and computational workflow. For this, we spiked a mock microbial community of well-defined composition (ATCC MSA-2002®) with AGS, a human gastric adenocarcinoma cell line, at increasing host: microbial ratios (10%, 70%, 90%, and 97% host cells). RNA was isolated, treated with DNAse, and depleted from prokaryotic and eukaryotic ribosomal RNA (rRNA). Sequencing was performed on the Illumina NovaSeq 6000 platform with high depth (15 Gbp/sample). Low-quality reads, rRNA and host sequences were removed from raw data. Then, taxonomic and functional profiling were performed using mapping-based approaches.
After testing several bioinformatics tools, we accurately reconstituted the taxonomic profile of the synthetic microbiome samples. These results were further validated by 16S rRNA transcript sequencing. Finally, we effectively identified a wide variety of microbiome functions, including several microbial enzymes and metabolic pathways, involved in nucleotide and amino acid biosynthesis.
Overall, we successfully implemented a MTX strategy using synthetic microbiome samples. This optimized workflow will now be applied to gastric tissue specimens to evaluate the functional activity of the gastric microbiome in non-cancerous and in cancer contexts.

J. Pereira-Marques: None. R.M. Ferreira: None. C. Figueiredo: None.

W1.4

RELATIONSHIPS OF THE GUT MICROBIOME WITH COGNITIVE DEVELOPMENT AMONG HEALTHY SCHOOL AGE CHILDREN

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***Objective*:** The gut microbiome might play a role in neurodevelopment; however, evidence remains elusive. We aimed to examine the relationship between the intestinal microbiome and cognitive development of school-age children.
Patients and Methods: This cross-sectional study included healthy Israeli Arab children from different socioeconomic status (SES). The microbiome was characterized in fecal samples by implementing 16S rRNA gene sequencing. Cognitive function was measured using Stanford-Binet test, yielding full-scale Intelligence Quotient (FSIQ) score. Sociodemographics and anthropometric and hemoglobin measurements were obtained. Multivariate models were implemented to assess adjusted associations between gut microbiome and FSIQ score, while controlling for age, sex, SES, physical growth and hemoglobin levels.
Results: Overall, 165 children (41.2% females) aged 6-9 years were enrolled. SES score was strongly related to both FSIQ score and the gut microbiome. Measures of α-diversity were significantly associated with FSIQ score, demonstrating more diverse, even, and rich microbiome with increased FSIQ score. Significant differences in fecal bacterial composition were found. FSIQ score explained the highest variance in bacterial β-diversity, followed by SES score. Several taxonomic differences were significantly associated with FSIQ score, including *Prevotella*, *Dialister*, *Sutterella*, *Ruminococcus callidus* and *Bacteroides uniformis*.
Conclusions: We demonstrated significant independent associations between the gut microbiome and cognitive development in school-age children.

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W1.5

ASSOCIATION OF STOMACH MICROBIOME WITH PROGNOSIS OF GASTRIC CANCER PATIENTS

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Introduction: Gastric carcinogenesis is associated with *Helicobacter pylori* (*H. pylori*) and alteration of stomach microbiome. Only limited knowledge exists regarding potential impact of stomach microbiome on the clinical phenotype of prognosis of gastric cancer patients. The aim of this study was to investigate the relationship between mucosal microbial community and prognosis of gastric cancer patients.
Materials and Methods: DNA from well-characterized paired gastric tumorous and adjusted non-tumorous tissue were obtained from 64 gastric cancer patients. Region V1-V2 of the 16S rRNA gene was amplified by PCR and barcoded for high throughput sequencing using Illumina platform. Clinical and pathological characteristics as well as survival data were available for follow up period of up to seven years.

Results: *H. pylori* was present at lower abundance in tumorous compared to adjacent tissues (*p*-value = 0.01). Tumour stage and histopathological Lauren's tumour classification were not associated with microbial changes. The overall survival analysis revealed *Fusobacterium* and *Prevotella* in tumorous tissue to be associated with worse prognosis. *Fusobacterium* was negatively correlated with the survival time (r = -0.27, *p*-value = 0.048) in tumorous tissues, while *Asinibacterium* in non-tumorous tissues correlated positively with overall survival of gastric cancer patients. Detailed taxonomic analysis revealed that *F. nucleatum* is the dominant *Fusobacterium* species in gastric cancer patients, while *F. periodonticum* is dominant in healthy individuals.
Conclusions: Mucosal microbiome of gastric cancer patients is associated with prognosis of gastric cancer patients. *Fusobacterium* and *Prevotella* in tumorous but not non-tumorous tissues were associated with worse prognosis.

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W1.6

MICROBIOME SIGNATURE OF METABOLICALLY HEALTHY OBESE INDIVIDUALS ACCORDING TO ANTHROPOMETRIC, METABOLIC AND INFLAMMATORY PARAMETERS

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***Objective*:** Recent studies have revealed that metabolically healthy obese (MHO) population have different clinical profiles and prognosis than metabolically unhealthy obese patients. This study aims to investigate the characteristics of gut microbiome in the MHO patients, and how they correlate with metabolic and inflammatory profiles.
Patients and Methods: 120 obese people without metabolic comorbidities were recruited, and their clinical phenotypes, metabolic and inflammatory parameters were analyzed. The fecal microbiome originating from bacterial cell and extracellular vesicle (EV) were profiled using 16S rDNA sequencing.
Results: The total study population could be classified into two distinct enterotypes (group I: Prevotellaceae-predominant, group II: *Akkermansia/Bacteroides* abundant), based on their stool EV-derived microbiome profile. When comparing the metabolic and inflammatory profiles, enterotype I correlated with higher levels of body mass index, total body fat mass, serum IL-1B, serum resistin than enterotype II (all $p < 0.05$). The microbial diversity in enterotype I were lower than those in enterotype II ($p < 0.001$), and the microbial composition, analyzed by unweighted unifrac distance, revealed distinct distribution between the two enterotypes (PERMANOVA $p = 0.001$). Enterotype, I had relatively higher abundance of Bacteroidetes, *Prevotellaceae, Prevotella*-derived EVs, and lower abundance of Actinobacteria, *Firmicutes, Proteobacteria, Akkermansia* and *Bacteroides*-derived EVs.
Conclusions: HMO patients can be categorized into two distinct enterotypes by the fecal EV-derived microbiome profile. The enterotypes may be associated with different metabolic and inflammatory profiles. Further studies are warranted to elucidate the long-term prognostic impact of EV-derived microbiome in the obese population.

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W2 Diagnosis, Epidemiology and Extragastric Diseases

W2.1

HELICOBACTER PYLORI OUTER MEMBRANE VESICLES ALTER ASTROCYTE AND NEURONAL FUNCTION *IN VITRO* AND *IN VIVO*

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***Objective*:** *Helicobacter pylori* (*Hp*) infects the stomach of half of the world's population. Importantly, chronic infection by this bacterium correlates with the appearance of several extra-gastric pathologies, including neurodegenerative conditions. Brain astrocytes become reactive and neurotoxic in such diseases, but how this gastric pathogen relates to these pathological processes in the central nervous system (CNS) is still unclear. The remote action of secreted outer membrane vesicles (OMVs) from the gastric niche is an emerging possibility. In this study, we evaluated the effect of *Hp* OMVs on astrocyte and neuronal functions *in vitro* and *in vivo*.

Materials and Methods: *Hp* 60190 OMVs were purified from liquid cultures by exclusion chromatography and characterized by nanotracking. DTNIC1 astrocytes were treated with OMVs and the effect on astrocytes was tested by immunoblot and immunofluorescence. CAD neurons were co-cultured with the OMV-exposed astrocytes. Additionally, Dir-labeled OMVs were injected into the tail vein of BALB/c mice, and their brain distribution was monitored. The effect on neuronal function was evaluated following neurite retraction by microscopy *in vitro* and neuronal damage *in vivo*.

Results: *Hp* OMVs triggered astrocyte reactivity, which promoted neurite retraction *in vitro. Hp* OMVs were detected in the brain of mice, indicating that these OMVs access the CNS. Furthermore, their distribution in the brain coincided with sites of astrocyte reactivity and neuronal damage.

Conclusions: *Hp* OMVs alter astrocyte and neuronal function *in vivo* and *in vitro*. Hence, *Hp* could trigger systemic effects through small vesicles that access the CNS and alter brain homeostasis.

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W2.2

NEUROTOXIC PROPERTIES OF *HELICOBACTER PYLORI* UREASE: A POSSIBLE LINK TO ALZHEIMER'S DISEASE?

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Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil.

Epidemiologic studies correlate *Helicobacter pylori* (*Hp*) and Alzheimer's disease (AD), revealing an increased proportion of *Hp*-positive cases among AD patients and that treatment of *Hp* infection can improve AD symptoms. Deposits of beta-amyloid peptide and hyperphosphorylated tau protein are present in AD's brain. The literature reported that rats treated ip with a filtrate of *Hp's* culture had hyperphosphorylated tau in the brain, suggesting that bacterial exotoxins could cross the blood brain barrier and directly induce tau's phosphorylation. *H. pylori*, which infects ~60% of the world population and can remain asymptomatic for decades, produces a pro-inflammatory urease (HPU). We have shown that HPU displays enzyme-independent effects eliciting cytokines and eicosanoid production, neutrophil activation, increased paracellular permeability, thereby promoting tissue damage. Here we demonstrated the neurotoxic potential of HPU in *in vitro* and *in vivo* models.

HPU-treated (50-300 nM) SH-SY5Y neuroblastoma cells produced reactive oxygen species (ROS) and had an increased intracellular [Ca^{2+}]. Incubated with HPU (50-300 nM), BV-2 microglial cells showed reduced viability, producing ROS, and cytokines IL-1β and TNF-α. Rats received HPU (5 µg, i.p.) daily for 1 week. Tau hyperphosphorylated at Ser199, Thr205, and Ser396 sites, with no changes in total tau or GSK-3β levels, and overexpression of Iba1 (microglial activation marker), were found in hippocampal homogenates. HPU was not detected in the brain homogenates. Behavioral tests indicated no cognitive impairments, suggesting a "prodromic" stage of neuroinflammation. Our findings support previous correlation data linking infection by *H. pylori* and tauopathies such as AD, possibly mediated by its urease.

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W2.3

HELICOBACTER PYLORI DIAGNOSTIC TESTS USED IN 35,000 PATIENTS IN EUROPE: RESULTS FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (*HP*-EUREG)

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***Objective*:** There are several methods, both invasive and non-invasive, to diagnose *H. pylori* infection. Our objective was to evaluate the tests used in Europe.
Materials and Methods: International prospective non-interventional registry evaluating the management of European gastroenterologists. Data were registered at AEG-REDCap e-CRF (2013-2021). Countries with >100 patients were included. The results were summarized as absolute and relative frequencies.
Results: 34,920 patients from 20 countries were analyzed (mean age 51 years, SD 14; 61% women). For initial diagnosis, invasive tests were performed in 19,801 cases (71%), non-invasive in 11,369 (41%), and both in 3,437 (12%), most frequently: histology (n=11,885, 43%), rapid urease test (n=10,636; 38%), and urea breath test (UBT) (n=7,577; 27%). According to age, an invasive test was indicated in 11,179 (77%) >50 years, and in 8,603 (65%) <50 years. Depending on the country, the use of invasive tests ranged from 29%-99% in <50 years, and 60%-99% in >50 years (Table 1). Regarding eradication, most of the tests were non-invasive (n=32,540, 93%), principally UBT (n=32,540; 78%). In 2,983 (9%) an invasive test was performed.

Conclusions: The use of diagnostic tests for both the initial diagnosis and for confirmation of eradication in Europe is heterogenous. The reasons for the apparent lack of adherence to the guidelines on the diagnosis of *H. pylori* should be explored.

TABLE 1. INVASIVE TESTS USED FOR THE INITIAL DIAGNOSIS OF *H. PYLORI* ACCORDING TO AGE.

	Patients with an invasive diagnostic test/ Total of patients n/N (%)	n patients <50 years with an invasive diagnostic test / N total patients <50 years (%)	n patients ≥50 years with an invasive diagnostic test / N total patients ≥50 years (%)
Azerbaijan	565/570 (99)	382/386 (99)	183/184 (99)
Croatia	277/338 (82)	70/99 (71)	207/239 (87)
France	101/107 (94)	46/49 (94)	55/58 (95)
Germany	101/132 (77)	40/55 (73)	61/77 (79)
Greece	497/541 (92)	184/211 (87)	313/330 (95)
Hungary	194/233 (83)	77/95 (81)	117/138 (85)
Ireland	221/313 (71)	90/164 (55)	131/ 149 (88)
Israel	59/103 (57)	21/52 (40)	38/51 (75)
Italy	2,213/2,629 (84)	904/1,117 (81)	1,300/ 1,485 (88)
Latvia	426/528 (81)	250/326 (77)	176/202 (87)
Lithuania	397/512 (78)	149/203 (73)	248/309 (80)
Norway	598/740, (81)	215/261 (82)	383/479 (80)
Portugal	337/347 (97)	103/107 (96)	233/239 (97)
Russia	3,520/5,245 (67)	1,871/2,879 (65)	1,648/2,364 (70)
Serbia	67/92 (73)	16/31 (52)	51/61 (84)
Slovenia	2,304/2,411 (96)	952/983 (97)	1,352/1,428 (95)
Spain	7,482/12,331 (61)	3,027/5,876 (52)	4,447/6,442 (70)
Turkey	247/264 (94)	137/150 (91)	110/114 (97)
United Kingdom	98/195 (50)	18/62 (29)	80/133 (60)
Ukraine	97/145 (67)	51/73 (70)	46/ 72 (64)
TOTAL	**19,801/27,776 (71)**	**8,603/13,179 (65)**	**11,179/14,554 (77)**

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W2.4

REAL-TIME ASSESSMENT OF *H. PYLORI* GASTRITIS GUIDED BY ENDOFASTER: A PROSPECTIVE COHORT STUDY.

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***Objective*:** Endofaster is an innovative technology complementing Upper-GI Endoscopy (UGE) for gastric juice analysis and detection of *H. pylori* infection in real-time. Aim of our study was to assess the diagnos-

tic performance of Endofaster and to use the instant detection of *H.pylori* to guide antibiotic susceptibility testing (AST).
Patients and Methods: Patients undergoing routine UGE were prospectively recruited. Intake of antibiotics but not the use of PPI during 2 weeks prior to endoscopy was an exclusion criteria. Gastric juice analysis was performed by Endofaster and diagnosis of *H. pylori* was made on real-time ammonium measurement (>62 ppm/ml). Gastric histology was assessed according to the Sydney system. Additional biopsies for culture-based AST were taken in case of *H. pylori*-detection. Diagnostic accuracy of Endofaster was determined using histology as gold standard.
Results: 127 patients (57 women, 55.6 ± 19 years) were enrolled. Gastric juice was analyzed in 118 patients. *H. pylori* infection was detected histologically in 32 (27.1%) patients. Overall, the sensitivity, specificity, accuracy, positive predictive value (PV) and negative PV of Endofaster were 90.6%, 95.4%, 94.1%, 87.9%, 96.5%, respectively. Ongoing therapy with PPI was associated with reduced diagnostic performance, with exception for specificity and NPV. In *H. pylori*-positive subjects 27 (84.4%) were therapy-naïve and 18 (56.3%) were infected with antibiotic-resistant strains. Resistance rates were 6,25% for clarithromycin, 34.4% for levofloxacin and 43.8% for metronidazole.
Conclusions: Endofaster provides the immediate diagnosis of *H. pylori*-infection with high accuracy. Diagnosis of *H. pylori* in real-time guides to perform additional susceptibility tests and the selection of an individually tailored eradication regimen.

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W2.5

PREVALENCE OF ANDRISK FACTORS FOR FAMILIAL *HELICOBACTER PYLORI* INFECTION IN CHINA: A NATIONWIDE FAMILY-BASED CROSS-SECTIONAL STUDY

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***Objective*:** Few epidemiological data on familial *H. pylori* infection (the rate of *H. pylori*-positive households among overall households) are available. The present study aimed to determine the prevalence of familial *H. pylori* infection, identify the associated risk factors inside home and assess the impact of the infected family members on childhood infection in China.
Patients and Methods: A cross-sectional epidemiological survey of *H. pylori* infection within households in mainland China was done and families containing two or more family members from 29 provinces were invited to participate the study. For eligible families, all members were asked to fill out a home-made pre-validated questionnaire and take ^{13}C urea breath test for *H. pylori* infection. *H. pylori* prevalence in families, all-age individuals and minors (<18 years old) were determined.
Results: A total of 31098 subjects from 10735 households were finally enrolled. *H. pylori* prevalence was 64.61% in families, 35.20% in all-age individuals and 20.21% in children. The independent intrafamilial risk factors were teacup sharing and big family size. In contrast, cohabitation with more generations in one household was a protective factor. Childhood infection was significantly associated with a positive *H. pylori* status of the father and the mother. Four patterns of *H. pylori* prevalence were classified in various provinces.
Conclusions: The familial *H. pylori* prevalence is much higher than the individual prevalence in China. Teacup sharing, big family size and less generations in one household are independent risk factors for familial *H. pylori* infection. The infected parents are potential sources for childhood *H. pylori* infection.

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W2.6

HIGH INCIDENCE OF RESISTANCE TO ANTIBIOTICS USED FOR ERADICATION OF *HELICOBACTER PYLORIIN* THE UK

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Treatment of *Helicobacter pylori* is becoming more problematic due to increasing antibiotic resistance rates globally. There is no routine surveillance of *H. pylori* antimicrobial sensitivities in the UK, and published data is lacking. This study aimed to characterise antimicrobial sensitivities of isolates collected in Nottingham since 2001. Gastric biopsy samples were collected, with informed written consent and ethics approval, from patients attending the Queen's Medical Centre in Nottingham for an upper GI tract endoscopy. Antibiotic sensitivity was assessed comparing disc diffusion and Etest methods. Of 241 isolates tested, 28% were resistant to clarithromycin, 68% to metronidazole, and 3% to amoxicillin, which are used in first-line therapies. For those used in second- and third-line therapies, 0% of isolates were resistant to tetracycline, 4% to levofloxacin and 13% to rifampicin. Multi-drug resistance was found in 33% of isolates. Resistance to clarithromycin increased dramatically between 2001-2005 and 2011-2018 (17% to 45%; p=0.04). Resistance rates were higher than had previously been estimated for UK isolates. Based on the resistance profiles, treatment failure is more likely to occur when patients are given first-line therapies without amoxicillin. We are now sequencing the genomes of resistant isolates, to gain insight into the relationship between genotypic and phenotypic resistance data.

S.N. Suffian: None. E. Garvey: None. J. Rhead: None. K. Robinson: None.

W3 Pathogenesis of *Helicobacter pylori*

W3.1

SINGLE-CELL TRANSCRIPTOMICS ATLAS OF *HELICOBACTER PYLORI* INFECTION-ASSOCIATED GASTRIC CARCINOGENESIS

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Objective*:** *Helicobacter pylori* (*H. pylori*) is the strongest risk factor for gastric cancer. Infection with *H. pylori* causes universal gastritis which can progress typically through the Correa's cascade to intestinal metaplasia and gastric cancer. Dissecting the cell lineage, molecular heterogeneity could contribute to a deeper understanding of cell-to-cell variation and reveal new diagnostic and therapeutic insights. ***Materials and Methods: Here, we performed sing-cell RNA sequencing (scRNA-seq) analysis to elucidate the comprehensive transcriptomic landscape of 124,548 cells from 18 patients across *H. pylori*-uninfected and -infected histological lesions with chronic gastritis, intestinal metaplasia, and gastric cancer. ***Results:*** We identified 26 distinct cell-lineage clusters that could be assigned 9 different cell types based on known marker genes. The proportion of epithelial cells was gradually decreased during gastric neoplastic progression, whereas the proportion of endothelia and myeloid cells was significantly higher in tumors. ***Conclusions:*** Intriguingly, we found increased epithelial cell proportions and decreased myeloid cell proportions in *H. pylori*-infected samples compared with *H. pylori*-uninfected samples. Subclustering analysis of all epithelial cells revealed divergent cell lineage states. Tumor cells possessed a higher CNV signal and were localized in gastric cancer tissues. Specifically, tumor cells displayed high levels of KRT17 and ISG15 genes that also gradually upregulated with the progression from gastritis, intestinal metaplasia to gastric cancer. Additionally, we found that almost all enterocytes were acquired from metaplastic tissues. A list of genes that are uniquely upregulated in the enterocyte includes KRT20, ANPEP, FABP1, and PHGR1. Trajectory analysis indicated that pit mucous cells could transdifferentiate into tumor cells.

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W3.2

THE CYTOLETHAL DISTENDING TOXIN MODULATES CELL DIFFERENTIATION AND ELICITS EPITHELIAL TO MESENCHYMAL TRANSITION

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We are frequently exposed to bacterial genotoxins, such as cytolethal distending toxin (CDT), a prevalent heterotrimeric toxin whose active moiety is its CdtB subunit. CdtB triggers potent DNA damage, predisposing factors in the development of cancers, in host cells. CDT from *Helicobacter hepaticus*, a mouse pathogen, was shown to be directly involved in the development of murine hepatocarcinoma. Preliminary studies have shown that CDT induces certain phenotypes reminiscent of epithelial to mesenchymal transition (EMT), a process by which cells lose their epithelial characteristics in favor of mesenchymal ones, conducive to cell motility. In the present study, we investigated the different steps of EMT using liver tissues of mice infected with *H. hepaticus*, as well as human epithelial cell lines and xenograft mouse models following *H. hepaticus* CdtB expression. Most of the different steps of the EMT process were reproduced throughout the studied models. Indeed, microarray data showed a CdtB-dependent regulation of EMT-related transcripts. The key transcriptional regulators of EMT (SNAIL1 and ZEB1) and EMT markers (Vimentin, Fibronectin and α5β1 integrin) were upregulated both at RNA and protein levels in response to CdtB. It also induced cell-cell junctions' disassembly, causing individualization of cells and acquisition of a spindle-like morphology. CdtB activated the expression and activity of matrix metalloproteases and increased cell motility. This study demonstrated that CDT/CdtB elicits EMT process activation, supporting the idea that infection with genotoxin-producing bacteria can promote malignant transformation.

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W3.3

EFFECTS OF CHRONIC *HELICOBACTER PYLORI* STRAIN PMSS1 INFECTION ON WHOLE BRAIN AND GASTRIC IRON HOMEOSTATSIS IN MALE INS-GAS MICE

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***Objective*:** Iron deficiency in humans is associated with long-term deficits in cognition and memory if left untreated. Infection with *Helicobacter pylori* has been linked to iron deficiency anemia, potentially exacerbated by the expression of the virulence factor *cagA* in some strains. Due to the prevalence of both iron deficiency and *H. pylori* infection, a high risk of comorbidity exists.
Materials and Methods: Male INS-GAS/FVB mice were infected with the CagA$^+$ strain pre-murine Sydney strain 1 (PMSS1) for 12-13 or 27-29 weeks. Whole blood, serum, stomach and brain were collected at necropsy for further analysis including bacterial colonization, complete blood counts, and measurement of various iron parameters.
Results: Gastric histopathology scores and inflammatory cytokines were significantly elevated in all infected mice compared to controls. Mice infected for 12-13 weeks demonstrated a lower serum ferritin and higher transferrin receptor saturation percentage. Mice at 27-29 weeks had significantly decreased erythrocyte count, hematocrit, serum hemoglobin, and increased serum total iron binding capacity. Gastric transcription of iron-regulatory genes *Hamp* and *Bmp4* were significantly downregulated at 27-29 weeks. In the brain, iron-dependent myelingergic and synaptic markers were significantly downregulated at 27-29 weeks.

Conclusions: Infection with a CagA active *H pylori* strain induces perturbations in iron homeostasis in INS-GAS mice in a similar manner as CagA inactive strains, suggesting that it is not entirely the CagA activity itself that contributes to iron dysregulation in this model, but rather a multitude of other pathogenic processes.

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W3.4

CD40-CD40L BLOCKADE ATTENUATES DISEASE IN A NEW MOUSE MODEL OF GASTRIC B CELL MALT LYMPHOMA

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***Objective*:** *Helicobacter pylori* infection is a major factor in mucosa-associated lymphoid tissue (MALT) lymphoma. Nevertheless, the rarity and indolence of this lymphoma, as well as the lack of practicable animal models, have impeded the development of new treatments. The aims of the study were to: 1) develop a practicable model of gastric MALT lymphoma; and 2) evaluate whether blockade of CD40-CD40L signalling, important in T cell-B cell interactions, may be a new therapeutic target for the treatment of this disease.
Materials and Methods: Gastric tissues from *Nlrc5* conditional knockout (KO) mice, which develop MALT at 3 months post-*Helicobacter* infection, were compared with those of human MALT lymphoma using multiplex immunohistochemistry and H&E staining. The therapeutic efficacy of CD40L blockade was assessed by flow cytometry and histology on tissues from mice receiving either anti-CD40 or isotype control antibodies. Serum antibody titres were measured by ELISA.
Results: The gastric lesions in *Nlrc5* KO mice are consistent with those of human MALT lymphoma, comprising lymphoepithelial-like lesions, centrocyte-like cells and B cell follicles infiltrated by dendritic cells (DCs), macrophages, and T cells. *Nlrc5* KO mice administered an anti-CD40L antibody, either coincident with or after establishment of *Helicobacter* infection, had significantly reduced MALT lymphomagenesis, when compared with animals receiving a control antibody. CD40L-treated mice had significantly reduced numbers of gastric DCs, $CD8^+$ and $Foxp3^+$ T cells, as well as decreased gene expression of B cell lymphoma-associated factors.
Conclusions: CD40L may be a promising therapeutic target for the treatment of human gastric MALT lymphoma.

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W3.5

TH1 CYTOKINES, ESPECIALLY TNF, CAUSE NF-κB2 DEPENDENT MORPHOLOGICAL CHANGES IN PRIMARY MOUSE GASTRIC ORGANOIDS (GASTROIDS)

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***Objective*:** *Helicobacter pylori* (*H. pylori*) is the most important risk factor for gastric cancer development. Infection results in elevated concentrations of Th1 cytokines such as TNF, interferon (IFN)-γ and interleukin (IL)-1β and these are believed to play important roles during gastric carcinogenesis. We have previously demonstrated that genetic deletion of the NF-κB2 gene protected *H. felis* infected mice against the development of gastric preneoplastic lesions *in vivo*.
Materials and Methods: 3-dimensional gastric organoids (gastroids) from C57BL/6 (wild-type) and NF-κB2-null mice were grown in UltiMatrix and maintained in growth factor enriched media. Gastroids were treated with TNF, IFN-γ and IL-1β (0-100ng/ml) for up to 72 hours and photomicrographs were taken every 24 hours. Gastroid area was measured using ImageJ.
Results: Concentrations ≥75ng/ml TNF and ≥10ng/ml IFN-γ significantly reduced the area of wild-type mouse gastroids, but IL-1β did not induce cause any significant morphological changes in C57BL/6 gastroids up to 72 hours. By contrast, NF-κB2-null gastroids showed no significant decrease in area, even 72 hours after 100ng/ml TNF treatment. The responses of NF-κB2-null gastroids to IFN-γ were partially attenuated compared to wild-type.
Conclusions: TNF and IFN-γ significantly inhibited the growth of wild-type mouse gastroids in a dose-dependent manner, while IL-1β caused no obvious effects on gastroids. NF-κB2 deletion completely protected gastroids from TNF induced death. We are using immunohistochemistry for Ki-67 and active Caspase3 to investigate whether these observations result from alterations in cell proliferation and/or apoptosis and intend to use this model system to investigate how human gastroids respond to the same stimuli.

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W3.6

ACE2 IS INVOLVED IN THE CARCINOGENIC PROCESS OF *HELICOBACTER PYLORI* INFECTION

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***Objective*:** As a SARS-CoV-2 receptor, ACE2 has attracted much attention in recent years. A clinical study showed that *Helicobacter pylori* (*H. pylori*)-positive patients infected with SARS-CoV-2 showed more severe gastrointestinal symptoms. However, the relationship between ACE2 and *H. pylori* infection is unknown.
Materials and Methods: An *in vitro* coculture system and an *in vivo* C57BL/6 mouse model of *H. pylori*-infected gastric epithelial cells were established. The effect of *H. pylori* infection *in vitro* and *in vivo* on ACE2 expression was detected by western blot, and the changes of ACE2 expression in gastric mucosa tissues of *H. pylori*-infected mice were also detected by IHC. At the same time, 28 pairs of gastric cancer and paracancer tissue specimens were collected in this study, and the expression differences of ACE2 in gastric cancer and paracancer tissues were detected. Finally, overexpression and knockdown ACE2 cell lines were constructed, and the effects of ACE2 on cell biological functions were detected by CCK8, EdU, plate clone formation, cell scratch repair assay and Transwell cell migration and invasion assay.

Results: *H. pylori* infection *in vitro* and *in vivo* can significantly up-regulate the expression of ACE2, and the expression of ACE2 in gastric cancer tissues is significantly higher than that in paracancer tissues. Cell biological function experiments showed that ACE2 overexpression significantly promoted the proliferation, migration and invasion of gastric epithelial cells.
Conclusions: *H. pylori* infection significantly upregulated the expression of the oncogene ACE2, suggesting that ACE2 may be involved in the pathogenesis of *H. pylori* infection.

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W4 Treatment of *Helicobacter pylori*

W4.1

MISTAKES IN EMPIRICAL ERADICATION THERAPIES FOR *HELICOBACTER PYLORI* IN 45,778 PATIENTS: DATA FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (*HP*-EUREG)

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***Objective*:** Failure of therapy with macrolides, quinolones or metronidazole is associated with increased *H. pylori* antibiotic resistance; so, prescribing the same antibiotic as in previous eradication treatment should be avoided. In addition, quinolones are not recommended in first-line therapy given the higher incidence of adverse events reported
Patients and Methods: International, multicenter, prospective, non-interventional registry of clinical practice of European gastroenterologists. Infected adult patients were registered from 2013 to 2021. A modified intention-to-treat analysis was performed
Results: 45,778 patients from 29 countries were included in analysis: Spain (40%), Russia (16%), Italy (10%), Slovenia (8.1%), and Lithuania (4.8%). First-line therapy was prescribed in 36,699 (80%) cases, second line in 6,435 (14%), and third- to sixth-line in 2,644 (5.7%). Among those first-line therapies, 952 (2.6%) included levofloxacin, with a decrease in the consumption over the years (from 15% in 2013 to

5.9% in 2021) and differing between countries (Italy 3.4%, Lithuania 2.3%, Russia 2.0%, Slovenia 0.5%, Spain 1.9%; p<0.001). After a first-line eradication failure, clarithromycin was repeated in second-line therapy in 788 patients (16%), metronidazole in 312 (18%) and levofloxacin in 43 (28%) cases (Table 1).
Conclusions: The erroneous administration of quinolones in first-line therapy has decreased in recently in Europe. After first line-therapy failure with either clarithromycin, levofloxacin or metronidazole, the same antibiotic is frequently prescribed in second-line therapy.

TABLE 1. ANTIBIOTIC PRESCRIPTIONS REPEATED IN SECOND-LINE THERAPY, BY COUNTRY.

Antibiotic	Total n (%)	Italy n (%)	Lithuania n (%)	Russia n (%)	Slovenia n (%)	Spain n (%)	Other n (%)	*p*-value
Clarithromycin	**788 (16.0)**	83 (13.8)	27 (10.7)	272 (46.8)	19 (5.6)	263 (10.3)	124 (21.1)	**<0.001**
Amoxicillin	**3,403 (70.7)**	410 (64.4)	243 (97.2)	435 (69.2)	191 (92.3)	1.695 (68.2)	429 (71.1)	**<0.001**
Metronidazole	**312 (17.6)**	3 (2.8)	1 (4.5)	21 (28.0)	11 (7.6)	198 (17.2)	78 (28.8)	**<0.001**
Levofloxacin	**43 (28.1)**	3 (11.1)	0 (0.0)	15 (71.4)	-	19 (22.9)	43 (28.1)	**<0.001**

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W4.2

H. PYLORI PHAGES: FROM GENOME RELEASE TO HOPE FOR USE AS THERAPY

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***Objective*:** The increasing antibiotic-resistant *Helicobacter pylori* infections worldwide and the ineffectiveness of treatments led the World Health Organization to designate clarithromycin-resistant *H. pylori* as a high-priority bacterium for antibiotic research and development. (Bacterio)phages, viruses that infect bacteria, showing effectiveness in the treatment of pathogenic bacteria, could be a promising alternative strategy in the fight against *H. pylori* infections.
Patients and Methods: In this work, a collection of 74 Portuguese *H. pylori*-clinical strains was used to screen for the presence of phage genes, using a new PCR-based method. Selected strains were subsequently sequenced and prophage isolation was attempted using UV radiation. Three phages were isolated, one of which was further characterized genetically and biologically.
Results: PCR-based detection indicated the presence of target phage sequences in 14 strains, and the induction strategies resulted in the release of a new phage. It presents a genome length of 31,162 bp with a G+C content of 37.1 %. This podovirus showed capability to form phage plaques in five strains, was stable under an *in vitro* gastric digestion model, and was able to maintain a *H. pylori* population at low levels for up to 24 h post-infection.
Conclusions: The new PCR screening method proved to be very effective in the selection of strains carrying prophages, resulting in the isolation of a new *H. pylori* phage. This phage presented very promising characteristics in terms of stability and efficacy, being therefore a small step towards the future use of phage therapy in the fight against *H. pylori* infections.

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W4.3

LONG-TERM CHANGES OF GUT MICROBIOTA AND ANTIBIOTIC RESISTOME AFTER *H. PYLORI* ERADICATION – A MULTICENTER RANDOMIZED TRIAL

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***Objective*:** We aimed to compare the efficacy and long-term changes of antibiotic resistome of gut microbiota after *Helicobacter pylori* eradication.

