Factor analysis of the Rome IV criteria for major disorders of gut-brain interaction (DGBI) globally and across geographical, sex and age groups

Jóhann P. Hreinsson, MD, PhD, Hans Törnblom, MD, PhD, Jan Tack, MD, PhD, Douglas A. Drossman, MD, PhD, William E. Whitehead, PhD, Shrikant I. Bangdiwala, PhD, Ami D. Sperber, MD, MSPH, Olafur S. Palsson, PsyD, Magnus Simrén, MD, PhD

PII: S0016-5085(23)00219-6
DOI: https://doi.org/10.1053/j.gastro.2023.02.033
Reference: YGAST 65581

To appear in: *Gastroenterology*
Accepted Date: 15 February 2023

Please cite this article as: Hreinsson JP, Törnblom H, Tack J, Drossman DA, Whitehead WE, Bangdiwala SI, Sperber AD, Palsson OS, Simrén M, Factor analysis of the Rome IV criteria for major disorders of gut-brain interaction (DGBI) globally and across geographical, sex and age groups, *Gastroenterology* (2023), doi: https://doi.org/10.1053/j.gastro.2023.02.033.

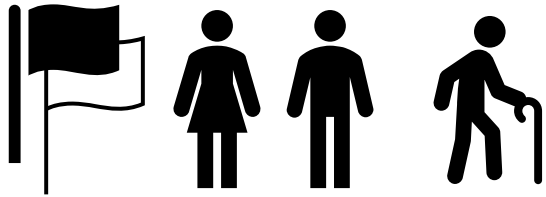
A **worldwide** survey to validate the **Rome IV criteria** on Disorders of the gut-brain interaction (DGBI)

GI symptom
GI symptom
GI symptom
GI symptom

DGBI

Factor analysis identifies clusters of GI symptoms, these clusters can represent DGBI

The Rome IV criteria were found to be valid for major DGBI across geographical regions, sex and age groups



Gastroenterology

Factor analysis of the Rome IV criteria for major disorders of gut-brain interaction (DGBI) globally and across geographical, sex and age groups

Short title: Factor analysis validates Rome criteria

Authors: Jóhann P. Hreinsson MD, PhD[1], Hans Törnblom MD, PhD[1], Jan Tack MD, PhD[1,2], Douglas A. Drossman MD, PhD[3], William E. Whitehead PhD[3], Shrikant I. Bangdiwala PhD[4,5], Ami D. Sperber MD, MSPH[6], Olafur S. Palsson PsyD[3], Magnus Simrén MD, PhD[1,3]

[1]Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.

[2]Translational Research Center for Gastrointestinal Disorders (TARGID), Department of Chronic Diseases and Metabolism (CHROMETA), KU Leuven, Leuven, Belgium

[3]Center for Functional Gastrointestinal and Motility Disorders, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

[4]Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, Ontario, Canada

[5]Population Health Research Institute, McMaster University, Hamilton, Ontario, Canada

[6]Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel

Grant support: This study was conducted under the auspices of the Rome Foundation.

Correspondence: Jóhann P. Hreinsson, Sahlgrenska University Hospital, Blå Stråket 5, postal code 41345, Gothenburg, Sweden. Email: hreinssonjp@gmail.com. Tel: +46722224033.

Disclosures: HT reports honoraria for lectures from Biocodex, Galapagos, Takeda, Tillotts, outside the submitted manuscript. OP reports support from the Rome foundation; and grants from NIH & NIMH, Royal DSM, outside the submitted manuscript; licence for metaMe Health; honoraria for lectures from Rome foundation, payment for expert testimonies from iHealth, support for attending meetings from Rome Foundation, stock in metaMe health. MS reports grant support from the Swedish state under the agreement between the Swedish government and the county councils, the ALF-agreement (ALFGBG-965173), the Swedish Research Council (2021-00947), and the Erling-Persson Foundation; and consulting fees from Danone Nutricia Research, Ironwood, Menarini, Biocodex, Genetic Analysis AS, DSM, Tillotts, Takeda, Arena, Kyowa Kirin, Adnovate, BioGaia and Pharmanovia, outside the submitted work, and honoraria for from Tillotts, Menarini, Kyowa Kirin, Takeda, Biocodex, AlfaSigma, Sanofi, Janssen Immunology, Pfizer, Ferrer, BioGaia and Falk Foundation, outside the submitted work. JPH, JT, DAD, WEW, SIB and ADS have no disclosures to declare related to this manuscript.

Authors' contributions

All authors took part in conceptualization and methodology of the study. JPH analyzed the data and drafted the manuscript. All other authors took part in interpreting the data and provided critical revision of the manuscript.

Data accessibility statement

The source datasets are available from the Rome Foundation for analyses under data use agreements for approved analysis and publication projects.

Abstract

Background & Aims: The Rome criteria are widely accepted for diagnosing disorders of gut-brain interaction (DGBI), but their global applicability has been debated. This study aimed to evaluate the validity of the Rome IV criteria by factor analysis globally, across geographical regions, by sex, and by age groups.

Methods: Data were collected in 26 countries using the Rome IV questionnaire. Forty-nine ordinal variables were used in exploratory factor analysis (EFA) to identify clusters of inter-correlated variables (factors) within the data set. Confirmatory factor analysis with predefined factors of the DGBI was compared to the factors in the EFA. Analyses were performed globally, for each geographical region, (North and Latin America, Western and Eastern Europe, Middle East, Asia), sex, and age groups (18-34, 35-49, 50-64, ≥65).

Results: 54,127 people were included. The EFA identified ten factors accounting for 57% of the variance: IBS, constipation, diarrhea, upper GI symptoms, globus, regurgitation/retching, chest pain, nausea/vomiting and two right upper quadrant pain factors. Most factors had close correspondence to a Rome IV criteria diagnosis, but notably, functional dysphagia and heartburn symptoms were often included in the same factor and/or in upper GI symptoms. Most factors were consistent across geographical regions, sex, and age groups, and compatible to the global results. All prespecified factors in the confirmatory analysis had a loading ≥0.4, indicating validity of the Rome IV criteria.

Conclusions: The results indicate that the Rome IV criteria for IBS, functional dyspepsia, functional constipation, globus and biliary pain are globally valid and represent universal diagnostic entities that are similar across sex and age groups.

Keywords: Functional gastrointestinal diseases.

Introduction

The Rome criteria are widely accepted as the main method for defining and diagnosing disorders of gut-brain interaction (DGBI), previously known as functional gastrointestinal (GI) disorders. These criteria, the most recent being the Rome IV criteria, are based on single symptoms or combination of symptoms within anatomical regions.[1]

The Rome criteria have been criticized for largely being based on expert opinion and lacking rigorous validation data.[2,3] One way of validating the Rome criteria in a data-driven manner is through factor analysis. Factor analysis is a statistical method that identifies potentially meaningful clusters of inter-correlated variables (factors) within a data set (*i.e.*, that tend to occur together), and these factors can then be labelled based on the common theme or significance of the items they contain.

Previous factor analyses have revealed symptom factors that show good conformity with the Rome I and II criteria for several DGBI.[4-6] More recently, analysis of population-based survey data from the USA, UK and Canada identified eight factors within the data set, six of which corresponded well to the Rome IV definitions of globus, functional heartburn, IBS, functional constipation, functional diarrhea, and chronic nausea and vomiting syndrome. The remaining two factors corresponded to the broader categories of gastroduodenal disorders and centrally mediated disorders of pain in the Rome IV criteria.[7]

Another recent study from the Rome Foundation Asian working team that included patients in several Asian countries, found several factors compatible with specific Rome IV diagnoses, but also reported two factors containing gas symptoms and meal-related bowel symptoms incompatible with the existing Rome IV diagnoses.[3] The validity of the Rome criteria has since then been debated[8,9] and their global validity questioned, which is reasonable as populations can vary significantly, including differences in sociocultural aspects and diet in Western countries and Asia.

Recently, a global population-based survey using the Rome IV questionnaire was undertaken.[10] This study electronically collected data from 26 countries in 6 geographical regions, which allows for detailed study of the validity of the Rome IV criteria and possible confirmation of the global existence in the general population of DGBI that correspond to the criteria.

Hence, the primary aims of the present analyses were to study the validity of the Rome IV criteria by factor analysis using a large set of data from a global population, and to compare their validity across geographical regions, as well as sex and age groups.

Methods

Study setting and participants

Data from the Rome Foundation Global Epidemiology Study (RFGES) were used in the current study, the methodology of which has previously been described in detail elsewhere.[10] Briefly, it was a survey study that included 33 countries, and for 26 of these countries the data were collected via the internet. In those 26 countries, participants were recruited on a nationwide basis by a large market research company (Qualtrics, LLC, Provo, UT, USA). The online surveys had built-in quality-assurance measures that ensured high-quality response sets without missing data, including attention-check questions, a speed-check, and response inconsistency assessment. In the remaining seven countries data were collected by personal interview as a household survey. A previous analysis has shown that prevalence rates of DGBI were lower for these countries when compared to countries surveyed via the internet, possibly due to individuals being less prone to answer sensitive questions included in the questionnaire.[10] Additionally, in contrast to the internet surveys, missing data was an issue in the household surveys. Therefore, these seven countries were excluded from the analysis to make the included sample more homogenous. Demographic parameters were predefined and controlled with quotas, including equal sex proportion, and age group proportions of 40% for 18 to 39 years, 40% for 40 to 64 years, and 20% for ≥65 years.

