# Chapter 3.5.

# Gastric cancer prevention efforts in Europe (EUROHELICAN, TOGAS, and HPSS projects)

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## Summary


- Four studies are currently under way in Europe: GISTAR, EUROHELICAN, TOGAS, and HPSS. An additional study is currently in the preparatory phase under the European Joint Action on Cancer Screening (EUCanScreen).
- The GISTAR study is a multicentre randomized trial in Latvia that is focusing on *H. pylori* eradication and pepsinogen testing as methods to reduce gastric cancer mortality in middle-aged people.
- Accelerating Gastric Cancer Reduction in Europe through *H. pylori* Eradication (EUROHELICAN), supported by the EU4Health programme, is assessing the feasibility, acceptability, and effectiveness of implementing a population-based *H. pylori* screen-and-treat programme in young adults (aged 30–34 years) in Slovenia.
- The Towards Gastric Cancer Screening Implementation in the European Union (TOGAS) study, also supported by the EU4Health programme, aims to evaluate three different approaches to gastric cancer screening: (i) an *H. pylori* screen-and-treat strategy in a young population (aged 30–34 years); (ii) upper endoscopic screening in individuals undergoing colonoscopy for colorectal cancer screening or surveillance; and (iii) long-term effects of *H. pylori* eradication, in a study in the GISTAR cohort (combining *H. pylori* detection and pepsinogen assessment).
- An *H. pylori* screen-and-treat study (European implementation study on simultaneous screening for gastric and colorectal cancers) within EUCanScreen

will address the potential of screening and treatment for *H. pylori* at the time of initiating colorectal cancer screening with a faecal immunochemical test (FIT).

- The United Kingdom *H. pylori* Screening Study (HPSS) has randomized 56 000 people aged 35–69 years (men) and aged 45–69 years (women) into screen-and-treat and control groups, with follow-up until 2024.
- Preliminary results from a survey conducted by the Thomas More University of Applied Sciences, Belgium, targeting representatives of policy-making authorities, suggest overall limited willingness and readiness among Member States of the European Union and the European Economic Area to implement gastric cancer screening.

Studies in the field of gastric cancer prevention through *H. pylori* screen-and-treat strategies are under way in Europe and are presented in this chapter. Four studies are currently under way in Europe: GISTAR, EUROHELICAN, TOGAS, and HPSS. An additional study is currently in the preparatory phase under the European Joint Action on Cancer Screening (EUCanScreen).

### 3.5.1 GISTAR

The GISTAR study (Multicentric Randomized Study of *H. pylori* Eradication and Pepsinogen Testing for Prevention of Gastric Cancer Mortality; ClinicalTrials.gov ID, NCT02047994) is a multicentre randomized study of *H. pylori* eradication and pepsinogen testing for gastric cancer prevention in middle-aged people. The study is run as a collaboration between the Institute of Clinical and Preventive Medicine of the University of Latvia and IARC [1]. The primary objective of the study is to determine whether *H. pylori* eradication combined with non-invasive screening and follow-up of precancerous lesions by measuring pepsinogen levels in the circulation reduces gastric cancer mortality in high-risk populations among individuals aged 40–64 years at enrolment.

The secondary objectives include analysis of the prevalence of *H. pylori* infection in the study populations, the success rates of *H. pylori* eradication therapy, the rates of resistance of *H. pylori* to the main antibiotics used in standard therapies, the potential

adverse effects of population-based eradication (including effects on the gut microbiome), and optimization of follow-up strategies, as well as a search for new biomarkers and optimization of the use of the available ones.

The key hypotheses of the GISTAR study are that: (i) *H. pylori* eradication in middle-aged people in a high-risk population with endoscopic follow-up of individuals with evidence of atrophic gastritis prevents gastric cancer mortality; (ii) *H. pylori* eradication is effective in preventing gastric cancer mortality even after the development of gastric mucosal atrophy; (iii) certain population subgroups can derive more benefit from *H. pylori* eradication and therefore could be targeted if general population eradication is not feasible; and (iv) a combination of biomarker screening and upper endoscopy is an appropriate strategy to prevent gastric cancer mortality in high-incidence areas.

The study flow chart in Fig. 3.5.1 shows the overall design of the study.