Patients and Methods: Eligible patients with *H. pylori* infection who failed after first-line eradication therapy were randomized to receive either levofloxacin quadruple therapy (esomeprazole, amoxicillin, metronidazole, and levofloxacin for 14 days, EAML) or bismuth quadruple therapy (esomeprazole, bismuth, tetracycline, and metronidazole for 10 days, BQ). The microbiota composition of fecal samples was profiled by shotgun metagenomic sequencing.

Results: 560 patients were randomized in a 1:1 ratio to receive either EAML for 14 days or BQ for 10 days. The eradication rates in the EAML and BQ groups were 87.9% (246/280) and 87.5% (245/280) (p=0.898), respectively. The transient perturbation of the diversity of fecal microbiota at week 2 was restored to basal state 1 year after EAML and BQ. There was a significant increase in total resistome after EAML (p=0.00017) and BQ (p=4.3x10^{-10}) at week 2, which were restored to pretreatment level since week 8. The resistance rates to levofloxacin, ciprofloxacin, ampicillin and various cephalosporins of *Escherichia coli* and *Klebsiella pneumonia* were significantly increased in the EAML group than in the BQ group at week 2, which were restored to pretreatment levels at week 8 and year 1.

Conclusions: Levofloxacin quadruple therapy is not inferior to bismuth quadruple therapy in the second-line treatment for *H. pylori* infection. The transient increase of antibiotic resistance/resistome and perturbation of diversity of fecal microbiota were largely restored to pretreatment level months to 1 year after eradication therapy.

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W4.4

COMPARISON OF EMPIRICAL FIRST-LINE TREATMENT BETWEEN TEGOPRAZAN *VERSUS* LANSOPRAZOLE-BASED QUADRUPLE THERAPY: DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL

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***Objective*:** Antibiotic resistance to *Helicobacter pylori* (*H. pylori*) infection, which ultimately results in eradication failure, has been an emerging issue. Recently, for the first-line empirical therapy bismuth-based quadruple therapy is suggested. However, there are few studies that compare the potassium-competitive acid blocker (TBMT) and proton pump inhibitor containing quadruple therapy (LBMT) The aim of the study was to investigate the efficacy and safety profiles of TMBT *vs.* LMBT *via* non-inferiority trial.
Patients and Methods: We included patients (> 18 years) with treatment naive *H. pylori* infection who visited the four university-affiliated hospitals between March and December 2021. After being randomly assigned to both groups in 1 to 1 manner, patient compliance, eradication success rate, and patient-reported side effects profiles were assessed.
Results: Of the 217 patients, six patients who withdrew consent were excluded. 105 patients [mean age: 58.0 ± 11.3, male, n = 61 (58.1%)] were treated with TBMT, and 106 patients [mean age: 57.9 ± 9.97, male, n = 59 (55.7%)] were treated with LBMT. In the Intention-to-treat analysis, the eradication rate was 77.8% (77/99) in the TBMT group and 75.5% (74/98) in the LBMT group (p=0.02). In the per protocol analysis, the eradication rate (primary endpoint) was 89.0% (73/82) in the TBMT group and 82.4% (70/85) in the LBMT group (p<0.01). The compliance (TBMT *vs.* LBMT, 95.4%, 96.7%, p=0.47) and side effects were not significantly different.
Conclusions: The TBMT is not inferior to LBMT, thus, TMBT could be used as the first-line empirical treatment for the *H. pylori* eradication regimen.

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W4.5

COMPARISON OF THE EFFECTIVENESS OF *HELICOBACTER PYLORI* ERADICATION REGIMENS BETWEEN THE ELDERLY AND NON-ELDERLY POPULATIONS: DATA FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (*HP*-EUREG)

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***Objective*:** It is important to assess the treatment efficacy and differences between the elderly and non-elderly populations. The aim of the study is to compare the efficacy of first- and second-line *H. pylori* eradication regimens between the elderly and non-elderly.
Materials and Methods: European multicenter registry of *H. pylori* infection management (*Hp*-EuReg) collecting data until 2022. Subjects were divided into the non-elderly (18-59 years) and elderly (≥60 years) groups. Per-Protocol (PP) and modified Intention-To-Treat (mITT) analyses were performed.
Results: Overall 34,994 (71%) non-elderly and 14,467 (29%) elderly patients were included. In first- and second-line treatment, quadruple therapies were prescribed in 45% and 51% of the cases, respectively, whereas triple therapies in 44% in both lines. The overall first-line treatment effectiveness was 89% by PP and 88% by mITT in the non-elderly, and 90% by PP and 89% by mITT in the elderly (p<0.05). The overall second-line treatment effectiveness was 84% both by PP and mITT analyses in both groups (p>0.05). The main 6 regimens by line and their effectiveness are reported in Table 1. The elderly group was associated with significantly higher overall mITT eradication rate in the first-line treatment.
Conclusions: The overall effectiveness and the effectiveness of most frequent first- and second-line *H. pylori* eradication regimens in Europe is suboptimal (<90%). Optimal effectiveness (>90%) was achieved with quadruple therapies. No clinically relevant differences between elderly and non-elderly patients were observed.

TABLE 1. AMOST FREQUENT FIRST- AND SECOND-LINE *H. PYLORI* ERADICATION PRESCRIPTIONS AND THEIR EFFICACIES IN THE NON-ELDERLY AND ELDERLY POPULATIONS.

Treatment	Comparison of first-line treatment regimens between the non-elderly and elderly populations					
	Non-Elderly (18-59 years)			Elderly (≥ 60 years)		
	Use, N	PP %(95% CI)	mITT %(95% CI)	Use, N	PP %(95% CI)	mITT %(95% CI)
Triple PPI+C+A	10,540	87 (86-87)	86 (85-87)*	4,065	88 (87-89)	87 (86-89)*
Triple PPI+C+M	1,150	86 (84-88)	86 (83-88)	491	83 (79-86)	83 (79-86)
Quadruple PPI+C+A+M	4,199	90 (89-91)*	89 (88-90)*	1,940	91 (90-93)*	91 (90-92)*
Quadruple PPI+C+A+B	3,489	92 (91-93)	92 (91-93)	1,086	91 (89-93)	90 (88-92)
Pylera® (single capsule)1	3,233	94 (93-95)	93 (92-94)	1,519	94 (93-95)	93 (92-95)
Sequential C+A+T	1,291	90 (88-92)*	90 (88-91)*	623	94 (92-96)*	94 (91-96)*

Treatment	Comparison of second-line treatment regimens between the non-elderly and elderly populations					
	Non-elderly (18-59 years)			Elderly (≥ 60 years)		
	Use, N	PP %(95% CI)	mITT %(95% CI)	Use, N	PP %(95% CI)	mITT %(95% CI)
Triple PPI+A+L	1,422	83 (80-85)	82 (80-84)	524	80 (76-84)	80 (76-83)
Triple PPI+C+A	323	78 (72-83)	78 (72-83)	102	84 (74-91)	84 (74-91)
Quadruple PPI+A+L+B	584	89 (86-92)	89 (86-91)	225	86 (80-91)	86 (80-91)
Quadruple PPI+C+A+M	234	84 (79-89)	84 (78-88)	91	86 (77-92)	86 (77-93)
Quadruple PPI+M+Tc+B	224	86 (80-91)	84 (78-88)	101	87 (78-93)	88 (79-94)
Pylera® (single capsule)1	843	89 (87-91)	89 (86-91)	384	92 (89-95)	91 (88-94)

PP – per protocol; mITT – modified Intention-To-Treat; 95% CI – 95% confidence interval; PPI – proton pump inhibitor; C- clarithromycin; A – amoxicillin; M – metronidazole; B – bismuth; T – tinidazole; L – levofloxacin; Tc – tetracycline; 1Pylera®: three-in-one single-capsule containing metronidazole, tetracycline and bismuth; * statistically significant differences between the age groups, p<0.05.

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W4.6

PILOT STUDIES OF VONOPRAZAN-CONTAINING *HELICOBACTER PYLORI* ERADICATION THERAPY

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***Objective*:** Vonoprazan-containing *Helicobacter pylori* eradication is reliably effective in Japan. Its effectiveness in other countries remains unclear. Here, we examined vonoprazan-*H. pylori* therapies in Thailand.
Patients and Methods: This was pilot study of 4 different vonoprazan-containing therapies. Subjects were randomized to: 14-day dual therapy (500 mg amoxicillin q.i.d. plus 20 mg vonoprazan b.i.d.), 14-day triple therapy (amoxicillin 1 g b.i.d., slow release clarithromycin-MR, 1 g daily plus vonoprazan 20 mg b.i.d.), 7-day high-dose vonoprazan triple therapy (amoxicillin 1 g b.i.d., clarithromycin-MR 1 g daily and 60 mg vonoprazan once daily), and 14-day vonoprazan triple therapy plus bismuth (amoxicillin 1 g b.i.d., clarithromycin-MR 1 g daily, vonoprazan 20 mg b.i.d., and bismuth subsalicylate 1,048 mg b.i.d.). Eradication was confirmed 4 weeks after therapy. Antimicrobial susceptibility and CYP3A4/5 genotyping were performed.
Results: A total of 100 *H. pylori*-infected patients (mean age 54.3±13 years, 51% men) were randomized. DemogrAll were CYP3A4 extensive metabolizers. Cure rates with both 14-day vonoprazan dual therapy and 14-day triple therapy were low: 66.7%; 95%CI=43-85% (14/21), and 59.3%; 95%CI=39-78%) (16/27), respectively. In contrast, 7-day high-dose vonoprazan triple therapy and 14-day vonoprazan triple plus bismuth proved effective 92.3%; 95%CI=75-99% (24/26) and 96.2%; 95%CI=80%-100% (25/26), respectively.
Conclusions: Vonoprazan dual and triple therapy were ineffective for *H. pylori* eradication. High dose vonoprazan triple therapy and vonoprazan triple therapy adding bismuth might be used as first line treatments in some regions with high efficacy irrespective of CYP3A4/5 genotype and clarithromycin resistance.

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W5 Microbiota Manipulation

W5.1

EFFECTS OF TRANSPLANT DOSE, ROUTE OF ADMINISTRATION, AND REPEATING ON THE OUTCOME OF FECAL MICROBIOTA TRANSPLANTATION FOR PATIENTS WITH IRRITABLE BOWEL SYNDROME

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***Objective*:** In a study of fecal microbiota transplantation (FMT) for IBS with a high efficacy, a protocol for FMT with a combination of favorable factors was used. The present study investigated some of these factors.

Patients and Methods: The study included 186 IBS patients who randomized 1:1:1 into transplant administrated to the colon (single LI), to the duodenum (single SI), or to the distal duodenum twice with a week interval (repeated SI). The fecal transplant dose was 90g. The patients provided a fecal sample and were asked to complete five questionnaires at the baseline, and at 3, 6, and 12 months after FMT. The fecal bacteria were analyzed using 16S rRNA gene PCR DNA amplification/probe hybridization covering the V3-V9 regions.
Results: The response rate was significantly higher in single SI than that of single LI at 12 months after FMT. The response rates did not differ between single SI and repeated SI at all observation times after FMT. Symptoms and quality of life improved in all the treated groups at all time intervals after FMT. The abdominal symptoms were significantly lower and quality of live higher in repeated SI group than those of single SI. The bacterial profiles changed in all groups at all observation intervals. However, these changes differed between single LI on and single SI/repeated SI.
Conclusions: Administrating fecal transplant to the small intestine is to prefer than that administrated to the large intestine. Repeating FMT had more effect on symptoms and quality of life than a single FMT.

M. El-Salhy: None. T. Hausken: None. J. Hatlebakk: None.

W5.2

THE EFFECT OF MULTI-STRAIN PROBIOTICS ON DIARRHEA IN PATIENTS WITH TYPE 2 DIABETES AND METFORMIN INTOLERANCE

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***Objective*:** Metformin may cause gastrointestinal (GI) side-effects, which may be caused by gut microbial composition changes and probiotic may have the potential to modulate it.
Patients and Methods: 37 patients with diabetes mellitus type 2 and metformin intolerance (inability to increase the dose above 1500 mg due to GI upset, based on the questionnaire adapted from L. Creight) were randomized to Sanprobi Barrier® multispecies probiotic or placebo twice daily in a 32-week prospective, single center, cross-over clinical trial. Patients were randomized on visit 2 (V2) to probiotic or placebo and received a 12-week treatment until V5, followed by a 4-week wash-out, cross-over at V6, and a 12-week treatment until V9, followed by 4-week wash-out. The frequency and intensity of diarrhea was assessed every 4 weeks using a 5-point scale questionnaire (the study protocol: clinicaltials.gov, NCT04089280). Friedman's tests with post-hoc Dunn's were used.
Results: In the probiotic/placebo sequence, the frequency and severity of diarrhea decreased for patients on probiotic, and it increased on placebo. As for the placebo/probiotic sequence the frequency of diarrhea was not significantly increased on placebo and reduced for those on probiotic. Diarrhea's severity decreased insignificantly on both probiotic and placebo (Table 1).

Conclusions: The use of multi-strain probiotic decreases significantly the frequency of diarrhea in metformin intolerant patients compared to placebo.

TABLE 1. THE PATIENTS' CHARACTERISTICS, TOGETHER WITH THE FREQUENCY AND SEVERITY OF DIARRHEA.

	Randomization: probiotic → placebo	**Randomization: placebo → probiotic**
Patients' clinical characteristics		
Number of patients	19	18
Men: number (%)	5 (26)	9 (50)
Age: mean ± SD, years (*p*=0.92)	64.4 ± 5.8	61.2 ± 7.7
Duration of diabetes: mean ± SD, years (*p*=0.99)	9.6 ± 5.8	10.1 ± 7.9
HbA1c value: mean ± SD, % (*p*=0.58)	7.4 ± 1.1	7.9 ± 2.7
The frequency of diarrhea: mean ± SD score (the lower, the better)		
Visit 2	3.0 ± 1.1 (randomization to probiotic)	1.0 ± 1.0 (randomization to placebo)
Visit 5	1.5 ± 1.2	2.2 ± 1.3
p-value (visit 2 *vs.* 5)	<0.01	>0.99
Visit 6 (cross-over)	1.3 ± 1.2 (cross-over to placebo)	1.7 ± 1.3 (cross-over to probiotic)
Visit 9	1.6 ± 1.1	1.1 ± 1.1
p-value (visit 6 *vs.* 9)	>0.99	>0.99
The severity of diarrhea: mean ± SD score (the lower, the better)		
Visit 2	3.4 ± 1.5 (randomization to probiotic)	3.3 ± 1.3 (randomization to placebo)
Visit 5	1.5 ± 1.3	1.8 ± 1.2
p-value (visit 2 *vs.* 5)	0.01	0.10
Visit 6 (cross-over)	1.2 ± 1.2 (cross-over to placebo)	1.6 ± 1.3 (cross-over to probiotic)
Visit 9	1.4 ± 0.9	0.9 ± 0.9
p-value (visit 6 *vs.* 9)	>0.99	>0.99

K. Nabrdalik: D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Sanofi, NovoNordisk, Sanprobi, Roche, Lilly, Abbot, Boehringer, Astra Zeneca. F. Consultant/Advisory Board; Modest; Boehringer, Polfa. K. Drożdż: None. H. Kwiendacz: D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Sanofi, NovoNordisk. K. Skonieczna-Żydecka: F. Consultant/Advisory Board; Modest; Sanprobi Sp. z o.o. Sp. k. I. Łoniewski: E. Ownership Interest (stock, stock options, patent or other intellectual property); Significant; Sanprobi Sp. z o.o. Sp. k. M. Kaczmarczyk: F. Consultant/Advisory Board; Modest; Sanprobi Sp. z o.o. Sp. k. J. Nalepa: None. F. Holleman: None. M. Nieuwdorp: F. Consultant/Advisory Board; Modest; Caelus health. J. Gumprecht: B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Modest; Eli Lilly, Sanofi, Bayer, Worldwide Clinical Trials. D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Novo Nordisk, Eli Lilly, Merck, Sharp&Dohme, Bioton (Poland), Adamed (Poland), Sanofi, Astra Zeneca, Boehringer Ingelheim, Berlin-Chemie. F. Consultant/Advisory Board; Modest; Novo Nordisk, Eli Lilly, Merck, Sharp&Dohme, Bioton (Poland), Adamed (Poland), Sanofi, Astra Zeneca, Boehringer Ingelheim.

W5.3

A MICROBIOTA TARGETED, MEDITERRANEAN DIET-BASED NUTRITIONAL EDUCATION PROGRAM POSITIVELY MODIFIES THE INTESTINAL MICROENVIRONMENT OF HEALTHY INDIVIDUALS

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***Objective*:** The Mediterranean diet (MED) modifies gut microbial composition. Here we describe the positive outcome of a pilot study based on MED nutritional scheme in twenty healthy individuals.
Materials and Methods: The MED nutritional scheme was prospectively applied for four weeks and involved dietary counseling and a daily physical activity measurement. We used Dietary questionnaires to evaluate MED adherence. Furthermore, complete blood counts, metabolic and inflammatory markers, and microbial and eukaryotic composition using 16S and 18S sequencing, respectively, were assessed at four weeks, six- and twelve-months post intervention.
Results: All participants (females - 65%, median age - 37), completed the four-week intervention. Adherence to MED increased from baseline to four weeks post intervention as reflected by a significant increase in dietary fiber consumption and decrease in saturated fat intake (both $p<0.05$). Moreover, a reduction in fecal calprotectin, total leukocytes, neutrophil and lymphocyte counts, within the normal range (all $p<0.05$) was observed. Microbial composition demonstrated significant positive correlations between adherence to MED and physical activity to levels of butyrate producers including *Faecalibacterium* and *Lachnospira.* Bacterial composition was associated with plant-based food intake, while fungal composition with animal-based food as well as olive oil and sweets intake. Lastly, increasing adherence to MED correlated with increased absolute abundances of multiple beneficial gut symbionts.
Conclusions: MED adherence is associated with reduction of inflammatory markers and beneficial microbial alterations in healthy individuals. Thus, MED nutritional education program may be used to modify the intestinal ecosystem with potential implications for microbiome mediated diseases.

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W5.4

FECAL MICROBIOTA TRANSPLANTATION (FMT) ON IRRITABLE BOWEL SYNDROME (IBS): A RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND STUDY

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***Objective*:** IBS is a common functional bowel disorder with recurrent abdominal pain. Gut microbial dysbiosis contributes to pathogenesis of IBS. Stool bank was successfully established in Thailand 2 years ago. FMT has provided tentative beneficial results in IBS patients in previous trials. This study aimed to compare efficacy of FMT with placebo in IBS patients.
Patients and Methods: Patients aged 18-70 years with IBS defined by Rome IV criteria at Thammasat University Hospital were enrolled between April and November 2021. Patients were randomized 1:1 to receive 50 grams of FMT or placebo via rectal enema. The primary outcome was clinical response defined by a decrease in IBS-symptom severity score (IBS-SSS) by ≥50 points at 4 weeks after FMT.
Results: Patients had mean age of 48.6 years and 40% were males. Baseline characteristics and mean IBS-SSS at baseline were comparable between groups. There was a significant improvement of IBS-

SSS (161.0±106.1 *vs.* 264.0±71.7, *p*=0.020), overall clinical response (2 weeks: 70% *vs.* 10%, *p*=0.020, 4 weeks: 80% *vs.* 20%, *p*=0.007), abdominal pain score (2 weeks: 4.3±1.3 *vs.* 5.8±1.4, *p*=0.025, 4 weeks: 2.8±1.8 *vs.* 5.2±1.8, *p*=0.008), and abdominal distension score (4 weeks: 3.0±2.6 *vs.* 5.4±1.8, *p*=0.028) after FMT compared with placebo. A significant mean reduction in abdominal pain score (-49% *vs.* -19%, *p*=0.045), and abdominal distension score (-53% *vs.* -19%, *p*=0.042) was demonstrated at 4 weeks after FMT. Quality of life scores significantly improved in FMT group (13.3±8.0 *vs.* 20.2±5.1, *p*=0.033). Only minor adverse events such as mild abdominal pain, nausea, and diarrhea, were reported and not different between groups. No serious adverse event was observed.
Conclusions: FMT *via* rectal enema improves overall clinical response, IBS-SSS and quality of life scores. FMT might be an alternative effective treatment for patients with IBS.

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W5.5

IMMUNE AND NON-IMMUNE CHANGES FOLLOWING FECAL MICROBIOTA TRANSPLANTATION IN EXPERIMENTAL COLITIS: EMERGING PATHWAYS OF FMT DERIVED MUCOSAL HEALING

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Objective**:** Several studies suggest a clear association to altered gut microbiota, impaired mucous layer and epithelial barrier disfunction in ulcerative colitis (UC). Fecal microbial transplantation (FMT) emerged as a promising therapeutic approach aimed at repopulating gut microbiota and indirectly influencing the recipient's immune system. Our study aims to evaluate the impact that FMT, using feces from UC patients, on microbiota composition and mucosal integrity in a murine model of colitis.
Materials and Methods: Mice (n=40), that were pre-conditioned for a week with a cocktail of broad-spectrum antibiotics to deplete most of the intestinal microbiota, then a 7-day DSS 3% treatment was carried out to induce the colitis and, during those days, two FMT infusion were performed. The mice were sacrificed at the end of seven days of recovery, and feces, colon and whole blood were collected.
Results: Disease activity index of murine colitis was ameliorated by the infusion of feces from inactive UC patients, associated with the decrease of LPS in serum, lower levels of pro inflammatory cytokines, an increase of FOXP3 and MUC2 as a marker of intestinal integrity. A modulation of gut microbiota was assessed after each phase of treatment.
Conclusions: Our study suggests the infusion of fecal suspension from inactive UC patients is able to induce an anti-inflammatory response at mucosal level. These data open new scenario about the use of autologous FMT in UC.

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W5.6

CHANGES IN GUT MICROBIOTA AFTER ANTIBACTERIAL THERAPY AMONG CHILDREN: PRELIMINARY DATA

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Objective**:** Children often receive antibacterial treatment due to concomitant diseases, thus, affecting gut microbiota. Spontaneous recovering of microbiota is suggested in children. The aim of the study was to analyse changes of gut microbiota composition in children after antibacterial treatment.

Patients and Methods: Parents of children receiving antibacterial therapy brought child's faecal samples before treatment, seven and 30 days after the treatment. The baseline composition of gut microbiota (16rRNS sequencing) was compared with further samples. Statistical analysis: ANOVA, Wilcoxon, Friedman test.
Results: Eleven children (F/M: 7/4; mean age 20,82 months) submitted faecal samples. The mean Shannon Index was 4.5 (SD±1.5) at baseline compared to 4.1 (SD±1.8) and 5.1 (SD±1.1) seven and 30 days after the treatment (p=0.5), showing marked intra-patient differences. The median relative abundance of *Bifidobacteriaceae* decreased from 49.4 (IQR: 14.2-74.4) at baseline to 9.8 (IQR: 0.01-39.5) and 32,1 (IQR: 7.3-49-2) seven and 30 days after treatment; p=0.05; being significantly lower 30 days after treatment compared to baseline: 24.4 (SD±24.4) *vs.* 48.6 (SD±33.1); p=0.009. Relative abundance of family *Lachnospiraceae* increased from 29.5 (IQR:10.1-81.7) at baseline to 41.1(24.2-88.9) one month after the treatment (p=0.05). *Erysipelotrichia* and *Coriobacteriia* was identified *de novo* among most abundant taxa.
Conclusions: Although strain diversity did not change significantly after antibacterial treatment, large inter-patient differences suggested individual response to the treatment. *Bifidobacteriacae* was the main taxonomic unit decreasing after antibacterial treatment, showing also tendency to increase after 30 days, thus indirectly suggesting spontaneous stabilization of microbiota. Increase of *Lachnospiracae* together with appearance of previously not identified taxa could be associated with selection of strains after antibacterial therapy.

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W6 Gastric Cancer and Carcinogenesis

W6.1

INCIDENCE OF GASTRIC CANCER AMONG LONG-TERM USERS OF PROTON PUMP INHIBITORS AFTER *HELICOBACTER PYLORI* ERADICATION; A POPULATION-BASED COHORT STUDY IN KOREA

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***Objective*:** Gastric cancer (GC) risk among *H. pylori* eradicated (HPE) long-term proton pump inhibitor (PPI) users is unclear.
Patients and Methods: We queried the 2009-2019 [j1] Korean National Health Insurance Services Database for patients aged > 40 years who had claimed for HPE during 2009-2014 [j2]. The incidence of GC after PPI exposure of 180 days of cumulative defined daily dose (cDDD) or more and that of < 180 cDDD were compared. Outcome was defined as GC development at least one year after HPE. Patients with any history of cancer, gastrectomy or endoscopic resection, or their follow-up data < 2 years were excluded. PPI users were matched to non-users using propensity scores (PS) within the same quartiles of follow-up duration. Development of GC among the tertiles of annual PPI dose were compared among PPI users.
Results: After PS matching, 144,091 pairs of PPI users and non-users were selected for analysis. During a median follow-up of 8.3 years (interquartile range, 6.8-9.6), there were 1,053 GC cases in PPI users and 948 in non-users. The incidence (95% confidence interval [CI]) of GC per 1,000 person-years was 0.90 (0.85-0.96) in PPI users and 0.81 (0.76-0.86) in non-users. When compared to non-users, adjusted

hazard ratio (aHR) for GC risk was 1.16 (95% CI, 1.06-1.27; *p* = 0.001) in PPI users. Among PPI users, patients in higher tertile for annual PPI dose showed higher GC development compared to lower tertile (aHR [95% CI] 3.87 [3.25-4.60].
Conclusions: After HPE, GC risk may be influenced by long-term PPI use.

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W6.2

ATROPHIC GASTRITIS AND GASTRIC CANCER TISSUE MIRNOME ANALYSIS

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Objective**:** Gastric cancer (GC) is one of the most frequently diagnosed tumor globally. GC is usually diagnosed at advanced stages resulting in poor prognosis. Clinical potential of miRNA profiling in the gastric cancerogenesis, especially in premalignant GC cases, remains unclear. We aimed to evaluate the atrophic gastritis (AG) and GC tissue miRNomes.
Patients and Methods: Study included a total of 125 subjects: Controls (CON), AG, and GC patients. All study subjects were recruited at the Departments of Surgery or Gastroenterology, Hospital of Lithuanian University of Health Sciences. Tissue samples was used for preparation of small RNA sequencing libraries and profiled using next-generation sequencing.
Results: Tissue analysis revealed 20 differentially expressed miRNAs in AG group compared to CON group, 129 deregulated miRNAs in GC compared to CON, and 99 altered miRNAs comparing GC and AG groups. MiRNAs hsa-miR-129-1-3p and hsa-miR-196a-5p were identified to be stepwise deregulated in healthy-premalignant-malignant sequence. Area under the curve (AUC)-receiver operating characteristic analysis revealed that expression level of hsa-miR-196a-5p is significant for discrimination of CON *vs.* AG, CON vs GC and AG vs GC and resulted in AUCs: 88.0%, 93.1% and 66.3%, respectively. Moreover, analysis revealed that hsa-miR-215-3p/5p and hsa-miR-934 were significantly deregulated in GC based on *H. pylori* status.
Conclusions: Comprehensive miRNome study provides evidence for gradual deregulation of hsa-miR-196a-5p and hsa-miR-129-1-3p in gastric carcinogenesis and found hsa-miR-215-3p/5p and hsa-miR-934 to be significantly deregulated in *H. pylori* carrying GC patients.

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W6.3

HELICOBACTER PYLORI TESTING AMONG INDIVIDUALS AT RISK OF GASTRIC CANCER: A POTENTIAL INTERCEPTION POINT TO REDUCE THE GASTRIC CANCER BURDEN IN THE US

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Objective**:** Although clinical trials have shown that *H. pylori* treatment reduces risk of developing gastric cancer and potentially prolongs survival, *H. pylori* testing is not consistently performed in the US, even among patients reporting gastric distress.

Patients and Methods: In a diverse retrospective cohort of 99 gastric cancer cases diagnosed at Duke University from 2002-2020 (57% Black and 43% white), we examined the association of *H. pylori* testing prior to cancer diagnosis with survival.
Results: Overall, 29 patients were tested for *H. pylori* prior to gastric cancer diagnosis (average 2.9 years before diagnosis), 68% of whom tested positive, but one had evidence of treatment. Using Cox proportional hazards regression modeling with inverse probability weighting for factors associated with receipt of testing (age, race, and insurance status), and adjusting for cancer treatment and stage at diagnosis, *H. pylori* testing prior to cancer diagnosis was associated with a reduced likelihood of death (HR 0.66, 95% CI 0.45-0.97, p=0.035). When including neighborhood-level socioeconomic status for the 83 North Carolina residents, the protective effect of *H. pylori* testing appeared even stronger (HR 0.48, 95% CI 0.31-0.75, p=0.001). Although in the US, gastric cancer accounts for the largest racial disparity in cancer death rates comparing Blacks to whites, in this analysis there was no significant difference in survival by race.
Conclusions: These findings support increased use of *H. pylori* testing among individuals at risk of gastric cancer and suggest this may be a potential interception point to reduce gastric cancer disparities in the USA.

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W6.4

OPTIMAL FOLLOW-UP PERIOD AFTER ENDOSCOPIC RESECTION OF EARLY GASTRIC CANCER: A MULTI-CENTER RETROSPECTIVE COHORT STUDY

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***Objective*:** Endoscopic resection (ER) is now accepted as a standard treatment modality for early gastric cancer (EGC). Since metachronous gastric neoplasm (MGN) is not uncommon after successful ER, periodic follow-up is recommended. However, there has been no report on optimal follow-up period so far. This study aimed to investigate an optimal follow-up period and investigate risk factors for MGN after successful ER for EGC.
Patients and Methods: Patients who underwent ER at three university hospitals from 2017 to 2020 were included. Patients were followed up once or twice a year. The interval from the time of endoscopic resection to the onset of MGN was identified, and risk factors for MGN were investigated.
Results: 774 patients were recruited in in this study, and 477 patients were included except for incomplete resection and follow-up loss. 209 patients were followed up annually, and 270 patients were followed up biannually. MGN was found in 19 patients during the follow-up period, and there was no significant difference in incidence between the two groups (p=0.878). In a univariate analysis of MGN incidence, severe atrophic gastritis was the only risk factor (odds ratio, 3.63; 95% confidence interval, 1.12-11.77; p=0.032). *Helicobacter pylori* infection or intestinal metaplasia were not significant risk factors in this study. All the MGN was resected endoscopically.
Conclusions: Annual follow-up is enough after successful ER for EGC.

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W6.5

IDENTIFICATION OF SEROLOGICAL MARKERS ASSOCIATED WITH GASTRIC CANCER IN TWO CHINESE STUDIES USING *HELICOBACTER PYLORI* MULTI-STRAIN MICROARRAYS

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Infections with *H. pylori* trigger antibody responses which can be used to estimate gastric cancer (GC) risk. So far, serological associations between *H. pylori* and GC were mainly studied using well-known cytotoxins, primarily CagA. In order to discover additional informative antigens, we performed an unbiased *de novo* identification using *H. pylori* microarrays, chip-scaled test systems. To generate these microarrays, we defined the minimal non-redundant proteome of five *H. pylori* strains of different origins (Chile, Korea, Latvia, Malaysia and UK) by clustering homologues. This resulted in 1,852 clusters, each consisting of proteins with an amino acid identity >70%. A representative of each cluster was displayed as an *in vitro* translated recombinant protein on our *H. pylori* microarrays. To identify GC associated antigens, microarrays were probed with sera from 63 GC cases and 63 controls from a Chinese cross-sectional study. A confirmatory study was performed using 136 GC cases and 136 matched controls from the prospective Linxian Nutrition Intervention Trial (NIT; China). Antigens contributing the most to a correct classification of GC were identified using iterative recursive feature elimination. Twenty-two promising candidates were transferred to the high-throughput platform multiplex serology to measure antibodies against the selected *H. pylori* antigens in a larger number of cases and controls (Shanxi ~850; NIT ~2,000). Beside well-known serological risk markers, we were able to identify further antigens significantly associated with GC, e.g., the outer membrane protein HopA. Informative serological markers beyond CagA enable the generation of enhanced GC risk models and potentially promote secondary prevention.

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W6.6

DISTINCT MUCIN-MICROBIOME SIGNATURES IN PATIENTS WITH GASTRIC CANCER

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***Objective*:** We performed high-throughput profiling to investigate interactions between mucin expression and bacterial communities in gastric cancer (GC) patients.
Materials and Methods: Tumour and adjacent normal tissue samples from three independent GC cohorts (n=106) and gastric biopsies from functional dyspepsia patients (n=20) were analysed for mucin expression by RT-qPCRs integrated with clinical data (age, gender, tumour stage/location, survival). Based on mucin expression, the adenocarcinomas were classified into gastric (predominantly MUC5AC, MUC6 and MUC1), intestinal (predominantly MUC2, MUC4 and MUC13), mixed (all types) and null (neither gastric nor intestinal) mucin phenotypes. The gastric microbiome (n=83) was determined using 16S rRNA sequencing. Taxonomy and community composition were determined, metagenome inferred, and microbial networks analysed.

Results: Our tumour samples were classified as gastric (13%), intestinal (19%), mixed (47%) and null (17%) mucin phenotypes. The intestinal and null phenotypes (p=0.01, log-rank test) as well as aberrant MUC13 expression (p=0.037, Wald test) associate with worse survival. Significant changes in Campylobacterota, Firmicutes, Bacteroidota and Proteobacteria abundancy between mucin phenotypes were found. Moreover, bacterial networks of intestinal and mixed mucin phenotypes were more complex and influenced by mucin-associated bacteria compared to the gastric and null phenotypes. *Bacteroides, Lachnoanaerobaculum, Limnohabitans, Methyloversatilis, Oribacterium, Reyranella* and *Sediminibacterium* are depleted in samples with high MUC13 expression while *Prevotella, Solobacterium, Leptotrichia, Veillonella* and *Neisseria* are enriched. The latter three genera have been linked to GC underlining their involvement in MUC13-driven carcinogenesis.
Conclusions: Our results highlight a key role for mucins in 1) GC prognosis and 2) shaping microbial networks in the tumour microenvironment.