Variables and definitions

Data from the survey included information on age, sex, country, and answers to the Rome IV diagnostic questionnaire, an extensive gastrointestinal symptom questionnaire that contains 26 to 86 items depending on skip patterns (answering yes to certain questions prompts follow-up questions).[11]

For the current analysis, geographical regions were defined as: *North America* – Canada and the United States of America; *Latin America* - Argentina, Brazil, Mexico and Colombia; *Western Europe* - Belgium, France, Germany, Netherlands, Italy, Spain, Sweden and the United Kingdom; *Eastern Europe* - Poland, Romania, and Russia; *Middle East* - Egypt, Israel, and Turkey; *Asia* - China, Japan, South Korea, and Singapore. Two additional

countries, Australia and South Africa, which could not be included in any of the above-mentions regions, were included in the global factor analysis.

Statistical analysis

To assess the validity of the Rome IV criteria in a data-driven manner, factor analysis was utilized. Only the ordinal items of the Rome IV questionnaire were used in the analysis as categorical variables are not eligible in factor analysis. These items, which represent self-reported frequency or characteristics of different gastrointestinal symptoms on either a 9- or 11-point Likert scale, are listed in Table 1. The item names in the table are shortened versions of the full Rome IV diagnostic questionnaire questions.[11]

First, all 49 gastrointestinal symptom items were used in an exploratory factor analysis (Table 1). Second, pre-specified factors that consisted of items belonging to certain diagnoses within the Rome IV criteria were used in confirmatory factor analysis. These pre-specified factors are based on DGBI defined in the Rome IV criteria by two or more items in the Rome IV questionnaire and are thereby eligible for factor analysis. The DGBI based on two or more items are globus, functional heartburn, functional dysphagia, functional dyspepsia, chronic nausea and vomiting syndrome, IBS, functional constipation, and biliary pain. The pre-specified factors are described in Table 1. The purpose of these analyses was to identify factors that consist of highly inter-correlated Rome IV questionnaire items in the exploratory factor analysis, and then compare these factors to the pre-specified factors used in the confirmatory factor analysis. Similarity between the factors in the exploratory and confirmatory factor analysis would indicate validity of the Rome IV criteria. Furthermore, the exploratory and confirmatory analysis were compared by root mean square error of approximation (RMSEA), with similar values indicating similar model fit, *i.e.*, how well it explains the data.

To assess whether the results from the global analysis were similar irrespective of geographical region, sex and age, the analysis was repeated across geographical regions, sex, and age categories (18-34, 35-49, 50-64 and ≥65 years). The results were compared to the global analysis by examining how well the factors corresponded to the ones identified in the global analysis, and by comparing the RMSEA from these sub-analyses to the RMSEA from the global analysis. An RMSEA value of zero indicates perfect fit, and values of <0.05 are considered a close fit and values of <0.08 a reasonable fit.[12]

Additionally, a sensitivity analysis was carried out. Of the 55 ordinal variables included in the main analysis, 11 are questions about right upper quadrant abdominal pain. These items are likely to be inherently correlated and take up a large magnitude of the variance in the data. Therefore, in the sensitivity analysis all questions on right upper quadrant abdominal pain were removed and the analysis repeated on the global sample. Similar results in the global analysis and the sensitivity analysis, with questions on right upper quadrant abdominal pain removed, would indicate that the inherent correlation of right upper quadrant abdominal pain questions does not affect the overall results.

In the exploratory analysis, varimax rotation was used, and item loadings of >0.4 and factors with an eigenvalue of ≥1 were considered relevant. Cross-loading items (items appearing in >1 factor) were kept in the analysis rather than dropping them as the aim of the study was to evaluate the Rome IV questionnaire in its entirety (i.e. its ordinal questions).[13] In addition to this, dropping cross-loading items from a model would ignore overlapping of symptoms in DGBI which is clinically unsound.

The Internet survey in the RFGES was reviewed by the Institutional Review Board (IRB) of the University of North Carolina at Chapel Hill before data collection started and was deemed exempt from IRB oversight due to the anonymity of the participants.

Results

Subjects

The total sample used for the analyses consisted of 54,127 study participants from 26 countries, with a mean age of 44.3 years (95% CI: 44.2-44.5). Age was comparable across countries except in Egypt where the mean age was slightly lower (Supplementary figure 1). In the overall global sample, the proportion of females was 49.1% (95% CI 48.9-49.5%). For all countries, the proportion of males was from 48.6-51.1% and females 48.9-51.4%, except for Egypt where the proportion of females was 30.3%. The numbers of participants in each geographical region were 4,052 in North America, 8,069 in Latin America, 16,314 in Western Europe, 6,106 in Eastern Europe, 6,042 in the Middle East and 9,487 in Asia. Coefficient alpha and split-half reliability were >0.9 for all analyses, indicating excellent internal consistency and reliability of the data.

Exploratory factor analysis

In the global exploratory factor analysis, there were ten factors with an eigenvalue of ≥1; these are represented as F1-F10 in Table 2 and on the left side of Figure 1. The factors identified, discussed in more detail below, included items that correspond with IBS, functional constipation, functional dyspepsia/upper GI symptoms, diarrhea, nausea and vomiting/regurgitation, globus, chest pain and right upper quadrant abdominal pain. The exploratory factor analysis was repeated across geographical regions, sex, and age groups. These sub-analyses yielded very similar results, with 9-10 factors that had an eigenvalue of ≥1 and similar items within each factor (Supplementary Figures and Tables 2-13).

Confirmatory factor analysis

In the global confirmatory factor analysis, all pre-specified factors (right side of Figure 1) had a loading of ≥0.4, meaning that the items of the pre-specified factors were highly correlated, thereby indicating validity of these factors that were based on the Rome IV criteria. The same was true across sub-analyses by geographical region, age, and sex (Supplementary Figures and Tables 2-13).

Comparison of exploratory and confirmatory factor analysis

The results from the exploratory and confirmatory factor analysis were compared graphically with two types of figures (Figure 1-2) which are explained in the figure legends and discussed in further detail with individual factors below. Furthermore, the analyses were compared by the RMSE. In the global exploratory analysis, the RMSE was low (0.0156), indicating an excellent model fit, and it was similar in all sub-analyses by geographical region, age, and sex (0.0154-0.0198). The RMSE in the confirmatory analyses was somewhat higher (0.0601-0.0721), but indicated a good fit, nonetheless. Detailed information on the RMSE by analysis are presented in Supplementary Table 1. The difference in the RMSE may suggest that the exploratory analysis better explained the data, indicating that the pre-specified factors of the Rome criteria in the confirmatory analysis may need adjustments. However, the discrepancy is at least partly explained by the fact that the exploratory factor analysis may overfit and that the confirmatory was restricted to fewer items.

Overall, these comparisons show that factors comparable to the pre-specified factors of Rome IV IBS, functional dyspepsia, functional constipation and globus were consistently identified across all exploratory analyses, indicating their validity both globally, and across geographical regions, sex, and age groups. Furthermore, chronic nausea and vomiting

syndrome, functional dysphagia, and functional heartburn had valid factor loadings (>0.4) in the confimatory analysis, but this was not consistently found in the exploratory analysis (Figure 1-2).

Factors

IBS

Factor F3 in the global exploratory factor analysis conformed well with the pre-specified IBS factor in the confirmatory analysis (Figure 1-2). Furthermore, it included items on meal-related abdominal pain and abdominal pain limiting usual activities. This factor was consistent across geographical regions, sex, and age. The factors in these sub-analyses were identical to that of the global analysis (Figure 2, Supplementary Figures/Tables 2-13) with the single exception of Eastern Europe, where the item "Pain anywhere in the abdomen" did not have a sufficiently high loading (0.36) to be included in the IBS-like factor (Supplementary Figure/Table 5).

Functional constipation

Factor F2 in the global exploratory analysis included items compatible with functional constipation (Figure 1-2). This factor was consistent across geographical regions, sex, and age (Figure 2, Supplementary Figures/Tables 2-13).

Functional dyspepsia / Upper GI symptoms

Factor 4 in the global analysis included all items compatible with the Rome IV diagnosis of functional dyspepsia (Figure 1-2). Additionally, it included bloating, nausea, and types of abdominal pain other than epigastric pain/burning, (Figure 1). These items were generally present in upper GI factors of all sub-analyses as well (Supplementary Figure/Table 2-13). The items of the pre-specified factors for the confirmatory analysis were consistently selected in the exploratory analysis across sub-analyses (Figure 2), except for North America, where two of the three items consistent with functional dyspepsia (early satiety and postprandial fullness) were not included in any exploratory analysis factor (Supplementary Figure/Table 2). Furthermore, the upper GI symptoms factor among young adults (age 18-34) did not include early satiety (Figure 2, Supplementary Figure/Table 10).

As items not included in the Rome IV definition of functional dyspepsia, such as bloating and nausea, were often included in the upper GI symptoms factor of exploratory factor analyses, the overlap of functional dyspepsia, nausea and bloating was analyzed. Figure 3 displays this overlap and demonstrates that even though a large proportion of patients with all three

symptoms of functional dyspepsia have nausea and bloating, a much larger proportion of patients has these symptoms without having functional dyspepsia.

Diarrhea

Factor F6 in the global analysis represented diarrhea, and was identical across geographical regions, sex, and age categories.

Nausea and vomiting / regurgitation

Factor F10 in the global analysis was compatible with chronic nausea and vomiting syndrome (Figure 1). However, in the sub-analysis of geographical regions, sex, and age groups, only females and people of ages ≥65 years had a factor compatible with chronic nausea and vomiting syndrome (Figure 2). Of note, for those in the ≥65 years age group the factor also contained items on regurgitation/retching (F2; Supplementary Figure 13). The item nausea was often included in an upper GI symptom factor, whilst vomiting either loaded with self-induced vomiting or was included in a factor describing regurgitation and retching (Supplementary Figures/Tables 2-13).

Factor 5 in the global analysis included items on regurgitation and retching, and this factor was quite consistent across sub-analyses, often including vomiting as well. The main exception was in the North America sub-analysis where the factor F1 included items on upper GI symptoms, regurgitation, nausea and vomiting (Supplementary Figure 2).