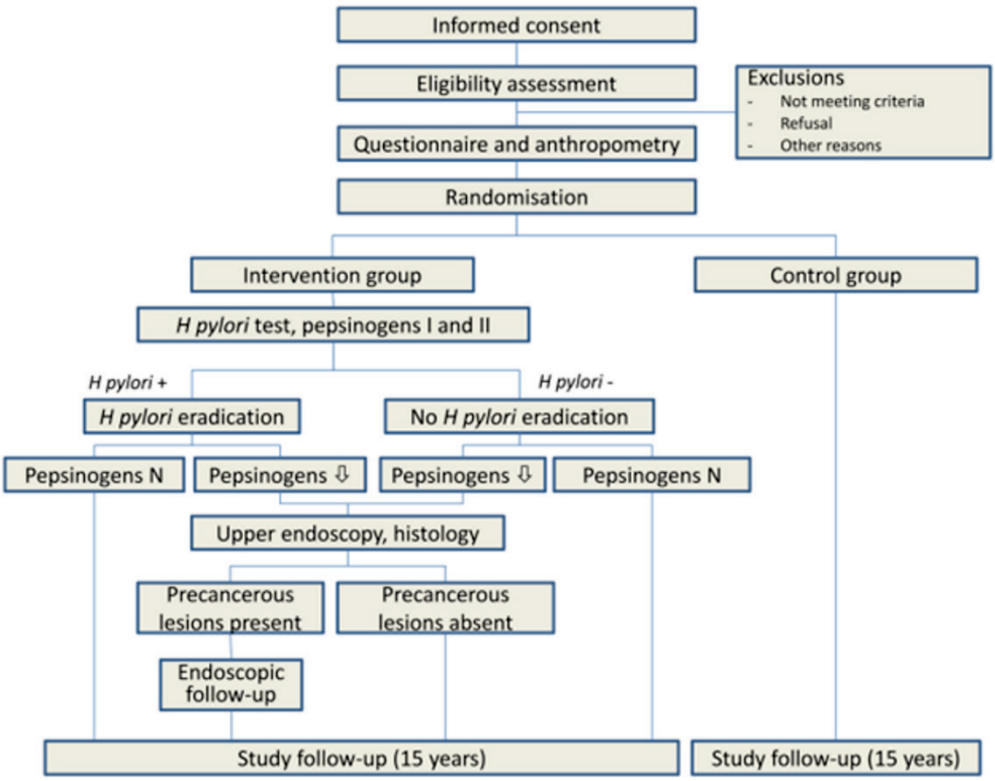


**Fig. 3.5.1.** Flow chart for the GISTAR study. Reproduced from Leja M et al. (2017) [1]. Copyright © 2017, Leja et al. Published by BMJ Publishing Group Ltd.

The recruitment centres for the main GISTAR study have been operating in regional cities and towns in Latvia. Apparently healthy, asymptomatic middle-aged participants (aged 40–64 years at recruitment) were enrolled in the study. Participants were interviewed to determine their socioeconomic status, lifestyle, environmental and occupational exposures, medical history, family history of disease, and dietary habits. Thereafter, participants were randomly assigned to either the intervention group or the control group.

The pilot study, which was designed to test the assumptions and tools, was followed by the general study. A total of 3447 participants were enrolled in the pilot study in 2013–2015; of those, 1724 were allocated to the intervention group and 1723 to the control group. Participants in the intervention group who tested positive for *H. pylori* infection (serology was used to detect the presence of the infection; whenever upper endoscopy was indicated, histology was considered as the confirmatory test) were offered *H. pylori* eradication treatment. Study participants with altered pepsinogen or gastrin-17 levels in the circulation were invited to undergo upper endoscopy. A randomly assigned subgroup with normal biomarker levels was invited to undergo upper endoscopy.

Based on the results of the pilot study, the general GISTAR protocol was modified. In particular, the primary detection method for *H. pylori* infection was changed from serology to the $^{13}$C-urea breath test (because of a relatively high proportion of false-positive serology tests), and the use of biomarkers was optimized.

The GISTAR general study was run after the pilot phase. The data from the pilot study were included in the overall GISTAR study statistics. The recruitment to the study was completed by 31 August 2023. By then, 11 223 participants had been randomized in 11 recruitment centres (these are the combined numbers for the pilot study and the general study). Of those, 344 were excluded due to several reasons; therefore, the number of study participants for the follow-up is 10 882. GISTAR study cohorts are currently being used in the EUROHELICAN study 2 and in Pilot 3 within the TOGAS project, to address the potential long-term effects of *H. pylori* eradication therapy.

### 3.5.2 EUROHELICAN

Accelerating Gastric Cancer Reduction in Europe through *H. pylori* Eradication (EUROHELICAN), an ongoing project supported by the EU4Health programme, aims to reduce the gastric cancer mortality related to chronic infection with *H. pylori*. The project consists of the following actions [2]:

- Assessment of the feasibility, acceptability, and effectiveness of implementing an *H. pylori* screen-and-treat strategy programme in young adults (aged 30–34 years) in Slovenia at the population level; this is the first time that this type of assessment has been done in Europe.
- Assessment of the potential long-term effects of previous *H. pylori* screen-and-treat programmes in a middle-aged population in Latvia.
- Analysis of two randomly selected groups of people with *H. pylori* infection, one with *H. pylori* eradicated and one with *H. pylori* not eradicated, with a follow-up of 5–10 years.
- External evaluation of the two studies conducted in Slovenia and Latvia, performed by the University Hospital of Nantes, France.
- Development of a Working Group Report, prepared by IARC, aiming to establish a set of minimum standards for the implementation and evaluation of population-based *H. pylori* screen-and-treat strategies through an expert Working Group Meeting.

The prospective non-interventional study was launched in Slovenia in 2023. This study is a joint action of the Slovenia National Institute of Public Health and the Community Healthcare Centre Dr Adolf Drolc Maribor.

The main questions that the study aims to answer are:

- Is the proposed population-based *H. pylori* screen-and-treat strategy feasible and acceptable in a community health service setting?
- Is the proposed population-based *H. pylori* screen-and-treat strategy effective in a community health service setting?

- What is the profile of adverse events in the participants who have been treated, and how does this profile relate to the results of the *H. pylori* screen-and-treat strategy and the demographic characteristics of the participants?
- What is the relationship between the living conditions during childhood reported by the participants and the results of the *H. pylori* screen-and-treat strategy?
- What is the association between alcohol consumption or use of tobacco products reported by the participants and the results of the *H. pylori* screen-and-treat strategy?