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POSTER

P01 Diagnosis of Helicobacter infection

P01.01

COMPARISON OF FOUR STOOL ANTIGEN TESTS FOR THE DETECTION OF *HELICOBACTER PYLORI*

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***Objective*:** Stool antigenic tests (SAT) are rapid, largely available, and non-invasive method for the diagnosis of *Helicobacter pylori* (*HP*) infection. We evaluated and compared the performance of 3 novel SAT devices, *H. PYLORI* QUIK CHEK™ (TECHLAB), *H. pylori* Ag Rapydtest® (APACOR) and Curian® HpSA® (MERIDIAN[2]) against our routine method, Helico HpSA Immunocard STAT!® (MERIDIAN[1]), for which the performance has been established extensively in previous studies (accuracy up to 97.5%).
Materials and Methods: We carried out a prospective comparison study using four cited devices on 124 stool samples obtained from consecutive non-duplicate patients between June and October 2021. Tests were performed according to the manufacturers' instructions and MERIDIAN[1] served as our reference method. Sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) for each test were calculated. Multiple aliquots of a positive sample were frozen at -80°C and tested with four devices at day 1, 7, 15 and 30, to evaluate the stability of samples storage. Two positive samples were tested with the four methods 3 times per day during 5 days for repeatability/reproducibility studies.
Results: Repeatability, reproducibility, and stability analyses showed excellent performance for all devices. Performance results are summarized in Table 1.
Conclusions: All tests were reliable showing a perfect specificity and PPV. APACOR has the shortest turn-around time to carry out. MERIDIAN[2] requires a reading device but reduces the subjectivity of the operator's reading.

TABLE 1. PERFORMANCE OF EVALUATED TESTS COMPARED TO THE ROUTINE METHOD.

Performance compared to the reference method (n=124; 28 positive & 96 negative results)	*H. PYLORI* QUIK CHEK™ (TECHLAB) Positives: n=22 & Negatives: n=102	*H. pylori* Ag Rapydtest® (APACOR) Positives: n=25 & Negatives: n=99	Curian® HpSA® (MERIDIAN) Positives: n=24 & Negatives: n=100
Sensitivity % (95% CI)	79 (66-84)	89 (76-92)	86 (73-90)
Specificity % (95% CI)	100 (96-100)	100 (96-100)	100 (96-100)
Accuracy %	96	98	97
NPV %	94	97	96

P01.02

SCREENING AND DIAGNOSIS OF *HELICOBACTER PYLORI* INFECTION AND AUTOIMMUNE GASTRITIS IN PATIENTS WITH CHRONIC PANCREATITIS

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The role of *H. pylori (HP)* infection and atrophic gastritis in the development and progression of chronic pancreatitis (CP) remains unknown. We screened patients with CP for *HP*-infection and autoimmune gastritis (AIG) and assessed gastric structure and function. Screening for *HP*-infection, gastric atrophy and AIG was assessed by pepsinogen-I (PG-I), PG-II, gastrin-17 (G-17), *H. pylori* IgG; anti-parietal-cell antibodies (APCA), anti-intrinsic-factor (AIF) using ELISA. 42 persons were involved (26 men, mean age 51.86±15.93 years): 30 with CP and 12 healthy controls. Mean levels of PG-I, PG-II, G-17, APCA and AIF in patients with CP were as follows: 138.67±54.39 µg/L; 17.46±11.86 µg/L; 10.15±10.55 pmol/L; 9.63±17.03 Cell U/mL and 9.32±10.31 Factor U/mL. AIG was observed in 46.67% of CP patients. APCA levels were higher in patients (p=0.015). We observed AIG more often in patients with severe structural pancreatis. *HP*-infection was found in 40% of CP patients, superficial *HP*-gastritis – in 30%, and atrophic gastritis – in 10%. PG-II levels were higher in males and in patients with advanced CP (p =0.048 and p=0.034). Grade of pancreatic structural changes did not correlate with gastric mucosal changes. In CP, AIF levels correlated positively with G-17. Patients with CP and concomitant autoimmune disease had increased risk of AIG and gastric atrophy in respect to lower levels of G-17 (p=0.000) and PG-I (p=0.002) and higher APCA (p=0.03). By iron-deficiency anaemia, we observed higher *HP*-titer in CP. Patients with CP are at risk of *HP* infection. Proper diagnostic algorithm for *HP*, AIG and atrophic gastritis allows their early verification, treatment and prevention of associated complications.

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P01.03

THE PRESENCE OF ANTI-PARIETAL CELL AUTO-ANTIBODIES COULD BE RELATED WITH THE RE-INFECTION OF *HELICOBACTER PYLORI*

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

METHOD: We analyzed 1,518 patients who complained with 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 autoantibodies and compared the frequencies between NUD and gastric neoplasia. Among patients with NUD, screening endoscopic examinations and *H. pylori* state were evaluated (n=295).
Results: The presence of autoantibodies 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 autoantibodies 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 autoantibodies (6/8, 75%, p<0.01).
Conclusions: It was unlikely that the presence of autoantibodies was a marker of gastric neoplasia, and *H. pylori* was a potential trigger of autoimmune gastritis. In patients with history of eradication, the presence of autoantibodies could predict the re-infection of *H. pylori.*

S. Lim: None. W. Chung: None.

P01.04

AUTOMATION OF RIDA®GENE *HELICOBACTER PYLORI* PCR ON THE INGENIUS® AUTOMATED SYSTEM

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Introduction: *Helicobacter pylori* PCR allows a sensitive detection of this bacterium and of mutations associated with macrolide resistance. The aim was to automate and evaluate the performance of the RIDA®GENE *H. pylori* PCR (r-Biopharm) on Ingenius (Elitech) on biopsies and stools.
Materials and Methods: 200 gastric biopsies were tested retrospectively. Digested material was transferred for analysis on Ingenius. An in-house *H. pylori* PCR was used as reference. 55 stools of known *H. pylori* status were also tested. Pretreated stools were analyzed on Ingenius according to the same protocol as the gastric biopsies.
Results: 98 of the 100 *H. pylori*-negative biopsies were detected as negative by Ingenius. Two biopsies were positive (Ct >35) but with no notion of *H. pylori* infection.
All of the 100 biopsies positive for *H. pylori* were detected positive on Ingenius. The macrolide-sensitive population and macrolide-resistant population were all perfectly detected. The sensitivity and NPV were 100%, specificity and PPV 98-100% for *H. pylori* detection and macrolide susceptibility categorization, respectively.
Analyses on stool samples yielded no false positives out of 30 expected negatives and 7 false negatives out of 25 expected positives: sensitivity of 72% and specificity of 100%. Macrolide resistance was not detected for 2 out of 6 expected resistant: sensitivity of 66.7% and specificity of 100%.
Conclusions: The performance of the RIDA®GENE *H. pylori* PCR on the Ingenius for gastric biopsies is excellent. The adaptation of this PCR on automated PCR systems is of real interest for microbiologists. Stool tests are less efficient.

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P01.05

COMPARISON OF DIFFERENT METHODS FOR THE DETECTION OF *HELICOBACTER PYLORI* IN THE PATHOLOGY DIAGNOSTICS

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***Objective*:** The diagnostic accuracy of the conventional histology stainings, immunohistochemistry (IHC) and molecular methods and their role in the routine pathology diagnosis of *Helicobacter pylori* is still controversial. Our aim was to compare these methods in a single-institution cohort.
Materials and Methods: Formalin-fixed paraffin-embedded gastric tissue samples from 67 patients with clinical request for *Helicobacter pylori* diagnostics were collected. Tissue sections were stained by Giemsa and *Helicobacter* IHC. DNA was isolated from further sections and PCR was performed using a newly designed primer amplifying a sequence containing 122 bp from the 23SrRNA gene of the bacterium.
Results: Of the 67 cases, 44 were positive for *Helicobacter pylori* by Giemsa, 44 by IHC and 53 by PCR. We found 14 cases with discrepancies. Two cases were negative by Giemsa but were positive by IHC and by PCR. In a single Giemsa and IHC positive case the PCR was negative. Two cases were positive by Giemsa but negative by IHC. One of them showed positivity by PCR, while the other was negative. 9 cases were negative by Giemsa and IHC but later proved to be positive by PCR.
Conclusions: IHC and PCR showed superior results in comparison with Giemsa. Among the IHC positive cases, high concordance was obtained with the PCR. However, considerable proportion of the IHC negative cases turned out to be positive by PCR. PCR, with its known high sensitivity, is suggested to be used in IHC negative cases with strong clinical and/or histological suspicion for *Helicobacter pylori* infection.

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P01.06

PCR IMPROVED DETECTION OF *HELICOBACTER PYLORI* IN UNSELECTED ADULT PATIENTS UNDERGOING ROUTINE GASTROSCOPY

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Accurate detection of *H. pylori* is essential for effective patient management. Reduced prevalence and wide usage of PPI's can negatively impact commonly employed tests, including rapid urease tests (CLO), culture and standard histological examinations. Additional tests in at risk patients could improve detection.
The aim was to compare the performance of a PCR-based assay for the detection of *H. pylori* versus routine histological testing in an Irish context.
Following ethical approval and informed consent, adults were prospectively recruited. During routine gastroscopy subjects had 2 additional antrum and corpus biopsies taken for DNA extraction and PCR using custom-designed primers for the urease gene. CLO tests and antral and corpus histology (H&E and IHC, where indicated in the hospital laboratory) were performed as standard.
In all, 118 patients with available histology and PCR results were included in the analysis. 27 had chronic active gastritis (CAG), of which 21 (78%), 20 (74%) and 13 (48%) had positive histology, PCR and CLO tests respectively. Of interest, in 44 subjects with chronic inactive gastritis (CIG), 11 (25%) had a positive PCR and only 1 (2%) positive histology. PCR detected the urease gene in 31 (26%) patients indicative of infection; 20 and 11 with CAG and CIG respectively. Based on PCR the sensitivity, specificity, PPV and NPV for histology were 65%, 98%, 9% and 89% respectively.

PCR-based testing should be included in cases where no Helicobacter-like organisms are detected on routine histology, particularly if the patient has a presentation of chronic gastritis irrespective of activity.

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P01.07

CAGA AND VACA GENOTYPES OF *HELICOBACTER PYLORI* STRAINS IN ESTONIA AND THEIR RESISTANCE TO ANTIBIOTICS

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***Objective*:** Estonia ranks as top 3 country for the prevalence of *Helicobacter pylori* (*HP*) with high gastric cancer incidence. Triple therapy is generally prescribed for *HP* eradication without prior antibiotic susceptibility testing (AST) or follow-up control. Here, we wish to map the pathogenicity and antibiotic resistance of *HP* strains circulating in Estonia.
Patients and Methods: 23 patients with different gastric problems who provided written informed consent were enrolled in the study approved by local ethics committee. Gastric biopsies from antrum and corpus were plated on Columbia blood agar. From each *HP*-positive biopsy, 6-14 colonies were picked for DNA extraction and PCR genotyping. AST was performed using E-test method from one colony of each biopsy.
Results: Out of 23 patients, 16 were *HP*-positive (70%). Using REP and RAPD PCR, we found that 5 patients (31%) were infected with the same *HP* strain in both antrum and corpus, while the rest of them had different *HP* subpopulations in different gastric regions or even within the same location. Many of the strains isolated were highly virulent, encompassing the CagA gene (7 patients, 44%) and VacA s1 allele [s1/m^1 in 5 patients (31%) and s1/m^2 in 8 patients (50%)]. Only 6 patients (38%) were infected with *HP* strains susceptible to all antibiotics tested. Resistance to ampicillin, clarithromycin and metronidazole was 18.8%, 43.8% and 37.5%, respectively.
Conclusions: We report for the first time in 20 years that *HP* strains in Estonia are highly virulent and resistant to many widely used antibiotics.

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P01.08

REAL-TIME PCR *HELICOBACTER PYLORI* TEST IN COMPARISON WITH CULTURE AND HISTOLOGY FOR *HELICOBACTER PYLORI* DETECTION AND IDENTIFICATION OF RESISTANCE TO CLARITHROMYCIN: SINGLE CENTER EXPERIENCE

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***Objective*:** The possibility to use RT-PCR, now widely used for COVID19 detection, and the availability of kits specific for *H. pylori*, encouraged us to include this test to our armamentarium to diagnose *H. pylori* and to detect its resistance to clarithromycin (CLA). We report here a single center experience in *H. pylori* detection and CLA susceptibility testing using three different methods: histology, culture and real-time PCR assay RIDA®GENE *HP*.
Patients and Methods: Thirty-eight symptomatic patients (mean age 41.9 years) underwent upper endoscopy during which 4 biopsies (2 antral and 2 corpus) were obtained for histology and 4 biopsies for culture with antibiogram and RT-PCR. We compared the results of *H. pylori* detection between histology, PCR and culture, and the results of CLA susceptibility testing between antibiogram based on culture and RT-PCR.
Results: Out of 38 patients, 18/34 (52.9%) were positive for *H. pylori* by both RT-PCR and histology, while only 17/38 (44.7%) were detected by culture. CLA resistance was found in 2 patients by both RT-PCR and culture (11.7%). In one patient, after double-checking, we obtained discrepant results. The minimal time for obtaining the antibiogram test response was of 9 days.
Conclusions: RIDA®GENE *H. pylori* assay and culture on gastric biopsies are comparable in their ability to detect *H. pylori* and its resistance to CLA and are easily feasible. Despite the small number of patients, we can say that RT-PCR was very convenient and gave a quick result of clinical value, justifying the reimbursement of this test now acted and which should occur soon in France.

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P01.09

EVALUATION OF THE ACCURACY OF THE "LIAISON® MERIDIAN *HELICOBACTER PYLORI* SA" STOOL ANTIGEN TEST FOR THE DIAGNOSIS OF *H. PYLORI INFECTION*: A SPANISH MULTICENTRE STUDY.

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***Objective*:** Detection of *Helicobacter pylori* by a stool antigen test (SAT) is an attractive non-invasive alternative. The aim of this study was to assess the accuracy of a new SAT, the automated LIAISON® Meridian *H. pylori* SA chemiluminescent immunoassay (CLIA) based on monoclonal antibodies, as compared to the ^{13}C-Urea Breath Test (UBT) gold standard.
Patients and Methods: This prospective multicentre study (9 Spanish centres) enrolled patients ≥ 18 years with clinical indication to perform UBT, both diagnosis pre- and post-treatment. Two UBT methods were used as available: mass spectrometer (MS), including citric acid (CA) in its protocol; and infrared spectrophotometer (IRS), without CA.

Results: 307 patients (145 naïve, 162 post-treatment) were analysed. Using recommended cut-off values (negative SAT <0.90, positive ≥1.10) the sensitivity, specificity, positive-predictive-value, negative-predictive-value and accuracy were 67%, 97%, 86%, 92% and 91%, respectively, obtaining an area under the curve (AUC) of 0.85. In total, 28/307 patients (7 false positives and 21 false negatives) presented a discordant result between SAT and UBT. Among the 21 false negatives, 4/6 tested with MS and 11/15 tested with IRS had a borderline UBT delta value. In 25/28 discordant samples, PCR targeting *H. pylori* DNA was performed and SAT accuracy was re-analysed, showing encouraging results (Table 1).
Conclusions: The new LIAISON® Meridian *H. pylori* SA SAT shows a good accuracy for diagnosing *H. pylori* infection.

TABLE 1. ACCURACY OF THE LIAISON® MERIDIAN *H. PYLORI* SA TEST.

Comparison SAT vs. UBT	Sensitivity 95% CI	Specificity 95% CI	PPV 95% CI	NPV 95% CI	LR+ 95% CI	LR- 95% CI	Global accuracy 95% CI	AUC 95% CI
Overall	67% (55-79%)	97% (95-99%)	86% (75-97%)	92% (88-95%)	23 (11-49)	0.34 (0.24-0.48)	91% (88-94%)	0.85 (0.78-0.92)
Naïve	74% (59-88%)	96% (92-100%)	89% (77-100%)	90% (84-96%)	19 (7-51)	0.27 (0.16-0.45)	90% (84-95%)	0.88 (0.80-0.96)
NDIRS Naïve	73% (54-92%)	93% (86-100%)	83% (65-100%)	89% (80-97%)	11 (4-29)	0.29 (0.15-0.55)	87% (80-95%)	0.86 (0.75-0.96)
IRMS Naïve	75% (51-99%)	100% (99-100%)	100% (96-100%)	92% (82-100%)	–	0.25 (0.11-0.58)	93% (86-100%)	0.91 (0.79-1.0)
Post-treatment	55% (31-78%)	98% (95-100%)	80% (56-100%)	93% (89-98%)	25 (8-82)	0.46 (0.29-0.73)	92% (87-96%)	0.79 (0.65-0.93)
NDIRS Post-Treatment	53 % (26-80%)	99% (96-100%)	90% (66-100%)	91% (85-98%)	46 (6-336)	0.48 (0.29-0.79)	91% (85-97%)	0.81 (0.67-0.95)
IRMS Post-Treatment	60% (7.1-100%)	96% (90-100%)	60% (7-100%)	96% (90-199%)	16 (3-75)	0,42 (0.14-1.22)	93% (86-100%)	0.78 (0.44-1.0)
Overall after performing RT-PCR in stool	94% (85-100%)	97% (95-99%)	86% (75-97%)	99% (97-100%)	35 (17-73)	0,07 (0.02-0.20)	97% (95-99%)	0.96 (0.91-1.0)
Naïve after performing RT-PCR in stool	91% (80-100%)	96% (93-100%)	89% (77-100%)	97% (94-100%)	25 (10-67)	0.09 (0.03-0.27)	95% (91-99%)	0.996 (0.99-1.0)
Post-treatment after performing RT-PCR in stool	100% (96-100%)	98% (95-100%)	80% (56-100%)	100% (99-100%)	50 (16-153)	0,00	98% (96-100%)	0.94 (0.88-1.0)

SAT: Stool Antigen Test; UBT: Urea Breath Test; CI: Confidence Interval; PPV: Positive predictive value; NPV: Negative predictive value; LR+: Positive Likelihood Ratio; LR−: Negative Likelihood Ratio; AUC: Area under the ROC Curve; IRMS: Isotope ratio mass spectrometer; NDIRS: Nondispersive isotope-selective infrared spectrometer; RT-PCR: Real-time polymerase chain reaction.

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P01.10

PRESENCE OF *H. PYLORI* AND NHPH IN CHILDREN WITH GASTRODUODENAL MANIFESTATIONS AT THE NATIONAL INSTITUTE OF PEDIATRICS IN MÉXICO

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***Objective*:** *H. pylori* (*Hp*) infects the human gastric mucosa and its prevalence in children is 20%-80% depending on the geographic region. Non-*Helicobacter pylori* gastric *Helicobacters* (NHPH) infect animals and humans. The frequency of NHPH in children is 2.7%. *Helicobacter* infection is associated with active chronic gastritis, peptic ulcer and MALT lymphoma.
The objective of the study was to analyze the frequency of *Hp* and NHPH species in Mexican children treated at the National Institute of Pediatrics.
METHOD: This study was approved by the National Institute of Pediatrics (NIP) research, ethics and biosafety committee. Participants come from gastroenterology service of the NIP, due to the presence of dyspeptic symptoms such as recurrent chronic abdominal pain and other symptoms suggestive of *Hp*. Gastric biopsies were collected per patient, it was homogenized, one part was used for *Hp* culture and the other for molecular identification of both *Hp* as well as NHPH species by endpoint PCR.
Results: A total of 196 children participated in this study; 121 (61.7%) were positive for the *Helicobacter* genus. 74/196 (37.7%) were positive only for *Hp* and 72/196 children (36.7%) were NHPH positive. Single and mixed infections were found in the gastric mucosa of these children, 49/196 (25%) were only positive for *Hp*; 47/196 (24%) only positive for NHPH and 25/196 (12.7%) had mixed infection between *Hp* and species NHPH.
Conclusions: 61.7% of the children were infected with *Helicobacter*. co-infection was found between *Hp* and NHPH. This work showed the frequency of zoonotic infection of *Helicobacter* in Mexican children with gastroduodenal manifestation.

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P02 Treatment of Helicobacter infection

P02.01

EFFECTIVENESS AND SAFETY OF AMOXICILLIN- AND FURAZOLIDONE-CONTAINING BISMUTH QUADRUPLE REGIMEN FOR HELICOBACTER PYLORI INFECTION IN REAL-WORLD PRACTICE

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***Objective*:** The eradication rate of *Helicobacter pylori* (*Hp*) has decreased largely because of high antibiotic resistance. We aimed to evaluate the effectiveness and safety of amoxicillin- and furazolidone-containing bismuth quadruple regimen for *Hp* eradication, based on real-world data.
Patients and Methods: This was a prospective observational study. From December 2019 to February 2022, patients who were confirmed to infected *Hp* by C-UBT value > critical value + 50% critical value, rapid urease test ≥ (++), histopathology, bacterial culture or stool antigen test received eradication treatment (acid suppressant, bismuth, amoxicillin and furazolidone) in *Hp* specialist clinics or partial general clinics for *Hp* eradication at our hospital. Within ±2 days after *Hp* eradication, adverse events (AEs) and compliance were obtained. At least 4 weeks after completion of therapy, *Hp* eradication was assessed by C-UBT or histopathology.
Results: A total of 625 patients completed this study, the overall eradication rates were 87.4% (546/625) by intention-to-treat (ITT) analysis and 89.5% (537/600) by per-protocol (PP) analysis. The ITT eradication rates for 10-day and 14-day regimen were 86.3% *vs.* 89.0% (p=0.328). The ITT eradication rates for initial treatment and rescue treatment were 88.7% *vs.* 79.8% (p=0.017). 89 patients (14.2%) expe-

rienced at least one AE, the majority of AEs were mild and overall compliance rate was 96.0%. The incidence of AEs for 10-day regimen was higher than 14-day regimen (16.8% *vs.* 10.2%, $p = 0.020$).
CONCLUSION: Amoxicillin- and furazolidone-containing bismuth quadruple regimen proved safe and provided fair initial eradication in real-world practice.

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P02.02

THE *IN VITRO* ACTIVITY OF POPLAR PROPOLISES AGAINST *HELICOBACTER PYLORI* GROWTH AND UREASE ACTIVITY

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In the last two decades, the alarming antibiotic resistance phenomenon became a key factor in the treatment failure of *H. pylori* infection. Searching of natural compounds with anti-*H. pylori* activity has gained popularity in scientific research focused on drug innovation because of their broad flexibility and low toxicity. The chemical composition of propolis extracts, obtained from different region of Georgia (Vasisubani, Ota, Misatske), was determined by ultra-high-performance liquid chromatography-diode array detector-mass spectrometry (UPLC-DAD-MS). The MIC and MBC of propolis extracts were tested using two-fold microdilution method with modification by addition after incubation of resazurin to visualize the growth of *H. pylori* ATCC 43504 and 10 clinical *H. pylori* strains with different resistance patterns. The phenol red method was used to screen the effect of propolis extracts on urease activity expressed as IC_{50}. Propolis samples were classified as poplar. Among phenolic compounds content caffeic acid prenyl or isoprenyl ester isomers II and IV as well as pinobanksin-3-O-acetate were confirmed in sample from Vasisubani. Propolis sample from Ota and Misatske were similar and contained mainly flavonid compunds: chrysin, pinocembrin, pinobanksin-3O-acetate, galangin. All tested propolises showed promising inhibitory activity against both reference *H. pylori* strain (MIC 15.6-31.3 mg/L) and clinical *H. pylori* strains (MIC50/90 31.3 mg/L). Urease activity was inhibited by the propolises with IC_{50} ranged from 233.6 mg/L and 456.1 mg/L (propolises from Misatske and Ota, respectively) to 1498.4 mg/l (propolis from Vasisubani). The propolises can be regarded as a useful natural preparation supporting the eradication *H. pylori* therapy.

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P02.05

SEVEN DAYS OF BISMUTH-BASED QUADRUPLE THERAPY IS EFFECTIVE FOR THE FIRST-LINE TREATMENT OF CLARITHROMYCIN-RESISTANT CONFIRMED *HELICOBACTER PYLORI* INFECTION

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***Objective*:** Point mutations in the 23S ribosomal RNA gene have been associated with *Helicobacter pylori* (*H. pylori*) clarithromycin resistance, and bismuth-based quadruple therapy (BQT) is one of the options for the treatment of clarithromycin-resistant *H. pylori*. Current *H. pylori* treatment guidelines recommend BQT for 10-14 days. This study aims to compare the eradication extents according to 7-day and 14-day BQT treatment for treatment-naïve clarithromycin-resistant confirmed *H. pylori* infection.

Patients and Methods: We retrospectively investigated treatment-naïve *H. pylori* infection cases from March 2019 to December 2020 where patients were treated with BQT. Clarithromycin resistance was identified with a dual-priming oligonucleotide-based multiplex polymerase chain reaction method. We reviewed a total of 126 cases. Fifty-three subjects were treated with a 7-day BQT regimen (7-day group), and 73 subjects were treated with a 14-day BQT regimen (14-day group). We evaluated the total eradication extent of the BQT and compared the eradication extents of the two study groups.
Results: Total eradication extent of *H. pylori* was 83.3% (105/126). The eradication extents of the two groups were as follows: 7-day group [81.1% (43/53)], 14-day group [84.9% (62/73), p = 0.576] by intention-to-treat analysis; 7-day group [95.6% (43/45)], 14-day group [92.5% (62/67), p = 0.522] by per-protocol analysis. The moderate or severe adverse event extents during the eradication were 30.2% (16/53) in the 7-day group and 19.2% (14/73) in the 14-day group (p = 0.165).
Conclusions: The 7-day BQT regimen was as effective as the 14-day BQT regimen in the eradication of treatment-naïve clarithromycin-resistant *H. pylori* infection.

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P02.07

ROLE OF COMPLIANCE IN *HELICOBACTER PYLORI* TREATMENTS: RESULTS FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (*HP*-EUREG)

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***Objective*:** The adherence to *Helicobacter pylori* eradication treatment is a cornerstone for achieving an adequate treatment efficacy. The objective of the study was to determine which factors could influence on the compliance of treatments.
Materials and Methods: Systematic prospective non-interventional registry (*Hp*-EuReg) of the clinical practice of European gastroenterologists. Compliance was adequate: >90% drug intake. Data collected until September 2021 at AEG-REDCap e-CRFand was subject to quality control. Modified intention-to-treat (mITT) analyses were performed. The multivariate analysis evaluated the factors associated with the effectiveness of the treatments and the compliance.

Results: Of the 38,698 records, 646 (1.7%) did not have adequate compliance. There was a higher non-compliance rate in patients prescribed with longer therapies (10-,14-days), rescue treatment, with uninvestigated/functional dyspepsia, and reporting adverse events. Non-adherence was lower in first-line as compared to rescue treatment (1.5% *vs.* 2.2%; *p*<0,001). Non-adherence in the three most frequent first-line treatments was significantly different: 1.1% with PPI-clarithromycin-amoxicillin; 2.3% with PPI-clarithromycin-amoxicillin-metronidazole; and 1.8% with bismuth quadruple therapy; and their effectiveness was significantly higher in compliant *vs.* non-compliant patients: 86% *vs.* 44%; 90% *vs.* 71% and 93% *vs.* 64%, respectively (*p*<0.001). In the multivariate analysis, the variable which was most significantly associated with higher effectiveness was the adequate compliance with the treatment (OR: 6.3; 95%CI: 5.2-7.7; *p*<0.001).
Conclusions: Compliance with *H. pylori* eradication treatment is very high. Factors associated with poor compliance: uninvestigated/functional dyspepsia, rescue-treatment, prolonged treatment regimens, the presence of adverse events, and the use of sequential and concomitant treatment. Adequate treatment compliance was the variable most closely associated with an eradication success.

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P02.08

ANNUAL ERADICATION RATES OF CONCOMITANT THERAPY AS FIRST-LINE TREATMENT FOR *HELICOBACTER PYLORI* INFECTION: A 10-YEAR RETROSPECTIVE DATA FROM A SINGLE CENTER IN KOREA

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***Objective*:** The eradication rates of standard triple therapy for *Helicobacter pylori* (*H. pylori*) infection have been reported to have decreased over the years due to antibiotics resistance. Concomitant therapy, one of non-bismuth quadruple therapy, has recently been suggested as one of the first-line treatment options for *H. pylori* infection in Korea. The aim of this study was to document whether the eradication rate of concomitant treatment has changed over the past 10 years.
PATIENST AND METHODS: A total of 1,287 patients with *H. pylori* infection who were treated with concomitant therapy (proton pump inhibitor, amoxicillin, metronidazole, and clarithromycin) for 5-10 days, and performed the test to assess the eradication from January 2010 to December 2019 were included in this study. Data were collected by retrospectively reviewing the medical records.
Results: The overall *H. pylori* eradication rate was 90.5%. Annual eradication rates from 2010 to 2019 were 88.2%, 92.4%, 90.2%, 87.8%, 94.0%, 93.1%, 89.0%, 88.9%, 89.4% and 90.6%, respectively, by per-protocol analysis. The eradication rate with first-line concomitant therapy has remained consistent over the past 10 years.
Conclusions: The overall eradication rate of concomitant therapy was about 90%, and annual eradication rate has not decreased over the past 10 years. Concomitant therapy could be the acceptable option as the first-line therapy for *H. pylori* in Korea.

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P02.09

RECURRENT NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING AMONG PATIENTS RECEIVING DUAL ANTI-PLATELET THERAPY

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***Objective*:** Patients who are receiving dual anti-platelet therapy (DAT) may suffer from recurrent gastrointestinal (GI) bleeding. We investigated clinical characteristics and associated factors of recurrent non-variceal upper gastrointestinal bleeding (NVUGIB) in patients receiving DAT.
Patients and Methods: We enrolled patients who received DAT and was diagnosed as NVUGIB during 2006 to 2020. NVUGIB was defined if definite bleeding focus was found on upper GI tract by esophagogastroduodenoscopy with either 1) associated symptoms (i.e., melena) or 2) anemia: decrease of serum hemoglobin more than 2.0 mg/dL from the baseline.
Results: A total of 138 patients who received DAT were diagnosed as NVUGIB. Patients were male-predominant (112, 81.2%), and bleeding was mostly from stomach (102, 73.9%) and peptic ulcer (83, 60.1%). Among them, 45 patients (32.6%) showed recurrent NVUGIB, and 21 patients (15.2%) expired during 16.2 months of follow-up (7 patients [5.0%] due to NVUGIB). Multivariate analysis showed that age was the significant factor for rebleeding (odds ratio [OR]: 1.043, 95% confidence interval [CI]: 1.001-1.088, *p*-value: 0.046), death (OR: 1.082, 95% confidence interval [CI]: 1.012-1.158, *p*-value: 0.022) and bleeding-related death (OR: 1.154, 95% confidence interval [CI]: 1.006-1.324, *p*-value: 0.040). Kaplan-Meier analysis showed that cumulative probability of rebleeding, death and bleeding-related death was significantly higher among patients ≥ 70 years compared with patients < 70 years (p=0.005, 0.001 and 0.025, respectively).
Conclusions: Clinicians need to be cautious of high possibility of rebleeding and mortality when manage elderly NVUGIB patients who receive DAT.

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P02.10

EFFECTIVENESS OF HIGH-DOSE RABEPRAZOLE TRIPLE THERAPY FOR *H. PYLORI* INFECTION IN ELDERLY PEOPLE AND ATROPHIC GASTRITIS

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***Objective*:** Rabeprazole is a potent PPI with less dependent on CYP2C19 polymorphism. Elderly people tend to resist eradication treatment, are more prone to antibiotic resistance against *H. pylori.* Atrophic gastritis involving the corporal mucosa is associate with reduced gastric acid secretion. We aimed to investigate the efficacy of high-dose rabeprazole triple therapy for *H. pylori* eradication in either elderly people or atrophic gastritis patients.
Patients and Methods: Total 103 patients with *H. pylori* infection by either a positive UBT or rapid urease test in Seoul Paik Hospital were recruited. Patients were treated with 14-day regimen of amoxicillin 1 g, clarithromycin 500 mg, rabeprazole 20 mg twice daily. After one month after treatment, UBT was performed to document the eradication.
Results: 103 patients completed the study included 53 males, 50 females, age range 34-83 years. The endoscopic features of subjects were 81 chronic atrophic gastritis, 36 intestinal metaplasia, 6 duodenal ulcer, 6 gastric ulcer, 5 lymphofollicular gastritis, 9 gastric polyp, 5 gastric adenoma, 3 EGC, 1 MALT lymphoma. The average *HP* eradication rate in all patients was 74.8%, in male 76.9%, in female 72.5%. Eradication rate by age was 63.6% over 70 years, 76.1% under 70 years. Eradication rate with or without gastric corporal atrophic gastritis was 65.9%, 76.1%.
Conclusions: High-dose rabeprazole triple therapy for 14 days was not superior to conventional triple therapy. *H. pylori* eradication rates in either elderly people or atrophic gastritis patients were lower than non-elderly, non-atrophic gastritis groups.

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P02.11

DIFFERENCES OF *HELICOBACTER PYLORI* DIAGNOSTICS AND TREATMENT IN THE ELDERLY AND NON-ELDERLY POPULATIONS: DATA FROM EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (*HP*-EUREG)

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***Objective*:** There might be some peculiarities in the diagnostics and treatment of *H. pylori* in the elderly population. The aim of the study was to compare the demographics, diagnostics and treatments of *H. pylori* infection in the elderly (≥60 years) and non-elderly (18-59 years).

Patients and Methods: European multicenter registry of *H. pylori* infection management (*Hp*-EuReg) collecting data until 2022. Subjects were divided into the non-elderly (18-59 years) and elderly (≥60 years) groups.