Globus

Factor F8 in the global analysis included those items consistent with the Rome IV diagnosis of globus, and this factor was identical across geographical regions, sex, and age groups.

Chest pain

Factor F9 in the global analysis included items on chest pain, with a burning sensation or food sticking after swallowing (Figure 1). These are the symptoms for diagnosis of functional heartburn and functional dysphagia, respectively. This factor was identical across all sub-analyses. The items “Heartburn” (used in diagnosing functional heartburn) and “Food stuck in chest” (used in diagnosing functional dysphagia) were often either included in upper GI symptom factors or not selected in the exploratory factor analysis results (Figure 2).

Right upper quadrant pain

Factors F1 and F7 in the global analysis included items on right upper quadrant abdominal pain, and they were partially compatible with biliary pain, but none of the factors included all

items used in the diagnosis of biliary pain according to Rome IV (Figure 2). These results were quite similar across sub-analyses, except for Asia, where only one factor included items on right upper quadrant abdominal pain.

Sensitivity analysis

The global analysis with items on right upper quadrant pain removed, for the reasons discussed above, yielded a near-identical result when compared to the original analysis in which they were included (Supplementary Figure/Table 14). The only differences were that belching loaded on the upper GI symptoms factor and nausea did not load with vomiting. These results indicate that even though a large proportion of the questions used in the exploratory analysis were on right upper quadrant abdominal pain, they did not affect the main results of the global analysis.

Discussion

The factor analysis study presented here provides the first comprehensive evaluation of the validity of the Rome diagnostic classifications of DGBI in a world-wide population sample. By taking advantage of the large RFGES internet survey dataset from 26 countries, our analyses have sufficient sample size to assess similarities and differences between gastrointestinal symptom groupings in different geographical world regions and demographic subgroups. Our results confirm that several key DGBI that have been defined in the Rome criteria by expert consensus are, indeed, distinct highly intercorrelated symptom clusters in factor analysis, and that these symptom constellations generally show striking similarity across different world regions and sex and age subgroups. This provides strong validation of the existing DGBI diagnostic classifications of the Rome IV criteria. However, in some cases, our analyses suggest specific additions or variations to the criteria that may be helpful for guiding further refinement of the DGBI diagnoses in the future.

Irritable bowel syndrome

A factor corresponding to IBS was consistently found globally and across geographical regions, sex, and age. These findings cement IBS as a clinical entity that is found in all populations. In the exploratory factor analysis, the IBS factor often included items on meal-related pain and abdominal pain limiting daily activities, which is in agreement with previous studies showing meal-related symptoms to be common among IBS patients[14,15] and that IBS is a disorder that affects patients' daily activities.[16] Based on these findings, it may be

reasonable to consider incorporating these variables in the Rome V criteria as supportive criteria, or to identify a subgroup of IBS. This is in line with recent data suggesting a distinct pathophysiology of meal-related pain, related to local responses to food allergens in the gut.[17,18]

Functional dyspepsia / upper GI symptoms

A factor compatible with functional dyspepsia was found across all analyses except for North America and was only partially compatible in young adults. Across both global and sub-analyses, the factor often included upper GI symptoms beyond those included in functional dyspepsia criteria. These additional upper GI symptom items were commonly pain symptoms, such as RUQ abdominal pain, heartburn, and pain anywhere in the abdomen, which is not surprising as one of the elements of functional dyspepsia is epigastric pain/burning. Furthermore, nausea and bloating were often included in factors corresponding to functional dyspepsia. This is reassuring as these symptoms are a part of the supportive criteria for functional dyspepsia[11], but they are probably too common in the general population to be included in the main criteria, as highlighted in Figure 3. In addition, the high prevalence of these symptoms partly explains lower loadings of items in the exploratory analysis compared to the confirmatory factor analysis. All these items (symptoms) correlate, but as many individuals in the general population report nausea and bloating, the correlation among the core items of functional dyspepsia is stronger. The explanation for the absence of a functional dyspepsia factor in the North America cohort is unclear. While epigastric pain was present, satiety and postprandial fullness were lacking in the North American exploratory factor analysis. An earlier telephone interview-based large population survey had reported a high prevalence of early satiation and postprandial fullness in the adult population in the U.S.A.[19] Factor and cluster analysis of this telephone survey did identify an early satiation/postprandial fullness factor. The reason for the discrepancy between both survey outcomes is not entirely clear. However, over the last decades, clinical and diagnostic trends in the U.S.A. have evolved to over-estimate reflux disease and under-estimate dyspepsia as a clinical entity.[20] In a setting where direct-to-patient advertisement is prominent, the general public may also be susceptible to the same trend, *i.e.* being more aware of and focused on their symptoms of heartburn or pain than other symptoms. The absence of a functional dyspepsia factor in North America was the only instance where a single geographical region was clearly different from the other regions, which can serve as a point of discussion for the upcoming Rome V criteria. With regards to young adults, early satiety may be a less

prominent symptom among those with functional dyspepsia compared to older functional dyspepsia cohorts.

Globus

The diagnostic entity of globus was clearly represented by a factor in all our analyses. Across global and sub-analyses, it always included the item "pain with swallowing". This item however, consistently had a lower loading than the two items used to define globus in the Rome criteria, meaning that a large proportion of those that reported the two items included in the criteria for globus did not report dysphagia. It is possible that a proportion of patients reporting symptoms compatible with globus also report dysphagia, so some of these patients may have undiagnosed conditions that can cause symptoms similar to globus.

Chronic nausea and vomiting, functional dysphagia and functional heartburn

The pre-specified factor of chronic nausea and vomiting syndrome in the confirmatory factor analysis was valid across global and all sub-analyses. However, the exploratory analysis did not consistently yield a factor compatible with this diagnosis. The same was true, and even more so, for functional dysphagia and functional heartburn. For chronic nausea and vomiting this may be explained partly by the fact that nausea is a fairly common symptom, which also has a strong correlation to other symptom constellations, such as the upper GI symptom factor, discussed above. For functional dysphagia and functional heartburn, no factor compatible with the two emerged from the exploratory analysis. The item "heartburn" was often included in the upper GI symptoms factor and the items "chest pain and burning sensation" (included in the pre-specified factor of functional heartburn) and "chest pain and food sticking after swallowing" (included in the pre-specified factor of functional dysphagia) were included in the same factor in the exploratory factor analysis. This may be explained in part by the fact that our analysis was limited to discrete variables of the Rome IV questionnaire, so important categorical variables used in the criteria could not be included. Furthermore, answers to the items "burning sensation" and "food sticking after swallowing" were both part of the same skip pattern question on chest pain, which may increase correlation between the items.

Regurgitation and retching

The global exploratory analysis and all sub-analyses often yielded a factor that described regurgitation/retching and was not compatible with any of the pre-specified factors of the confirmatory analyses. Conceivably, some of these patients may represent those with

rumination syndrome, which has recently been shown to be more common than previously thought [21].

Right upper quadrant pain

In the global analysis and sub-analyses, one or two factors that contained items on right upper quadrant pain were identified, but they did not fully meet the criteria for biliary pain (except in Asia). This may be explained by the commonness of right upper qudrant symptoms and their propensity to correlate, while biliary pain is rare, which may lead to factor analysis choosing a right upper quadrant pain factor over a biliary pain factor as it explains more of the data.

Validity of anatomical regions

As previously explained, a cornerstone of the Rome criteria is the classification of diseases by anatomical regions.[1] In exploratory factor analysis globally and across geographical regions, sex, and age, individual factors predominantly included items restricted to anatomical regions, reaffirming the approach of classifying DBGI by anatomical regions.

Comparison to previous literature

The results of the current study are mostly in line with a previous paper using factor analysis to validate Rome IV criteria in a smaller sample size,[7] where factors corresponding to IBS, globus, functional constipation and diarrhea were identified, as well as an upper GI symptom factor that included all three items of functional dyspepsia. Siah et al. reported factors containing gas symptoms and meal-related bowel symptoms in their recent study performed in an Asian population presenting to gastroenterology clinics.[3] The results of the current study did not show factors compatible to the abovementioned factors reported by Siah et al; neither in the global analysis nor in the Asia sub-analysis. This discrepancy may be explained by the larger Asian sample size in the current study compared to the study by Siah et al., n=9,487 and n=1,805, respectively. Furthermore, the study by Siah et al. was not population-based and included certain items that were not assessed in the current study and utilized a Rome III criteria questionnaire adapted for Asian languages and culture which is different from the Rome IV questionnaire used in the current study.

Strengths and limitations

Factor analysis requires variables to be ordinal or continuous in nature, whereas categorical variables such as responses to yes or no question, cannot be included. However, the number of categorical variables in the survey that could not be included was 14, and 10 of them asked

about duration of a symptom. Therefore, we find it unlikely that this had a significant impact on how variables clustered, or the conclusions drawn from both the exploratory and confirmatory factor analyses. Additionally, diagnoses based on only one ordinal variable could not be included in the analysis as they cannot logically constitute a factor. The results of the current study must be interpreted with this in mind Another point of consideration is that the analysis is based on the Rome IV questionnaire and will be biased towards nuances within the questionnaire, for example questions that are a part of the same skip pattern, may tend to correlate. However, we believe that these limitations had minimal effects on the findings in our analyses due to the extensive nature of the Rome IV diagnostic questionnaire, which covers most known GI symptoms, as well as the fact that nearly all of the key DGBI symptoms are assessed in the questionnaire with either 9-point or 11-point ordinal frequency scales, which are well suited for factor analysis. Lastly, cultural differences and differences in the interpretation of questions in the Rome IV questionnaire are important factors to consider, but difficult to objectively define and account for in the analyses. However, to minimize the effect of these variables, a great effort was made to translate the Rome questionnaire as accurately as possible, using professional translators and following accepted guidelines for translation of questionnaires. In addition, in countries where multiple languages are spoken the participants had a choice of languages to use. For example, French and English in Canada, French and Dutch in Belgium, Hebrew, Arabic, Russian, and English in Israel. If the original translation was for another country, e.g., French for France, it was carefully localized into French for Canada and French for Belgium.