Participants ($n$ = 2000) are being randomly selected from young adults (aged 30–34 years) who are registered at the primary level of care at the Community Healthcare Centre Dr Adolf Drolc Maribor. They are tested for the presence of active infection with *H. pylori* using locally validated serology and the urea breath test (UBT) as a confirmatory test. Participants with *H. pylori* infection are offered bismuth-based quadruple therapy. Eradication of *H. pylori* infection is confirmed by the UBT at least 1 month after completion of treatment. Participants with a positive test result after the second UBT are retreated with a second-line modified bismuth-based quadruple therapy, and the success of eradication is verified with the UBT. Participants in whom two rounds of treatment have failed are referred to a gastroenterologist for susceptibility-based antibiotic therapy.

For each of the participants, compliance with testing and treatment, treatment outcomes, adverse events, and reasons for withdrawal of participation are monitored. The feasibility and sustainability of the proposed *H. pylori* screen-and-treat strategy will be evaluated using several key performance indicators that follow the structure of the five principal areas of feasibility. Several secondary participant outcomes will be also measured to provide additional evidence for and against the potential future implementation of a population-based *H. pylori* screen-and-treat programme in Slovenia.

The results of this study will enable the project to be scaled up to the national level and will serve as a model for the implementation of this strategy in the rest of Europe. The results will also contribute to the implementation of one of the goals of Europe's Beating Cancer Plan: preventing gastric cancers caused by *H. pylori* infection [3].

Finally, the real-world data from this study will be used in a Working Group Report, prepared by IARC, which will describe a set of minimum standards for the implementation of population-based *H. pylori* screen-and-treat programmes at the international level.

Interim results as of 30 September 2024 are as follows:

- Invitations sent, 4000 participants.
- Response rate, 1490 participants (37.2%).
- Exclusion criteria, 28 participants (2.1%).
- Serology, 1159 participants (147 participants positive; 12.7%).
- UBT, 54 participants (79.6% positive; 3.7% grey zone).
- Treatment started, 25 participants.
- Treatment completed, 13 participants (eradication rate, 92.3%).

The study will be enlarged by inviting other European countries to follow the same strategy as part of the TOGAS project (see Section 3.5.3) (Fig. 3.5.2).

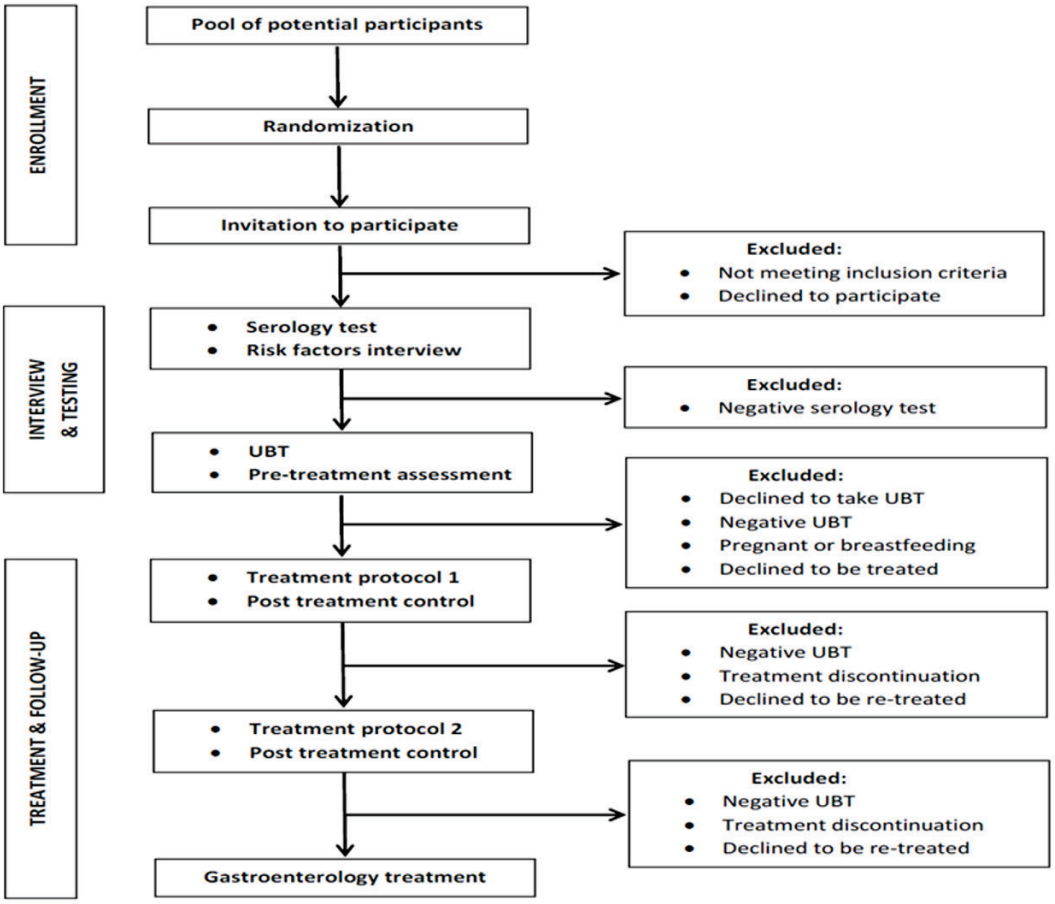


**Fig. 3.5.2.** Flow charts for the EUROHELICAN and TOGAS studies. UBT, urea breath test. Source: Tepeš et al. (2024) [4]

### 3.5.3 TOGAS

The Towards Gastric Cancer Screening Implementation in the European Union (TOGAS) project, which is also supported by the EU4Health programme, has been designed to provide the missing evidence that is needed for recommending appropriate implementation of gastric cancer screening across the European Union (EU) [5]. This includes the evaluation of various strategies that could be effective for reducing gastric cancer mortality in EU countries with varying burdens of gastric cancer and varying prevalence of *H. pylori* infection.