Results: Results are presented in Table 1. 14,467 elderly and 34,994 non-elderly patients were included. Elderly patients had more concurrent medications and drug allergies ($p<0.05$). There were significant differences in most of main *H. pylori* diagnostic tests before and after the treatment between groups. The duration of first-line treatment in the elderly and non-elderly was 7 days in 14% and 12%, 10 days in 50% and 49%, and 14 days in 36% and 40%, respectively, ($p<0.05$ for all groups), but no significant differences in prescribed PPI doses were found. In second-line treatment, no differences in treatment durations were reported; however, low-dose PPIs were more frequently prescribed in the elderly and high-dose PPIs in the non-elderly. No differences were found in overall treatment compliance, but the AEs rate was lower in the elderly ($p<0.05$).

Conclusions: Age group differences were reported in concurrent medications, drug allergies, AEs and prescribed regimens both in first- and second-line treatments. Treatment compliance was similar between groups.

TABLE 1. THE MAIN DIFFERENCES IN THE DEMOGRAPHICS, DIAGNOSTICS AND TREATMENT OF *H. PYLORI* BETWEEN THE ELDERLY AND NON-ELDERLY POPULATIONS.

	Elderly (≥60 years)	Non-elderly (18-59 years)	*p*-value
Gender, N (%)			
Total	14,467 (29%)	34,994 (71%)	<0.05
Male	5,365 (37%)	14,244 (41%)	<0.05
Female	9,093 (63%)	20,730 (59%)	<0.05
Average age (mean and standard deviation)	68.1±6.3	42.8±10.7	<0.05
Main treatment indications, N (%)			
Functional dyspepsia	5,111 (36%)	13,248 (38%)	<0.05
Peptic ulcer disease	2,893 (20%)	5,094 (15%)	<0.05
Main symptoms, N (%)			
Dyspepsia	10,571 (73%)	27,070 (77%)	<0.05
Heartburn	3,831 (26.3%)	9,183 (26.5%)	>0.05
Concurrent medications, N (%)	7,364 (55%)	8,834 (27%)	<0.05
Drug allergies, N (%)	796 (6%)	1,306 (4%)	<0.05
Main diagnostic methods pre-treatment, N (%)			
Histology	6,840 (47%)	13,191 (38%)	<0.05
Rapid urease test	5,463 (38%)	13,138 (38%)	>0.05
Urea breath test	3,550 (25%)	10,702 (31%)	<0.05
Main diagnostic tests post-treatment, N (%)			
Urea breath test	9,544 (66%)	21,755 (62%)	<0.05
Stool antigen test	1,968 (13.6%)	5,401 (15.4%)	<0.05
Histology	715 (5%)	1,529 (4%)	<0.05
Treatment compliance, N (%)	12,938 (97%)	31,270 (97%)	>0.05
First-line prescriptions, N (%)			
Triple-therapy	4,851 (42%)	12,492 (45%)	<0.05
Quadruple-therapy	5,182 (45%)	12,641 (46%)	<0.05
Second-line prescriptions, N (%)			
Triple-therapy	788 (43%)	2,134 (45%)	<0.05
Quadruple-therapy	956 (52%)	2,393 (51%)	<0.05
PPI potency in first-line treatment, N (%)			
Low	5,275 (46%)	12,312 (45%)	>0.05
Standard	2,726 (24%)	6,831 (25%)	>0.05
High	3,516 (31%)	8,539 (31%)	>0.05
PPI potency in second-line treatment, N (%)			
Low	750 (40%)	1,691 (36%)	<0.05
Standard	423 (23%)	1,059 (23%)	>0.05
High	705 (38%)	1,983 (42%)	<0.05
First-line treatment duration, N (%)			
7 days	1,583 (14%)	3,170 (12%)	<0.05
10 days	5,700 (50%)	13,351 (49%)	<0.05
14 days	4,185 (37%)	11,019 (40%)	<0.05
Second-line treatment duration, N (%)			
7 days	75 (4%)	197 (4%)	>0.05
10 days	1,023 (56%)	2,618 (56%)	>0.05
14 days	744 (40%)	1,881 (40%)	>0.05
Adverse events (AEs)			
Overall, N (%)	3,062 (23%)	8,144 (25%)	<0.05
Treatment cessation due to AEs, %	1.5%	1.2%	>0.05

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P02.12

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

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***Objective*:** 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.
Patients and Methods: We prospectively enrolled treatment-naïve patients with *H. pylori* infection from 4 hospitals in Korea. We enrolled 225 (72.1%) patients at the time of this preliminary analysis. 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's susceptibility test. The empirical group was treated with a concomitant regimen.
Results: After randomization, 24 (10.7%) patients dropped out. The *H. pylori* eradication rates in the tailored and empirical groups were 83.7% and 83.1% (p=1.000) in the ITT analysis and 93.9% and 92.5% (p=0.747) 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 (8.0% *vs.* 33.3%, p<0.001). Taste alteration and dizziness of grade 2 or higher were less common in the tailored group as well (1.9% *vs.* 21.1%, p<0.001 and 1.2% *vs.* 7.0%, p=0.041, respectively).
Conclusion Culture-based tailored therapy seems to be effective and safe as a primary treatment for *H. pylori* infection.

TABLE 1. ERADICATION RATES ACCORDING TO ANTIBIOTICS RESISTANCE PROFILE (PP ANALYSIS).

Clarithromycin	Metronidazole	Regimen	Total number (n)	Eradication success (n)	Eradication rate (%)
Empirical group (n=53)					
Susceptible	Susceptible	PAMC	30	30	100
Susceptible	Resistant	PAMC	11	11	100
Resistant	Susceptible	PAMC	7	6	85.7
Resistant	Resistant	PAMC	5	2	40.0
Tailored group (n=148)					
Susceptible	Susceptible	PAC	88	82	93.2
Susceptible	Resistant	PAC	22	21	95.5
Resistant	Susceptible	PAM	26	25	96.2
Resistant	Resistant	PBTM	12	11	91.7

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P02.13

THE ERADICATION RATE OF *HELICOBACTER PYLORI* OF CONCOMITANT THERAPY WAS HIGHER THAN SEQUENTIAL THERAPY AND TRIPLE THERAPY WITH TEGOPRAZAN, POTASSIUM COMPETITIVE ACID BLOCKER

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***Objective*:** The decline of *Helicobacter pylori* (*H. pylori*) eradication rates with standard triple therapy resulted in a search for novel therapies for first-line therapy of *H. pylori* infection. Murakami reported that eradication rate of vonoprazan, Japanese potassium competitive acid blocker (P-CAB) triple therapy was higher than PPI triple therapy. The aim of the study is to compare the efficacy of concomitant therapy with sequential therapy and triple therapy with Korean P-CAB as the first-line therapy of *H. pylori* eradication.
PATIENS AND METHODS: Total 900 patients were divided into 3 groups, and each group was treated with a different eradication therapy. The first group was simultaneously treated with rabeprazole, amoxicillin clarithromycin, and metronidazole for 7 days (concomitant therapy group). The second group was treated with rabeprazole and amoxicillin for 5 days, followed by rabeprazole, clarithromycin, and metronidazole for 5 days (sequential group). The final group was treated with tegoprazan, potassium competitive acid blocker, instead of PPI and amoxicillin and clarithromycin (K-CAB group).
Results: The eradication rates were 92.3% (277/300) in the concomitant group, 84.4% (253/300) in the sequential group (p<0.05), and 79.4% (238/300) in P-CAB group (p<0.05).
Conclusions: The eradication rates of concomitant therapy were higher than sequential therapy and triple therapy with tegoprazan, Korean K-CAB.

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P02.14

THE INFLUENCE OF PROBIOTIC SUPPLEMENTATION ON THE ERADICATION RATES AND RECRUDESCENCE OF *HELICOBACTER PYLORI*: A DOUBLE-BLIND RANDOMIZED CLINICAL TRIAL

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***Objective*:** Although the effects of probiotic supplementation on *Helicobacter pylori (H. pylori)* eradication therapy have been studied, we do not fully understand them. The purpose of this study is to analyze the effect of continuous probiotic intake on eradication rates and recrudescence after fully completing a course of *H. pylori* therapy.
METHOD: We prospectively performed a randomized double-blind placebo-controlled trial from June 2018 to June 2020. We enrolled and treated 270 patients with a standard triple regimen for *H. pylori* eradication. We randomized the subjects to either receive a probiotic as adjunctive therapy (*Enterococcus faecium* 4.5 x 10^8 and *Bacillus subtilis* 5.0 x 10^7, Medilac-S®, Hanmi Pharmaceuticals, Seoul, Korea) or a placebo (one tablet three times daily) for 28 days following *H. pylori* eradication. For the subjects who had successful eradication, we conducted a second ^{13}C-UBT (urea breath test) after six months.
Results: The probiotic and placebo group eradication rates were 77.1% and 72.4% (p = 0.48) in per-protocol analysis, and 67.4% and 65.9% in intention-to-treat analysis (p = 0.43). After six months, 149 patients had follow-up visits and four patients had recrudescence (2.7%). The probiotic and placebo groups had no statistical difference in recrudescence rates. Of the 76 patients who complained of non-ulcer dyspepsia, 60 (78.9%) had symptom relief after six months. This beneficial effect was typical for postprandial distress syndrome (p = 0.02).
Conclusions: Consecutive probiotic supplementation as adjunctive therapy following *H. pylori* eradication therapy had little beneficial effect on the eradication rate or prevention of recrudescence.

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P02.15

A RANDOMIZED MULTICENTER CONTROLLED TRIAL TO COMPARE *HELICOBACTER PYLORI* ERADICATION RATES BETWEEN THE EMPIRICAL CONCOMITANT THERAPY AND TAILORED THERAPY BASED ON 23S RRNA GENE POINT MUTATIONSÌ

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***Objective*:** We compared the *H. pylori* eradication rates of the empirical concomitant therapy (CoT) and the tailored therapy (TaT) using DPO-PCR to detect mutations in the 23S rRNA gene that are related to clarithromycin resistance.
Patients and Methods: Between June 2020 and May 2021, 290 patients were enrolled and randomly assigned into two groups. In the CoT group, the patients received rabeprazole 20 mg, amoxicillin 1 g, clarithromycin 500 mg, and metronidazole 500 mg twice daily for 14 days. In the TaT group, point mutation-negative patients received rabeprazole 20 mg, amoxicillin 1 g, and clarithromycin 500 mg twice daily for 14 days; the point mutation-positive patients received rabeprazole 20 mg twice daily, metronidazole 500 mg thrice daily, and bismuth 120 mg and tetracycline 500 mg four times daily for 14 days.
Results: A total of 290 and 261 patients were included in the ITT and PP analyses, respectively. The point mutations were identified in 28.6% of the patients. The eradication rates showed no significant difference between the two groups as per ITT (CoT, 82.8% and TaT, 85.5%, $p = 0.520$) and PP (CoT, 88.6% and TaT, 94.6%, $p = 0.084$) analyses. In point mutation-positive patients, the eradication rates of the CoT group were lower than those of the TaT group as ITT (69.8% and 87.5%, $p = 0.050$) and PP (76.9% and 97.1%, $p = 0.011$) analyses.
Conclusions: CoT and TaT showed similar overall eradication rates for *H. pylori*. However, CoT eradication rate was suboptimal, especially in point mutation-positive patients.

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P02.16

SERBIAN DATA OVERVIEW FROM APRIL 2021 TO APRIL 2022: EVALUATION FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (*HP*-EUREG)

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***Objective*:** *Helicobacter pylori* (*H. pylori*) is a transmissive pathogen that causes a wide range of gastric lesions. Optimal clinical management remains a challenge considering growing antimicrobial resistance. Our aim was to analyse current trends in eradication therapy and its effectiveness in Serbia.
Materials and Methods: An observational multicentric prospective study was conducted in Serbia, as part of the European registry on *H. pylori* management (*Hp*-EuReg), from April 2021 to April 2022. Assessed data included demographics, treatment indication, diagnostic tests, previous eradication attempts, current treatment regimen, *modified intention-to-treat (mITT)* and *per protocol (PP)* effectiveness analyses, safety, and antimicrobial resistance. Data was quality checked.
Results: Overall 283 patients were included with a mean age of 55±15 years, 64% women. Main treatment indication was functional dyspepsia (39%), the most used diagnostic test was histology (51%). Overall eradication rate was 95% (PP) and 94% (mITT). Mostly prescribed first-line therapy was quadruple-clarithromycin+amoxicillin+metronidazole, with an effectiveness of 96% (p<0.001). Second-line main treatment choice was triple-amoxicillin+levofloxacin, with an effectiveness of 95% (p<0.05). Single-capsule Pylera® was mostly used as a third-line therapy, with 100% effectiveness (p<0.05). Longer treatment duration was associated with a higher eradication rate in first-line therapy (p<0.05). Clarithromycin resistance rate in first-line was 23% while quinolone resistance rate was 8.5%. Overall adverse events incidence was 9.3%, therapy compliance was >90%.
Conclusions: Considering the high eradication rate, 14-day concomitant non-bismuth quadruple therapy is a reasonable first choice in treatment-naive patients, while quinolone-based therapy and single-capsule Pylera® are good rescue therapy options.

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P02.17

THE EFFECT OF VITAMIN C SUPPLEMENT TO STANDARD TRIPLETHERAPY FOR ERADICATION OF *HELICOBACTER PYLORI*

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***Objective*:** *Helicobacter pylori* (*H. pylori*) infection is higher in developing countries. Therefore, several clinical studies have shown different results in the effects of vitamin C oral supplement on *H. pylori* eradication. The aim was to evaluate the effect of the addition of vitamin C to standard triple therapy on the eradication rate of *H. pylori* infection.
Methodology*:* In one year period, patients (18-57 years old) with dyspeptic symptoms, diagnosed with histologically confirmed *H. pylori* infection were included and randomized into two groups. The STT group (65 patients) treated with standard therapy (pantoprazole, amoxicillin and clarithromycin for 14 days; the STV group (69 patients) was given the standard regimen and vitamin C. Eradication rate was evaluated five weeks after the cessation of treatment via Ammonia Breath Test ("Helic- test" Association of Medicine and Analytic. St. Petersburg).
Results: this study included 134 patients (mean age: 37.3±11.6 years; female 69%). *H. pylori* infection in male higher than in female. Eradication rate was recorded over 55%, it was 46% with a STT group ,65% with STV group. There was no statistical difference between the two groups (p=0.17). However, the symptoms were improved in the two groups.
Conclusions: The triple therapy with Vitamin C supplement achieved an eradication rate over 55% in group participants. It does not improve the eradication rate of *H. pylori*. Further studies with larger Randomized controlled trials are required. Routine monitoring the local antibiotic resistance is important for the successful treatment of *H. pylori* infection in Libya.

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P02.18

EMPIRICAL FIRST-LINE TREATMENT USE AND EFFECTIVENESS TRENDS IN EUROPE IN THE PERIOD 2013-2021: RESULTS FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (*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: International multicenter prospective non-interventional registry aimed to evaluate the decisions and outcomes of *H. pylori* management by European gastroenterologists. Data were registered at AEG-REDCap e-CRF until December 2021. Modified intention-to-treat (mITT) and time trend analyses were performed.

Results: Overall 35,203 (71%) were first-line empirical prescriptions. The most common prescribed treatments in 2013-21 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 25% in 2020/21. Non-bismuth concomitant therapy use decreased from 21% in 2013/14 to 13% in 2020/21, while Pylera® increased from 0-1% in 2014/2015 to 17% in 2020/21. An increase in the average duration of treatments from 9.8 days to 13 days in 2013-2021 and on the daily high-dose of PPIs was identified. There was a 10% overall improvement in first-line mITT overall effectiveness from 2013 (85%) to 2021 (94%) (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.

TABLE 1. PRESCRIPTIONS AND EFFECTIVENESS TRENDS OF FIRST-LINE EMPIRICAL TREATMENTS IN EUROPE IN THE PERIOD 2013-2021.

Year	2013	2014	2015	2016	2017	2018	2019	2020	2021
Quadruple-C+A+B	2.0%	2.7%	6.8%	20.5%	13.7%	21.7%	10.8%	9.8%	10.3%
Single-capsule*	0.1%	0.0%	0.5%	13.2%	24.5%	18.7%	21.7%	16.5%	18.2%
Quadruple-M+Tc+B	2.1%	1.9%	0.5%	0.2%	0.4%	0.5%	1.4%	1.2%	1.1%
Concomitant-C+A+M/T	21.8%	21.5%	27.0%	22.7%	20.9%	8.0%	13.4%	12.8%	13.1%
Sequential-C+A+M/T	11.8%	3.5%	1.9%	0.9%	0.5%	0.7%	0.11%	0.1%	0.3%
Triple-A+L	2.3%	2.2%	3.1%	1.8%	0.3%	0.3%	0.4%	0.3%	0.4%
Triple-A+M	3.6%	3.0%	1.7%	0.8%	0.9%	0.5%	1.9%	0.7%	1.0%
Triple-C+M	3.4%	6.4%	8.8%	6.3%	1.4%	0.7%	1.1%	10.2%	4.9%
Triple-C+A	48.5%	54.6%	44.7%	29.2%	32.1%	31.0%	35.2%	34.6%	32.7%

Continued

TABLE 1. *(Continued)* **PRESCRIPTIONS AND EFFECTIVENESS TRENDS OF FIRST-LINE EMPIRICAL TREATMENTS IN EUROPE IN THE PERIOD 2013-2021.**

Year	2013	2014	2015	2016	2017	2018	2019	2020	2021
Length									
7 days	27.5%	28.1%	24.4%	16.2%	7.9%	1.7%	2.1%	4.5%	2.9%
10 days	55.1%	52.6%	55.1%	46.5%	47.2%	41.6%	34.7%	29.4%	34.1%
14 days	17.4%	19.3%	20.4%	37.3%	44.9%	56.7%	63.2%	66.1%	62.9%
PPI acid inhibition*									
Low	66.6%	56.6%	47.3%	37.9%	39.7%	25.0%	30.1%	45.3%	40.5%
Standard	16.9%	25.5%	26.7%	24.1%	23.7%	41.3%	30.9%	19.5%	25.4%
High	16.5%	17.9%	26.0%	38.0%	36.6%	33.7%	39.0%	35.2%	50%
Eradication rate (mITT)	85.0%	85.1%	85.7%	87.6%	87.7%	91.4%	91.5%	92.7%	92%

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.

O.P. Nyssen: F. Consultant/Advisory Board; Significant; Mayoli, Allergan. Á. Pérez-Aísa: None. D. Vaira: None. L. Jonaitis: None. B. Tepes: None. D. Bordin: None. A. Keco-Huerga: None. A. Lucendo: None. L. Vologzhanina: None. L. Bujanda: None. N. Brglez Jurecic: None. A. Lanas: None. M. Leja: None. G. Babayeva: None. F. Lerang: None. L. Moreira: None. I. Puig: None. F. Mégraud: None. C. O'Morain: None. J.P. Gisbert: F. Consultant/Advisory Board; Significant; Mayoli, Allergan, Diasorin, Gebro Pharma, Richen.

P02.19

BISMUTH QUADRUPLE REGIMEN CONTAINING FURAZOLIDONE AND TETRACYCLINE ACHIEVED EXCELLENT ERADICATION EFFICACY AGAINST *HELICOBACTER PYLORI*, BOTH FOR INITIAL TREATMENT AND RESCUE TREATMENT

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***Objective*:** The eradication rate of *Helicobacter pylori* (*Hp*) has decreased largely because of high antibiotic resistance. We aimed to evaluate the effectiveness and safety of bismuth quadruple regimen containing furazolidone and tetracycline for *Hp* infection from evidence based on real-world data.
Patients and Methods: From December 2019 to February 2022, patients who were confirmed to infected *Hp* by C-UBT value > critical value + 50% critical value, rapid urease test ≥ (++), histopathology, bacterial culture or stool antigen test received eradication treatment (acid suppressant, bismuth, furazolidone and tetracycline) in *Hp* specialist clinics or partial general clinics at our hospital. Within ±2 days after *Hp* eradication, adverse events (AEs) and compliance were obtained. At least 4 weeks after completion of therapy, *Hp* eradication was assessed by C-UBT or histopathology.
Results: A total of 495 patients completed this study, overall eradication rates were 96.2% (476/495) by intention-to-treat (ITT) analysis and 98.3% (465/473) by per-protocol (PP) analysis. The ITT eradication rates for 10-day and 14-day regimen were 96.1% *vs.* 96.5% (p=0.819). The ITT eradication rates for initial treatment and rescue treatment were 96.2% *vs.* 96.1% (p=1.000). 100 patients (20.2%) experienced at least one AE, most AEs were mild and overall compliance rate was 95.6%. The incidence of AEs for 10-day regimen was lower than 14-day regimen (18.2% *vs.* 27.0%, p=0.039).
Conclusions: Bismuth quadruple regimen containing furazolidone and tetracycline achieved excellent *Hp* eradication efficacy in real-world practice, both for initial treatment and rescue treatment, with good compliance and tolerance.

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P02.20

EFFICACY AND SAFETY OF GASTROCUR® IN COMBINATION WITH PANTOPRAZOLE IN PATIENTS WITH *HELICOBACTER PYLORI*

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***Objective*:** The rate of antibiotic resistance in *H. pylori* increase in recent years, which has led to a decreased *H. pylori* eradication rate. Alternative antibiotic-free *H. pylori* therapies, such as phytotherapy, potentially can be used to combat this pathogen.
The aim was to test whether dihydroquercetin (Gastrocur®) in combination with pantoprazole in patients with *H. pylori.*
Patients and Methods: 10 patients with infection were given Gastrocur® two capsules three times a day in combination with pantoprazole 40 mg once a day for four weeks. A special condition was the compliance with Gastrocur® temperature regime of storage from +4° to +10°. All underwent ^{13}C-urea breath test before and after 4 weeks of treatment. Intention-to-treat (ITT), per-protocol (PP) analyses were performed to assess the effectiveness of therapy.
Results: The effectiveness of therapy was 20% (ITT) and 22.2% (PP). 80% of patients had completely regress symptoms of dyspepsia by the 14th day of therapy, with the effect remaining for a month after the end of therapy. Three patients had bloating, five had diarrhea no more than three times a day during the first two weeks of therapy, and these adverse events resolved spontaneously, no additional therapy was required. One patient dropped out of the study due to an exacerbation of pityriasis rosea on the 21st day of therapy, which regress in two days after stopping of treatment.
Conclusions: Gastrocur® in combination with pantoprazole led to the eradication of *H. pylori* in 20% (ITT). No serious adverse events have been reported.

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P02.21

EFFECTIVENESS AND SAFETY OF HIGH-DOSE DUAL THERAPY: RESULTS OF THE EUROPEAN REGISTRY ON THE MANAGEMENT OF *HELICOBACTER PYLORI* INFECTION (*HP*-EUREG)

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***Objective*:** Randomized clinical trials and meta-analyses, primarily from Asian countries, have reported good effectiveness with high-dose dual therapy (HDDT) when prescribed as *H. pylori* infection first-line or rescue treatment. However, combining amoxicillin with PPIs in several European countries yielded suboptimal results. We aim to analyze the effectiveness, compliance and safety of HDDT in real clinical practice.
Materials and Methods: An international, multicenter, prospective non-interventional Registry aimed at evaluating the decisions on and outcomes of *H. pylori* management by European gastroenterologists. All infected adult cases receiving HDDT (amoxicillin 1,000 mg three times a day plus a PPI), with or without bismuth, in any treatment line and for at least 10 days up to June 2021 were included. Sixty patients received HDDT (98% compliance), 19 of them as first-line and 41 as rescue treatment.
Results: Overall HDDT effectiveness was 52% (per-protocol) and 51% (modified intention-to-treat). HDDT was more effective as first-line than as rescue treatment, but the difference was not statistically significant (mITT 65% *vs.* 45%, p=0.171). Effectiveness was worse when patients had previously received metronidazole (mITT 32% *vs.* 70%, p<0,05), tetracycline (mITT 26% *vs.* 69%, p<0.05) or rifabutin (mITT 25% *vs.* 65%, p<0.005). Adding bismuth to HDDT in rescue treatment did not yield better results. Adverse event incidence was 30%, diarrhea being the most common (20% of patients); no serious events were reported.
Conclusions: HDDT is safe and has good compliance but is not a good option in European first-line or rescue *H. pylori* treatment, even adding bismuth.

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P02.22

LESSONS IN *HELICOBACTER PYLORI* TREATMENT FAILURE:A RESTROSPECTIVE STUDY

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***Objective*:** In recent years, the eradication rate of *Helicobacter pylori* has been decreasing in China. Most people pay attention to the antibiotic resistance and host factors of Helicobacter pylori, whereas few studies have reported the iatrogenic factors of eradication failure. Therefore, the aim of the study is to learn from the lessons of these related iatrogenic factors.
Patients and Methods: Totally 508 patients who experienced Helicobacter pylori eradication failure were included in this study conducted from December 2019 to February 2022. All the patients completed a questionnaire including baseline characteristics, medication period, regimens used, dosage, adhenrence, and time intervals in rescue treatment.
Results: 5.5% of all the patients (5.5%, 28/508) were allergic to penicillin and 50.6% of them underwent rescue therapy. 18.5% of the patients (18.5%, 89/480) with non-penicillin allergy used one or two highly resistant antibiotics as first-line treatment in triple therapy and 11.9% of them (11.9%, 57/480) used two highly resistant antibiotics in quadruple therapy, including other unrecommended antibiotics. Ninety-eight patients (19.3%, 98/508) had a short duration of the treatments, and 59 patients (11.6%, 59/508) were given levofloxacin-containing regimens as first-line eradication. 178 recipes containing highly resistant antibiotics were reused in 85 patients (33.1%, 85/257) in rescue therapy. 64.3% of the rescue therapies were given in an interval of less than 6 months.
Conclusions: We evaluated the unreasonable iatrogenic factors of Helicobacter pylori eradication. In future research, we need to pay more attention to the unreasonable factors in Helicobacter pylori eradication and standardize the treatment regimens, so as to better manage the patients with Helicobacter pylori infection.

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P02.23

MANAGEMENT OF GASTROINTESTINAL METAPLASIA WITH *HELICOBACTER PYLORI* IN A RETROSPECTIVE COHORT OF PATIENTS IN THE SOUTHEASTERN US

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***Objective*:** Clinical guidelines for GIM management do not incorporate *H. pylori*-specific factors and are ambiguous regarding consideration of race/ethnicity.
Patients and Methods: In a newly established cohort of 144 patients with endoscopic evidence of *H. pylori* infection and GIM, seen at Duke University 2015-2019, we assessed practice patterns. In a subset, we determined the association of *H. pylori* virulence factors and load at baseline endoscopy with persistent *H. pylori* infection.
Results: Among these diverse patients (72% Black, 28% white), clinical biopsies of gastric antrum and corpus were only separated 32% of the time, with no difference by race. *H. pylori* therapy was common in patients with GIM (90% treatment rate), but eradication testing was low at 42% (40% Black and 49% white). Additionally, repeat endoscopy occurred 26% of the time (23% Black and 34% white). Of those who underwent repeat testing after *H. pylori* therapy, 75% were cured and 25% had persistent *H. pylori*. Among 32 patients with subsequent endoscopies, 100% of the persistent infections had detectable CagA and VacA i1, compared to 71% and 80% of cleared infections, respectively. Persistent infections were also associated with a higher *H. pylori* 16S load than cleared infections (median 4.87 compared to 1.95, p=0.10) with no differences by race in load. CagA and VacA i1 were more common in Black IM patients than white (86% *vs.* 60%, and 100% *vs.* 50%, respectively).
Conclusions: Incorporation of *H. pylori*-specific factors into risk-stratification strategies for patients with GIM may help to address health disparities in the US.

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P02.24

CLINICAL PHENOTYPES THROUGH *MACHINE LEARNING* OF FIRST-LINE TREATED PATIENTS IN EUROPE DURING THE PERIOD 2013-2021: DATA FROM THE EUROPEAN REGISTRY ON *H. 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 were 1) To determine the most important treatment characteristics used in the European Registry on the management of *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 September 2021, were included in the analysis. A *Random Forest* method was used to determine the 'most important' variables: therapeutic indication, treatment scheme, duration of treatment, proton-pump inhibitor (PPI) dose, compliance, and patient's country.

Results: In total, 29,771 European patients were analysed. Table 1 shows that the average treatments' effectiveness raised from 86.3% in 2013 to 93,6% in 2021. The lowest effectiveness was obtained in cluster #3 in 2016 This cluster was composed of 7-day PPI-clarithromycin-amoxicillin therapy (92.3% cases) mainly in Slovenia, Lithuania, and Latvia. The highest effectiveness was in cluster #1 in 2021, also with PPI-clarithromycin-amoxicillin therapy (93.3% cases), but with a 14-day duration (98.4%) in Azerbaijan (83.8%) and Slovenia (11.8%).
Conclusions: Cluster analysis allowed both to identify patients with homogeneous treatment groups, and to assess the different first-line treatments effectiveness depending on the therapy scheme, its compliance, region, and year visit.

TABLE 1. TRENDS IN THE OVERALL EFFECTIVENESS (BY MODIFIED INTENTION-TO-TREAT, PER CLUSTER) BETWEEN 2013 AND 2021 IN EUROPE.

year	# of clusters (# of patients)	*Effectiveness % (number of patients) per cluster				
		1	2	3	4	5
2013	3 (3,243)	87.8 (548)	85.4 (1,432)	85.6 (1,263)		
2014	3 (4,307)	90.6 (374)	86.5 (2,613)	84.0 (1,320)		
2015	3 (3,651)	89.3 (335)	86.9 (2,629)	84.7 (687)		
2016	3 (4,268)	91.4 (2,376)	86.7 (1,452)	**80.7 (540)**		
2017	3 (3,637)	85.0 (301)	92.2 (1,749)	83.4 (1,587)		
2018	4 (3,535)	90.1 (2,084)	93.4 (793)	91.8 (304)	88,7 (354)	
2019	4 (3,335)	90.1 (1,088)	91.0 (943)	84.8 (257)	90,9(1,047)	
2020	4 (3,281)	90.5 (232)	85.8 (1,299)	94.4 (1,057)	92.8 (693)	
2021	3 (3,354)	**96.4 (1076)**	92,4 (929)	92.1 (1,349)		

O.P. Nyssen: F. Consultant/Advisory Board; Significant; Mayoli, Allergan. A. Sanz-García: None. G. Ortega: None. J.P. Gisbert: F. Consultant/Advisory Board; Significant; Mayoli, Allergan, Diasorin, Gebro Pharma, Richen.

P02.25

REINFORCED MEDICATION ADHERENCE IMPROVES *H.PYLORI* ERADICATIONRATE IN DEVELOPING COUNTRIES: A SYSTEMATIC REVIEW AND META-ANALYSISOF RANDOMIZED CONTROLLED TRIALS

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***Objective*:** We conducted a systematic review and meta-analysis of RCTs to assess the effect of medication adherence on *H. pylori* eradication rates in developing countries.
Materials and Methods: A systematic review was conducted in international databases (Web of Science, Cochrane Library, PubMed, and EMBASE) and national databases (CBM, WanFang Data, CNKI, and VIP Database) to identify relevant RCTs frominception to April 2022. The Cochrane Collaboration's tool for assessing the risk of bias in RCTs was used to assess the quality and risk of bias of the included studies. The core indicator was the changes in eradication rates after enhanced adherence. Meta-analysis was performed to estimate the pooled relative risk (RR) with 95% confidence intervals (CI) using R4.1.2.
Results: A total of 3286 patients with confirmed *HP* infection were included in 19 RCTs. Interventions include telephone, message, WeChat, and combined regime. The results of meta-analysis showed that the eradication rate of the intervention group was significantly different from that of the control group in the intentional analysis (ITT) [RR=1.25, 95%CI (1.12, 1.31), p<0.0001] and compliance protocol analysis (PP) [RR=1.16,95% CI (1.08, 1.24), p<0.0001]. The compliance of the intervention group was high [RR=1.27,95%-CI (1.16, 1.40), p<0.0001], the incidence of adverse reactions was lower than the control group [RR=0.72,

95%CI (0.52, 0.99), *p*=0.04], gastrointestinal symptom relief was better than control group [RR=1.23, 95%CI (1.06, 1.43), *p*=0.005], the patient satisfaction [RR=1.26, 95%CI (1.19, 1.35), *p*<0.0001] and disease knowledge rate [SMD=1.82, 95%CI (0.77, 2.86), *p*=0.0007] were better than the control group. Egger funnel plot suggested that there was no potential publication bias among included studies (*p*=0.718).
Conclusions: Reinforced medication adherence improves H. pylori eradication rate in developing countries.

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P02.26

ANALYSIS OF DYNAMICS OF DIAGNOSIS AND TREATMENT OF *HELICOBACTER PYLORI* IN UKRAINE

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***Objective*:** The goal is analysis of dynamics methods for diagnosing *Helicobacter pylori* infection and schemes of anti-*Helicobacter pylori* therapy (AHPT) in Ukraine.
Patients and Methods: 689 patients were examined in *Hp*-EuReg – EUROPE (from 2013 to 01.05.2022). The nosologies diagnosed: Non-Investigated Dyspepsia (2, 0.3%), Functional Dyspepsia (2, 0.3%), Duodenal Ulcer (117, 17.0%), Gastric Ulcer (15, 2.2%), chronic atrophic gastritis (552, 80.2%). For the primary diagnosis of Helicobacter: Histology (431, 62.7%), Serology (145, 21.1%), Rapid Urease Test (96, 14.0%), Stool Antigen Polyclonal Test (11, 1.6%), Stool Antigen Monoclonal Test (10, 1.5%), No test performed (5, 0.7%), 13C Urea Breath Test (1, 0.1%), 14C Urea Breath Test (1, 0.1%). AHPT: Dual (3, 0.4%), Triple (338, 49.1%), Quadruple (338, 49.1%), Other (10, 1.5%). The patients are taking pre- and probiotics: No (522, 75.9%), Yes – Probiotics (167, 24.3%), Yes – Prebiotics (2, 0.3%). To control the eradication: Serology (3, 2.7%), Stool Antigen Monoclonal Test (95, 84.8%), Stool Antigen Polyclonal Test (4, 3.6%), Histology (9, 8.0%), Rapid Urease Test (2, 1.8%).
Results: The most effective eradication scheme is Quadruple with the addition of Bismuth salts of tripotassium dicitrate (BTD) lasting 10-14 days (90.6 and 92.1%), as well as schemes with the inclusion of probiotics for 10-14 days AHPT (eradication efficiency is 91.8 and 96.2%).
Conclusions: Ways to increase the effectiveness of AHPT in Ukraine: adding BTD to therapy and duration of therapy for at least 10-14 days, adding probiotics to treatment regimens.