Strengths of the study are its enormous sample size allowing for sub-analyses across geographical regions, age, and sex. Further strengths are its population-based design and electronical data gathering that made sure missing values were non-existent in the data set and that inconsistent or careless symptom reporting was minimized.

Conclusion

This factor analysis on a global population-based sample showed that the Rome IV criteria have validity across the world's populations and confirm the existence of IBS, functional dyspepsia, functional constipation, and globus as consistent diagnostic entities across geographical regions, sexes, and different age groups. Furthermore, the results indicate that functional dysphagia, functional chest pain, and chronic nausea and vomiting may require criteria modification in the upcoming Rome V criteria.

Tables

Table 1: *All ordinal items of the Rome IV questionnaire. The Rome IV factors refer to pre-specified factors used in confirmatory factor analysis. "Other items" refers to items not included in the pre-specified factors.*

Rome IV pre-specified factors	Items
Globus	Lump in throat last 3 months. Lump in throat when not eating.
Functional heartburn	Chest pain as burning sensation. Heartburn.
Functional dysphagia	Chest pain and food sticking after swallowing. Food stuck in chest.
Functional dyspepsia	Postprandial fullness. Early satiety. Epigastric pain/burning.
Chronic nausea and vomiting syndrome	Nausea. Vomiting.
IBS	Pain anywhere in the abdomen. Abdominal pain related to defecation. Abdominal pain related to stool consistency. Abdominal pain related to stool frequency.
Functional constipation	Hard stools. Infrequent stools. Straining during bowel movements. Incomplete bowel emptying. Anorectal obstruction/blockage. Manual maneuvers to facilitate defecation.
Biliary pain	Right upper quadrant pain. Long-lasting right upper quadrant pain. Right upper quadrant pain of steady severe level. Right upper quadrant pain goes away between episodes. Right upper quadrant pain limits usual activities.
Other items	Pain with swallowing. Chest pain, Epigastric pain/burning improved by defecation. Self-induced vomiting. Food coming back up after swallowing. Retching. Vomiting when food comes back up. Food coming back up is recognizable. Belching. Abdominal pain related to a meal. Abdominal pain limits usual activities. Loose stools. Loose stools following a meal. Urgency. Bloating/abdominal distention. Right upper quadrant pain related to defecation. Right upper quadrant pain related to posture. Right upper quadrant pain improved by medicine. Right upper quadrant pain accompanied by nausea or vomiting. Right upper quadrant pain accompanied by back or right shoulder blade pain. Right upper quadrant pain waking one up. Fecal incontinence. Anorectal pain.

Table 2: *Results from exploratory factor analysis on the global sample. Items represent the variables included in the analysis, F1-F10 represent the factors from the analysis, item loadings ≥0.4 are marked in bold.*

Item	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Lump in throat last 3 months	0.081	0.12	0.076	0.25	0.11	0.068	0.075	**0.74**	0.11	0.078
Lump in throat when not eating	0.13	0.13	0.13	0.13	0.14	0.079	0.077	**0.81**	0.16	0.072
Chest pain as burning sensation	0.18	0.13	0.13	0.19	0.16	0.088	0.093	0.17	**0.7**	0.077
Heartburn	0.11	0.11	0.13	**0.41**	0.17	0.099	0.14	0.13	0.27	0.065
Chest pain and food sticking after swallowing	0.17	0.12	0.12	0.13	0.21	0.085	0.087	0.18	**0.61**	0.12
Food stuck in chest	0.14	0.17	0.12	0.35	0.23	0.091	0.1	0.28	0.29	0.12
Postprandial fullness	0.14	0.2	0.14	**0.47**	0.17	0.11	0.093	0.16	0.13	0.11
Early satiety	0.15	0.19	0.14	**0.43**	0.16	0.11	0.071	0.14	0.12	0.16
Nausea	0.25	0.15	0.15	**0.42**	0.22	0.096	0.052	0.16	0.13	**0.4**
Vomiting	0.16	0.11	0.06	0.24	0.25	0.09	0.041	0.099	0.08	**0.72**
Pain anywhere in the abdomen	0.28	0.18	**0.48**	**0.54**	0.091	0.1	0.2	0.093	0.065	0.045
Abdominal pain related to defecation	0.13	0.19	**0.76**	0.15	0.1	0.14	0.19	0.086	0.096	0.05
Abdominal pain related to stool consistency	0.13	0.22	**0.84**	0.13	0.1	0.18	0.17	0.088	0.085	0.065
Abdominal pain related to stool frequency	0.16	0.21	**0.8**	0.13	0.12	0.18	0.14	0.087	0.1	0.076
Hard stools	0.11	**0.59**	0.13	0.091	0.078	0.012	0.068	0.072	0.065	0.062
Infrequent stools	0.11	**0.51**	0.072	0.078	0.067	0.056	0.057	0.038	0.05	0.059
Straining during bowel movements	0.098	**0.8**	0.16	0.12	0.076	0.052	0.084	0.071	0.052	0.034
Incomplete bowel emptying	0.11	**0.73**	0.19	0.18	0.092	0.17	0.11	0.089	0.054	0.015
Anorectal obstruction/blockage	0.15	**0.83**	0.15	0.15	0.1	0.087	0.087	0.079	0.074	0.045
Manual maneuvers to facilitate defecation	0.16	**0.5**	0.043	0.068	0.11	0.062	0.049	0.068	0.1	0.11
RUQ pain	**0.49**	0.2	0.21	**0.43**	0.093	0.11	**0.44**	0.11	0.07	0.037
Long-lasting RUQ pain	**0.72**	0.21	0.21	0.22	0.093	0.12	0.27	0.095	0.054	0.019
RUQ pain of steady severe level	**0.79**	0.22	0.19	0.18	0.12	0.12	0.16	0.1	0.094	0.058
RUQ pain goes away between episodes	0.19	0.12	0.2	0.11	0.04	0.077	**0.74**	0.058	0.042	0.016
RUQ pain limits usual activities	**0.67**	0.18	0.16	0.15	0.14	0.12	0.14	0.096	0.14	0.14
Pain with swallowing	0.18	0.16	0.12	0.12	0.2	0.083	0.056	**0.53**	0.27	0.14
Chest pain	0.15	0.13	0.11	0.35	0.1	0.085	0.11	0.2	**0.5**	0.089
Epigastric pain/burning	0.38	0.14	0.2	**0.53**	0.21	0.093	0.098	0.11	0.22	0.11
Epigastric pain/burning improved by defecation	0.24	0.12	0.29	0.31	0.19	0.09	0.16	0.09	0.22	0.048
Self-induced vomiting	0.11	0.1	0.07	0.041	0.2	0.081	0.051	0.08	0.092	**0.52**
Food coming back up after swallowing	0.11	0.14	0.089	0.35	**0.61**	0.1	0.089	0.13	0.1	0.14
Retching	0.18	0.15	0.12	0.14	**0.77**	0.1	0.066	0.13	0.14	0.17
Vomiting when food comes back up	0.19	0.14	0.14	0.14	**0.71**	0.1	0.067	0.11	0.12	0.24
Food coming back up is recognizable	0.095	0.11	0.092	0.12	**0.52**	0.084	0.077	0.092	0.11	0.094
Belching	0.17	0.14	0.1	0.36	0.26	0.095	0.042	0.12	0.13	0.13
Abdominal pain related to a meal	0.29	0.18	**0.56**	0.26	0.15	0.16	0.13	0.087	0.13	0.067
Abdominal pain limits usual activities	0.38	0.19	**0.53**	0.26	0.14	0.14	0.068	0.11	0.11	0.1
Loose stools	0.12	0.097	0.16	0.12	0.085	**0.83**	0.08	0.058	0.053	0.063
Loose stools following a meal	0.12	0.09	0.2	0.091	0.1	**0.77**	0.079	0.063	0.066	0.058
Urgency	0.18	0.21	0.2	0.15	0.12	**0.54**	0.082	0.08	0.092	0.083

Bloating/abdominal distention	0.16	0.35	0.2	**0.44**	0.086	0.17	0.19	0.1	0.03	0.0062
RUQ pain related to defecation	0.38	0.23	0.33	0.1	0.13	0.15	0.4	0.089	0.093	0.085
RUQ pain related to posture	0.32	0.16	0.17	0.12	0.093	0.077	**0.62**	0.079	0.11	0.06
RUQ pain improved by medicine	0.28	0.11	0.13	0.14	0.12	0.071	**0.48**	0.053	0.14	0.072
RUQ pain and nausea/vomiting	**0.5**	0.17	0.13	0.15	0.22	0.13	0.17	0.098	0.14	0.29
RUQ pain and back/right shoulder blade pain	**0.49**	0.2	0.12	0.19	0.15	0.1	0.25	0.1	0.18	0.12
RUQ pain waking one up	**0.58**	0.17	0.14	0.15	0.18	0.14	0.18	0.089	0.17	0.16
Fecal incontinence	0.14	0.085	0.066	0.18	0.15	0.25	0.048	0.064	0.11	0.17
Anorectal pain	0.2	0.34	0.17	0.33	0.14	0.12	0.11	0.097	0.11	0.092