The results from this project will aid policy-makers in incorporating gastric cancer screening into their health-care priorities while balancing its effectiveness, feasibility, and acceptability with potential long-term adverse effects.

To achieve the set goals and generate additional information to fill the gaps in knowledge and understand the unmet needs for gastric cancer prevention, the following specific objectives have been designed:

- Assess the current situation and needs in EU Member States and target populations in the area of gastric cancer prevention.
- Assess the appropriateness of various gastric cancer screening modalities for use in the EU.
- Ensure that the TOGAS results are sustainable by using an effective dissemination strategy and coordinating the methodology with approaches used in the EU. This will involve gathering not only important data from the field studies but also critical information from the decision-makers, other stakeholders, and target populations. Furthermore, cost–effectiveness modelling of intervention strategies to reduce gastric cancer-related mortality will be performed to guide the decision-makers on the most appropriate and cost-effective strategy.

### *TOGAS pilot studies*

Each of the pilot studies addresses a different aspect of gastric cancer prevention:

- Pilot 1: *H. pylori* screen-and-treat strategy in a young population in six EU countries.
- Pilot 2: Possibility of detection of gastric precancerous lesions and *H. pylori* infection by adding a systematic upper digestive endoscopy to screening upper endoscopies in individuals undergoing colonoscopy (in people aged 50–74 years) within colorectal cancer screening programmes or for surveillance in seven EU countries.
- Pilot 3: Assessment of potential long-term effects of *H. pylori* eradication therapy (using data from the GISTAR cohort).

Fig. 3.5.3 shows the design of the TOGAS pilot studies.

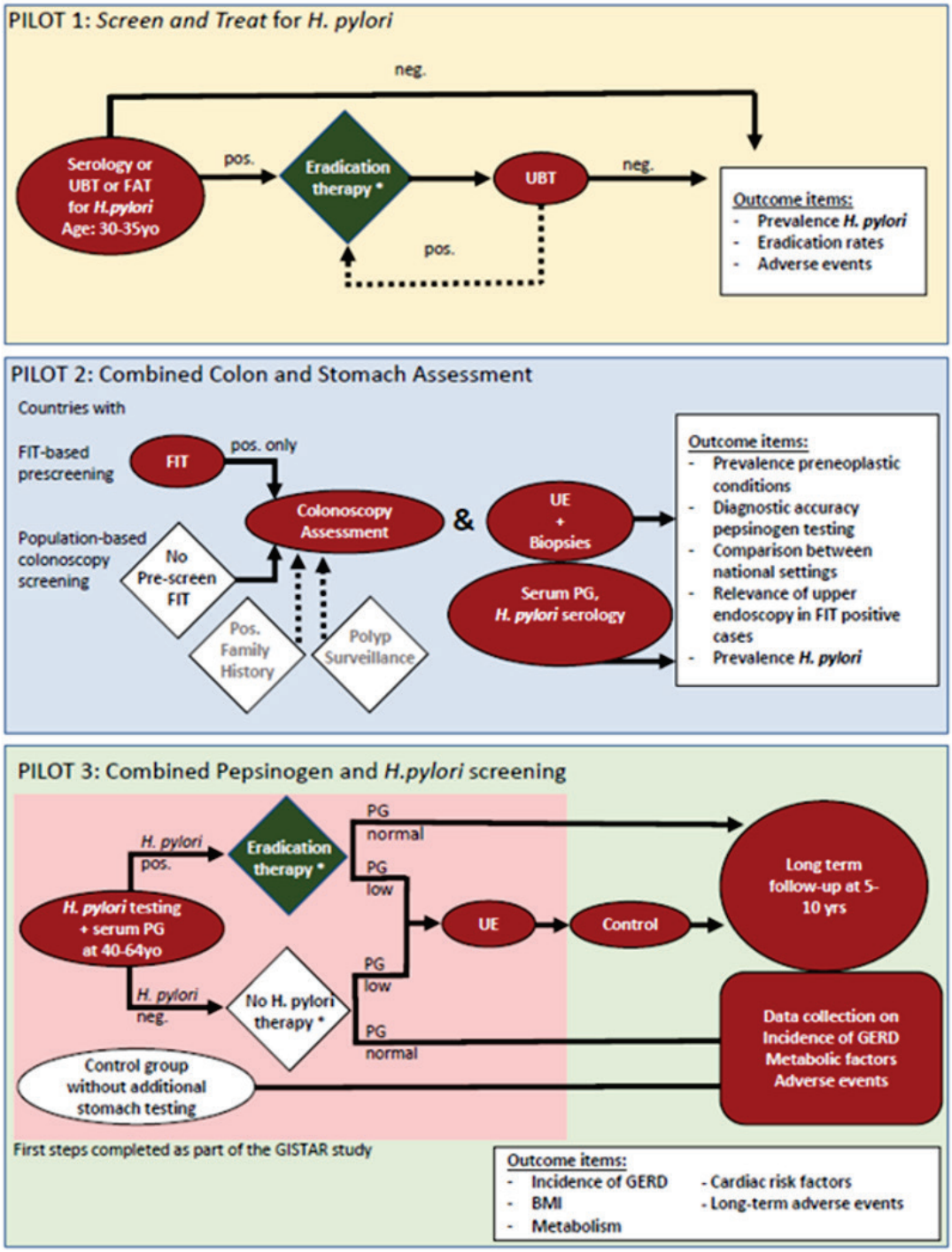


**Fig. 3.5.3.** TOGAS pilot studies. BMI, body mass index; FAT, faecal antigen test; FIT, faecal immunochemical test; GERD, gastro-oesophageal reflux disease; neg., negative; PG, pepsinogen; pos. positive; UBT, urea breath test; UE, upper endoscopy; yo, years old. Source: European Commission (2024) [6].