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P02.27

THE COMPARISON OF STANDARD TRIPLE THERAPY EFFECTIVENESS AFTER ADDITION OF *SACCHAROMYCES BOULARDII*

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***Objective*:** The meta-analysis on *Saccharomyces boulardii* supplementation to *Helicobacter pylori* eradication suggests significant decrease of adverse events and increased the effectiveness. A lower induction of resistome could become an important argument of recommending this therapy.
The aim was to compare the effectiveness of standard regimens with and without addition of *Saccharomyces boulardii.*
Patients and Methods: Eradication subgroup of this clinical trial underwent urea breath test (UBT); positive patients were allocated into four eradication subgroups – standard triple therapy (Amoxicillin 1000 mgx2, Clarithromycin 500 mgx2 and Esomeprazole 40 mgx2) 10 or 14 days with or without addition of 500 mg *Saccharomyces boulardii*. Control UBT was performed six months later.

Results: We acquired data from 246 patients. The overall effectiveness was 87.0% (CI 95 – 82.8-91.2%). In the 10 days subgroup without probiotics (n=49) it was 85.7% (CI 95 – 75.9-95.5%); with probiotics (n=76) - 89.4% (CI 95 – 82.6-96.4%), *p*=0.529. In its turn, in the group of 14 days without probiotics (n=62) it was 85.5% (CI95 76.7-94.3%); and with probiotics - 86.4% (CI 95 77.7-95.1%), *p*=0.880. There was no significant difference of effectiveness between subgroups; we noticed a slight tendency of higher effectiveness in 10 days probiotic subgroup.
Conclusions: The significantly lower frequency of adverse events in probiotic subgroups was proved in the previous part of this study. The ongoing research on resistome induction will complement the results.
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P02.28

EXPERIENCE WITH SINGLE-CAPSULE BISMUTH QUADRUPLE THERAPY IN 6,000 PATIENTS FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (*HP*-EUREG)

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***Objective*:** There has been 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 was to evaluate the effectiveness and safety of the single capsule.
Materials and Methods: Systematic prospective registry of the clinical practice of gastroenterologists in the European Registry on *Helicobacter pylori* management (*Hp*-EuReg) collecting all 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, at AEG-REDCap e-CRF until February 2021. Modified intention-to-treat (mITT) and per-protocol (PP) analyses were performed. Data were subject to quality review.
Results: Overall, 6,069 (12%) received single-capsule bismuth-quadruple therapy achieving a high eradication rate based on the mITT (92%) and PP (93%) analyses, especially in first-line treatment (93%) but it had also high effectiveness as a rescue therapy, both in second line (89%) or subsequent lines of therapy (3rd-6th lines: 86%) (Table 1). Compliance was the factor most closely associated with effectiveness. Adverse events were generally mild-to-moderate and transient; leading to discontinuation of treatment in 1.8% of patients; 0.1% reported a serious adverse event.

Conclusions: Treatment with 10-day 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 favourable safety profile.

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

	Use, N (%)	mITT, N (%)	95% CI	PP, N (%)	95% CI
Overall	6,069 (12*)	5,676 (92)	(91-92)	5,551 (93)	(92-93)
1st line (naïve)	4,378 (72)	4,108 (93)	(92-94)	4,026 (94)	(93-94)
2nd line	1,118 (18)	1,038 (89)	(87-91)	1,013 (90)	(88-92)
3rd line	451 (7,4)	419 (89)	(85-92)	406 (90)	(86-93)
Rescue (3rd to 6th line)	573 (9,4)	530 (86)	(83-89)	530 (86)	(85-91)

*Of the total of treatments included in the Hp-EuReg up to December 2021 (i.e., N= 49,739); mITT: modified intention-to-treat; PP: per-protocol, N: total number of patients analysed.

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P02.29

TAILORED THERAPY WITH BISMUTH ADD-ON STANDARD TRIPLE THERAPY VERSUS CONCOMITANT THERAPY: AS A FIRST-LINE REGIMEN OF *HELICOBACTER PYLORI* INFECTION

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***Objective*:** As a first-line regimen for *Helicobacter pylori* (*H. pylori*) infection, the eradication rate of concomitant therapy (CT) has been known to be higher than the other regimens. We aim to evaluate the efficacy of tailored therapy (TT) with bismuth add-on standard triple therapy (STT) compared to CT.
Patients and Methods: A consecutive study was undertaken from September 2020 to September 2021. Two gastroenterology specialists participated in this study; one prescribed TT, and the other prescribed CT. 210 patients with *H. pylori* infection were enrolled. In the TT group (n=108), clarithromycin resistance tests with detection of point mutations by multiplex PCR were done before eradication therapy. The patients negative for the point mutation received STT for 14 days, and the patients positive for the point mutation took bismuth add-on STT for 14 days. Control group (n=108) received CT for 10 days.
Results: The eradication rate of the TT group was 85.2% (92/108) and 87.6% (92/105) in the intention-to-treat (ITT) and per-protocol (PP) analysis. In the CT group, the eradication rate was 80.6% (87/108) and 81.3% (87/107) in the ITT and PP analysis. There were no statistical differences of eradication rates between two groups in both the ITT and PP analyses (p=0.79, p=0.42). The frequency of clarithromycin resistance estimated by multiplex PCR was 33.3% (36/108) and the eradication rate with bismuth add-on STT was 77.8% (28/36) in the clarithromycin-resistant subjects.
Conclusions: The strategy of TT with bismuth add-on STT could be advisable without the concerns about further accumulation of antibiotic resistance.

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P02.30

COMPARISON OF TEGOPRAZAN-BASED VERSUS LANSOPRAZOLE-BASED *HELICOBACTER PYLORI* ERADICATION THERAPY: A PROPENSITY SCORE MATCHING ANALYSIS

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***Objective*:** Tegoprazan is a novel potassium-competitive acid blocker developed in Korea. Several studies have shown a superior efficacy of vonoprazan-based *Helicobacter pylori* (*H. pylori*) eradication therapy; however, there have been few reports on tegoprazan-based *H. pylori* eradication therapy. Therefore, we aimed to evaluate the efficacy of tegoprazan-based eradication therapy compared to lansoprazole-based eradication therapy.
Patients and Methods: From January 2021 to February 2022, 72 patients underwent tegoprazan-based 1st-line concomitant therapy and 176 patients underwent lansoprazole-based 1st-line concomitant therapy in Pusan National University Hospital. After optimal propensity score matching analysis, 144 patients (72 patients in each treatment group) were selected in the study. Successful eradication was defined as a negative ^{13}C-urea breath test 4-6 weeks after completion of the treatment.
Results: In 72 patients who received tegoprazan-based concomitant therapy for 7 or 10 days, *H. pylori* infection was eradicated in 67 patients (93.1%). In 72 patients who received lansoprazole-based concomitant therapy for 7 or 10 days, the infection was eradicated in 66 patients (91.7%). Although the eradication rate was higher in the tegoprazan-based treatment group, there was no significant difference in eradication rate between the two groups (p = 0.754). In subgroup analysis, there was no significant difference in eradication rate according to treatment duration in both groups.
Conclusions: Tegoprazan-based concomitant therapy was not superior to lansoprazole-based concomitant treatment as the first-line treatment in Korea.

TABLE 1. *H. PYLORI* ERADICATION RATES OF TEGOPRAZAN-BASED AND LANSOPRAZOLE-BASED CONCOMITANT THERAPIES.

	Number	Eradication rate
1st-line tegoprazan based concomitant therapy		
7 days	28	92.9% (26/28)
10 days	44	93.2% (41/44)
1st-line lansoprazole based concomitant therapy		
7 days	1	100% (1/1)
10 days	71	91.5% (65/71)

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P02.31

AN EVOLVING RESISTANT PANDEMIC. RISING COMMUNITY *H. PYLORI* TREATMENT FAILURE TO CLARITHROMYCIN-BASED TRIPLE THERAPY, AN OBSERVATIONAL STUDY

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Clarithromycin-based triple therapy is commonly prescribed as a first-line treatment for *H. pylori* in Ireland. Worldwide, increased clarithromycin resistance has been reported. It is unclear whether this is due to personalised antibiotic exposure inducing resistance over time, or endemic community prevalence of a resistant strain of *H. pylori*, acquired from youth. We hypothesise that older age cohorts would have increased exposure to antibiotics and that increased resistance rates, leading to treatment failure with age, would support a developed resistance model.

All patients referred for their post-eradication 13C-urea breath test (UBT), having received clarithromycin-based triple therapy (40mg esomeprazole b.i.d., 500 mg clarithromycin b.i.d., amoxicillin 1 g b.i.d. for 14 days) between 2019 and 2022 were identified and included in the analysis. Following clarithromycin triple therapy, a positive UBT, delta-over-baseline >4, was considered a surrogate marker of clinical resistance.
482 patients were identified [mean age=50.6±16.8; 45.6% (n=220) male, 54.4 (n=262)]. The overall clarithromycin resistance rate was found to be 25.5% (n=123). We found no statistical difference in resistance rates across ages or between age groups, divided into decades analysed *via* two-way ANOVA. It was also found that failure rates were comparable for both male and female patients [21.8% (n=48) *vs.* 28.6% (n=75), respectively, Fisher's exact test, p=0.094].
Across adult age groups, clarithromycin resistance has reached alarmingly high levels with 1 in 4 patients failing first-line therapy. In addition, it suggests a high community prevalence of clarithromycin-resistant *H. pylori*. The authors propose that clarithromycin-based triple therapy should no longer be used without sensitivity testing as a treatment for *H. pylori* in Ireland.

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P02.32

EFFECTIVENESS OF TREATMENTS AGAINST *HELICOBACTER PYLORI* ACCORDING TO RESISTANCE TO CLARITHROMYCIN: DATA FROM THE EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (*HP*-EUREG)

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***Objective*:** The treatments including clarithromycin are the most frequently used in first line; however, the resistance to clarithromycin in naïve patients is more than 20%.
The Objective was to assess the effectiveness of first-line *H. pylori* treatments in Europe according to the resistance to clarithromycin.
Materials and Methods: Non-interventional, prospective, multicenter, international European registry on the management of *H. pylori* (*Hp*-EuReg). All culture-diagnosed infected adult patients were registered at AEG-REDCap e-CRF from 2013 to 2021. Per-protocol (PP) analysis was performed based on the presence or absence of bacterial resistance to clarithromycin in treatment-naïve patients.
Results: In total, 2,479 culture-naïve patients were included. Of these, 627 (25%) reported resistance to clarithromycin. The eradication rate with the standard triple therapy (PPI+clarithromycin+amoxicillin) in patients susceptible to clarithromycin was 92% (424/460). The eradication rate in these clarithromycin-susceptible patients was higher both with the concomitant regimen (PPI+clarithromycin+amoxicillin+metronidazole) and with the sequential treatment with tinidazole (95%, 882/929), and also with the bismuth quadruple regimen (PPI+bismuth+tetracycline+metronidazole) as single capsule (100%, 67/67) (p<0.05). In those patients with bacterial resistance to clarithromycin, the effectiveness of the standard triple therapy decreased to 75% (9/12), and the eradication rate with the concomitant and sequential regimen was 87% (314/361; p<0.05); while the effectiveness with the single-capsule bismuth-containing quadruple was 93%.

Conclusions: In those European regions where the *H. pylori* resistance rate to clarithromycin is high, therapy with the bismuth quadruple regimen is the best eradication option. Other alternatives that approach 90% eradication despite clarithromycin resistance are the non-bismuth quadruple concomitant and sequential regimens.

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P02.33

USING WATERCRESS EXTRACT AGAINST THE VIRULENCE FACTOR UREASE AS A POTENTIAL TREATMENT FOR *HELICOBACTER PYLORI* INFECTION

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***Objective*:** *Helicobacter pylori* has a highly active virulence factor, urease, which metabolises urea to ammonia causing a localised increase in pH within the stomach. This forms a protective microenvironment around the *H. pylori* allowing colonisation within the stomach which is associated with chronic inflammation and an increase in the risk of gastric cancers. Here we describe the use of a specific watercress extract developed to maximize urease inhibiting effect as a novel mechanism for potentially treating *H. pylori* infections.
Materials and Methods: *In silico* docking experiments were performed with Cresset™ Flare software using the crystal structure of *H. pylori* and compounds found within watercress extract. *In vitro* enzymatic assays of whole-cell assays using *Proteus mirabilis*, using the Berthelot method, were used to measure urease activity.
Results: Results show that certain compounds within the watercress extract appear to dock into the active site and to the active site flap of *H. pylori* urease. Further *in vitro* experimentation showed that watercress extract was able to inhibit the urease from *P. mirabilis*. Interestingly, a negative reduction in the ammonia was observed, this indicated that the watercress extract was able to scavenge the excess ammonia. We propose this occurs due to the isothiocyanates forming a thiourea upon reaction with ammonia.
Conclusions: Watercress extract exhibits urease inhibitory properties initially predicted using *in silico* docking and then confirmed with *in vitro* enzymatic assays. Further work is required to examine the mechanism of ammonia scavenging and investigate the effect of watercress extract on *H. pylori* urease.

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P02.34

WHY VONOPRAZAN DUAL AND TRIPLE THERAPIES FAILED TO ACHIEVE ACCEPTABLE CURE RATES IN THE US/EUROPEAN TRIALWHY VONOPRAZAN DUAL AND TRIPLE THERAPIES FAILED TO ACHIEVE ACCEPTABLE CURE RATES IN THE USA/EUROPEAN TRIAL

D. Y. GRAHAM
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***Objective*:** Whether vonoprazan clarithromycin triple and or dual therapy is effective therapy for *H. pylori* in western countries remains unclear.
Materials and Methods: The US/European a clinical *H. pylori* eradication trial compared vonoprazan or lansoprazole amoxicillin/clarithromycin triple therapies or high dose amoxicillin dual therapy randomized trials.

Results: Both the dual and triple therapies failed to achieve cure rates of 90% or greater despite (compared to Japan) increasing the duration from 7 to 14-days and increasing clarithromycin dosage. Surprisingly, the cure rate for lansoprazole triple therapy in clarithromycin susceptible infections was only 70%. Discussion: Potential causes of the poor outcomes include a) issues with therapy including dosage, duration, timing of drug administration, and failure to achieve a sustained intragastric pH of ~6), b) issues with the bacterium (i.e., emergence of resistance during therapy, or c) issues with patients (e.g., poor adherence). The fact that the PPI-based therapy provided unexpectedly low cure rates with initially susceptible infection suggests resistance emerged during therapy (e.g., because pf hetero-resistance). Unfortunately, the protocol did not include susceptibility with the test of cure. The low cure rate with dual therapy is most consistent with failure of vonoprazan to reliable achieve an intragastric pH ~6 in this western population (insufficient vonoprazan dosage). Whether taking the antibiotics 30 minutes before meals played a role in the relatively poor outcome is also unclear.
CONCLUSION: Potential causes of the unexpectedly poor results with a highly successful therapy in Japan have been identified and can be directly studied in future trials.

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P02.35

14-DAY VONOPRAZAN-BASED QUADRUPLE THERAPY FOR *HELICOBACTER PYLORI* ERADICATION IN AREAS WITH HIGH CLARITHROMYCIN RESISTANCE: A PROSPECTIVE RANDOMIZED STUDY (VQ-*HP* TRIAL)

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***Objective*:** Potassium-Competitive Acid blocker (P-CAB) is a new drug and stronger acid-inhibition than proton pump inhibitor. P-CAB-based regimen provided high effectiveness for *H. pylori* eradication in Japan but not in other countries yet. This study aims to evaluate efficacy of vonoprazan-based quadruple therapy for *H. pylori* eradication in Thailand.
Materials and Methods: This preliminary prospective randomized study was to compare *H. pylori* eradication between 7-day and 14-day vonoprazan-based quadruple therapy containing vonoprazan 20 mg twice daily, bismuth subsalicylate 1,024 mg twice daily, metronidazole 400 mg 3 times daily and tetracycline 500 mg 4 times daily. CYP3A4/5 genotyping (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-urea breath test (UBT) at least 4 weeks after treatment completion.
Results: 275 dyspeptic patients undergoing upper GI endoscopy were enrolled. *H. pylori* prevalence was 30.5% (84/275 patients). 81 patients (42 males, 39 females, mean age 53.3 years) could complete their treatment regimens (41 and 40 patients for 7-day and 14-day regimen, respectively). Antibiotic resistance was 37.5%, 28.5%,37.5% for clarithromycin, metronidazole, and levofloxacin, respectively. CYP3A4 genotype revealed 100% extensive metabolizers. CYP3A5 genotype demonstrated 4.7%, 71.4%, 23.8% for poor, intermediate and rapid metabolizers, respectively. *H. pylori* eradication rates for 7-day and 14-day regimens were 85.3% and 95% respectively, *p*-value=0.08. No serious adverse reaction was observed. More data collection will be performed and reported soon.
Conclusions: 14-day vonoprazan-based quadruple therapy provide an excellent cure rate for *H. pylori* infection in areas with high clarithromycin resistance regardless of CYP3A4/5 genotype. This 14-day regimen could be use as alternative first-line treatment for *H. pylori* eradication.

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P03 Gastric cancer

P03.01

LOCAL RECURRENCE AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION OF EARLY GASTRIC CANCER

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Introduction: Endoscopic submucosal dissection (ESD) is considered the treatment of choice for early gastric cancer (EGC)with a negligible risk of lymph node metastasis. However, locally recurrent lesions on artificial ulcer scars are difficult to manage. Therefore, predicting the risk of local recurrence after ESD is important to manage and prevent the event. This study aimed to elucidate risk factors associated with local recurrence after ESD of EGC.
Patients and Methods: Between November 2008 and February 2016, consecutive patients (n=641; mean age, 69.3±9.5 years; men,77.2%) with EGC who underwent ESD at a single tertiary referral hospital were retrospectively analyzed to evaluate the incidence and factors associated with local recurrence. Local recurrence was defined as the development of neoplastic lesions at or adjacent to the site of the post-ESD scar.
Results: *En bloc* and complete resection rates were 97.8% and 93.6%, respectively. The local recurrence rate after ESD was 3.1%. The mean follow-up period after ESD was 50.7±32.5 months. One case of gastric cancer-related death (0.15%) was noted, wherein the patient had refused additive surgical resection after ESD for EGC with lymphatic and deep submucosal invasion. Lesion size ≥15 mm, incomplete histologic resection, undifferentiated adenocarcinoma, scar, and absence of erythema of the surface were associated with a higher risk of local recurrence.
Conclusions: Predicting local recurrence during regular endoscopic surveillance after ESD is important, especially in patients with a larger lesion size (≥15 mm), incomplete histologic resection, surface changes of scars, and no erythema of the surface.

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P03.02

LONG TERM OUTCOMES OF ENDOSCOPIC TREATMENT FOR EARLY GASTRIC CANCER IN EXTREMELY ELDERLY PATIENTS

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***Objective*:** Limited data exist that describes the long-term outcomes of endoscopic resection of early gastric cancer (EGC) for very elderly patients. The aim of this study was to determine the appropriate treatment strategy and identify risk factors for mortality for these patients.
METHOD: Patients diagnosed with gastric cancer who underwent endoscopic resection were identified using National Health Insurance Data and were divided into 3 groups; very elderly (≥85 years; 118 patients), elderly (65-84 years; 4,583 patients), and non-elderly (≤64 years; 3,725 patients). We compared the long-term and short-term outcomes among the 3 groups and the standard mortality ratio (SMR) was calculated to evaluate mortality in relation to the expected incidence of death in the general population.
Results: The overall survival (OS) and gastric cancer-specific survival (CSS) were significantly lower in the very elderly compared to elderly or non-elderly (for very elderly, elderly, and non-elderly, 10 years OS were 62.7%, 85.3%, and 96.5%; and 10-year CSS were 89.8%, 98.3%, and 99.6%). The risk factor associated with CSS was congestive heart failure (HR 2.86, 95% CI 1.51-5.41). However, significantly decreased SMR was observed among the non-elderly, elderly, and very elderly groups (SMR = 0.45, 0.30, and 0.23, respectively, $p<0.001$). Readmission rate and mortality within 3 months after endoscopic resection were significantly higher in the very elderly group than non-elderly or elderly groups.
Conclusions: The endoscopic resection for EGC is an acceptable treatment for very elderly patients, and it may play a role in achieving survival comparable to the general population.

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P03.03

HYDROGEN SULFIDE DONOR DIMINISHES *HELICOBACTER PYLORI* INFECTION-INDUCED PROCARCINOGENIC HUMAN GASTRIC FIBROBLASTS ACTIVATION

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***Objective*:** Recently, the high ratio of gastric cancer (GC) incidence, metastasis and recurrence has been related to the asymptomatic *Helicobacter pylori* (*Hp*) infections. The limited efficiency of GC treatment strategies is also increasingly attributed to the activity of tumor stroma with the key role of cancer-associated fibroblasts (CAFs). We have recently reported, that *Hp* (cagA+vacA+)-activated rat gastric fibroblasts induced dedifferentiation, pluripotency and invasiveness of gastric epithelial cells. Herein, we assessed the influence of *Hp* infection on human gastric fibroblasts, define possible mechanisms of their activation and to reduce this process by sodium hydrosulfide (NaHS), the fast-releasing donor of physiological mediator, hydrogen sulfide (H_2S).
Materials and Methods: Human fibroblasts isolated from the biopsies of patients without systemic inflammatory, autoimmunological diseases and *Hp* infection, qualified to laparoscopic, sleeve gastrectomy were infected with live *Hp* (cagA+vacA+). For auto- and paracrine TGFβ signaling inhibition SB-431542 (ALK5/TGF-β type I receptor inhibitor, non-toxic dose of 10 μM/L) was used and compared with the effect of NaHS (non-toxic 50 μM). Markers of fibroblast activation and corresponding signaling pathways were determined with RT-PCR, Western Blot and Immunofluorescence.
Results: *Hp* utilized TLR2, TLR-4, STAT3 and NF-κB (relA) pathways to activate human fibroblasts towards CAFs characterized with $Snail^+Twist^+$ phenotype and intense Twist and Snail incorporation into the nucleus and these effects were abrogated by SB-431542. This inhibitory effect was even more profound after NaHS co-incubation which caused downregulation of these components of pro-inflammatory pathway.
Conclusions: H_2S donors seem to act as promising anti-inflammatory factors inhibiting CAFs activation during *Hp* infection.

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P03.04

ASSOCIATION OF *HELICOBACTER PYLORI* INFECTION AND ORAL HYGIENE IN PATIENTS WITH GASTRIC ADENOCARCINOMA IN SÃO PAULO, BRAZIL

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***Objective*:** There is inconsistent evidence about the link of *Helicobacter pylori* infection (*H. pylori*) and oral hygiene, this study aims to investigate association of *Helicobacter pylori* infection (*H. pylori*) and oral hygiene on patients with gastric adenocarcinoma (GAd).
Patients and Methods: All cases from case control study on GAd from AC Camargo Cancer Center, São Paulo, Brazil were recruited between February, 2016 and July, 2019. Cases were compared due to presence or absence of *H. pylori* using Pearson's X^2 or exact test when appropriate. Univariate and multiple logistic regression were performed, statistical significance was 5%.
Results: Among 214 GAd cases 87.4% (187/214) tested for *H. pylori*, 78% (146/187) were negative and 22% (41/187) positive. When compared by presence of *H. pylori* (negative *vs.* positive) the majority

was male (65.1% *vs.* 51.2%), white (63.7% *vs.* 75.6%), high school (69.1% *vs.* 78.1%), reported no periodontal disease (88.4 *vs.* 95.1%) and clinical stage I/II (41.8% *vs.* 56.1%). Cases with *H. pylori* positive referred more often than those without infection to brush their teeth 3 or more times/day (82.9% *vs.* 54.8%, *p*=0.001) and floss daily (58.5% *vs.* 35.6%, *p*=0.023). Multivariate analysis adjusted by sex and age, chance of *H. pylori* positive in GAd cases was increased by brushing 3 or more times/day (OR 3.94; 95%CI 1.60-9.71) compared to 1-2 times/day and clinical stages I/II (OR 3.17; 95%CI 1.21-8.35) and III (OR 3.12; 95% CI 1.04-9.35) compared to IV.
Conclusions: There was higher chance of having H.pylori among GAd cases clinical stage I/II and III and those referred to brush their teeth 3 or more times/day.

T. Tiengo: None. G.A. Fernandes: None. M.P. Curado: None.

P03.05

THE EFFECT OF *HELICOBACTER PYLORI* TREATMENT ON THE RISK OF GASTRIC CANCER IN GENERAL POPULATION. A NATIONWIDE POPULATION-BASED COHORT STUDY

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***Objective*:** *Helicobacter pylori* (*HP*) treatment has been thought to reduce the risk of gastric cancer (GC) occurrence. However, previous studies focused high-risk patient of GC. We investigated the effect of *HP* treatment on GC prevention in the general population.
Materials and Methods: We obtained medical records of general population from the Common Data Model-converted sample cohort of National Health Insurance Service of Korea. All included subjects were 1) ≥40 years of age; 2) had undergone upper endoscopy within a year; and 3) not had gastric surgery previously. The target cohort was *HP* treatment group, and comparator was the persons without *HP* treatment. Among the *HP* treatment recipients, the incidence of GC was investigated for every 3 years after *HP* treatment.
Results: After large-scale 1:4 propensity score matching, 2,735 and 5,328 subjects were included. During the median 6.5 years, the GC incidence showed lower trend in the *HP* treatment cohort compared to non-*HP* treatment cohort [hazard ratio: 0.76; 95% confidence interval: 0.50-1.13; *p*-value=0.19]. After *HP* treatment, however, the incidence of gastric cancer consistently decreased over time, and showed a more marked decrease as the age increased (*p* for time trend <0.001) (Table 1).
Conclusions: Treatment of *HP* showed a tendency to lower the risk of GC in the general population. The incidences of GC according to the period after *HP* treatment were significantly decrease.

TABLE 1. THE INCIDENCE OF GC ACCORDING TO THE PERIOD AFTER HP TREATMENT IN DIFFERENT AGE GROUPS.

	Years after HP treatment			
Age group	2-4 years	5-7 years	8-10 years	*p* for trend
41-50	0.23% (41/17,573)	0.15% (27/17,532)	0.09% (15/17,505)	<0.001
51-60	0.44% (68/15,441)	0.23% (36/15,373)	0.08% (13/15,337)	<0.001
61-70	0.74% (62/8,385)	0.36% (30/8,323)	0.18% (15/8,293)	<0.001
71-80	1.08% (27/2,510)	0.56% (14/2,483)	0.04% (1/2,469)	<0.001

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P03.06

HUMORAL IMMUNITY IN PATIENTS WITH CHRONIC GASTRITIS, CHRONIC ATROPHIC GASTRITIS AND GASTRIC CANCER WITH *H.PYLORI* INFECTION.

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Researh Institute of Medical Problems of the North, Krasnoyarsk, Russian Federation.

***Objective*:** The aim of the work was to evaluate the features of the humoral immunity in patients with chronic, chronic atrophic gastritis and gastric cancer associated with *H. pylori* infection.
Patients and Methods: 85 patients with chronic gastritis (CG), 25 patients with chronic atrophic gastritis (CAG), 50 patients with gastric cancer (GC) and 100 practically healthy volunteers were examined. Quantitative determination of IgA, IgM, IgG, IgE was carried out by enzyme immunoassay using reagent kits manufactured by ZAO Vector-Best. Statistical data processing was carried out using Statistica 7.0 (StatSoft, OK, USA).
Results: In patients with CG, CAH and GC, there was an increase in IgG compared with the control group (p_{1-2}=0,01; p_{1-3}=0,001; p_{1-4}=0,001). In patients with CG and CAH, there was a decrease in IgA compared with the control group. In patients with GC, there was an increase in IgA compared with the control group and groups of patients with CG and CAH.
Conclusions: In patients with CG and CAH, unidirectional changes in the humoral link of immunity were observed, increased IgG parameters and reduced IgA were detected, which indicates a long-term chronic persistence of infection in the gastric mucosa. In the pathogenesis of H.pylori-associated diseases, the presence of a permanent bacterial infection has been proven. Hypergammaglobulinemia of the main classes was detected in gastric cancer patients: IgA, IgM, IgG, which is probably due to a combination of acute and chronic inflammatory process in the gastric mucosa.

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

P03.07

CHEMILUMINESCENT ACTIVITY OF NEUTROPHILIC GRANULOCYTES IN PATIENTS WITH GASTRIC DISEASES ASSOCIATED WITH *H. PYLORI* INFECTION.

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***Objective*:** The aim of the work was to study the chemiluminescent activity of neutrophilic granulocytes in patients with chronic, chronic atrophic gastritis and gastric cancer associated with *H. pylori* infection.
Patients and Methods: 85 patients with chronic gastritis (CG), 25 patients with chronic atrophic gastritis (CAG), 50 patients with gastric cancer (GC) and 100 practically healthy volunteers were examined. Estimation of spontaneous and induced chemiluminescence of NCs was carried out on a CL3604 chemiluminescent analyzer (method de Sole et al, 1983). Statistical data processing was carried out using Statistica 7.0 (StatSoft, 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 CAH, the activity of NG is increased, increased indicators of maximum intensity, time to reach the maximum, area under the curve in spontaneous and induced CL, and an activation index are detected. In patients with gastric cancer, neutrophil activity is reduced, indicators of maximum intensity, time to reach maximum in spontaneous and induced CL are reduced, parameters of the area under the curve of spontaneous and induced CL and the activation index are increased.
Conclusions: The increased activity of nonspecific defense cells in CAH is explained by the presence of an infectious agent and the severity of changes in the gastric mucosa. In patients with GC, the most severe immune lesions are detected, probably due to the depletion of the body's reserves and the toxic effect of the tumor.

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

P03.08

RISK OF GASTRIC CANCER AMONG PATIENTS WITH NEWLY DIAGNOSED ULCERATIVE COLITIS: A NATIONWIDE POPULATION-BASED STUDY

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Objective**:** Few studies have investigated the risk of gastric cancer (GC) in ulcerative colitis (UC), with inconsistent results. This study assessed GC risk in patients with newly diagnosed UC.
Materials and Methods: Using claims data of the Korean National Health Insurance (NHI) from January 2006 to December 2015, we identified incident UC patients. UC was defined using the International Classification of Diseases-10 codes and UC-specific prescriptions. Age and sex-matched non-UC individuals during the same period were randomly selected as controls from the NHI database. Hazard ratios (HRs), adjusted for covariates, were calculated using multivariate Cox proportional-hazards regression.
Results: From 2006 to 2015, 30,546 patients diagnosed with UC and 88,829 matched non-UC individuals were included. GC developed in 77 (0.25%) UC and 383 (0.43%) non-UC individuals. The HR for GC in UC patients was 0.60 (95%CI: 0.47-0.77) compared to non-UC individuals. When stratified according to age and sex, the HR for late-onset UC (≥40 years) was 0.63 (95%CI: 0.49-0.80) compared to non-UC for the same age, and the HR of male UC patients was 0.55 (95%CI: 0.33-0.89), compared to non-UC men. Among UC patients, the HR for age ≥40 years was 23.37 (95%CI: 6.38-85.64).
Conclusions: UC patients had a decreased GC risk compared to non-UC individuals. In particular, UC patients aged ≥40 years and male UC patients had a decreased risk of GC compared to non-UC individuals. However, among UC patients, late-onset UC (≥40 years) had a higher risk of GC than early-onset UC.

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

P03.09

OUTCOMES OF CONVENTIONAL METHOD VERSUS POCKET-CREATION METHOD FOR ENDOSCOPIC SUBMUCOSAL DISSECTION OF GASTRIC BODY TUMORS USING A DUAL KNIFE

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Objectives**:** Various endoscopic submucosal dissection (ESD) methods for gastric tumors have been tried. However, no studies have yet compared results according to ESD method for gastric body tumors using a dual knife. The objective of this study was to compare outcomes of two ESD methods for gastric body tumors: pocket-creation method and conventional method.
Patients and Methods: Patients who underwent ESD for gastric body tumor were retrospectively reviewed. Patients were divided into two groups according to the ESD method: conventional method (group I) and pocket-creation method (group II). Characteristics of patients and tumors, hospitalization period, incidence of complications, resection margin status, incidence of surgical operation, procedure time, and laboratory findings were investigated.
Results: Of the total of 100 patients, 52 belong to group I and 48 to group II. All tumors were successfully resected *en bloc*. Resection margin involvement was found in 6 (11.5%) of group I and 6 (12.5%) of group II. Complications were observed in 7 (13.5%; major complication 5, minor 2) of group I and 8 (16.7%; major 2, minor 6) of group II. There were no significant differences in ESD outcomes such as hospitalization period, incidence of complications, resection margin status, incidence of surgical operation, procedure time, or inflammatory response after ESD between the two groups.
Conclusions: Both methods are suitable for treating gastric body tumors with adequate treatment success rates and comparable complication rates.