References

1. Drossman DA, Hasler WL. Rome IV-Functional GI Disorders: Disorders of Gut-Brain Interaction. *Gastroenterology* 2016; **150**(6): 1257-61.
2. Holtmann GJ, Talley NJ. Inconsistent symptom clusters for functional gastrointestinal disorders in Asia: is Rome burning? *Gut* 2018; **67**(11): 1911-5.
3. Siah KTH, Gong X, Yang XJ, et al. Rome Foundation-Asian working team report: Asian functional gastrointestinal disorder symptom clusters. *Gut* 2018; **67**(6): 1071-7.
4. Talley NJ, Boyce P, Jones M. Identification of distinct upper and lower gastrointestinal symptom groupings in an urban population. *Gut* 1998; **42**(5): 690-5.
5. Whitehead WE, Bassotti G, Palsson O, Taub E, Cook EC, 3rd, Drossman DA. Factor analysis of bowel symptoms in US and Italian populations. *Dig Liver Dis* 2003; **35**(11): 774-83.
6. Talley NJ, Holtmann G, Agréus L, Jones MJTAjog. Gastrointestinal symptoms and subjects cluster into distinct upper and lower groupings in the community: a four nations study. 2000; **95**(6): 1439-47.
7. Clevers E, Whitehead WE, Palsson OS, et al. Factor Analysis Defines Distinct Upper and Lower Gastrointestinal Symptom Groups Compatible With Rome IV Criteria in a Population-based Study. *Clin Gastroenterol Hepatol* 2018; **16**(8): 1252-9 e5.
8. Siah KTH, Gwee KA. Rome IV Exploratory Model Closely Resemble Asian Functional Gastrointestinal Disorder Symptom Clusters. *Clin Gastroenterol Hepatol* 2019; **17**(5): 1002.
9. Clevers E, Whitehead WE, Palsson OS, et al. Rome IV Exploratory Model Closely Resemble Asian Functional Gastrointestinal Disorder Symptom Clusters Reply. 2019; **17**(5): 1002-4.
10. Sperber AD, Bangdiwala SI, Drossman DA, et al. Worldwide Prevalence and Burden of Functional Gastrointestinal Disorders, Results of Rome Foundation Global Study. *Gastroenterology* 2021; **160**(1): 99-114 e3.
11. Palsson OS, Whitehead WE, Van Tilburg MA, et al. Development and validation of the Rome IV diagnostic questionnaire for adults. 2016; **150**(6): 1481-91.
12. Browne MW, Cudeck R. Alternative ways of assessing model fit. Newbury Park, CA: Sage; 1993.

13. Ferguson E, Cox T. Exploratory Factor Analysis: A Users' Guide. *International Journal of Selection and Assessment* 1993; **1**(2): 84-94.

14. Bohn L, Storsrud S, Tornblom H, Bengtsson U, Simren M. Self-reported food-related gastrointestinal symptoms in IBS are common and associated with more severe symptoms and reduced quality of life. *Am J Gastroenterol* 2013; **108**(5): 634-41.

15. Colomier E, Melchior C, Algera JP, et al. Global prevalence and burden of meal-related abdominal pain. *BMC Med* 2022; **20**(1): 71.

16. Goodoory VC, Ng CE, Black CJ, Ford AC. Impact of Rome IV irritable bowel syndrome on work and activities of daily living. *Aliment Pharmacol Ther* 2022; **56**(5): 844-56.

17. Fritscher-Ravens A, Pflaum T, Mosinger M, et al. Many Patients With Irritable Bowel Syndrome Have Atypical Food Allergies Not Associated With Immunoglobulin E. *Gastroenterology* 2019; **157**(1): 109-18 e5.

18. Aguilera-Lizarraga J, Florens MV, Viola MF, et al. Local immune response to food antigens drives meal-induced abdominal pain. *Nature* 2021; **590**(7844): 151-6.

19. Camilleri M, Dubois D, Coulie B, et al. Prevalence and socioeconomic impact of upper gastrointestinal disorders in the United States: results of the US Upper Gastrointestinal Study. *Clin Gastroenterol Hepatol* 2005; **3**(6): 543-52.

20. Pleyer C, Bittner H, Locke GR, 3rd, et al. Overdiagnosis of gastro-esophageal reflux disease and underdiagnosis of functional dyspepsia in a USA community. *Neurogastroenterol Motil* 2014; **26**(8): 1163-71.

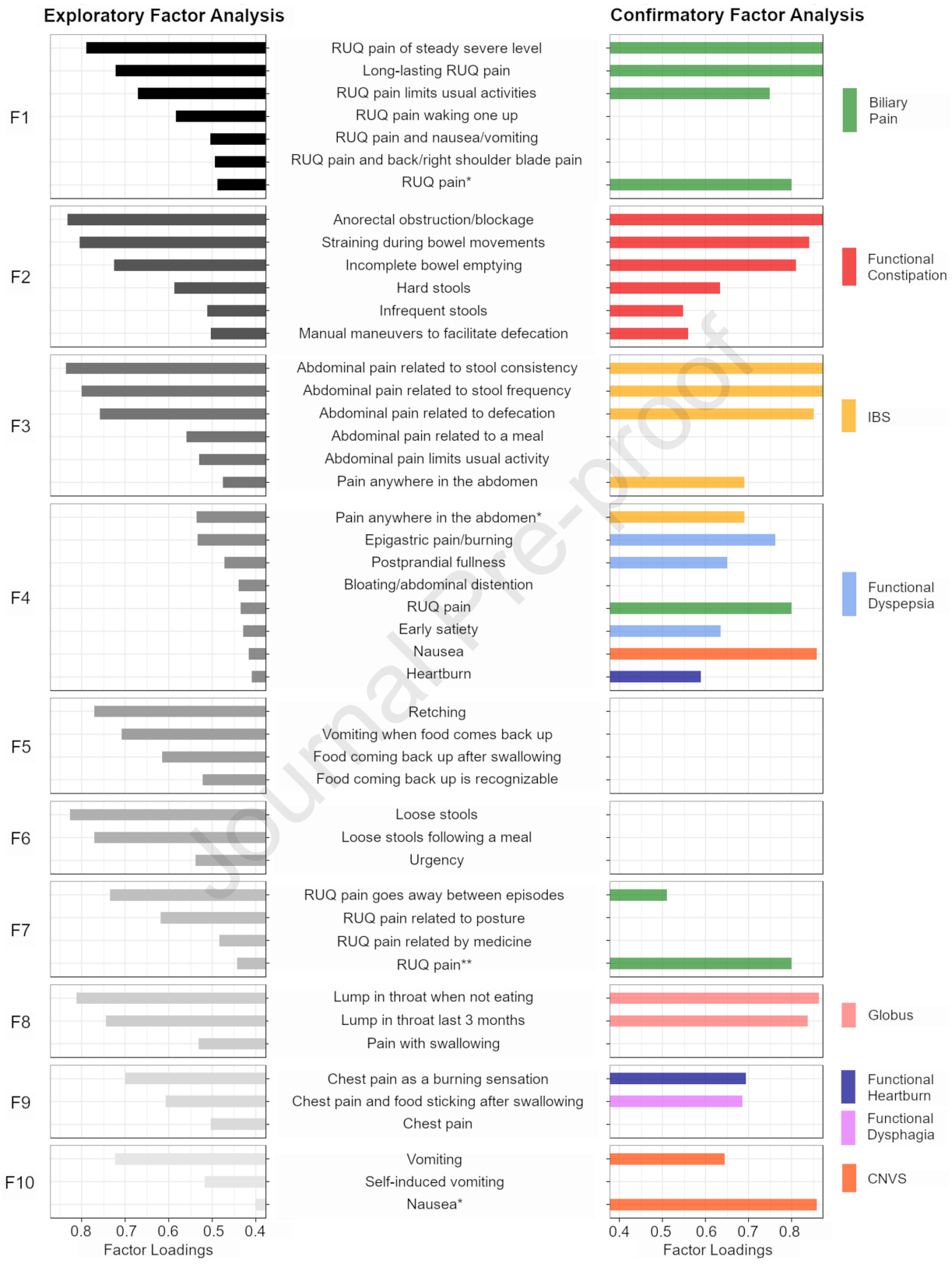
21. Josefsson A, Hreinsson JP, Simren M, et al. Global Prevalence and Impact of Rumination Syndrome. *Gastroenterology* 2022; **162**(3): 731-42 e9.