### *Pilot 1:* H. pylori *screen-and-treat strategy in a young population in six EU countries*

In 2024, a prospective non-interventional population screen-and-treat study for *H. pylori* eradication as a method of primary prevention of gastric cancer was launched in six EU countries (Croatia, Ireland, Latvia, Poland, Romania, and Slovenia). A total of 13 600 randomly selected members of the population, aged 30–34 years, will be invited to participate in the study, with the aim of reaching at least 6800 study participants. This study is coordinated by the Slovenia National Institute of Public Health and uses the same protocol as the EUROHELICAN study (Fig. 3.5.2). Some centres are using serology and a confirmatory UBT as the method of *H. pylori* detection; in some other centres, the UBT is used only as the primary test. The first-line treatment is offered according to the local recommendations, mainly 14-day bismuth-based quadruple therapy or 10-day single-capsule bismuth, metronidazole, and tetracycline combination therapy; 14-day clarithromycin-based triple therapy is also used in some centres.

### *Pilot 2: Combined colon and stomach assessments*

Screening for *H. pylori* infection and associated gastric lesions during upper digestive endoscopy performed in combination with screening colonoscopy is being addressed in Pilot 2. It is expected to include a total of 1600 participants in seven centres in Germany, France, Ireland, the Netherlands, Latvia, Lithuania, and Portugal.

Individuals presenting for screening or surveillance colonoscopy, including individuals with a positive faecal occult blood test (FOBT) or faecal immunochemical test (FIT) result, are invited to undergo a screening oesophago-gastro-duodenoscopy (OGD) in the same session. Patients who are undergoing colonoscopy for symptom investigation, individuals with genetic cancer syndromes, or people who have undergone an OGD within the past 3 years are excluded. The study protocol includes high standard operating procedures for OGD, such as the use of virtual chromoendoscopy, gastric biopsy sampling, imaging, and reporting, as well as histopathology assessment and serology testing.

The primary end-point of this study is the detection of gastric cancer or gastric pre-neoplastic lesions or conditions that need endoscopic surveillance or further therapy as defined by national and international guidelines. The secondary end-points include assessing the quality of the endoscopy, assessing the endoscopist's performance in

detecting other relevant gastric lesions, and identifying oesophageal or duodenal conditions.

On the day of the procedure, blood samples are obtained for the analysis of serum pepsinogens and *H. pylori* serology in order to provide input on the yield of serological screening for gastric lesions at the time of a screening colonoscopy, including the sensitivity, the specificity, and the area under the curve (AUC) of pepsinogens for the detection of advanced gastric precancerous lesions.

#### *Pilot 3: Combined pepsinogen and* H. pylori *screening*

Assessment of potential long-term effects is performed in participants who have been treated with *H. pylori* eradication therapy 5–10 years previously, and comparisons will be made with a matched group of study participants who have not been offered eradication treatment (i.e. participants recruited in the GISTAR cohort). Major concerns about negative effects of the eradication will be addressed, including potential increase in gastro-oesophageal reflux disease, negative metabolic effects (including increase in body weight), and laboratory parameters of cardiovascular risk patterns.

A total of 3000 study participants are expected to be recruited, and matched analyses with the data that were initially reported will be conducted.

### *European countries' willingness and readiness to implement gastric cancer screening*

The TOGAS project aims to provide the knowledge needed to design and implement an effective gastric cancer prevention strategy in the EU. The results of this project will help policy-makers to incorporate gastric cancer screening into their cancer control strategies.

A European Commission report, *Cancer screening in the European Union*, prepared by the European Commission's Group of Chief Scientific Advisors, recommended that "the countries with the highest gastric cancer incidence and death rates should consider screening for *H. pylori*" [7]. Researchers from the Thomas More University of Applied Sciences, Belgium, in collaboration with partners from the TOGAS consortium, have evaluated the willingness and readiness of Member States to implement gastric cancer screening.

### *Methods*

The willingness and readiness of Member States to implement gastric cancer screening were evaluated using an online survey, conducted in English. The survey targeted representatives of policy-making authorities in the Member States of the EU and the European Economic Area (EEA).

Invitations to participate were distributed in the newsletter of the European Commission Joint Research Centre, in emails to participants in the EUCanScreen project, and in announcements made during EU SANTE Working Group meetings. Given the specialized nature of the survey and the limited number of people capable of answering all the questions, reaching the target audience was challenging.

The survey was open from 29 February 2024 to 10 January 2025 and included questions on the following topics:

- Current practices with respect to gastric cancer screening [see Note 1 in Box 3.5.1].
- Plans for implementing a gastric cancer screening programme, the reasons for doing so, and the perceived desirability and feasibility of implementation [see Note 2 in Box 3.5.1].
- Availability of and reimbursement of costs for diagnostic tools and therapeutic options to reduce gastric cancer incidence, and medications used in regimens for *H. pylori* eradication [see Note 3 in Box 3.5.1].
- Readiness of the health-care system to implement gastric cancer screening [see Note 4 in Box 3.5.1].

A total of 27 policy advisers, legal advisers, medical professionals, and public health professionals from 19 Member States have completed the survey. The survey respondents represent ministries of health, cancer screening authorities, and other authorities with similar responsibilities [see Note 5 in Box 3.5.1].