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P03.10

A MODIFIED ENDOSCOPIC FULL THICKNESS RESECTION FOR GASTRIC SUBEPITHELIAL TUMORS FROM MUSCULARIS PROPRIA LAYER

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***Objective*:** The removal of subepithelial tumors (SETs) is challenging, particularly in tumors originating from the muscularis propria (MP) in the upper gastrointestinal (GI) tract, owing to the high risk of perforation. We developed mechanical spray lumpectomy (MSL), which is a novel method to safely and easily remove the tumor. This study aimed to evaluate the feasibility and safety of MSL as a novel endoscopic treatment for gastric subepithelial lesions.
Patients and Methods: We performed MSL in a total of 13 patients with upper GI SETs originating from the MP layer. First, mucosectomy was performed using a conventional snare. Repeated injections were performed towards the subserosal layer. After injection, the lesion was mechanically pushed to separate the MP layer using an endoscopic cap. Finally, the mucosa, submucosa, and MP layer with SETs were completely dissected using the spray coagulation mode, and the remaining defect was closed with clipping.
Results: All tumors were completely resected. The mean procedure time was 84.38 ± 41.73 min. There were four leiomyomas, six GI stromal tumors, one mucosa-associated lymphoid tissue lymphoma, and two ectopic pancreases. Although small perforation occurred in only one case, the defect was successfully closed using hemostatic clipping. Moreover, no serious complications related to MSL were encountered during or after the procedure. No residual lesion or recurrence was observed during the follow-up period.
Conclusions: Mechanical spray lumpectomy can be a novel method that provides a safe and minimally invasive endoscopic treatment for upper GI SETs originating from the MP layer.

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P03.11

LONG-TERM CLINICAL OUTCOMES OF ENDOSCOPIC TREATMENT OF GASTROINTESTINAL STROMAL TUMORS IN STOMACH

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***Objective*:** Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors in stomach. We evaluated the long-term clinical outcomes of endoscopic treatment for gastric GISTs.
Patients and Methods: This is a retrospective study that enrolled 135 cases of gastric subepithelial tumors (SETs) resected by endoscopic procedures and confirmed as GISTs by histopathology from 2005 to 2019. The immediate and long-term clinical outcomes were analyzed retrospectively.
Results: The mean age was 57.9 years, and the mean tumor size was 2.1 cm. Of the tumors, 43.0% were located in the corpus, followed by the fundus (26.7%) and cardia (17.0%). Most tumors (85.2%) were resected by endoscopic submucosal dissection. Macroperforation occurred in 4.4% and microperforation in 6.7% of the cases. The R0 resection rate was 15.6%. However, complete resection by the endoscopic view was 90.4%, of which 54.8% were in the very-low-risk group, followed by the low (28.1%), intermediate (11.9%), and high-risk groups (5.2%). During 36.5 months of follow-up, recurrence was found in four (3.4%) of the 118 patients who were monitored for more than six months.
Conclusions: Despite the low R0 resection rate, the endoscopic treatment of a GIST appears to be a feasible procedure with a relatively low rate of recurrence in selected cases.

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P03.12

SERUM LEVELS OF INTERLEUKIN-16 IN PATIENTS WITH *HELICOBACTER PYLORI* INFECTION

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H. pylori is the main cause of peptic ulcer disease, and a major risk factor for gastric adenocarcinoma. The pleiotrophic cytokine interleukin-16 (IL-16) is involved in the development and progression of several inflammatory conditions. Elevated serum concentrations of IL-16 were reported previously in gastric cancer patients compared with healthy controls, however, the relationship between IL-16 production and *H. pylori* infection is unclear. The aim of this study was to examine the serum concentrations of IL-16 in *H. pylori* positive patients and investigate potential links with disease.
We investigated the relationship between IL-16 responses and virulent *H. pylori* strains, and associations with presence and severity of gastric mucosal histopathology, and the impact of *H. pylori* eradication. Levels of IL-16C (processed mature form) were measured using a commercial ELISA kit. IL-16 was detected in all serum samples examined, with no differences between 46 *H. pylori*-infected and 29 uninfected patients. IL-16C levels were not significantly associated with gender or smoking status, and there were no differences according to whether the colonizing strain was *cagA* positive or negative. No link was detected between IL-16 concentration and histopathological changes in the gastric mucosa, and there were no significant differences in serum IL-16 levels before and after *H. pylori* eradication. Interestingly, patients with gastric cancer had significantly reduced concentrations of serum IL-16C, compared to those with peptic ulcer disease. This requires further investigation.

S.A. Alzahrani: None.

P03.13

CLINICAL OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC MUCOSA-ASSOCIATED LYMPHOID TISSUE LYMPHOMA: A CASE SERIES

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***Objective*:** Eradication of *Helicobacter pylori (H. pylori)* is the treatment of choice for gastric mucosa-associated lymphoid tissue (MALT) lymphoma. However, only 15.5% of patients with *H. pylori*-negative gastric MALT lymphoma achieved clinical remission with eradication therapy. We report a series of patients with gastric MALT lymphoma treated with endoscopic submucosal dissection (ESD).
Materials and Methods: We performed a computerized search of the de-identified clinical data warehouse of the Asan Medical Center, a tertiary hospital in Seoul, Korea. We reviewed medical records of patients with gastric MALT lymphoma treated with ESD between 2008 and 2020.
Results: A total of six patients with gastric MALT lymphoma were treated with ESD. Reasons for ESD are as follows: recurrence after remission without *H. pylori* re-infection and *H. pylori*-negative MALT lymphoma. Two patients were diagnosed with gastric MALT lymphoma and improved after eradication treatment, but they relapsed about 36 months and 41 months without *H. pylori* re-infection. Four patients had *H. pylori*-negative gastric MALT lymphoma. They were single lesions localized to mucosa on endoscopic ultrasound (EUS). ESD procedures were performed without complications. They remain in clinical remission status until the last follow-up [median 58 months (range: 7-160)].
Conclusions: ESD was safe and effective for properly selected patients with gastric MALT lymphoma. ESD can be considered a therapeutic option when the lesion is single and confined to the mucosal layer in patients with *H. pylori*-negative MALT lymphoma.

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P03.14

REFLUX ESOPHAGITIS ASSOCIATED WITH FALSE NEGATIVE CASES IN PEPSINOGEN TESTING FOR PRECANCEROUS GASTRIC LESIONS

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***Objective*:** The aim was to investigate whether individuals with reflux esophagitis and precancerous gastric lesions (PGL) are more likely to have a false negative pepsinogen (Pg) test result.
Materials and Methods: Serum PgI and II were measured for participants aged 40-64 years with PGL confirmed by endoscopy with biopsy within the "Multicentric randomised study of *Helicobacter pylori* eradication and pepsinogen testing for prevention of gastric cancer mortality: the GISTAR study". Participants with PGL and decreased Pg levels (Pg I /Pg II ≤ 2 and Pg I ≤ 30 ng/mL) were placed in the true positive group (TP), with the rest in the false negative group (FN). A multivariable model was built for FN and reflux esophagitis. Factors that were associated with FN in our previous analyses were included - smoking, alcohol, fruit and vegetable consumption, and *H. pylori* (biopsy), adjusting for age, sex, income, and proton pump inhibitor use.
Results: Reflux esophagitis was present in 48/364 (13.2%) participants; 72.9% of those with reflux esophagitis and 39.6% of those without were FN (p<0.01). In multivariate analysis, FN was associated with reflux esophagitis (OR 4.5, 95% CI 2.0-9.9), current smoking (OR 3.3, CI 1.7-6.6), *H. pylori* (OR 2.8, CI 1.6-4.5), and inversely with higher income (OR 0.3, CI 0.1-0.7).
Conclusions: Individuals with reflux esophagitis may require a modified approach in screening for PGL with Pg testing in order to decrease the rate of FN. Funding. Project ESF No. 8.2.2.0/20/I/006; ERDF No. 1.1.1.1/18/A/184.

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P03.15

CURRENT STATUS OF THERAPEUTIC ENDOSCOPY AND CHANGES IN GASTRIC CANCER INCIDENCE IN KOREA

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***Objective*:** This study was aimed to investigate the current clinical status of endoscopic treatment for premalignant lesion and early gastric cancer in Korea based on a National Health Insurance (NHI) database between 2010 and 2018.
Materials and Methods: The claims data of endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) in Korean NHI were reviewed using material codes of Health Insurance Review and Assessment Service between January 2010 and December 2018. The current clinical status was analyzed in terms of treatment pattern, final diagnosis, changes in gastric cancer incidence.
Results: The diagnosis rate of advanced adenoma and gastric cancer through the National Cancer Screening Project changed from 0.24% and 0.83% in 2013 to 0.20% and 0.63% in 2018. The number of ESD cases conducted increased from 2,558 in 2011 to 18,821 in 2018, and the number of EMR cases increased from 11,251 in 2011 to 18,717 in 2018. While the number of gastric cancer diagnoses through the National Cancer Screening Project increased from 7,232 in 2010 to 9,990 in 2017, the overall number of gastric cancer patients decreased from 30,714 in 2010 to 29,685 in 2017.
Conclusions: Endoscopic treatment for premalignant lesions and early gastric cancer has gradually increased, and such preventive treatment has the potential to affect the reduction or stasis of gastric cancer incidence.

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P03.16

THE VOLATILOMIC SIGNATURE OF *HELICOBACTER PYLORI*

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***Objective*:** Volatiles released by human body form a specific chemical pattern that can be employed for the diagnosis of gastric cancer. However, given that *H. pylori* is the main cause of gastric cancer, its presence complicates the volatilome, because the bacteria emit volatiles, resulting in confounders for gastric cancer detection via the volatilomic approach. Knowledge on the *H.pylori*-related volatilomic profile is needed to support non-invasive gastric cancer volatile diagnostic approaches. The aim of this study was to identify volatiles that are specific to *H. pylori*.
Materials and Methods: *H. pylori* were cultivated in a glass flasks using materials that have low volatile emission. Altogether 30 *H. pylori* cultures were prepared. Volatiles released by the *H. pylori* were captured from the headspace of the bacteria culture using headspace needle trap extraction and analyzed by gas chromatography-mass spectrometry.
Results: Sixty-one volatiles were identified, representing different chemical families. Forty-one volatiles were produced, and twenty volatiles were consumed by the cultures. Amongst the identified compounds were DMS, 2-butanol, tetrahydrofuran, trichloromethane, 3-methylbutanal, bromodichloromethane, isobutyronitrile, 3-methyl-1-butanol, DMDS, 2-pentanone, toluene and 2,4-dimethyl-1-heptene.
Conclusions: The results suggest that the VOCs emitted by the *H. pylori* culture form a specific chemical fingerprint that can potentially be used for the identification of this bacterial species. This knowledge does not only explain the origin of some volatile markers that have been tentatively assigned as gastric cancer biomarkers, but they can also be used for volatile elimination purposes in tests using the human volatilome to identify gastric cancer.

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P04 Helicobacter infection - pathogenesis and host response

P04.01

MODULATION OF THE *HELICOBACTER PYLORI* INTERACTION WITH HOST CELLS THROUGH MYCOBACTERUM BOVIS ONCO-BCG BACILLI *IN VITRO* AND *IN VIVO*

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Introduction: *Helicobacter pylori* (*Hp*) colonize gastric mucosa through mucin-(MUC5). Increasing *Hp* antibiotic resistance and escaping the immune system by *Hp* prompt the search for new anti-*Hp* formulations. *Mycobacterum bovis* onco-BCG(Biomed) bacilli are used in bladder cancer therapy due to immunomodulatory properties.
The aim was to examine in *Caviae porcellus* (permission No58/ŁB45/2016), and incell cultures *in vitro*, the ability of onco-BCG to reduce MUC5 and *Hp* adhesion and upregulate phagocytosis.

Materials and Methods: Animals were inoculated *per os* with 0,85%NaCl, *Hp*, onco-BCG, onco-BCG/*Hp*. After 7/28 days *Hp* infection was confirmed. MUC5 and *Hp* binding were assessed in gastric tissue stained with anti-MUC5 or anti-*Hp* fluorescent antibodies. MUC5 was also assessed in *Caviae porcellus* primary gastric epithelial cells non exposed or exposed 24h to *Hp* components: glycine extract, CagA protein, UreA, lipopolysaccharide or treated 2h with onco-BCG and then 24h with *Hp* components. To evaluate *Hp* binding, cells were grown 2h with *Hp*, onco-BCG or onco-BCG/*Hp*. Phagocytic activity (Vybrant™) and reactive oxygen species (dihydroethidine) in THP-1 monocytes (ATCC®TIB-202™) were assessed by fluorescence (FU) after 15/30 min.
Results: Onco-BCG reduced MUC5 and *Hp* adhesion (50%) in infected animals and in cells pulsed *in vitro* with Hp components, $p<0.05$. Phagocytic activity of monocytes treated with *Hp* was $7.8x10^5$FU *vs.* $3.6x10^6$FU after exposure to onco-BCG and *Hp*, $p<0.05$. Similarly, ROS increased up to $1x10^5$FU *vs.* $4x10^4$FU, $p<0.05$.
Conclusions: Onco-BCG by diminishing MUC5 in gastric cells reduce *Hp* adhesion and stimulate monocytes to phagocytosis. *This research was financially supported by the University of Lodz, Poland (*15/GNZPA/2022*), as part of the project: Excellence Initiative-Research University.*

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P04.02

GASTRIC COINFECTION WITH THIOPEPTIDE-POSITIVE *CUTIBACTERIUM ACNES* ALTERS *HELICOBACTER PYLORI*-INDUCED PATHOGENESIS IN MURINE MODEL OF GASTRIC CANCER

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***Objective*:** *Helicobacter pylori* (*H. pylori*) causes gastritis progressing to neoplasia, during which the transcription factor FOXM1 becomes increasingly expressed in humans and mice. Other gastric bacteria may also play a role in *H. pylori* pathogenesis. *Cutibacterium acnes* (*C. acnes*), a commensal in multiple organs, is isolated from stomachs of *H. pylori*-colonized humans. Given some *C. acnes* strains produce thiopeptides inhibiting FOXM1 expression, we asked whether coinfection with thiopeptide-positive *C. acnes* alters *H. pylori*-induced pathogenesis.
Materials and Methods: Germ-free INS-GAS mice were dosed with *H. pylori*, *H. pylori* then *C. acnes* one week later, *C. acnes* then *H. pylori* two weeks later, *C. acnes*, or remained uninfected. At 17 weeks post-infection, histopathology, bacterial colonization, gastric cytokine mRNA expression analysis, and gastric tissue cytokine array were performed. Serum antibodies for *H. pylori* and *C. acnes* were measured by ELISA, and RORγT expression in gastric lymph node CD4+ T cells were evaluated by flow cytometry.
Results: Total histopathology scores did not differ between coinfection groups and *H. pylori* alone. Infection with *C. acnes* then *H. pylori* reduced *H. pylori* gastric colonization. Coinfected males exhibited reduced gastric pro-inflammatory cytokines; males dosed with *H. pylori* followed by *C. acnes* had reduced gastric FOXM1 expression compared to *H. pylori* alone. Serum pro-inflammatory IgG2a antibodies and gastric lymph node RORγT expression were lower in coinfected mice compared to *H. pylori* alone.
Conclusions: This study demonstrates that coinfection of thiopeptide-positive *C. acnes* with *H. pylori* perturbs biomarkers of importance in *H. pylori*-induced pathogenesis.

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P04.03

HELICOBACTER PYLORI AND SARS-COV-2 ASSOCIATION: A COINCIDENCE OR A PATHOGENETIC CORRELATION?

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***Objective*:** The correlation between Covid-19 and non-respiratory bacteria is unexplored. The following considerations led us to investigate a possible correlation between *HP* and SARS-CoV2: SARS-CoV-2 binds ACE-2 receptors to enter cells, which are widely expressed in the GI tract. In addition, *HP* is known to increase the expression of ACE-2 receptors.
Materials and Methods: This study aims to investigate, by C13 Urea BT, the prevalence of *HP* infection and the DOB (delta over baseline), in pre-pandemic period and during COVID-19 pandemic to evaluate whether SARS-CoV-2 and *HP* infection association is only due to chance or whether represents a pathogenetic correlation. This is a retrospective preliminary study on 1532 randomized patients: 825 and 707 referring respectively to pre-pandemic and pandemic period.
Results: Only 490 patients underwent C13 Urea BT for the diagnosis of *HP* infection: 229 and 261 respectively during pre-pandemic and pandemic period. In pre-pandemic period 54 patients tested positive for *HP* (23.58%), while in pandemic period 87 (33,33%) resulted positive with a DOB of 40.4 ± 17.5, significantly higher when compared to the mean value found in pre-pandemic period: 17.4 ± 16.5.
Conclusions: SarS-CoV-2 and *HP* infection may influence each other. GI morphological and functional alterations due to SarS-CoV-2 infection, which can promote *HP* colonization and replication, need further investigation. Neglecting the search for *HP*, also due to difficulties encountered in this period to access BT, represented a risk condition for gastric diseases (e.g., peptic ulcer disease, gastritis, stomach cancer), especially considering the remarkable elevation of the bacterial load.

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P04.04

ENTEROHEPATIC *HELICOBACTER* SPECIES DIFFERENTIALLY MODULATE THE GASTROINTESTINAL MICROBIOME &IT CAN IMPACT *HELICOBACTER PYLORI* PATHOGENESIS

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***Objective*:** Enterohepatic *Helicobacter species* (EHS) colonize the human gastrointestinal tract (GIT), but their potential in modulating the GIT microbiome and *Helicobacter pylori* (*Hp*)-induced gastric pathology is not fully appreciated. The aim of this study was to characterize EHS effects on the GIT microbiome in *Hp*-infected mice.
Materials and Methods: Female C57BL/6 mice were dosed with *H. hepaticus* (*Hh*), *H. muridarum* (*Hm*) or coinfected with *Hp*SS1 (*HhHp* or *HmHp*). Mice were euthanized at 6- and 11-months post Hp inoculation. The V4-V5 regions of bacterial 16S rRNA gene were amplified from gastric and cecal DNA of all the mice and sequenced with an Illumina MiSeq instrument. Microbiome analyses were performed using QIIME 2 (2018.6) functions.
Results: Irrespective of Hp status and timepoints, *Hh* infection significantly decreased alpha diversity in the gastric microbiomes but increased alpha diversity in the cecal microbiomes compared to Hm infection (p<0.02). In the gastric microbiome, *Hh* and *HhHp* infection increased relative frequencies (RF) of *L. reuteri* (58-64%) but decreased *L. salivarius* RF (~1%) compared to Hm and *HmHp* infection (no *L. reuteri*, 14-17% RF for *L. salivarius*). In the cecal microbiome, *Hh* and *HhHp* mice had more *Muribaculaceae* (12-16% RF) and less *Parabacteroides* (1-2% RF) *vs. Hm* and *HmHp* mice (~1% RF for *Muribaculaceae,* 12-14% for *Parabacteroides*).
Conclusions: *Hh* and *Hm* coinfection with Hp had different impacts on both the gastric and cecal microbiome. This difference could potentially contribute in part to our findings that coinfection with Hh and Hm aggravated and attenuated *Hp*-induced gastric pathology respectively (IAI79: 3861, 2011).

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P04.05

TYPHLOCOLITIS ASSOCIATED WITH *H. MASTOMYRINUS* IN *GPT* DELTA C57BL/6J TRANSGENIC COLONY WITH A NATURALLY ACQUIRED IMMUNODEFICIENCY

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***Objective*:** Murine enterohepatic *Helicobacter* species (EHS) are opportunistic Gram-negative, microaerophilic, spiral-shaped bacteria that have the potential to cause hepatitis, typhlocolitis, and hepatic and colonic malignancy in susceptible strains. An outbreak of *H. mastomyrinus* was recently identified in a transgenic colony of *gpt* delta C57BL/6J transgenic mice. Our aim was to evaluate the host-pathogen interaction and elucidate the mechanism of immune deficiency.
Materials and Methods: Immunophenotyping of age- and sex-matched *gpt* delta and wild-type (WT) C57BL/6J mice was performed by flow cytometry. Peripheral and mesenteric lymph nodes, spleen, and peripheral blood were analyzed. In addition, *H. mastomyrinus* was isolated from naturally infected animals and used for experimental infection of age-matched *gpt* delta and WT male mice. Histological analysis of the liver and gastrointestinal tract was performed.
Results: Flow cytometric analysis revealed ~50% decrease in the $CD3^+$ and $CD4^+CD25^+CD127^{low}$ T cell populations in the transgenic mice relative to WT controls, despite no changes in the ratio of CD4:CD8 T cells. Experimental infection of *H. mastomyrinus* resulted in significant typhlocolitis in the *gpt* delta mice as early as 6 weeks post-infection. Further histological analysis revealed a significant increase in colonic hyperplasia of infected *gpt* delta mice compared to infected WT mice.
Conclusions: Our results indicate that the transgenic colony has acquired an immunodeficiency, particularly in the $CD3^+$ and regulatory T cell populations, thus making them susceptible to opportunistic infections, including *H. mastomyrinus*. Further investigation is warranted to determine the etiology of the acquired immunodeficiency in this transgenic colony.

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P04.06

HELICOBACTER PYLORI INFECTION INDUCES FERROPTOSIS IN GASTRIC EPITHELIAL CELLS AND MEDIATES INFLAMMATORY RESPONSES

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***Objective*:** Studies have found that ferroptosis is involved in the occurrence and development of immune, inflammatory and infectious diseases. *Helicobacter pylori* (*H. pylori)* infection can induce inflammatory responses through multiple pathways. Whether ferroptosis and its induced inflammatory response are involved in the pathogenesis of *H. pylori* has not yet been reported.
Materials and Methods: Transmission electron microscopy was used to observe changes in cell ultrastructure, detect changes in ROS levels, detect changes in intracellular ferrous ions, changes in mitochondrial membrane potential and changes in ferroptosis-related proteins to evaluate the effect of *H. pylori* infection on cell ferroptosis. *In vitro* experiments to evaluate the effects of ferroptosis inducers and inhibitors on inflammatory factors.
Results: Transmission electron microscopy showed that *H. pylori*-infected cells showed typical ferroptosis symptoms, such as decreased mitochondria, increased membrane density, and decreased or disappeared mitochondrial ridges. *H. pylori* infection *in vitro* and *in vivo* significantly upregulated the

level of ROS and the content of intracellular ferrous ions and resulted in a significant decrease in mitochondrial membrane potential. Western blot results showed that *H. pylori* infection significantly upregulated the expression of COX2 and downregulated the expressions of GPX4 and SLC7A11 *in vitro* and *in vivo*. In addition, *in vitro* experiments showed that ferroptosis inducers could further promote the up-regulation of pro-inflammatory cytokines (IL-1β, IL8 and TNF-α) induced by *H. pylori* infection, while ferroptosis inhibitors could inhibit their expression.
Conclusions: *H. pylori* infection induces ferroptosis in gastric epithelial cells and mouse gastric mucosal cells and mediates inflammatory responses.

H. Wang: None. J.F. Rong: None. Y. Xie: None.

P04.07

REGRESSION OF FOLLICULAR GASTRITIS AFTER SUCCESSFUL ERADICATION OF *HELICOBACTER PYLORI*

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Objective**:** Follicular gastritis is characterized by goose-flesh or chicken-skin-like appearance usually on the anterior aspect of the proximal antrum. It is manipulated that new onset *Helicobacter pylori* (*H. pylori*) infection in adulthood induced immature and aggressive tissue response, thus, resulted in large lymphoid follicles on the mucosa. Here, we evaluated the effect of *H. pylori* eradication on the regression of follicular gastritis.
Patients and Methods: Among individuals who underwent upper gastrointestinal endoscopy, patients with follicular gastritis were selected. *H. pylori* infection status was evaluated, and eradication therapy was done. Follow-up upper gastrointestinal endoscopy was performed, and we monitored the change of follicular gastritis in those patients.
Results: A total of 199 patients were diagnosed as follicular gastritis: 56 men and 143 women with mean age of 50.3 (range 30.5-74.4), 187 patients (94.0%) had concomitant *H. pylori* infection and 12 patients (6%) were uncertain for *H. pylori* infection. 99 patients who had follow-up endoscopy were included in the final analysis. 83 patients (88.9%) underwent eradication for *H. pylori* and 75 succeeded in eradication. 74 out of 75 (98.7%) patients showed complete remission of follicular gastritis. One patient still had follicular gastritis after 40.9 months follow-up despite of successful *H. pylori* eradication. Among 24 patient who had persistent *H. pylori* infection showed sustained follicular gastritis.
Conclusions: Follicular gastritis was successfully improved by *H. pylori* eradication. Further studies are warranted to confirm the long-term effect of *H. pylori* eradication in terms of prevention of lymphofollicular malignancy, such as MALT lymphoma, or diffuse-type gastric cancer.

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P04.08

THE NOTCH PATHWAY TRANSCRIPTION FACTOR HES1 REGULATES EXPRESSION OF THE PRO-INFLAMMATORY CYTOKINE IL-8 DURING *H. PYLORI* INFECTION

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Objective**:** Accumulating evidence supports an important role for the Notch pathway transcription factor HES1 in inflammation and immunity.
Aim: Determine the expression and function of HES1 during *H. pylori* infection.

Materials and Methods: RNA was collected from AGS and MKN45 gastric epithelial cells infected with *H. pylori* and from infected and uninfected antral biopsies. AGS cells were transfected with pCMV6-HES1 (NM_005524) Human Tagged ORF Clone (ORIGENE) or pCMV6-AC-GFP control vector (ORIGENE) using Lipofectamine LTX (Thermofisher). Gene expression was calculated by RT-qPCR. The Student's T-test and Mann-Whitney U-test identified significance (P<.05) for cell culture and tissue, respectively.
Results: *H. pylori* infection led to significant decreases in *HES1* mRNA expression in AGS and MKN45 cells. A 38% decrease in *HES1* level was observed in the gastric mucosa of *H. pylori*-infected patients (N=25) compared to uninfected controls (N=17; *p*=.02). *HES1* plasmid transfection was effective at increasing the expression of *HES1* >2,000 fold, compared to untransfected cells and empty vector samples in AGS cells (*p*=.004 and *p*=.004, respectively). *H. pylori*-mediated induction of *IL-8* was significantly augmented in cells over-expressing *HES1* (224-fold) compared to untransfected (91-fold; *p*<.001) or control vector transfected cells (102-fold; *p*<.001). *H. pylori* did not significantly increase *TNF* expression in HES1 over-expressing cells (13-fold) compared to untransfected (12-fold) and control vector transfected cells (14-fold).
Conclusions: *HES1* expression is decreased in *H. pylori* infected epithelial cells and tissue. *HES1* over-expression in AGS cells augments induction of *IL-8* but not *TNF.* Further research will identify additional targets of *H. pylori* mediated *HES1* suppression.

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P04.09

INTERFERENCE OF LPS *H. PYLORI* WITH IL-33-DRIVEN REGENERATION OF *CAVIAE PORCELLUS* PRIMARY GASTRIC EPITHELIAL CELLS AND FIBROBLASTS

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Introduction: Lipopolysaccharide-(LPS) of *Helicobacter pylori*-(*Hp*) causes disintegration of gastric tissue cells *in vitro*. It has been suggested that Interleukin (IL)-33 is involved in gastric tissue healing.
The aim of the study was to confirm the role of IL-33 as pro-regenerative molecule on the level of gastric barrier and to examine how *Hp* LPS affects regeneration of gastric barrier initiated by IL-33.
Materials and Methods: Primary gastric epithelial cells from *Caviae porcellus* (permission No58/ŁB45/2016) or reference fibroblasts (CRL-1405, ATCC, Washington DC, USA) were transfected with siRNA IL-33 (Santa Cruse Biotech, Dallas, TX, USA). Cells with inactivated IL-33 gene were propagated in the culture medium alone or in medium supplemented with exogenous IL-33 (Thermo Fisher Scientific, Waltham, MA, USA) and/or *Hp* LPS. Cell migration was assessed (scratch assay) in conjunction with oxidative stress (4-hydroksynonenal immunofluorescent staining, Cell Signaling, Danvers, MA, USA) and apoptosis (immunostaining of pro- or anti-apoptotic proteins, Cell Signaling, Danvers, MA, USA), activation of extracellular signal-regulated kinase-Erk (immunostaining of pErk, Cell Signaling, Danvers, MA, USA), production of collagen I and soluble ST2 (IL-33 decoy) (ELISA, MyBiosource, San Diego, CA, USA).
Results: Control cells, not treated with LPS were able to migrate in the presence of IL-33. This pro-regenerative activity of cells was related to enhanced collagen I production in the presence of IL-33. Migration of cells treated with *Hp* LPS was inhibited, even in the presence of IL-33. This could be due to increased oxidative stress and apoptosis induced by *Hp* LPS, enhanced Erk activation, sST2 elevation and modulation of collagen I production.
Conclusions: The recovery of gastric barrier cells during *Hp* infection potentially can be affected due to downregulation of pro-regenerative activity of IL-33 by LPS *Hp*. *This research was financially supported by the University of Lodz, Poland (25/IDUB/MLOD/2021), as part of the project: Excellence Initiative-Research University.*

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P04.10

THE INTERPLAY BETWEEN *HELICOBACTER PYLORI* VIRULENCE GENE EXPRESSION AND HOST CELL RESPONSES

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***Objective*:** Chronic inflammation caused by *Helicobacter pylori* infection is the primary risk factor for the development of gastric cancer and is influenced both by bacterial virulence as well as host immune responses. Lactate utilization and lactobacilli have been reported to play a key role in the pathogenicity of many bacteria, however it has been incompletely studied in *H. pylori* so far.
Materials and Methods: qPCR was performed to measure expression levels of *H. pylori* virulence genes. Human gastric epithelial cell line AGS was used in adhesion assays to study the attachment levels of the bacteria in the presence or absence of lactate. Proinflammatory cytokines released by human macrophages was measured by ELISA and their phagocytic ability was studied by flow cytometry.
Results: We showed that certain adhesins can be regulated in the presence of lactate by distinct two component systems within the bacterium. From the host side we observed that production of proinflammatory cytokines by macrophages infected with *H. pylori* was dampened in the presence of lactate. Our studies have explored the role of lactobacilli in *H. pylori* infection and show that they can interact directly with host cells, thereby influencing the immune response to the bacteria via the diverse ADAM17 pathway.
Conclusions: Our findings show multifaceted roles of lactate during *H. pylori* infection, and how the host immune system responds to the infection in the presence of lactate. Further, we show the underlying mechanisms of the antagonistic effects that lactobacilli have against *H. pylori* by interaction with the host.

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P04.13

MATRIX METALLOPROTEINASE (MMP)-7 MRNA ABUNDANCE IS INCREASED IN GASTRIC MUCOSA OF PATIENTS WITH *H. PYLORI* GASTRITIS AND GASTRIC PRE-NEOPLASIA

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***Objective*:** Gastric cancer develops following a series of premalignant changes driven by *Helicobacter pylori* infection. Matrix metalloproteinase (MMP)-7 is an endopeptidase involved in the maintenance, degradation and remodelling of extracellular matrix. Predominantly expressed in epithelial cells, MMP-7 has been linked to the tissue response to *H. pylori* and the development of epithelial malignancies. We have investigated gastric MMP-7 expression in patients with *H. pylori* and gastric pre-neoplasia.
Materials and Methods: Gastric biopsies were taken with informed consent from patients attending diagnostic upper gastrointestinal endoscopy. Real-time quantitative polymerase chain reaction was used to assess the relative abundance of MMP-7 mRNA versus GAPDH. Following exclusions, 441 patients were divided into four groups for analysis. These were “normal” patients [*H. pylori* negative, no proton pump inhibitor (PPI) use and normal gastric histology; n=112], patients using regular PPIs (*H. pylori* negative and normal histology; n=108), patients with *H. pylori* gastritis, but no gastric pre-neoplasia (n=140) and patients with confirmed gastric pre-neoplasia (n=81).

Results: Median relative abundance of MMP-7 mRNA in normal subjects was 0.120. This was significantly increased in patients with confirmed *H. pylori* infection (0.839, $p<0.001$), but was unchanged in patients taking PPIs (0.204, not significant). Patients with gastric antral and corpus pre-neoplasia also showed increased MMP-7 abundance compared to normal subjects (0.328, $p<0.01$ and 0.986, $p<0.001$ respectively), but were not significantly different when compared to *H. pylori* gastritis.
Conclusions: Gastric MMP-7 expression was significantly increased in *H. pylori* gastritis and gastric pre-neoplasia but was not reliably able to distinguish between these conditions.

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P04.14

A MIRNA-MRNA NETWORK TO STUDY THEIR ROLE IN *HELICOBACTER PYLORI* INDUCED GASTRIC CANCER

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Helicobacter pylori (*H. pylori*) expresses a spectrum of virulence factors that dysregulate host intracellular signaling pathways. In addition to proteins, the role of regulatory RNAs, like miRNAs are being currently investigated in order to obtain better understanding of the role of the bacteria in the progression of gastric cancer. It has been reported that miRNAs are deregulated following both *H. pylori* infection as well during gastric cancer. Studies have also been conducted to characterize miRNA expression signatures in *H. pylori*-infected and noninfected human gastric mucosa. However, most of these works are study of individual miRNAs. In order to have a holistic view, our research meticulously tried constructing and analyzing a miRNA-mRNA network of the gastric epithelial cells and analyze the divergence of the same network in *H. pylori*-induced gastric cancer using a systems biology approach. Using this model, we aim to compare the effects induced by the differential expression of the miRNAs before and after carcinogenesis. We also aim to highlight potential target miRNAs and identify the hub genes of the network. Identification of the miRNAs would lead to better understanding of not only the pathophysiology of the system; but also help in the pinpointing of novel cancer biomarkers and therapeutic targets.

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P04.15

STUDY OF NEUTROPHIL EXTRACELLULAR TRAPS (NETS) IN *HELICOBACTER PYLORI* INFECTION

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Helicobacter pylori (*Hp*) is a pathogen which colonizes the human gastric mucosa from childhood and remains throughout lifetime. Prevalence of *Hp* infection worldwide varies from 24% in Oceania to 70% in Africa and increases the risk of gastric cancer development. During *Hp* infection, the first cells recruited are the neutrophils, infiltrating the lamina propria thereby, becoming the hallmark of the infection. Previously, we have demonstrated the presence of neutrophil extracellular traps (NETs) in gastric biopsies of patients diagnosed with *Hp* chronic gastritis. CagA is a major *Hp* virulence factor that deregulates host cell functions such as proliferation, apoptosis and chromosomal integrity. Its pathogenic activity is partly regulated by tyrosine phosphorylation on repeated EPIYA-motifs. In this prospective study we aimed to determine the putative role of CagA in the formation and activity of NETs during *Hp* infection.