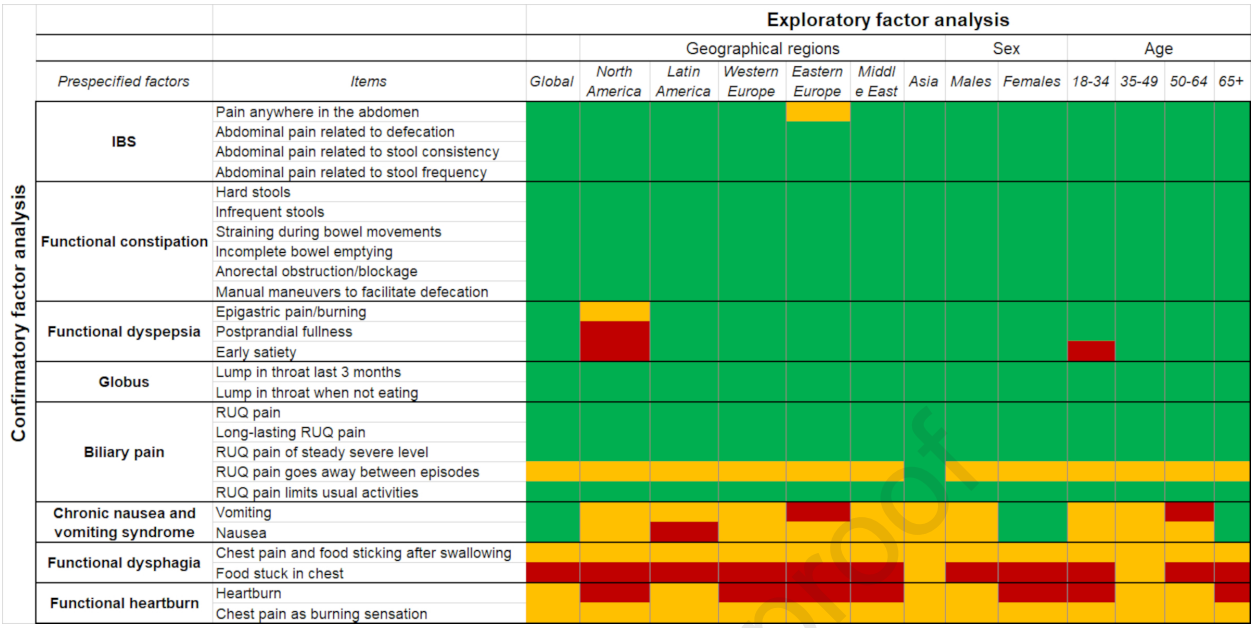
Figures

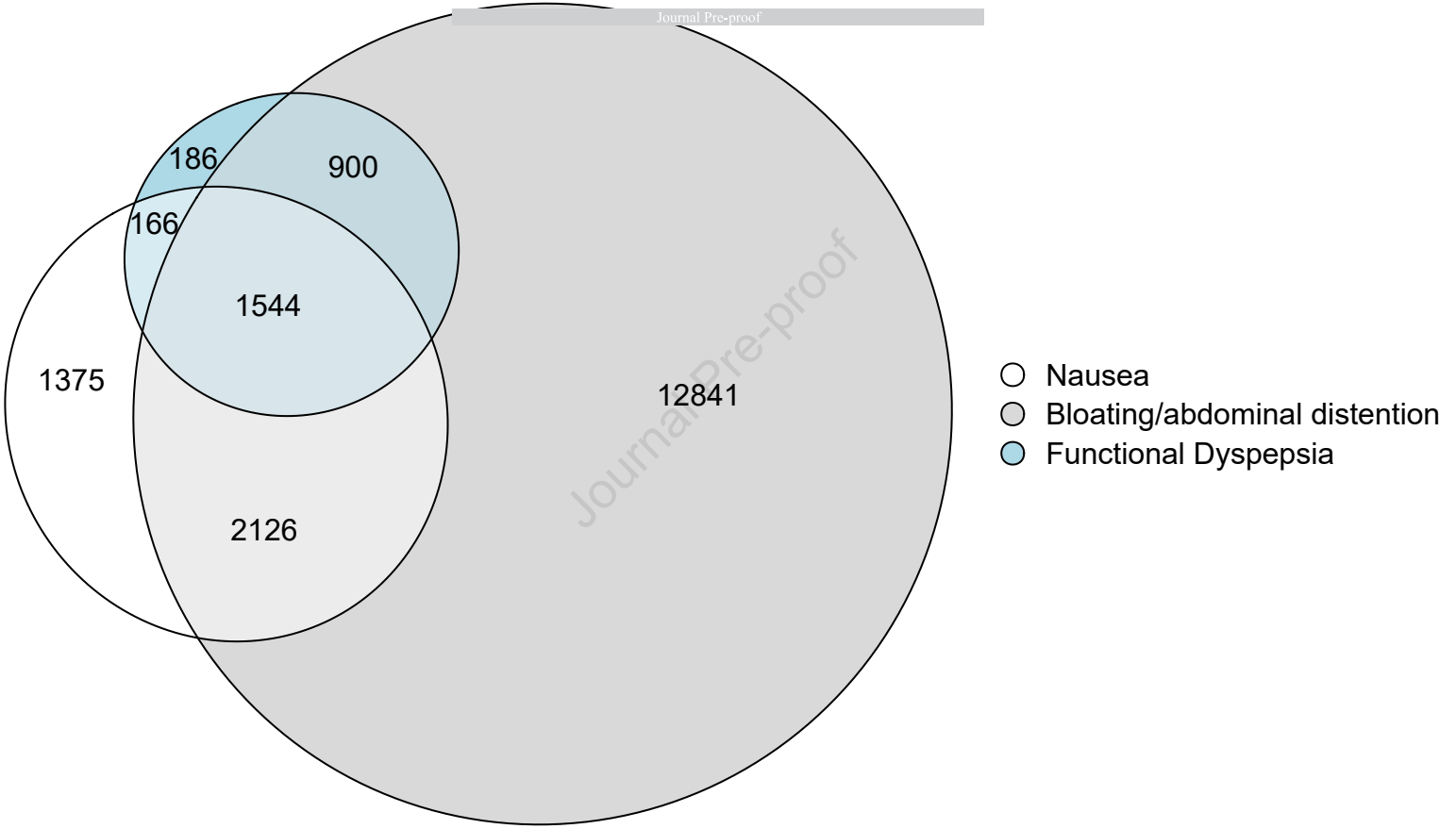
Figure 1: *Results from the Exploratory (left) and confirmatory factor analysis (right). Graphs on the left represent factor loadings of the items (displayed in the middle of the figure) selected in the exploratory analysis, where F1-10 on the left-hand side represent the factors identified in the exploratory factor analysis. Factors were categorized by the variance they explained, with F1 explaining the greatest amount. The predetermined factors in the confirmatory analysis are represented by colors, the key can be found on the right side of the graph. Grouping of color-coded items of the pre-specified factors on the right side indicates that it corresponds well to a factor from the exploratory analysis. Items that appear more than once are marked by "*".*

Figure 2: *An overview of how well items of the exploratory analysis corresponded to the items of the confirmatory analysis, both globally and by sub-analysis. The first two columns show the pre-specified factors of the confirmatory factor analysis and their items. Green-colored boxes represent items that were selected in the exploratory analysis and included in a factor that corresponded well to the confirmatory analysis. Yellow-colored boxes represent items that were selected in the exploratory analysis but included in a factor that did not correspond well to the confirmatory analysis. Red-colored boxes represent items that were not selected in the exploratory analysis.*

Figure 3: *A Euler diagram displaying the overlap of patients with functional dyspepsia symptoms (early satiety, epigastric pain/burning, post-prandial fullness), bloating and nausea. The frequency threshold for bloating and nausea was reporting symptoms two to three days a month or more frequently. Numbers of subjects displayed in the graph are an approximation.*







What You Need to Know

BACKGROUND AND CONTEXT

The Rome Criteria for disorders of the gut-brain interaction (DGBI) have been criticized for being largely based on expert opinion. The current study examined the validity of the Rome IV criteria in a global sample of individuals, this was done with factor analysis.

NEW FINDINGS

The analysis indicated that the Rome IV criteria for IBS, functional dyspepsia, functional constipation, globus and biliary pain are valid both globally as well as by geographical region, age, and sex.

LIMITATIONS

Factor analysis can only be performed on ordinal/continuous variables, therefore, the analysis was limited to DGBI that are based on two or more ordinal variables. Cultural and linguistic differences between geographical regions.

CLINICAL RESEARCH RELEVANCE and BASIC RESEARCH RELEVANCE

The results of the study affirm many DGBI within the Rome IV criteria, which strengthens the Rome criteria in a data-driven manner. Certain DGBI, *e.g.* chronic nausea and vomiting syndrome, were not as clearly valid in the analysis which may prompt their modification in the upcoming Rome V criteria.

Lay summary

Factor analysis on a global sample of patients validates major disorders of the gut-brain interaction (DGBI). This was true for sub-analyses by geographical regions, sex, and age groups.

Factor analysis confirms validity of Rome IV criteria for major disorders of gut-brain interaction (DGBI) globally across geographical regions, and by sex and age groups

Supplementary material

Contents

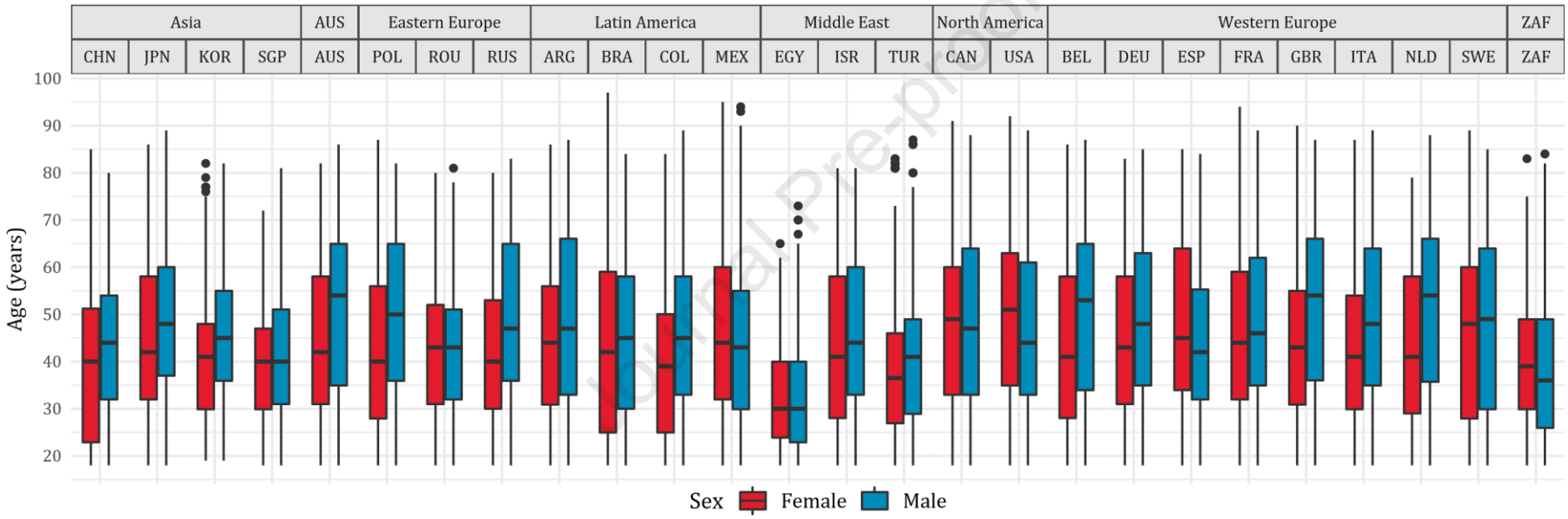
Figure and Table Guide

In Figures 2-14: Results from the Exploratory (left) and factor analysis (right). Graphs on the left represent factor loadings of the items (displayed in the middle of the graph) selected in the exploratory analysis, where "F" and the number on the left-hand side represent the factors from the analysis. Factors were categorized by the variance they explained, with F1 explaining the greatest amount. The pre-specified factors in the confirmatory analysis are represented by colors, the key for these colors is on the right-hand side of the graph.