### *Outcomes*

- Currently, no EU or EEA Member State has a population-based gastric cancer screening programme [see Note 6 in Box 3.5.1]. Of 39 respondents from 16

Member States, 25 indicated that policy-makers in their country are not considering implementing such a programme.

- According to respondents from Belgium, Ireland, Latvia, Lithuania, and Portugal, there is an ongoing debate about the implementation of a gastric cancer screening programme [see Note 7 in Box 3.5.1].
- Respondents from Croatia, Italy, Lithuania, Portugal, and Slovenia deemed implementation of gastric cancer screening both desirable and feasible. The respondent from Greece found it desirable but not feasible, and the respondents from France and Ireland found it feasible but not desirable. The most common reason cited for finding screening undesirable was "gastric cancer is not a major problem in my country". The primary reason for considering screening unfeasible was "limited resources and higher priority for other cancer screening programmes".
- The most highly rated factors influencing the decision to implement gastric cancer screening include the gastric cancer incidence rate, the impact on mortality and incidence rates, and cost–effectiveness [see Note 8 in Box 3.5.1].
- In most responding countries, the diagnostic tools and therapeutic options to reduce gastric cancer incidence and the medications used in regimens for *H. pylori* eradication are available and the costs are reimbursed.
- According to the respondents, 14 Member States have guidelines for *H. pylori* eradication medications, and 6 have a policy or guideline for gastric cancer screening in high-risk groups or in patients with precancerous lesions [8].

**Box 3.5.1. Notes**

Note 1. The following questions were posed:

"Does your country or region currently have a gastric cancer screening programme?", followed by questions on the screening method used, the target group, the frequency, and available documentation.

"Does your country or region have a policy or guideline for gastric cancer screening in high-risk groups or surveillance of patients with precancerous lesions?", with among others the answer categories "Yes, surveillance of high-risk individuals (e.g.

family members of patients with precancerous lesions)" and "Yes, screening of high-risk individuals (e.g. family members of patients with gastric cancer)". This question was followed by questions on available documentation, method, target group, etc.

Note 2. The following questions were posed:

"Are policy-makers in your country considering implementing a population-based gastric cancer screening programme?", followed by a question on the screening method being considered to be used.

"Listed below are factors which might play a role in the decision to implement a gastric cancer screening policy or programme in your country or region. Please indicate the importance of each factor on a scale from 1 (not important at all) to 10 (very important)."

"Taking into account the importance of the factors related to gastric cancer screening in your country or region, do policy-makers in your country or region consider the implementation of a gastric cancer screening programme desirable?", followed by a question in which "desirable" was replaced by "feasible". Respondents who answered that the implementation of gastric cancer screening was not desirable or feasible were asked about the reasons why they think so.

Note 3. The following questions were posed:

"This question is about the availability of diagnostic tools and therapeutic options. Listed below are the diagnostic tools and therapeutic options to reduce gastric cancer incidence. Please indicate whether or not they are available for routine practice in your country or region."

For each of the available tools and options, a follow-up question on availability was posed. The same questions were asked for "medications used in regimens for *H. pylori* eradication". Included diagnostic tools and therapeutic options: upper gastrointestinal endoscopy, biopsy histology taken during upper gastrointestinal endoscopy, rapid urease test if taken during upper gastrointestinal endoscopy, antibiotic sensitivity testing for *H. pylori*, sedation (e.g. propofol deep sedation) during upper gastrointestinal endoscopy, blood test for pepsinogen I and pepsinogen II detection, upper gastrointestinal series (X-ray), C-urea breath test (UBT), *H. pylori* stool antigen test (SAT), *H. pylori* IgG group antibody detection in blood, medication

for *H. pylori* eradication (first-line therapy), and medication for *H. pylori* eradication (second-line therapy). Included medications: bismuth (e.g. subcitrate, subsalicylate), tetracycline (e.g. hydrochloride), combined bismuth–tetracycline–metronidazole capsule (e.g. Pylera), clarithromycin, amoxicillin, metronidazole, levofloxacin, rifamycins (e.g. rifampicin, rifabutin), and potassium-competitive acid blockers (P-CABs) (e.g. vonoprazan).

Note 4. The readiness of the health-care system was measured by posing questions on the existence of a governance structure dedicated to cancer screening programmes, a central IT platform for cancer screening data, funding, upper gastrointestinal endoscopy capacity, *H. pylori* eradication guidelines, etc.

Note 5. The survey was completed by 19 public health professionals, 13 policy advisers, 8 medical professionals, 2 researchers, 1 manager, and 4 professionals combining two of these functions; 22 respondents answered on behalf of a cancer screening authority, 15 on behalf of a ministry of health, 1 on behalf of both, and 9 on behalf of other relevant authorities. Complete responses were received from Belgium, Croatia, Czechia, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, the Netherlands, Portugal, Romania, Slovakia, Slovenia, and Spain. Incomplete responses were received from Austria, Denmark, and Hungary.

Note 6. A respondent from Denmark did indicate that Denmark does have a population-based gastric cancer screening programme. However, this was contested by the TOGAS consortium members who reviewed the report.

Note 7. Respondents from Italy (Marche Region), Latvia, and Slovenia indicated that the decision to start a pilot population-based gastric cancer screening programme has been made.

Note 8. Other answer categories were: diagnostic yield of current screening methods, gastric cancer mortality rate, expected adherence rate, costs of the programme, availability of resources in the health-care system such as human resources and infrastructure, number of short-term adverse events, number of long-term adverse events, number of late-stage diagnoses, and *H. pylori* prevalence.