For this purpose, we cultured human peripheral blood neutrophils isolated from healthy donors with the P12 *Hp* reference strain containing EPIYA-ABCC motifs, its isogenic mutant containing EPIYA-ABCCC motifs, the corresponding ΔCagA mutant and two freshly isolated clinical *Hp* strains. Neutrophils demonstrated the capacity to phagocytose all *Hp* strains (visualized by confocal microscopy) and accordingly produce ROS (detected by flow cytometry), with the latter being significantly lower compared to neutrophils phagocytosing *E. coli* (positive control on NET formation). Interestingly, although neutrophils demonstrated NET release as a response to *Hp*, these NETs were degraded and demonstrated only faint presence of usual NET-related proteins. These findings suggest possible mechanisms of *Hp* evasion of neutrophilic immune response.

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P04.16

HELICOBACTER PYLORI INFECTION INHIBITS P53 AND PROMOTES MITOPHAGY THROUGH MITF

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Objective*:** Mitophagy is a type of selective autophagy that is essential for maintaining cellular homeostasis. *Helicobacter pylori* (*H. pylori*) infection is closely related to the development of gastric cancer (GC), however, the mechanism by which *H. pylori* infection regulates mitophagy in GC remains unclear. ***Materials and Methods: *In vivo* and *in vitro* models of *H. pylori* infection were constructed to study the relationship between *H. pylori* infection and mitophagy. The interaction between p53 and MITF was verified by immunoprecipitation (CO-IP). Overexpression of p53 and ROS inhibitor NAC treatment were used to study the relationship between p53, mitoSOX and MITF in GC, and the role of MITF in mitophagy induced by *H. pylori* infection.
Results: *H. pylori* infection can upregulate mitoSOX production and induce mitochondrial membrane depolarization, mitochondrial fission and mitophagy in GC. NAC treatment can reduce mitoSOX production and reduce mitophagy induced by *H. pylori* infection. *H. pylori* infection can up-regulate the expression of MITF and knocking down MITF can inhibit the mitophagy induced by *H. pylori* infection. NAC treatment could attenuate the upregulation of MITF expression induced by *H. pylori* infection. *H. pylori* infection can downregulate the expression of p53. MITF protein interacts with p53 protein in GC cell. Overexpression of p53 weakens the expression of MITF by inhibiting the production of mitoSOX, thus weakening the mitophagy induced by *H. pylori* infection.
Conclusions: *H. pylori* infection regulates mitochondrial oxidative stress through p53, thus mediating MITF to regulate mitophagy in GC.

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P04.17

THE ROLE OF PARAOXONASE 1 IN *HELICOBACTER* INDUCED GASTRITIS

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***Objective*:** High doses and/or inadequate removal of reactive oxygen species result in oxidative stress, which may cause severe metabolic malfunctions and damage to biological molecules including tissue DNA. An elevated oxidative status has been found in many types of cancer cells and *Helicobacter* infection. Paraoxonase 1 is one of the endogenous free radical scavenging systems in the human and believed to be involved in the protection against oxidative stress. But there was no study about differential paraoxonase 1 expression in *H. pylori* infection. In this study, we investigated the changes of paraoxonase-1 expression in the *H. pylori* infection.

Materials and Methods: To investigate the effect of *Helicobacter pylori* infection on the expression of paraoxonase 1, the gastric tissues from eighteen patients with *Helicobacter pylori* infection were used before and after eradication. The degree of oxidative stress in the tissues was evaluated by malondialdehyde. Expression of paraoxonase 1 and malondialdehyde were assessed by immunohistochemistry.
Results: The intensity of immunohistochemical stain on malondialdehyde and paraoxonase 1 was significantly elevated in pre-eradication state compared to post-eradication (1.77 *vs.* 1.05 and 1.83 *vs.* 1.11, $p<0.05$, respectively). The expression of paraoxonase 1 and malondialdehyde in *H. pylori* infection was a statistically significant correlation (r=0.586, $p=0.001$).
Conclusions: Paraoxonase 1 must be the antioxidant enzyme in *Helicobacter* induced gastritis.

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P04.18

HELICOBACTER PYLORI INFECTION INHIBITS P53 AND PROMOTES GLYCOLYSIS THROUGH PGK1

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***Objective*:** Phosphoglycerate kinase 1(PGK1) is a key enzyme in the glycolysis pathway and is closely related to the development of various cancers. However, the mechanism of PGK1 in gastric cancer (GC) and its relationship with *Helicobacter pylori* (*H. pylori*) infection remain unclear.
Materials and Methods: *H. pylori* positive and negative gastric tissue samples were collected to detect the expression of PGK1. *In vitro* and *in vivo H. pylori* infection model, the relationship between PGK1 and *H. pylori* was studied. The effects of PGK1 on cell proliferation, invasion, migration and glycolysis were verified by CCK-8 and EdU cell proliferation, colony formation, Transwell and lactic acid detection. The interaction between PGK1 and p53 was determined by immunoprecipitation.
Results: We found that PGK1 was highly expressed in GC tissues compared to adjacent noncancerous tissues. During the progression from mild chronic non-atrophic gastritis to GC, the expression of PGK1 gradually increased in human gastric tissue and was associated with *H. pylori* infection. PGK1 overexpression promotes GC cell proliferation, invasion and migration, whereas PGK1 knockdown inhibits GC cell proliferation, invasion and migration. *H. pylori* infection promotes the entry of PGK1 into mitochondria, upregulates lactate, ECAR, and downregulates OCR in GC. PGK1 protein interacts with p53 protein in GC cell. Overexpression of p53 suppressed *H. pylori* infection-induced lactate elevation by reducing PGK1 expression.
Conclusions: This study showed that *H. pylori* infection plays a key role in the development of GC by regulating the expression of PGK1 through p53.

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P04.19

SALVIA CADMICA EXTRACTS RICH IN POLYPHENOLS NEUTRALIZE A DELETERIOUS EFFECTS OF OXIDATIVE STRESS DRIVEN BY *HELICOBACTER PYLORI* LIPOPOLYSACCHARIDE IN CELL CULTURES OF GASTRIC EPITHELIAL CELLS OR FIBROBLASTS

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Introduction: High rate of *Helicobacter pylori*-(*Hp*) resistance to antibiotics requires finding new therapeutic formulations.

The aim was to examine antibacterial activity of *Salvia cadmica* Boiss. extracts (roots/aerial parts) towards *Hp* strains resistant to clarithromycin and/or metronidazole. To determine whether extracts neutralize oxidative stress and apoptosis driven by *Hp* lipopolysaccharide-(LPS) and promote cell regeneration *in vitro*.
Materials and Methods: Hydromethanolic extracts (20:80 v/v) from roots/aerial parts of seed-derived plants were tested for biosafety (ISO norm 10993-5) in the MTT-(3(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) reduction assay. Anti-Hp activity was tested in the microdilution assay. *Caviae porcellus* gastric epithelial cells (permission No. 58/ŁB45/2016) or fibroblasts (CRL-1405, ATCC, Washington DC, USA) exposed to *Hp* LPS and/or *S. cadmica* extracts, were tested for the rate of oxidative stress using 3-nitrotyrosine, apoptosis (immunostaining), cell migration (scratch assay) as well as the level of phosphorylated extracellular signal-regulated kinase-(pErk) or pro-regenerative collagen I and interleukin (IL)-33 production (ELISA).
Results: The minimal inhibitory concentration-(MIC) of root extract for reference *Hp* ranged from 39-78 µg/mL. The MIC for clinical *Hp* isolates was in the range 95-1560 µg/mL. Aerial part extract showed a weaker inhibitory effect towards reference *Hp* (MIC range 78-156 µg/mL), and clinical isolates (MIC range 390-1560 µg/mL). *S. cadmica* extracts effectively diminished oxidative stress and cell apoptosis, driven by *Hp* LPS, and promoted cell migration in conjunction with restoring collagen I and IL-33 production, while diminishing Erk activation.
Conclusions: The *S.cadmica* extracts with anti-*Hp* activity, diminish oxidative stress and apoptosis induced by *Hp* LPS and promote cell regeneration and thus are promising for the development of therapeutic formulations. *This research was financially supported by the National Center of Science, Poland, Miniatura 5 (DEC-2021/05/X/NZ6/00105).*

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P04.20

TREFOIL FACTOR 1 SILENCING DURING *HELICOBACTER PYLORI* CHRONIC INFECTION

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The gastric mucosa is considered the first defensive barrier to bacterial infections, secreting several protective molecules and mediators which represent the “mucosal defense”. One of these factors is the Trefoil Factor 1 (TFF1) which binds *Helicobacter pylori* in the mucus layer and reduces inflammation caused by the infection. Indeed, TFF1 is upregulated during the acute phase of bacterial infection, while it is gradually silenced when the infection becomes chronic, and the cytokines reach higher levels. The silencing of this factor prompts to loss of gastric mucosa protection and plays a determining role in the subsequent development of gastric cancer; because of its features, TFF1 is considered a gastro-specific tumor suppressor gene and is found downregulated in more than 50% of gastric tumor tissues. One of the hypothesized mechanisms leading to the silencing of multiple protective factors is triggered by a chronic inflammatory response of the host organism following the failed clearance of the pathogen. Since TFF1 was shown to be downregulated during chronic infection of *Helicobacter*, we investigated the molecular mechanisms leading to TFF1 silencing. Our data suggest that among the mostly released cytokines during *H. pylori* infection, IFNγ is the one that significantly reduces TFF1 expression in gastric cells. This transcriptional repression seems to occur through a specific transcription factor, C/EBPβ which binds three regions of TFF1 promoter, particularly under IFNγ stimulation. Remarkably, chemical inhibition of DNA methylation reverts C/EBPβ binding to TFF1 promoter and restores TFF1 expression.

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P05 Epidemiology

P05.01

HELICOBACTER PYLORI RESISTANCE TO ANTIBIOTICS IN HIV- COINFECTED INDIVIDUALS IN THE RECENT YEARS

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***Objective*:** HIV infection induces immune dysfunction leading to frequent infections, the treatment of which may affect the antibiotic susceptibility to various agents including *Helicobacter pylori*. This study analyzed rates and the trend of *H. pylori* antibiotic resistance in patients living with HIV (PLWH) and HIV-negative individuals (controls).

Patients and Methods: We selected all individuals with gastric sample culture positive for *H. pylori* infection and had available antibiogram between 01/2016 and 12/2021. Data collected were demographics and HIV status.

Results: A total of 3080 gastric sample cultures positive for *H. pylori* infection (185 PLWH 2895 controls) were selected. Compared to controls, PLWH were more males (57 *vs.* 42.2 %), older (42 *vs.* 38.1 years), originating from sub-Saharan Africa (50.4 *vs.* 7.9 %), and harbored significantly more antibiotic-resistant *H. pylori* strains (82.3 *vs.* 65.1%), with significantly higher rates of resistance to levofloxacin (35.8% *vs.* 24.0%), and metronidazole (70.4% *vs.* 50.1%); rate of resistance to clarithromycin was similar (24.7% *vs.* 22.0%).

Conclusions: Overall *H. pylori* antibiotic resistance is significantly more common in HIV-infected people than in the general population in the recent period. The diagnosis method of *H. pylori* infection in PLWH should include an antimicrobial susceptibility test.

TABLE 1. YEARLY EVOLUTION OF OVERALL H. PYLORI ANTIBIOTIC RESISTANCE; N NUMBER OF POSITIVE SAMPLES.

AntibioticResistance		years					
	HIV status	2016	2017	2018	2019	2020	2021
Clarithromycin	Hiv-negative	23.8%	28.9%	20.1%	17.8%	23.0%	21.8%
	(n)	(50/210)	(127/440)	(119/591)	(101/567)	(108/470)	(129/591)
	HIV-positive	13.8%	26.8%	42,3%	28.1%	12.5%	19.4%
	(n)	(4/29)	(11/41)	(11/26)	(9/32)	(2/16)	(6/31)
Metronidazole	HIV-negative	47.6%	45.7%	45.0%	48.3%	56.3%	57.4%
	(n)	(100/210)	(201/440)	(266/591)	(273/565)	(264/469)	(339/591)
	HIV-positive	72.4%	78.1%	53.9%	75.0%	50.0%	70.0%
	(n)	(21/29)	(32/41)	(14/26)	(24/32)	(8/16)	(21/30)
Levofloxacin	HIV-negative	20.5%	24.3%	25.1%	23.1%	23.2%	25.4%
	(n)	(43/210)	(107/440)	(148/590)	(131/567)	(109/470)	(150/591)
	HIV-positive	31.0%	39.0%	42.3%	21.9%	56.3%	38.7%
	(n)	(9/29)	(16/41)	(11/26)	(7/32)	(9/16)	(12/31)

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P05.03

SEROPREVALENCE OF ANTI CAGA *HELICOBACTER PYLORI* AMONG LIBYAN DYSPEPTIC CHILDREN FROM URBAN AND RURAL COMMUNITY

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***Objectives*:** The relationship between *Helicobacter pylori* (*H. pylori*) and dyspepsia was confirmed. The cytotoxic associated gene A (*cagA*) is an important virulence factor. No data of anti-cagA *H. pylori* in Libya. The aim was to determine prevalence of anti CagA *H. pylori* among the dyspeptic children in Tripoli & Al-Komes regions**.**
Patients and Methods: A blood sample collected from (350) & (120) dyspeptic children attending the gastroenterology units of Alkomes Hospital & Tripoli Children Hospital, respectively. Using ELISA to detect anti-CagA IgG & questionnaire covering socio-demographic variables completed by interview.
Results: In Alkomes, seroprevalence of *H. pylori* was (74%), anti CagA (10%), higher in males (46%) than in females (35%) a significant difference ($p = 0.04$). In Tripoli, anti-*H. pylori* (84%), anti CagA (13%). *H. pylori* infection was (51%) higher in females (62%) than in males (39%). In both regions, there was gradual increase with age.
Conclusions: In Tripoli & Al-Komes regions, *H. pylori* infection found in high rate among the dyspeptic children which might be related to socioeconomic status and living conditions as major risk factors for *H. pylori* infection. Our data indicate that the detection of the pathogenicity marker (*cagA*) of *H. pylori* infected is important. However, larger studies in other regions of Libya should be conducted to confirm the study finding. This finding highlighted the importance of screening children with dyspepsia in urban and rural Libyan regions. However, additional research in other areas of Libya should be conducted in the future to confirm the study's findings.

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P05.04

THE CURRENT PREVALENCE OF *HELICOBACTER PYLORI* INFECTION AMONG LIBYAN TYPE TWO DIABETIC MELLITUS PATIENTS: A MULTICENTER STUDY

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***Objective*:** Diabetes Mellitus (DM) is a common endocrine disease, DM patients suffer more frequently from complicated infections compared with non-DM, one of is *Helicobacter pylori* (*H. pylori*) occur earlier in life with high frequency in developing countries. The aim was to determine prevalence of *H. pylori* in T2 diabetic patients in two regions of Libya.
Patients and Methods: The study comprised (200) T2DM, (100) non-diabetic resident in Benghazi, other group include (157) T2DM, (160) non-diabetic from Tripoli region attending hospitals in both cities of Libya. A Blood sample was taken from all participants for anti-*H. pylori* IgG. The seroprevalence determined with ELISA method (Biotech USA), questionnaire covering sociodemographic variables were completed by interview.
Results: In Tripoli, among T2DM patients' prevalence of *H. pylori* was (79%), compared to non-DM (73%). *H. pylori* was higher in females than in males. There was gradual increase with age. In Benghazi T2DM group, *H. pylori* was (72%) in T2DM patients with highly significant difference (p=0.000), *vs.* to non-DM (49%), was no statistical difference in *H. pylori* seropositivity according to gender and education level in T2DM and non-DM.

Conclusions: The findings confirm in Tripoli, Benghazi regions, prevalence of *H. pylori* was higher in groups of T2DM & Non-diabetic participants of this population study. Appropriate prevention and control measures is needed. Community Health authority should plan to educate the population on health and hygiene practices to reduce DM, and risk of contracting the *H. pylori*. However, larger studies should be conducted to confirm the study finding.

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P05.05

IDENTIFICATION OF DRINKING WATER SOURCES IN PATIENTS WITH *HELICOBACTER PYLORI* INFECTION FROM BACĂU COUNTY, ROMANIA

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***Objective*:** Worldwide, *Helicobacter pylori* (*H. pylori*) infection affects about 80% of the world population. It is important to identificate the common risk factors in the transmission of *H. pylori* infection. Drinking water is a possible source of *H. pylori* infection.
Patients and Methods: A number of 115 patients from Bacău County were tested for *H. pylori* infection between October 2019 and November 2020. *H. pylori* infection was diagnosed by fecal antigen test. Patients were analysed by demographic criteria (age, sex, environment of origin). All patients were asked about the source of drinking water they use.
Results: Of the 115 patients analysed, 73 (63.47%) patients were identified with *H. pylori* infection (fecal Ag). Patients with *H. pylori* infection used as a source of water from the locality distribution network 26/73 (35.62%), 21/73 (28.77%) well water, 19/73 (26.02%) bottled water, 7/73 (9.59%) spring water. Regarding the environment of origin, we found *H. pylori* infection in 36/73 (49.31%) patients from urban areas and 37/73 (51.69%) patients from rural areas. Regarding the water source used, urban patients used bottled water (21/36, 58.33%), 15/36 patients (41.66%) used water from the city's supply network.
Conclusions: Following the study performed on a number of 115 patients from Bacău County who were analysed regarding H. pylori infection and the water source used, we can consider water as a possible risk factor for *H. pylori* infection. Priority testing of all individual water sources in rural and urban areas may decrease the prevalence of *H. pylori* infection/reinfection in this region.

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P05.06

EXPLORATORY ANALYSIS OF THE EATING HABITS OF PATIENTS WITH GASTRIC ADENOCARCINOMA: A CASE-CONTROL STUDY IN THE CENTRAL BRAZIL REGION

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***Objective*:** Gastric adenocarcinoma (AdG) is the most common type of upper gastrointestinal cancer and dietary habits are an important risk factor for the incidence of gastric cancer. The aim of this study was to analyze the eating habits of patients with AdG in a case-control sample in Goiânia-Brazil.

Materials and Methods: In this hospital-based case-control study, data were collected between April 2019 and June 2021 using a questionnaire on sociodemographic data, lifestyle and eating habits. One hundred cases and 295 controls were included in the study. The chi-square test was applied to verify differences in sociodemographic and lifestyle characteristics and the Kruskal-Wallis test to compare the mean ages of cases and controls. Exploratory Factor Analysis was performed to identify food preference for cases and controls.
Results: Of the one hundred patients with AdG, 56% were men, 43% were aged between 56 and 65 years and 23% were illiterate. There was a higher consumption of in natura or minimally processed foods in the cases and hospital controls group and a higher consumption of ultra-processed foods in the endoscopic control. Some ultra-processed foods, such as sweets in general and sweet drinks, were three times more consumed by patients with AdG when compared to hospital controls.
Conclusions: In this exploratory analysis, it was possible to verify differences in eating habits in patients with AdG, endoscopic and hospital controls. These results need to be further investigated to elucidate the association between dietary habits and AdG in the Central Brazil region.

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P05.07

EVALUATION OF INTRA-FAMILY AGGLOMERATION IN THE TRANSMISSION OF *HELICOBACTER PYLORI* INFECTION IN PATIENTS FROM BACĂU COUNTY, ROMANIA

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***Objective*:** The aim of this study is to evaluate the rol of intra-family agglomeration and the presence of toilet in house in the transmission of *Helicobacter pylori* (*H. pylori*) infection.
Patients and Methods: A number of 115 patients hospitalized in Emergency Bacău Hospital were analysed between October 1, 2019 and November 1, 2020. *H. pylori* infection was diagnosed by fecal antigen test. All patients were asked about the intra-family agglomeration and the presence of toilet in the house.
Results: Prevalence of *H. pylori* infection depending on intra-family agglomeration and the presence of toilet in the house.
Conclusions: Intra-family agglomeration is a risk factor for transmitting *H. pylori* infection, especially during childhood. The small area of the house can be a risk factor in transmitting *H. pylori* infection. The absence of the bathroom inside the home is a risk factor in the transmission of *H. pylori* infection.

TABLE 1. THE PREVALENCE OF HP INFECTION DEPENDING ON INTRAFAMILIAL AGGLOMERATION.

Number of people in the house		*H. pylori* +		*H. pylori* –	
		No. of people	%	No. of people	%
11-3		53	72.61	39	92.85
≥ 4		20	27.39	3	7.15
House	1-2 rooms	31	42.46	6	14.28
	3 rooms	12	16.43	7	16.66
Bloc	1-2 rooms	25	34.24	19	45.22
	3 rooms	5	6.85	10	22.85
Toilet	In the yard	31	42.46	8	19.04
	In the house	42	57.53	34	80.95
Total = 115		**73 patients**		**42 patients**	

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

P05.08

ASSOCIATION OF ALCOHOL CONSUMPTION AND *HELICOBACTER PYLORI* INFECTION IN CENTRAL BRAZIL

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***Objective*:** *Helicobacter pylori* infection has a prevalence of about 80% in developing countries and is associated with lifestyle. The aim of the study was to verify the association between *H. pylori* infection and alcohol consumption.

Materials and Methods: This is a cross-sectional study nested in a hospital-based case-control, carried out in the Midwest region of Brazil in the period 2019-2022. Data were collected through structured questionnaires. Patients of both sexes, aged between 18 and 75 years, undergoing upper digestive endoscopy were recruited. Categorical variables were compared using Pearson's chi-square test and continuous variables using Student's *t*-test, with a significance level of 5%. The study was approved by the Research Ethics Committee of Fundação Antônio Prudente (Opinion No.: 3,174,666).

Results: Of the 163 individuals, 43.6% were positive for *H. pylori* infection. Among the infected patients, 60.6% were women, 50.1% were under 50 years of age, 59.1% were married, 50.7% had only basic education, 38.0% were underweight or eutrophic, 31.8% were alcoholics, 25.8% were former alcoholics, 52.6% had consumed alcohol for more than 20 years, 71.8% consumed more than recommended by the World Health Organization (30 g/day for men and 20 g/day for women). However, no significant differences were observed between the variables.

Conclusions: It is concluded that there was no association between alcohol consumption and *H. pylori* infection. More comprehensive studies are needed to elucidate alcohol consumption and *H. pylori* infection in Brazil.

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P05.09

ASSOCIATION OF TOBACCO CONSUMPTION AND *HELICOBACTER PYLORI* INFECTION IN DYSPEPTIC PATIENTS IN CENTRAL BRAZIL

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***Objective*:** *Helicobacter pylori* infection is associated with lifestyle and has a high prevalence in developing countries. Therefore, this study investigated the association between smoking and *H. pylori* infection in central Brazil.

Materials and Methods: This is a cross-sectional study that analyzed 162 questionnaires on the lifestyle of patients undergoing gastric endoscopy in a reference hospital. *H. pylori* infection was confirmed by histopathological examination. Categorical variables were compared by Pearson's chi-square test, with a 5% significance level. Odds ratios and 95% confidence intervals were calculated.
Results: The prevalence of *H. pylori* infection was 43.83% (71/162). Among infected patients, the mean age was 49.84 ± 14.61, 59.15% (42/71) were women, 60.56% (43/71) never smoked, 29.58% (21/71) were former smokers, 9.86% (7/71) were smokers. There was no significant difference between the presence of infection and these variables. A higher proportion (63.64%) of uninfected individuals smoked below average (≤12 cigarettes per day), but there was no difference compared to the infected group. In the analysis adjusted for sex, body mass index, and number of cigarettes per day, a higher chance that individuals with *H. pylori* infection were men was observed (OR = 4.8, 95% CI: 1.4-16.8). The result of the association between the average amount of cigarettes per day (>12 cigarettes) and *H. pylori* infection was OR = 1.5, 95% CI: 0.5-4.9.
Conclusions: There was no association between tobacco consumption and *H. pylori* infection in this study.

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P05.10

RESEARCH TRENDS ON THE RELATIONSHIP BETWEEN MICROBIOTA AND *HELICOBACTER PYLORI* FROM 1983 TO 2021: A BIBLIOMETRIC ANALYSIS

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***Objective*:** In recent years, more and more studies have found that other bacteria besides *Helicobacter pylori* (*H. pylori*) exist in the stomach, and *H. pylori* infection may cause gastrointestinal flora imbalance. This study aimed to access the current status and research trends of microbiota and *H. pylori*.
Materials and Methods: Publications from January 1, 1983 to July 22, 2021 were retrieved from the Web of Science Core Collection database and screened according to inclusion criteria. Different kinds of software, SPSS21.0, VOSviewer, CiteSpace, and the online bibliometric analysis platform were used to analyze the selected literatures and visualize the results.
Results: A total of 1,320 articles from 58 countries were included in the analysis, and the results showed an overall upward trend in the number of publications published annually. The most productive country was China, while the United States has the most total citations and Estonia has the most average citations. *Helicobacter* was the most productive journal. The most prolific and most cited author was FOX JG from Massachusetts Institute of Technology, which was the most prolific research institution. "*Helicobacter pylori*" appeared most frequently as a keyword, and "metagenomics", as an important microecological technology, appeared more and more frequently in recent years.
Conclusions: This study summarized the characteristics of these articles, and these results can help relevant researchers understand the panorama of microbiota and *H. pylori* related research, and determine the further research direction, and also help relevant researchers choose suitable partners or journals.

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P05.11

THE FREQUENCY OF EROSIONS AND ULCERS OF THE STOMACH AND DUODENUM IN PATIENTS WITH COVID-19 INFECTION

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***Objective*:** COVID-19 infection is a global health problem. Recently, serious attention has been drawn to erosive and ulcerative lesions in the gastric and duodenal mucosa in patients with COVID-19 infection (Melazzini F. et al, 2020).
Patients and Methods: Esophagogastroduodenoscopy was performed in patients treated in the hospital for COVID-19 infection therapy with heartburn, dyspepsia, or signs of gastrointestinal bleeding. A total of 387 patients underwent endoscopy (116 men and 271 women, mean age 65.4 years). The classification of ulcer bleeding was performed according to J.A. Forrest (1974). *Helicobacter pylori* infection was determined by morphological and urease methods in all 387 patients.
Results: The frequency of the *Helicobacter pylori* infection in the examined persons was 82.2%. Gastric erosions were registered in 34.1% of COVID-19 patients with gastroenterological complaints (in 24.1% of men and 38.4% of women; p=0.01); duodenal erosions were identified in 10.3% of individuals (in 19.8 men and 6.3% of women; p<0.001). The frequency of gastric ulcers was 3.4% (9.5% in men and 0.7% in women; p<0.001), the frequency of duodenal ulcers was 6.7% (16.4% in men and 2.6% in women; p<0.001) in the examined persons. Gastroduodenal bleeding was detected in 5.7% of the patients (in 12.1% of men and 3.0% of women; p<0.001) and was associated with ulcerative defects in 81.8% of cases.
Conclusions: A high frequency of gastroduodenal ulcers and erosions was determined in COVID-19 patients, which may be associated with the combined effect of *Helicobacter pylori*, medicines and COVID-19 infection.

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P05.12

NATIONWIDE STUDY OF PREVALENCE RATES AND ANTIBIOTIC RESISTANT PATTERNS OF *H. PYLORI* INFECTION IN THAILAND COMPARING TO ASIAN COUNTRIES

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***Objective*:** *H. pylori* infection results in many diseases and impacts quality of life of many people in the world including Thailand. Our study aimed to provide prevalence of *H. pylori* infection and antibiotic resistance in Thailand and ASEAN countries.
Patients and Methods: Patients underwent esophagogastroduodenoscopy from January 2004-February 2021 in Thailand were included. Antibiotic susceptibility testing of *H. pylori* was performed which determines MICs of antibiotic including amoxicillin, clarithromycin, levofloxacin, metronidazole, and tetracycline.

Results: Total of 12,531 patients including 5,021(40.1%) men and 7,510 (59.9%) women with mean age of 56.9±14.8 years were included. The prevalence of *H. pylori* infection was 28.2% (95% CI: 27-29%). Decreasing prevalence of *H. pylori* infection was observed during 2014-2021, compared with from 2004 to 2013 (24.5% [95% CI: 24-25%] *vs.* 36.3% [95% CI: 35-38%], $p<0.001$). The prevalence of *H. pylori* resistance varied during 2004-2021 such as amoxicillin (median 1.9%, IQR 0-4.7%), clarithromycin (median 4.9%, IQR 2.7-16.0%), metronidazole (median 41.4%, IQR 36.2-48.6%), tetracycline (median 1.3%, IQR 0-2.8%), and levofloxacin (median 7.7%, IQR 0-24.0%). Clarithromycin-, metronidazole- and levofloxacin-resistant *H. pylori* stains were significantly increased between 2004 and 2013, compared with between 2014 and 2021 ([3.8% *vs.* 17.4%, $p<0.001$], [36.3% *vs.* 46.7%, $p=0.002$], and [6.7% *vs.* 23.2%, $p<0.001$], respectively). Prevalence of *H. pylori* infection in Thailand also compared with other countries in ASEAN.
Conclusions: *H. pylori* infection is decreasing over the past 18 years in ASEAN. Pattern of *H. pylori* antibiotic resistance demonstrated increasing in clarithromycin, metronidazole, and levofloxacin resistance especially in the recent years.

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P05.13

POTENTIAL RISK OF PROTON PUMP INHIBITORS FOR PARKINSON'S DISEASE: A NATIONWIDE NESTED CASE-CONTROL STUDY

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***Objective*:** The use of proton pump inhibitors (PPIs) is a potential risk factor for neurodegenerative diseases; however, its role in Parkinson's disease (PD) remains unclear. We aimed to investigate the association of PPI use with the risk of PD.
Materials and Methods: We used data queried from the Korean National Health Insurance Services Database. We included patients newly diagnosed with PD from January 2010 to December 2019 (N=31,326) and healthy controls matched by age, sex, body mass index, diabetes, hypertension, stroke, and dementia at a 1:4 ratio (N=125,304). Cumulative defined daily doses (cDDDs) of PPIs were extracted from treatment claims. We examined the association of PPI use with the risk of PD using conditional logistic regression. To prevent protopathic bias, we excluded patients with PD diagnosed within a 1-year lag period after PPI exposure. Additionally, we applied 2- and 3-year lag periods for sensitivity analysis.
Results: PPI use was associated with an increased PD risk when a 1-year lag period was applied between PPI exposure and PD development (adjusted odds ratio 1.10, 95% confidence interval 1.07-1.13). There was a significant positive dose-response relationship between the cDDDs of PPIs and PD development (p for trend < 0.001). Similar results were obtained using the 2- or 3-year periods. Finally, PPI use increased the risk of PD in patients aged ≥50 years but not those aged <50 years.
Conclusions: We observed the association between PPI use and the risk of PD.

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P06 Microbiology and genomics of Helicobacter

P06.02

NOVEL *HELICOBACTER* SPP. ISOLATED FROM WILD MICE IN MASSACHUSETTS, UNITED STATES

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Objective**:** Enterohepatic *Helicobacter* species (EHS) colonize the gastrointestinal tracts of humans and animals and are associated with gastrointestinal diseases. *Helicobacter* species in wild mice have been detected by PCR, but their zoonotic potential is unknown and their potential for pathogen introduction into laboratory animals exists. In this study, novel EHS were cultured and taxonomically classified from three different species of wild mice captured in seven different towns in Massachusetts, United States.
Materials and Methods: Feces and cecum tissues collected from live trapped house mice (*Mus musculus*), deer mice (*Peromyscus leucopus*), and meadow jumping mice (*Zapus hudsonius*) were subjected to microaerobic culture on blood agar or antibiotic-selective agar plates. Suspected isolates were subjected to 16S rRNA gene and whole genomic sequence analyses for taxonomical identification.
Results: *Helicobacter* species were isolated and identified by 16S rRNA sequence as *H. rodentium* from 2/7 of house mice. Eighteen EHS strains were isolated from 22 deer mice which included *H. mystomyrinus* and three different novel species. Sixteen EHS with identical 16S rRNA sequences and identified as a novel species were isolated from 21 meadow jumping mice. Virulence genes for cytolethal distending toxin (CDT) and the type VI secretion system (T6SS) were detected in selected novel *Helicobacter* spp. Whole genome sequence analysis indicated four of the species were identified as novel EHS.
Conclusions: *Helicobacter spp.* commonly colonize wild mice. Novel EHS isolation from wild mice and whole genomic sequence analysis of these novel bacteria provide further understanding of the taxonomy and epidemiology of *Helicobacter* genus.

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P06.03

LNCRNA LUCAT1 INCREASES THE ONCOGENIC PROPERTIES OF GASTRIC CANCER CELLS AND MACROPHAGES BY REGULATING MIF EXPRESSION IN *H. PYLORI*-INDUCED GASTRIC CANCER

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Objective**:** Long non-coding RNAs (lncRNAs) are proven to play critical roles in cancer biology. Tumor-associated macrophages predominantly induced to be polarized into M2, a pro-tumorigenic type when recruited with the tumor tissue and thereby favoring the tumorigenesis. In our study, we aim the possible mechanisms of the regulatory link between lncRNAs and macrophages in gastric cancer caused by *H. pylori*.
Materials and Methods: Differentially expressed lncRNAs between *H. pylori*-CagA+ infected and control AGS cells, and between cagA vector-transfected and control AGS cells were identified by RNA-seq and validated by qRT-PCR. Next, we built a co-culture system to explore the interaction between THP-1 macrophage cells and AGS cells in the presence of *H. pylori*-CagA+.