In Tables 2-14: The column "Item" represents all variables that were included in exploratory factor analysis. The factors derived from the analysis are represented with "F" and a number. The factor loading of each item is displayed in the table, where loadings defined as meaningful (>0.4) are marked in bold.

Supplementary Figure 1

Supplementary figure 14: *Boxplots comparing the age of patients by sex and country. Geographical regions are listed in the panels at the top of the graph, and their respective countries in the panels below.*

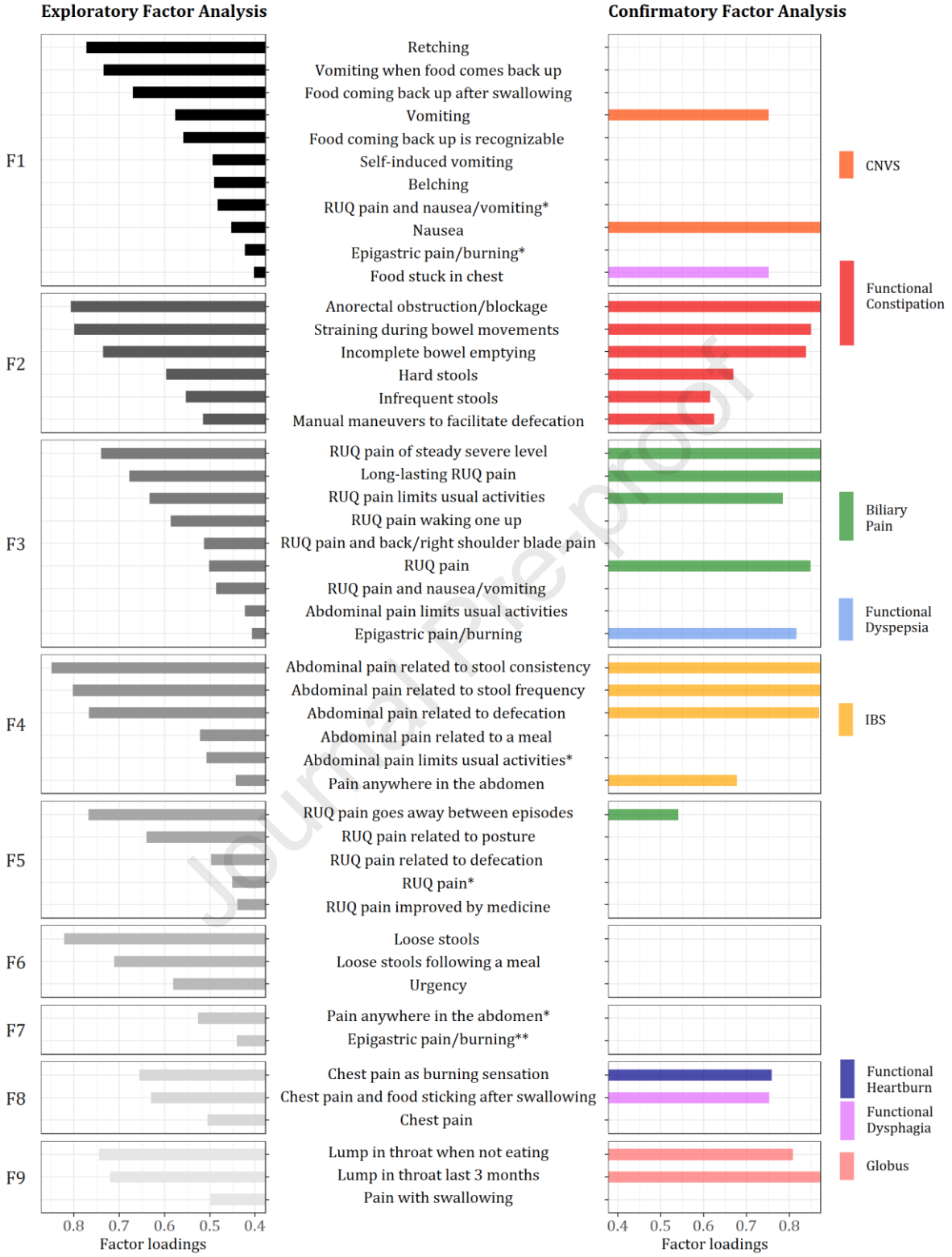


Supplementary table 1 – RMSE across analyses

Table 1 Root mean square error of exploratory and confirmatory factor analysis across global and sub-analyses.

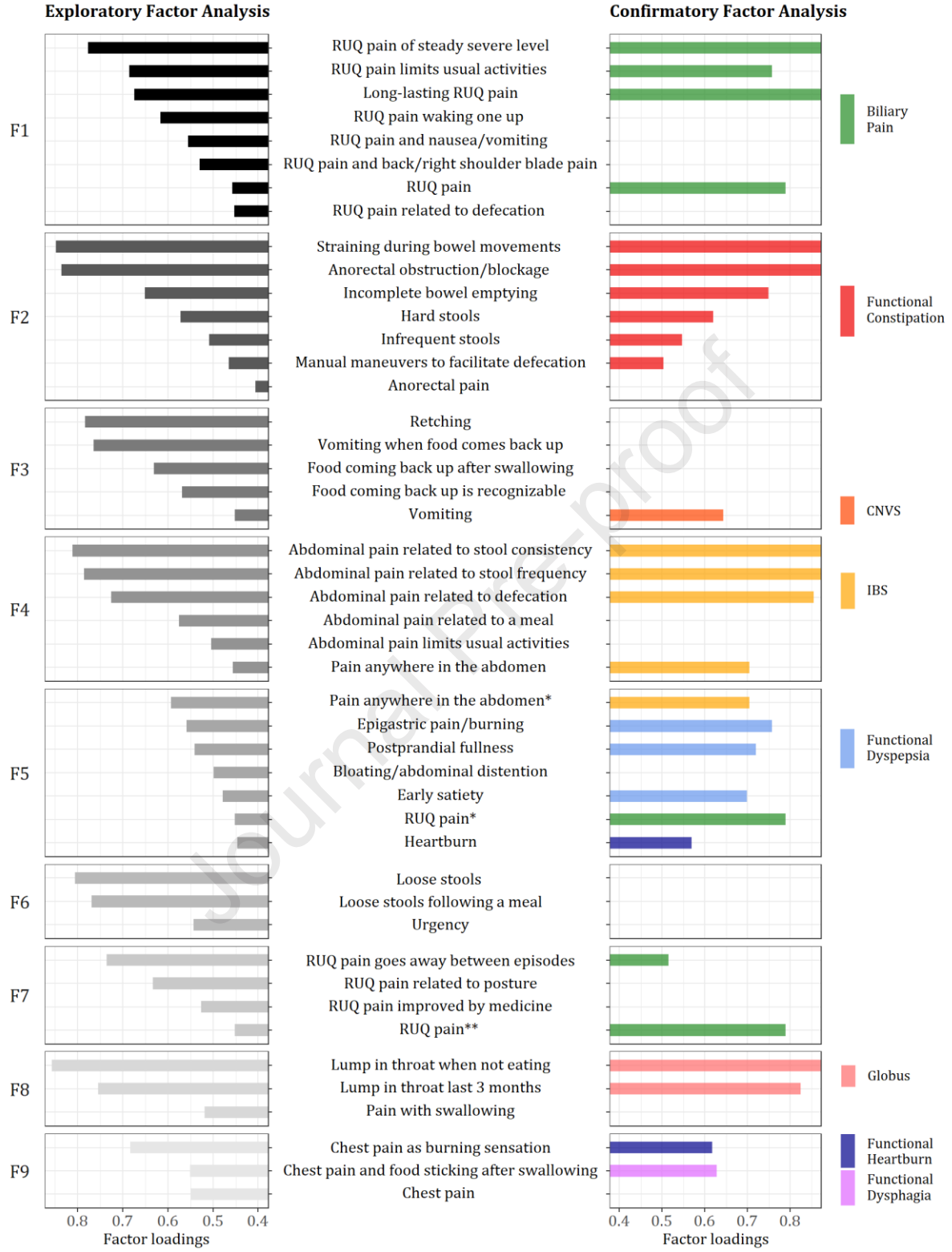
	Root mean square error (RMSE)	
	Exploratory factor analysis	Confirmatory factor analysis
Global	0.0156	0.0667
North America	0.0178	0.0744
Latin America	0.0188	0.0675
Western Europe	0.0176	0.0677
Eastern Europe	0.0187	0.0681
Middle East	0.0170	0.0663
Asia	0.0188	0.0707
Males	0.018	0.0672
Females	0.0165	0.0665
Age 18-34	0.0195	0.0635
Age 35-49	0.0154	0.0687
Age 50-64	0.0170	0.0700
Age 65+	0.0198	0.0690