*Source:* Compiled from Takens et al. (2025) [8].

### *Discussion*

The results suggest limited willingness of EU and EEA Member States to implement gastric cancer screening. However, the Member States expressing interest in the implementation of screening tend to have a relatively high incidence of gastric cancer. This aligns with the recommendation that “the countries with the highest gastric cancer incidence and death rates should consider screening for *H. pylori*” [7].

Health-care systems in the surveyed Member States generally seem prepared to support the implementation of gastric cancer screening. However, certain components of the health-care infrastructure present challenges to widespread implementation. Future efforts should focus on addressing these hurdles to facilitate the adoption of effective

## *TOGAS general population survey*

Initial insights into the willingness of European citizens to participate in gastric cancer screening were gathered from a general population survey conducted in 19 countries as part of the TOGAS project.

Currently, no effective screening method to prevent gastric cancer is available in Europe. Screening programmes depend on uptake. Therefore, before designing a gastric cancer screening programme, it is important to understand the willingness of the general population to participate and to understand any specific barriers or motivators to participation in screening. Surveys and preference studies for cancer screening programmes have previously been used to understand how such programmes can be optimized to maximize uptake. Digestive Cancers Europe, a TOGAS consortium member, designed and commissioned an online survey in 19 EU Member States to fulfil these objectives.

### *Methods*

The willingness of citizens to participate in gastric cancer screening was evaluated using an online survey. The survey was conducted in 19 EU Member States among members of the general population aged 18–70 years in the local language of each country. The data were collected between February and July 2024 and were subsequently analysed at the Thomas More University of Applied Sciences, Belgium. There were at least 1000

respondents from each Member State; the number ranged from 1039 in Austria to 1123 in Poland. The data were weighted to achieve representativeness for age and sex.

The survey contained questions about various topics, including:

- knowledge about gastric cancer and gastric cancer testing;
- motivators and barriers to participation in screening;
- perceptions of different methods of gastric cancer screening; and
- attitudes towards *H. pylori* bacterial infection screening.

### *Preliminary outcomes*

Awareness:

- Fewer than one third (31%) of respondents were aware of the risk factors for gastric cancer; country responses ranged from 20% in Belgium to 52% in Romania.
- Fewer than one quarter (24%) of respondents were aware of the symptoms of gastric cancer; country responses ranged from 17% in Belgium to 35% in Romania.
- Only 4% of respondents were familiar with the procedures involved for testing for risk of gastric cancer; a further 18% said they know a little about the procedures involved.

Motivators and barriers to participation in gastric cancer testing:

- The two main reasons that would motivate people to participate in gastric cancer testing were “being advised by their health-care provider to take part in testing” (47%) and “having symptoms that might indicate gastric cancer” (46%).
- The motivations differed significantly across countries. For example, whereas 68% of respondents in Slovenia said that being advised by their health-care provider to take part in testing would motivate them to do so, only 17% of respondents in Romania said the same.
- The two most important reasons that would prevent people from participating in gastric cancer testing were “concern about the possible discomfort associated with testing” (27%) and “financial constraints” (26%).

- In most Member States, “concern about the possible discomfort associated with testing” was the main barrier to participation. In Finland, Latvia, Poland, and Romania, “financial constraints” were the biggest barrier.

Perceived level of comfort of different screening methods:

- More than half (52%) of respondents expected a biopsy to be uncomfortable or very uncomfortable. The percentage of respondents who thought a biopsy would be uncomfortable was the highest in Croatia, at 64%, and the lowest in Germany, at 46%.
- Respondents were even more concerned about upper endoscopy. Most respondents (63%) expected an upper endoscopy to be uncomfortable or very uncomfortable. The percentage of respondents who thought an upper endoscopy would be uncomfortable was the highest in Finland, at 79%, and the lowest in Germany, at 53%.

Willingness to undergo gastric cancer testing:

- Overall, 57% of respondents said they would be willing to participate in gastric cancer testing, based on the information they had read.
- There were significant differences between certain countries. Respondents in Ireland showed the greatest willingness to undergo testing; 71% said they would, and only 8% said they would not. At the other end of the scale, in Hungary only 41% of respondents said they would be willing to undergo gastric cancer testing, and almost one quarter (24%) of respondents said they would not.
- By far the main reason people would be willing to participate in screening is that they would want to know if they had gastric cancer; 75% of respondents agreed with this.
- Of those respondents who said they were unwilling to undergo gastric cancer screening, the main reason was concern about the procedures being too invasive or uncomfortable; 46% of respondents agreed with this. In Croatia, this percentage was 62%. Other cited reasons included people trusting in their health and being convinced they do not have gastric cancer (21%) and not wanting to know if they had gastric cancer (15%).

Willingness to undergo *H. pylori* testing:

- Overall, 72% of respondents said they would be willing to undergo *H. pylori* testing, based on the information they had read. The willingness to participate varied from 61% in Hungary to 79% in Portugal.
- The main reason people would be willing to participate in *H. pylori* testing is to know whether they have an *H. pylori* infection; 70% of respondents agreed with this.
- Of those respondents who said they were unwilling to undergo *H. pylori* testing, the main reasons were concerns about the procedure being too invasive or uncomfortable (21%), being convinced they do not have an *H. pylori* infection (20%), and not wanting to know if they do (19%).