Results: We validated that the expression of LUCAT1 was significantly up-regulated after of both *H. pylori*-CagA+ infection and cagA transfection. The knock down of LUCAT1 significantly attenuated the proliferation, migration, and invasion of AGS and MKN74 cells. The infection of *H. pylori*-CagA+ increased secretions of inflammatory cytokines which produced a huge chemotactic effect on THP-1 cells. In our study, LUCAT1 up-regulated macrophage migration inhibitory factor (MIF), one of the crucial cytokines involved in cancer and inflammation in AGS and THP-1 cells. We found that LUCAT1 increased by *H. pylori*-CagA+ infection up-regulates MIF in AGS cells and subsequently MIF polarizes surrounding THP-1 macrophages into M2 macrophages. In turn, M2 macrophages activate carcinogenesis in gastric cancer.
Conclusions: Our findings provide important insights for the potential development of lncRNA-based targeted approaches for the treatment of *H. pylori*-related gastric cancer.

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P06.04

ASSOCIATION OF THE *HELICOBACTER PYLORI* VIRULENCE GENE *OIPA* WITH THE SEVERITY OF GASTRODUODENAL DISEASES

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Objective**:** *Helicobacter pylori* (*H. pylori*) infection is associated with gastroduodenal diseases. Approximately half of the world's population is infected, and the prevalence in Brazil is up to 91%. The clinical outcome of infection is associated with an imbalance in the parasite-host relationship. The *outer inflammatory protein A* (*oipA*) gene is an important virulence factor and plays the role of adhesin. The aim of this study was to evaluate the prevalence of *H. pylori* infection and the association of the *oipA* gene with the severity of gastroduodenal diseases in dyspeptic patients in the Central region of Brazil.
Materials and Methods: Molecular screening of the microorganism was performed by the polymerase chain reaction using the 16S primer (rRNA). Positive samples were submitted to *oipA* gene amplification. Infected patients had lesions categorized as non-severe, including duodenitis, esogaphagitis, gastritis, and ulcers, and severe, with gastric adenocarcinoma (AdG), gastric atrophy, and intestinal metaplasia.
Results: A total of 155 patients, 67.7% were positive for the infection and 36% were infected with *H. pylori oipA+* strains. About 18% of patients infected with the *H. pylori oipA+* strain were diagnosed with some severe disease. AdG was the most frequent, with 10.5%. The result of the analysis between the association of genotype and disease severity was OR = 0.247, 95% CI: 0.0804 – 0.7149 and p=0.007.
Conclusions: The *H. pylori oipA* genotype was associated with the severity of gastroduodenal diseases. The molecular characterization of circulating strains will contribute to precision medicine, impacting the diagnosis and treatment of patients.

D.N. Maciel: None. A.F.P.L. Ramos: None. G.R. Maximo: None. L.P. Assunção: None. T. Tiengo: None. M.P. Curado: None. L.T. Rasmussen: None. A.J.V. Blanco: None. M.S. Barbosa: None.

P06.05

REFRACTORY H.PYLORI INFECTION AND GASTRIC MICROBIOTA

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***Objective*:** The aim of the study was to investigate the effect of refractory *Helicobacter pylori* infection on the diversity, composition and function of gastric flora.
Patients and Methods: We designed a clinical study involved with 32 subjects who were divided into three groups: 1. nAGHp. a group: *H. pylori* positive was first found in non-atrophic gastritis; 2. nAGHp. b group: *H. pylori* negative in non-atrophic gastritis; 3.EFHp. a group: Refractory *H. pylori* infection. Gastric mucosa samples were collected for 16S rRNA sequencing analysis.
Results: There are significant diffrences between *H. pylori* positive group and *H. pylori* negative group in species diversity, gastric flora structure and bacterial function. The results of LEfSe analysis suggested that the beneficial *Lactobacillus* in *H. pylori* positive group was significantly enriched than that in refractory *H. pylori* infection group. The bacterial interaction network diagram suggested that the interaction between bacteria in refractory *H. pylori* infection group decreased. We found that the refractory *H. pylori* infection group gastric microbiota was enriched in energy metabolism, bacteria secretion system, glutathione metabolism, protein folding and associated processing, surful metabolism, membrane and intracellular structural molecules, lipopolysaccharide biosynthesis, ubiquinone and other terpenoid-quinone biosynthesis, inorganic ion transport and metabolism as well as metabolism of cofactors and vitamins compared with *H. pylori* positive group by PICRUST2 analysis.
Conclusions: *H. pylori* infection is an important factor affecting the diversity, composition and function of normal gastric flora. Multiple *H. pylori* eradication history can lead to imbalance of gastric mucosal flora to a certain extent, which is mainly reflected in inhibiting the growth of beneficial *Lactobacillus* in the stomach, and multiple *H. pylori* eradication history can change some functions of gastric flora.

J. Wang: None. Y. Xie: None. D. Liu: None.

P06.06

WHOLE GENOME SEQUENCING OF VACA ALLELIC VARIANTS OF THE MOUSE COLONISING *HELICOBACTER PYLORI* STRAIN PMSS1

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Helicobacter pylori (Hp) infection prevalence has declined over recent decades, whilst autoimmune diseases have become more common. Several groups report a protective link between *Hp* infection and multiple sclerosis (MS), and evidence suggests the VacA toxin may play a role in this. To identify which VacA polymorphic types are involved, we aimed to create *vacA* isogenic mutants for use in *in vitro* and *in vivo* models. The *vacA* gene of strain PMSS1 [wild-type (WT) s2i2 *vacA*] was mutated to create variants with more active s1i1 and s1i2 *vacA* types. As PMSS1 has an active *cag* pathogenicity island (*cag*PAI), we also constructed *vacA* variants in a *cagE* null background to study toxin effects in the presence and absence of functional *cag*PAI. Mutations were confirmed by PCR and Sanger sequencing, prior to whole genome MiSeq sequencing. Between 1 to 6 unexpected nonsynonymous mutations were found within the PMSS1 WT and six *vacA* mutant genomes. All strains possessed a single nucleotide difference from the published PMSS1 sequence within the *fur* (ferric uptake regulation) gene. This polymorphism was found in at least 6 other wild-type *Hp* strains. Five mutants contained a mutation within *rpoA* (RNA polymerase subunit alpha), but protein structural modelling software suggested this amino acid change is not within an essential protein domain and would not alter the predicted secondary structure. Relatively few secondary mutations were found within the wild-type and *vacA* variant strains. The constructed mutants are therefore suitable for future mechanistic studies of their impact on MS *in vivo*.

J.L. Stephens: None. J. Rhead: None. D. Letley: None. K. Robinson: None.

P07 Helicobacter and extragastroduodenal disease

P07.01

ASSOCIATION BETWEEN *HELICOBACTER PYLORI* AND HYPERTENSION IN DYSPEPTIC PATIENTS IN CENTRAL-WESTERN BRAZIL

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***Objective*:** *Helicobacter pylori* is a bacterium that colonizes the gastric mucosa and causes tissue damage to the host. In addition, it may play a role in the genesis of hypertension. The aim of this study was to evaluate the association between *H. pylori* infection and hypertension in dyspeptic patients treated at a referral hospital in Goiânia, Goiás.
Materials and Methods: This is a cross-sectional study, where 156 questionnaires were applied to patients undergoing upper endoscopy with biopsy. The data were analyzed by absolute and relative frequencies, measures of central tendency and dispersion, Pearson's chi-square, with a 5% significance level, and logistic regression, with a 95% confidence interval.
Results: The prevalence of *H. pylori* was 45.5% (71/156). In the *H. pylori*-positive group 60.6% were women (43/71), 50.7% were over 50 years old (36/71) and 36.6% were underweight or eutrophic (26/71). In the *H. pylori*-negative group, 76.5% were women (65/85), 57.6% were 50 years old or less (49/85) and 45.9% were underweight or eutrophic (39/85). Males were more likely to be infected by the bacteria (OR = 2.63, 95% CI: 1.26-5.50). In the infected group, 43.7% (31/71) of the subjects were hypertensive, and in the negative group 32.9% (28/85). There was no statistical difference between the groups (OR = 1.54, 95% CI: 0.71-3.34).
Conclusions: Males were more likely to be infected by the bacteria and no association was found between *H. pylori* infection and hypertension.

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P07.02

ASSOCIATION BETWEEN *HELICOBACTER PYLORI* INFECTION AND ANEMIA IN DYSPEPTIC PATIENTS SEEN AT A REFERENCE HOSPITAL IN CENTRAL-WESTERN BRAZIL

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***Objective*:** *H. pylori* infection is related to gastric diseases, such as gastritis, ulcer and gastric cancer. However, there is recent evidence that the infection is associated with extragastric diseases. This study investigated the association between *H. pylori* infection and anemia.
Materials and Methods: This is a cross-sectional study, in which 156 questionnaires of patients undergoing upper digestive endoscopy followed by biopsy were analyzed. Categorical variables were compared by Pearson's chi-square test with 5% significance level and univariate and multiple unconditional binary logistic regression model were applied for the analysis of odds ratios and 95% confidence intervals.

Results: The prevalence of *H. pylori* infection in the study population was 45.5% (71/156). In the *H. pylori* negative group, 76.5% (65/85) were female, 57.7 (49/85) were 50 years of age or younger, and 81.2% (69/85) declared themselves non-white (black, brown, and Asian). Among infected participants, 60.6% (43/71) were female, 50.7% (36/71) were between 51 and 75 years old, and 70.4% (50/71) were non-white. The variable sex showed a statistical difference (p = 0.03) between groups and regression adjusted OR = 0.45, 95% CI: 0.22-0.91. Anemia was present in 31.8% (27/85) in the negative group and 29.6% (21/71) in the infected group, p = 0.904 and the adjusted regression was OR = 0.96, 95% CI: 0.45-2.05.
Conclusions: Females were less likely to be infected by the bacteria and the presence of anemia was not associated with *H. pylori* infection.

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P07.03

EFFECTS OF *HELICOBACTER PYLORI* ON FAECAL CALPROTECTIN IN DEVELOPMENT COLORECTAL CARCINOMA

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***Objective*:** Faecal calprotectin (FC) is a known marker of colonic inflammation. There is evidence of elevated FC levels in patients with *Helicobacter pylori* (*HP*) infection and in patients with colorectal cancer (CRC). Chronic inflammation and HP have been associated with increased risk for CRC. Aim of this study was to find differences in FC levels in patients with CRC regarding HP infection.
Patients and Methods: Study was performed in UHC Sestre milosrdnice, Zagreb. Patients with CRC and healthy controls were enrolled from February 2020 - 2022. FC was measured and the presence of HP was determined using a stool antigen test. The Kruskal Wallis test was used to compare groups.
Results: There were 150 patients,88 with CRC (32 with *HP*) and 62 controls (16 with *HP*). FC median and interquartile range for patients with CRC and *HP* was 280 [118-606] mg/kg, CRC without *HP* 116 [40-266] mg/kg, controls with *HP* 37 [20-114] mg/kg, and controls without *HP* 21 [20-58] mg/kg. Results were significantly different (H=39.6, p<0.05). Post-hoc analysis showed significantly higher FC levels in patients with CRC and *HP* infection compared to patients with CRC without *HP* (p<0.05), as well as in patients with CRC compared to controls regardless of *HP* (p<0.05)
Conclusions: Our results confirm the association of chronic colonic inflammation and CRC, but also imply there is an additional effect of *HP* on colonic inflammation in patients with CRC. Further studies in order to clarify the potential role of FC in patients with *HP* and CRC are needed.

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P07.04

HELICOBACTER PYLORI INDUCES HEPATIC LESIONS IN A MOUSE MODEL OF GASTRIC CARCINOGENESIS

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Gastric cancer, the 4th cause of cancer mortality worldwide, is mainly caused by a chronic infection with the bacterium *Helicobacter pylori* which colonizes the stomach lifelong. It induces chronic gastritis, evolving in some cases to intestinal metaplasia, dysplasia and adenocarcinoma. Many studies have tried to correlate Helicobacter infection with disease in extra-gastric digestive organs like the liver where different strains were found. In mice, *Helicobacter hepaticus* colonizes the liver leading to

chronic active hepatitis and hepatocellular carcinoma. However, whether human strains of *H. pylori* can induce liver lesions remains unknown. This study evaluated the consequences of mice infection with different strains of gastric Helicobacters on their liver. In this double-blind study, histopathological analysis of HES-stained paraffin-embedded liver tissue sections were scored for inflammation and other lesions. Mice infected with *H. pylori* were found to develop liver inflammation and steatosis, known precursor lesions of liver carcinogenesis. Understanding the impact of *H. pylori* infection on extra-gastric lesions could help *in fine* prevent the emergence of other digestive-track related diseases.

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P08 Microbiota in health and disease

P08.01

UREASE AS MOTOR PROTEIN FOR TRANSLOCATION OF EXTRACELLULAR VESICLES OF GASTRIC YEAST

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***Objective*:** Urease exhibits high translocation property in the presence of urea. One gastric yeast with urease activity and intracellular *H. pylori* (*HP*) was used to study the role of urease in translocation of extracellular vesicles (EVs) released from the yeast.
METHOD: For EVs isolation, fresh culture of yeast on brucella blood agar was suspended in PBS, centrifuged at 4000, then 10000 and finally 100,000 g. Pellet with EVs was resuspended in 250 µL PBS. Test plates were prepared with upper half containing plain agar and 10-100 mM concentrations of inhibitor ($ZnCl_2$) or 2, 4 and 6% of inducer (urea) and lower half containing urea-phenol red agar (UPA). Forty µL volumes of vesicles were inoculated into wells made in the upper half of the agar. Plates were incubated at room temperature and observed for the appearance of pink color in the UPA.
Results: With inhibitor in the upper half, pink color in UPA appeared longer than 16 hr due to slower translocation of vesicles. With inducer in the upper half, pink color appeared shorter than 16 hr due to faster translocation of vesicles. Urease was induced by urea and inhibited with $ZnCl_2$ due to substitution of Ni by Zn.
Conclusions: Results of this study suggest urease as a motor protein that powers the translocation of vesicles. Urease is regarded as a moonlighting protein with several different activities. These might explain the advantage of having urease. Whether the urease activity originates from the yeast host or the intracellular *HP*, needs further studies.

A. Hatefi: None. F. Siavoshi: None.

P08.02

EXTRACELLULAR VESICLES FROM H. PYLORI & GASTRIC YEAST EXHIBIT UREASE ACTIVITY

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***Objective*:** *H. pylori* (*HP*) 16S rDNA and proteins were previously detected in extracellular vesicles (EVs) from a gastric yeast by PCR and immunogold method, respectively. Here, urease activity of released EVs from *HP* and yeast was examined.
Materials and Methods: One *HP* and one yeast isolate from two different gastric biopsies that both exhibited urease activity were used. Light microscopy and amplification of *ureAB* gene showed the occurrence of intracellular *HP* inside the yeast vacuole. For EVs isolation, cultures of yeast and *HP* on brucella blood agar were suspended in PBS, centrifuged at 4000, then 10000 and finally 100,000 g.

Pellets were resuspended in 250 µL PBS. A 40- µL volume of each suspension was used for urease activity on urea-phenol red agar (UPA). Second 40 µL was first treated (1hr) with 10-40 and 100 mM $ZnCl_2$ for urease inhibition and then inoculated on UPA. Plates were examined every hr for color change.
Results: EVs of both *HP* and yeast changed the color of UPA to pink within 1-3 hr due to strong urease activity. This urease activity was partially inhibited by $ZnCl_2$ at concentrations of 10-40 mM and completely inhibited at 100 mM.
Conclusions: Urealytic activity of EVs from *HP* and yeast was due to urease. This urease activity was strong, indicating the high efficiency of the enzyme carried by EVs. The urease activity of yeast might originate from intracellular *HP* or other bacteria. Further studies are warranted to reveal the important roles urease plays in *HP* and yeast.

A. Hatefi: None. F. Siavoshi: None.

P08.03

IDENTIFICATION OF NON-*H. PYLORI* GASTRIC BACTERIA WHICH STIMULATE INTERLEUKIN-8 PRODUCTION IN GASTRIC EPITHELIAL CELLS

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***Objective*:** Mucosal atrophy and reduced gastric acidity caused by chronic *H. pylori* infection leads to overgrowth of non-*H. pylori* gastric bacteria (NHGB). We aimed to investigate their ability of inducing IL-8 production from gastric epithelial cells and to demonstrate the underlying mechanism.
Materials and Methods: We collected gastric juice from 13 patients with gastric cancer. After culture, isolated NHGB were identified with 16S rRNA gene sequencing. Human gastric epithelial cells (AGS) were co-cultured with the bacteria, and interleukin-8 (IL-8) concentrations in cell culture supernatants were quantified by Enzyme-Linked Immunosorbent Assay. We additionally performed inhibition assays using inhibitors to TLR4, NOD1, mitogen-activated protein kinases (MAPKs), and transcription factors, to reveal the mechanism of pathogen recognition, intracellular signal transduction and translational regulation of IL-8 by the bacteria.
Results: Sixteen species of NHGB were isolated. After inoculation to AGS cells, *Neisseria perflava* potently stimulated IL-8 secretion, which was attenuated by concurrent treatment with NOD1 inhibitor. When AGS cells were co-treated with *N. perflava* and inhibitors of ERK, p38 or JNK, respectively, to determine the role of MAPKs in IL-8 production, IL-8 production was significantly reduced after treatment with p38 inhibitor. The cells produced significantly reduced level of IL-8 on stimulation with *N. perflava*, when pretreated with NF-κB inhibitor.
Conclusions: We demonstrated that *N. perflava* induces MAPK phosphorylation and NF-κB activation *via* a NOD1-dependent mechanism in gastric epithelial cells. *N. perflava* may contribute to the inflammation in gastric mucosa, and subsequent carcinogenesis process.

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P08.04

TREATMENT OF NON-EROSIVE REFLUX DISEASE AND CHANGE OF ESOPHAGEAL MICROBIOME: A PROSPECTIVE MULTICENTER STUDY

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Introduction: The pathogenesis of non-erosive reflux disease (NERD) has not been fully evaluated. We aimed to evaluate the treatment response of proton pump inhibitors (PPI) in patients with NERD and changes in microbial composition and biologic marker expression on esophageal mucosa after PPI therapy.

Patients and Methods: Patients was diagnosed with NERD were enrolled and received 20 mg of esomeprazole for 8 weeks. The treatment response was evaluated using the patient assessment of upper gastrointestinal symptom severity index questionnaire at baseline, week 4, and week 8. Esophageal mucosal markers and oropharyngeal and esophageal microbiomes were analyzed in patients who had required upper gastrointestinal endoscopy for screening.
Results: In 62 enrolled patients, complete and partial response rates at week 8 were 60.0% and 32.7%, respectively, for heartburn, and 61.8% and 29.1%, respectively, for regurgitation. After eight weeks of PPI therapy, the expression level decreased in several inflammatory cytokines, includingIL-6, IL-8, and NF-κB. In the microbiome analysis, Streptococcus, Haemophilus, Prevotella, Veillonella, Neisseria, and Granulicatella were prevalent regardless of timing (baseline *vs.* week 8) and organs (oropharynx *vs.* esophagus). However, the overall composition of the oropharyngeal microbiome was distinguished from that of the esophageal microbiome (p=0.004). After the PPI therapy, this difference was not identified.
Conclusions: Half-dose of PPI for eight weeks was effective for symptom control in NERD. It reduced the expression of several inflammatory cytokines in the esophagus. There was a significant difference in the microbial composition between oropharynx and esophagus in patients with NERD; however, it disappeared after PPI therapy.

S. Lee: None.

P08.05

NEUROTOXIC AND PRO-INFLAMMATORY PROPERTIES OF *PROTEUS MIRABILIS* UREASE

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Proteus mirabilis (Pm) is an opportunistic pathogen in humans, causing mainly urinary infection and meningitis. Moreover, studies have associated Pm to Parkinson's disease. Urinary diseases caused by Pm are facilitated by ammonia derived from urea cleaved by urease (PMU), one of its virulence factors. We previously reported non-enzymatic properties, such as pro-inflammatory and neurotoxic activities, for distinct ureases including that of *Helicobacter pylori.* Here, we assessed the neurotoxic potential of PMU in cultured cells and in mice. Purified PMU was tested in human embryonic kidney (HEK293) and neuroblastoma (SH-SY5Y) cells, and in murine microglia (BV-2). Incubation with PMU (nanomolar range, 6 or 24 h) did not affect viability and no ammonia was detected in the culture's supernatants. In PMU-treated SH-SY5Y, increased cytosolic [Ca^{2+}] and ROS production were detected, while in BV-2 and HEK293 cells, PMU induced synthesis of cytokines IL-1β and TNF-α. Texas Red-labeled PMU was found in the cytoplasm and nucleus of the cells, consistent with its two bipartite nuclear localization sequences. Mice were treated ip with 20 µg PMU/daily for 1 week and submitted to behavioral tests 8 and 16 days after the last injection. Alterations of mice performances were seen in the plus elevated maze, dark-light box and tail suspension tests while no changes were observed in the pole, wire hanging and rotarod tests. Our data showed that PMU displays pro-inflammatory properties beyond the urinary system, affecting the central nervous system and derived cells from it, suggestive of a role in neuroinflammation and in neurodegenerative diseases.

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P08.06

PROTON PUMP INHIBITORS USE AND THE RISK OF RHEUMATOID ARTHRITIS: A NATIONWIDE COHORT STUDY

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***Objective*:** Proton-pump inhibitor (PPI)-induced hypochondria can change the composition of the gut microbiota, inducing overgrowth of small bowel bacteria, which has been suggested to promote the development of rheumatoid arthritis. In this study, we aimed to investigate the association between PPI use and the risk of seropositive rheumatoid arthritis (RA).
Materials and Methods: A retrospective cohort study was conducted using the Korean National Health Insurance Service-National Sample Cohort, a nationwide population-based representative sample, from January 1, 2006, to December 31, 2019. PPI use was identified from treatment claims and considered as a time-varying variable.
Results: The hazard ratio (HR) for RA comparing PPI users to non-PPI users was 2.23 [95% confidence interval (CI), 1.50-3.31]. When adjusted for multiple confounders, including age, sex, body mass index, smoking, and alcohol intake, the association was still significant (HR, 1.77; 95% CI, 1.19-2.65). In addition, there was a trend toward a higher risk for RA with increasing duration (reference: PPI use ≤90 days; PPI 91-180 days: HR 1.43, 95% CI 0.98-2.09; PPI use ≥181 days: HR 2.17, 95% CI 1.59-2.96). In sensitivity, nested case-control study with different lag period (1 year and 2 years) showed significant association PPI use and risk for RA.
Conclusions: This current national wide cohort study suggests that PPI use was associated with an increased risk of rheumatoid arthritis, with a higher risk observed in individuals with a longer duration of PPI use. Clinicians should consider rheumatoid arthritis as a potential risk when prescribing PPI.

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P08.09

DSS-INDUCED INTESTINAL HYPERPERMEABILITY IS MICROBIOME-DEPENDENT AND DISPLAYS REGIONAL VARIABILITY

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***Objective*:** Dextran sodium sulphate (DSS) animal models are used to study barrier dysfunction in the pathogenesis of inflammatory bowel diseases. We aimed to study the effect of the gut microbiota on barrier function in DSS-treated mice.
Materials and Methods: An antibiotic cocktail was administered to 12-week-old C57Bl6/J mice *via* oral gavage twice daily for 10 days to deplete the gut microbiome, whereas controls were administered water. Then, animals were treated with 3% DSS or vehicle for 7 days. Subsequently, Ussing chamber experiments were performed to assess intestinal permeability in distal colon (DC), proximal colon (PC) and terminal ileum (TI) in the 4 groups (vehicle vs DSS, with or without antibiotic pre-treatment, n=10-11 animals/group).
Results: In DC of control animals exposed to DSS, the median paracellular flux of 4kDa FITC-dextran after 3 hours was increased threefold compared to vehicle-treated animals (p=0.0006), but no changes were seen in PC or TI. Similarly, median transepithelial resistance (TEER) was decreased twofold in DC (p=0.0009) but not in PC or TI. Microbiome depletion per se did not disrupt barrier function at any site. Furthermore, microbiome depletion prevented the DSS-induced changes in the flux of FITC-dextran or TEER in DC.
Conclusions: DSS exposure affects the intestinal barrier function in DC but not in PC or TI in conventional mice. Although depletion of gut microbiota does not affect the barrier function by itself, it prevents DSS-induced intestinal hyperpermeability in DC. Therefore, the gut microbiome is an important mediator in the development of disease in DSS animal models.

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P08.10

GLUTEN FREE DIET BASED ON PASTA MADE WITH SORGHUM FLOUR REDUCES GASTROINTESTINAL SYMPTOMS AND AMELIORATES DYSBIOSIS

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***Objective*:** Identifying new gluten-free foods is desirable, indeed the gluten-free diet (GFD) is the only therapy available to date for celiac disease and the best approach for non-celiac gluten sensitivity (NCGS). The aim of this study is to evaluate the role of sorghum in celiac and NCGS patients.
Patients and Methods: This study is a real-life experience of GFD based on pasta made with sorghum flour. The patients affected by celiac disease and NCGS, already on a GFD, were consecutively enrolled. All patients were asked to take at least 70g of sorghum pasta 4 times a week, in addition to their regular diet for a treatment period of 4 weeks. Clinical and laboratory data were collected according to clinical practice.
Results: A total of 8 celiac disease patients (4female, median age 43 years) and 25 NCGS (17female, median age 40 years) were include in this study. All patients reported good acceptance and palatability of Sorghum pasta. Patients improved their symptoms, such as diarrhea (72%), bloating (45%), asthenia (30%) and chronic fatigue (15%) or others. Furthermore, patients affected by SIBO showed resolution without taking antibiotics or probiotics. In particular, we report a case of a patient with SIBO characterized by high production of methane and dysbiosis (reduced Firmicutes/Bacteroidetes ratio) showed a marked reduction in the production of methane after 4 weeks of GFD with sorghum.
Conclusions: These preliminary data, based on real life experience, show the importance of sorghum in GFD and suggest new scenarios in the design of clinical trials for diseases that benefit from GFD.

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P08.11

FECAL MICROBIOME TRANSPLANTATION FOR RECURRENT CDI: TREATMENT EFFICACY AND SAFETY WITH ORAL CAPSULES

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***Objective*:** Fecal microbiome transplantation (FMT) is novel and effective treatment for recurrent and refractory CDI. Already existing upper and lower GI FMT methods show excellent efficacy and safety. However, the least invasive FMT method by oral capsules is infrequently used. In this study we analyze oral capsules primary efficacy and safety profile.
Patients and Methods: This study included 30 patients that underwent FMT for recurrent CDI from 2017 to 2021. Each patient was given 50 oral capsules with frozen material for a single day. All patients received CDI treatment with oral vancomycin 500 mg q.i.d. for at least five days and oral PPI before procedure. After FMT patients were followed-up for at least 2 months. Data about CDI reoccurrences, health status was gathered and analyzed.
Results: 30 patients (median age 71 years) received FMT via oral capsules. 22 patients had clinical remission after first FMT resulting in 73.34% primary cure rate. 8 patients had recurrent diarrhea within 8 weeks. During follow-up time no serious adverse events or FMT related deaths were noted.
Conclusions: FMT with oral capsules is safe, less invasive FMT method with adequate procedure efficacy. Further studies are welcome to analyze the most effective and safe FMT method for clinical practice.

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P08.12

THE USE OF FECAL MICROBIOTA TRANSPLANTATION FOR RECURRENT *CLOSTRIDIOIDES DIFFICILE* INFECTION: BRAZILIAN EXPERIENCE

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***Objective*:** The treatment of recurrent Clostridioides difficile infection (CDI) is a challenge in countries where fecal microbiota transplantation (FMT) is not widely available. There are few reports in Latin America and most without structuring a stool bank. Data on effectiveness and safety of FMT in emerging countries are scarce.
***Objective*:** To describe the initial experience of the first fecal microbiota transplantation center in Brazil for the treatment of recurrent CDI using frozen samples.
Materials and Methods: A prospective pilot study that FMT was performed by colonoscopy using frozen samples from stool bank. CDI was confirmed using GDH test followed by toxigenic culture and/or A/B toxin detection. C. difficile isolates were submitted to ribotyping and antimicrobial susceptibility tests.
Results: Over two years, there were 11 FMT for recurrent CDI, with a median age of 68 (23-87). Most patients (60%) had severe CDI and a median of 3 previous episodes (1-4). Primary resolution with single FMT was 80% and overall resolution after second FMT was 90%. Failure was not related to severity of CDI (p=0.273), bowel preparation (p=0.345), comorbidities (p=0.809), number of previous episodes (p=0.457). No serious adverse events were described during follow-up of 26.6 (26.6-38.2) months. Mild adverse events occurred in 54.5%, mostly transient abdominal discomfort. Toxigenic C. difficile isolates belongs to ribotypes (RT) 106, 014/020, 131, 076 and 037. All isolates were susceptible to metronidazole and vancomycin.
Conclusions: FMT is a safe and effective treatment for recurrent CDI in this cohort of Brazilian patients.

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P08.13

STERILE FECAL FILTRATE TRANSFER FOR THE TREATMENT OF HEPATIC ENCEPHALOPATHY

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Introduction: Hepatic encephalopathy (HE) remains one of the most debilitating complications of liver cirrhosis. Gut microbiome has been linked to the severity of HE, while recent randomized controlled trials showed FMT to be safe and effective in HE treatment, however this procedure comes with possible risks, including infections. A pilot study showed sterile fecal filtrate transfer (FFT) to be effective in reversing dysbiosis and treating recurrent Clostridium Difficile infection.
Materials and Methods: We have aimed to investigate safety and efficacy of sterile fecal filtrate in the treatment of hepatic encephalopathy. Sterile fecal filtrate from a healthy tested donor stools was prepared following the methods described by Ott SJ. Seven patients with hepatitis C virus or alcohol induced cirrhosis and HE have been enrolled in the study. Severity of HE and liver function was monitored for a month after a procedure. 16S rRNA sequencing was performed primers to determine fecal microbiome composition before, one week and one month after the FFT.
Results: No adverse events were registered. Significant shifts in microbiome composition were observed in 3/7 patients, with an increase in Shannon alpha diversity index, reduction in abundance of Proteboacteria phylum, and a shift towards donors' microbiome composition. No significant clinical effect on HE was observed after FFT.

Conclusions: Sterile fecal filtrate transfer resulted in significant shifts in stool microbiota composition for a portion of the patients, however we have not witnessed any clinical benefits for these patients.

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P08.14

OPTIMIZATION OF SAMPLES PREPARATION CONDITIONS FOR CIRCULATING MICROBIOME STUDIES

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Recent studies show that bacterial sequences are found in the human blood. Presumably circulating bacterial sequences could be used to diagnose, predict, or monitor various health conditions. The influence of different preparation conditions is an important aspect using samples from biobanks or comparing results from different studies. In this study, we aimed to analyze how 4 different criteria (blood collection tube, centrifugation, volume, and DNA extraction kit) impact on circulating bacterial composition. Blood samples of 4 individuals were collected into a three different sample collection tubes: K2EDTA Plasma tube, Sodium Citrate plasma tube, and Gel tube for blood serum. Tubes were centrifugated at standard and double centrifugation condition. DNA extraction was performed out of 100, 200, and 500 µl. For DNA extraction were used three different isolation kits: Norgen Plasma/Serum Cell-Free Circulating DNA Purification Micro Kit, Applied Biosystems MagMAX Cell-Free DNA Isolation Kit, and Qiagen QIAamp MinElute ccfDNA Mini Kit. All samples were subjected to 16S rRNA V1-V2 library preparation and sequencing. In total, 216 DNA and 18 control samples were included in the study. According to PERMANOVA, PCoA, Mann-Whitney and FDR tests the choice of a blood collection tube type, centrifugation type, and input volume had slight effect on the microbiota composition. While the choice of DNA extraction kit had greatest effect on bacterial composition. Bacterial profiles of samples prepared with Qiagen and MagMAX DNA extraction kit were more like each other and significantly differed from the samples prepared with the Norgen DNA extraction kit.

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P08.15

A NOVEL *CAMPYLOBACTER* SP. AND *HELICOBACTER HEPATICUS* ISOLATED FROM NILE RATS (*ARVICANTHIS NILOTICUS*)

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***Objective*:** *Campylobacter* species can cause diarrheal diseases in humans due to consuming contaminated food or close contact with infected animals. *H. hepaticus* has been linked to hepatitis, hepatocellular carcinoma, inflammatory bowel diseases, and colon cancer in certain immunodeficient and immunocompetent mice. The Nile rat, with similar nutritional correlates to humans, is used to study metabolic syndrome associated with diet-induced type 2 diabetes. To understand the microbiome composition in the gastrointestinal tract of these rats, *Helicobacter* and *Campylobacter* spp. screens were performed.

Materials and Methods: Feces from 10 rats were subjected to microaerobic culture on blood agar or antibiotic-selective agar plates. Suspected isolates were subjected to biochemical characterization and16S rRNA gene and whole genomic sequence analyses.
Results: *Campylobacter* species were isolated from 9 fecal samples. 16S rRNA sequences of all isolates were identical and shared 98% identity with *C. novaezeelandiae* isolated from birds. Virulence genes for cytolethal distending toxin (CDT) and a type VI secretion system were detected in the genomes. CDT activity was confirmed by cytotoxicity to HeLa cells. Biochemical characterization and whole genome sequence analyses indicated the isolates are a novel *Campylobacter* species most closely related to *C. cuniculorum* isolated from rabbits. To our knowledge for the first time, *H. hepaticus* was isolated from the feces of rats (5/10) and confirmed by 16S rRNA and whole genomic sequence analyses.
Conclusions: A novel *Campylobacter* species and *H. hepaticus* were isolated from Nile rats used as an animal model for diabetes. These bacteria have pathogenic and zoonotic potential and may in certain circumstances confound experimental results.

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