Overall willingness to participate in gastric cancer screening:

- After completing the survey and reading the information associated with it, 64% of respondents said they would be willing to participate in a gastric cancer screening programme; 11% said they would not, and 25% said they do not know. The willingness to participate varied from 54% in the Netherlands to 77% in Ireland.

### *Discussion*

The preliminary results suggest that most citizens would be willing to participate in gastric cancer screening and *H. pylori* testing, once they understand what is involved. However, there is a substantial minority who say they would not participate or are undecided. In addition, current levels of awareness – of gastric cancer risk factors and symptoms and of gastric cancer screening – are relatively low. This reinforces the need for awareness campaigns and education to encourage widespread uptake of gastric cancer screening.

The barriers to participation appear to be more pronounced in certain countries. For example, in Hungary, nearly one quarter (24%) of respondents said they were unwilling to undergo gastric cancer testing. More research may be needed to understand the perceptions and beliefs of people in different countries to help overcome specific national barriers.

Concern about the possible discomfort of testing is a key barrier to participation; respondents were concerned about the uncomfortable nature of biopsy and, in particular, of upper endoscopy. This finding aligns with research in countries where gastric cancer screening is already in place, where concern about endoscopy appears to be a key barrier to participation. For example, in a study in China only 56.2% of respondents stated that they would schedule an endoscopy if they had symptoms; the main concern was pain and other discomfort associated with the procedure [9]. Understandably, very few people are currently aware of what gastric cancer testing entails. Education about the procedure and what to expect will need to be a significant focus in the rollout of gastric cancer screening in the EU. As always, health-care providers have an essential role in advising and educating their patients who are at the relevant age.

Concern about financial constraints is also a substantial barrier to participation, particularly in Finland, Latvia, Poland, and Romania. Reassurances that screening will be free at the point of delivery will need to be emphasized, reducing financial barriers.

In general, EU populations appear to be prepared to participate in gastric cancer screening, but there are clear barriers to uptake that will need to be addressed proactively through educational and awareness initiatives.

### 3.5.4 HPSS

One trial that is currently in progress is the United Kingdom *H. pylori* Screening Study (HPSS). This trial addresses the question “Does *H. pylori* screening and the treatment of individuals with positive test results prevent gastric cancer, and if so, to what extent?” The eradication treatment used in this trial was 30 mg of lansoprazole, 400 mg of metronidazole, and 250 mg of clarithromycin, all taken twice a day for 7 days. The trial was funded by the Cancer Research Campaign (now part of Cancer Research UK) and the British United Provident Association (BUPA) Foundation. In 1997–2006, 56 000 people aged 35–69 years (men) and aged 45–69 years (women) were randomized by week of attendance at one of 10 well-person screening clinics held by BUPA. All participants had to be United Kingdom residents and had to be registered with a National Health Service general practitioner, to enable their National Health Service records to be flagged so that automatic notifications would be sent to the study centre in the event of cancer registration or death.

Participants were randomly allocated, by week of attendance, to a screen-and-treat group or a control group. The standard analysis method for this study would be to compare the number of gastric cancer cases in the screened group and the control group, but the study protocol specified a more powerful statistical analysis. Because there is no expectation of an effect of treatment in *H. pylori*-negative participants, these participants can be ignored and the incidence of gastric cancer will be compared in the *H. pylori*-positive participants in the two randomized arms. Thus, the primary analysis for the trial will compare individuals in the treated and control arms who tested positive for *H. pylori* infection in the blood sample they provided at the time of randomization and who developed gastric cancer.

More detailed information about the trial design is provided in Chapter 4.5 (subsection 3) of IARC Working Group Report No. 8 [10]. It is anticipated that cancer registrations and death certifications in trial participants will be accrued until December 2024 and that analyses will be completed during 2025.

### 3.5.5 Future directions

There is an evidence gap between international recommendations and real data from application studies. Studies in the field of gastric cancer prevention through *H. pylori* screen-and-treat strategies are under way in Europe and are presented in this chapter. Certain aspects need to be addressed in studies to be planned for the future.

The optimal age for *H. pylori* screen-and-treat interventions should be still determined. The ongoing studies have suggested that the participation rate could be suboptimal in the young age group; however, a subfraction of individuals may have passed the “point of no return” by the age they are eligible for colorectal screening.

The potential combination of an *H. pylori* screen-and-treat strategy with colorectal cancer screening programmes, in particular with FIT screening, should be analysed for the implementation possibilities in Europe. Pilot 2 within the TOGAS project will address the prevalence of high-risk precancerous lesions at the time that the target population for colorectal cancer screening are undergoing colonoscopy. The possibility of combining FIT with *H. pylori* stool antigen testing will be further

addressed in a study (European implementation study on simultaneous screening for gastric and colorectal cancers) within EUCanScreen.

The risk of inducing an increased long-term gut resistome with *H. pylori* eradication regimens still needs to be addressed and monitored. Furthermore, the effects of an *H. pylori* screen-and-treat strategy on gastric cancer mortality as well as overall mortality need to be monitored; realistically, this could be done within implementation studies.

Public awareness campaigns about *H. pylori* infection and related diseases, especially gastric cancer, are needed, because knowledge among important stakeholders is still limited. The studies that are in progress in Europe can contribute some valuable data that can help in the organization and implementation of future national *H. pylori* screen-and-treat programmes. These programmes should be organized as cancer screening programmes [11] with a programme council and a steering committee at the national level and a network of primary care medical and laboratory facilities. A central data capture system should be provided for the assessment of quality indicators and programme monitoring.

In summary, implementation studies would be important to monitor effects and potential risks of population-based *H. pylori* screen-and-treat strategies.

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