Supplementary Figure and Table 2 - North America



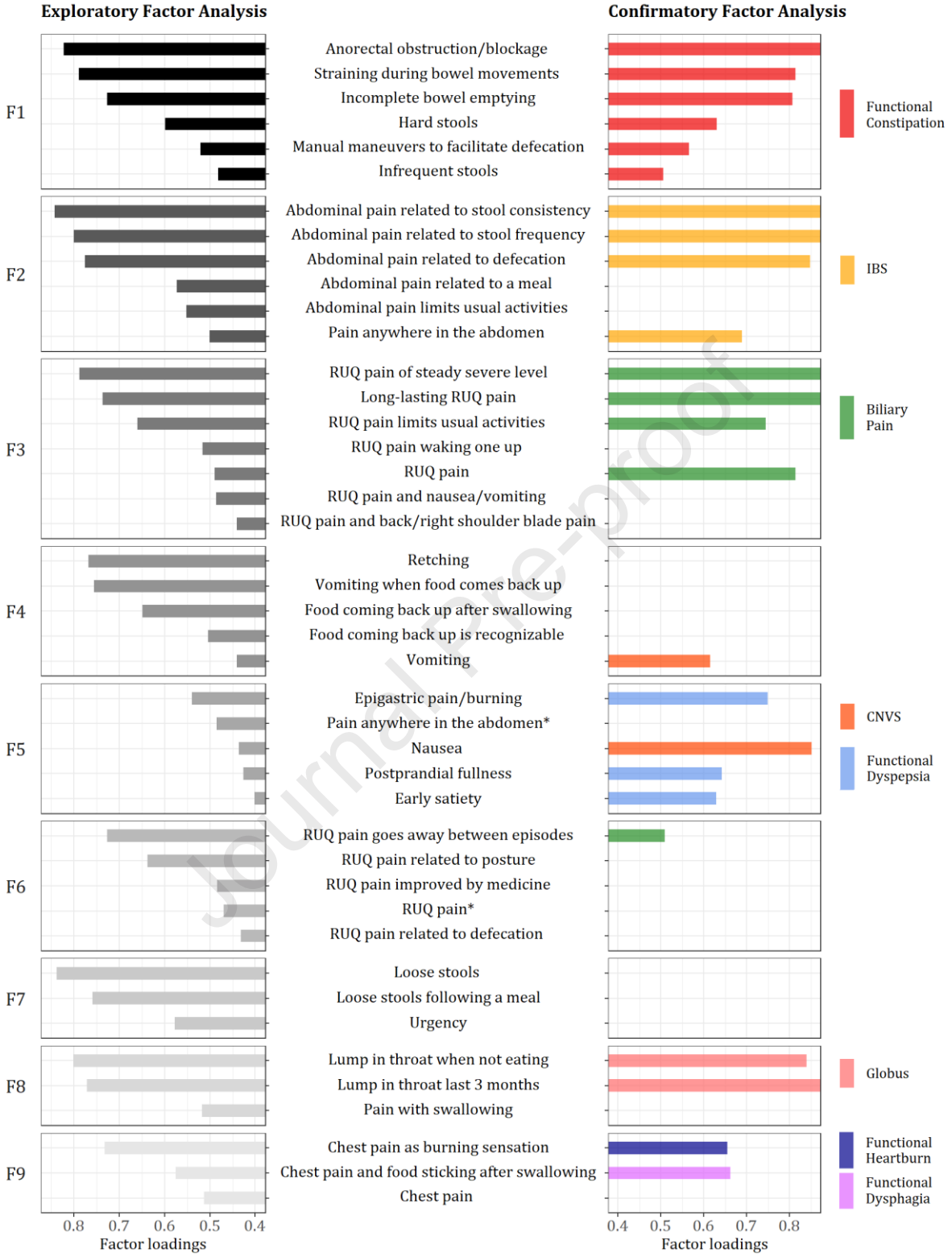
Item	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lump in throat last 3 months	0.28	0.15	0.11	0.11	0.09	0.1	0.23	0.14	**0.72**
Lump in throat when not eating	0.24	0.15	0.13	0.15	0.097	0.08	0.084	0.15	**0.74**
Chest pain as burning sensation	0.3	0.16	0.18	0.15	0.13	0.092	0.12	**0.66**	0.15
Heartburn	0.27	0.17	0.065	0.15	0.13	0.13	0.32	0.28	0.12
Chest pain and food sticking after swallowing	0.39	0.16	0.17	0.12	0.088	0.11	0.041	**0.63**	0.17
Food stuck in chest	**0.4**	0.2	0.11	0.12	0.12	0.096	0.29	0.34	0.28
Postprandial fullness	0.33	0.21	0.19	0.12	0.12	0.1	0.38	0.19	0.17
Early satiety	0.33	0.21	0.18	0.13	0.063	0.14	0.38	0.12	0.15
Nausea	**0.45**	0.16	0.34	0.15	0.056	0.17	0.39	0.12	0.16
Vomiting	**0.58**	0.14	0.22	0.078	0.042	0.17	0.24	0.13	0.15
Pain anywhere in the abdomen	0.19	0.21	0.34	**0.44**	0.2	0.14	**0.53**	0.11	0.14
Abdominal pain related to defecation	0.14	0.2	0.084	**0.77**	0.24	0.15	0.1	0.12	0.1
Abdominal pain related to stool consistency	0.13	0.23	0.13	**0.85**	0.21	0.18	0.068	0.097	0.083
Abdominal pain related to stool frequency	0.17	0.21	0.17	**0.8**	0.19	0.2	0.1	0.094	0.094
Hard stools	0.18	**0.6**	0.13	0.14	0.093	0.012	0.073	0.12	0.082
Infrequent stools	0.14	**0.55**	0.15	0.087	0.1	0.068	0.065	0.08	0.045
Straining during bowel movements	0.12	**0.8**	0.11	0.18	0.11	0.089	0.12	0.065	0.075
Incomplete bowel emptying	0.13	**0.74**	0.13	0.21	0.15	0.19	0.18	0.045	0.099
Anorectal obstruction/blockage	0.18	**0.81**	0.17	0.16	0.11	0.13	0.12	0.08	0.11
Manual maneuvers to facilitate defecation	0.29	**0.52**	0.19	0.058	0.083	0.11	0.013	0.14	0.11
RUQ pain	0.21	0.23	**0.5**	0.2	**0.45**	0.14	0.38	0.13	0.13
Long-lasting RUQ pain	0.19	0.22	**0.68**	0.22	0.32	0.14	0.21	0.078	0.082
RUQ pain of steady severe level	0.27	0.25	**0.74**	0.17	0.21	0.15	0.15	0.11	0.11
RUQ pain goes away between episodes	0.028	0.13	0.17	0.22	**0.77**	0.091	0.13	0.061	0.054
RUQ pain limits usual activities	0.31	0.22	**0.63**	0.15	0.18	0.16	0.13	0.13	0.11
Pain with swallowing	0.38	0.19	0.21	0.09	0.078	0.095	0.079	0.29	**0.5**
Chest pain	0.28	0.13	0.18	0.14	0.14	0.1	0.31	**0.51**	0.21
Epigastric pain/burning	**0.42**	0.17	**0.41**	0.16	0.082	0.11	**0.44**	0.25	0.16
Epigastric pain/burning improved by defecation	0.33	0.17	0.27	0.29	0.14	0.11	0.22	0.27	0.096
Self-induced vomiting	**0.49**	0.13	0.16	0.072	0.065	0.17	0.0096	0.18	0.14
Food coming back up after swallowing	**0.67**	0.19	0.11	0.14	0.15	0.1	0.29	0.13	0.14
Retching	**0.77**	0.19	0.21	0.13	0.12	0.11	0.074	0.11	0.14
Vomiting when food comes back up	**0.73**	0.18	0.22	0.17	0.11	0.12	0.1	0.093	0.12
Food coming back up is recognizable	**0.56**	0.15	0.098	0.1	0.11	0.079	0.029	0.14	0.084
Belching	**0.49**	0.16	0.24	0.12	0.049	0.12	0.25	0.18	0.15
Abdominal pain related to a meal	0.26	0.21	0.31	**0.52**	0.13	0.18	0.24	0.15	0.1
Abdominal pain limits usual activities	0.23	0.22	**0.42**	**0.51**	0.072	0.16	0.29	0.092	0.13
Loose stools	0.19	0.12	0.15	0.18	0.1	**0.82**	0.12	0.071	0.074
Loose stools following a meal	0.19	0.13	0.14	0.22	0.09	**0.71**	0.077	0.09	0.057
Urgency	0.25	0.24	0.21	0.19	0.12	**0.58**	0.13	0.082	0.095
Bloating/abdominal distention	0.16	0.35	0.17	0.19	0.19	0.2	0.39	0.055	0.11
RUQ pain related to defecation	0.21	0.25	0.33	0.31	**0.5**	0.14	0.028	0.11	0.06
RUQ pain related to posture	0.18	0.18	0.26	0.21	**0.64**	0.092	0.064	0.1	0.087
RUQ pain improved by medicine	0.28	0.17	0.25	0.14	**0.44**	0.078	0.071	0.16	0.11
RUQ pain and nausea/vomiting	**0.48**	0.23	**0.49**	0.1	0.18	0.19	0.077	0.15	0.1
RUQ pain and back/right shoulder blade pain	0.29	0.23	**0.51**	0.13	0.25	0.13	0.095	0.21	0.12
RUQ pain waking one up	0.35	0.21	**0.59**	0.15	0.21	0.19	0.1	0.17	0.13
Fecal incontinence	0.38	0.12	0.17	0.11	0.094	0.31	0.16	0.17	0.13
Anorectal pain	0.35	0.33	0.23	0.18	0.093	0.18	0.26	0.15	0.15

Supplementary Figure and Table 3 - Latin America



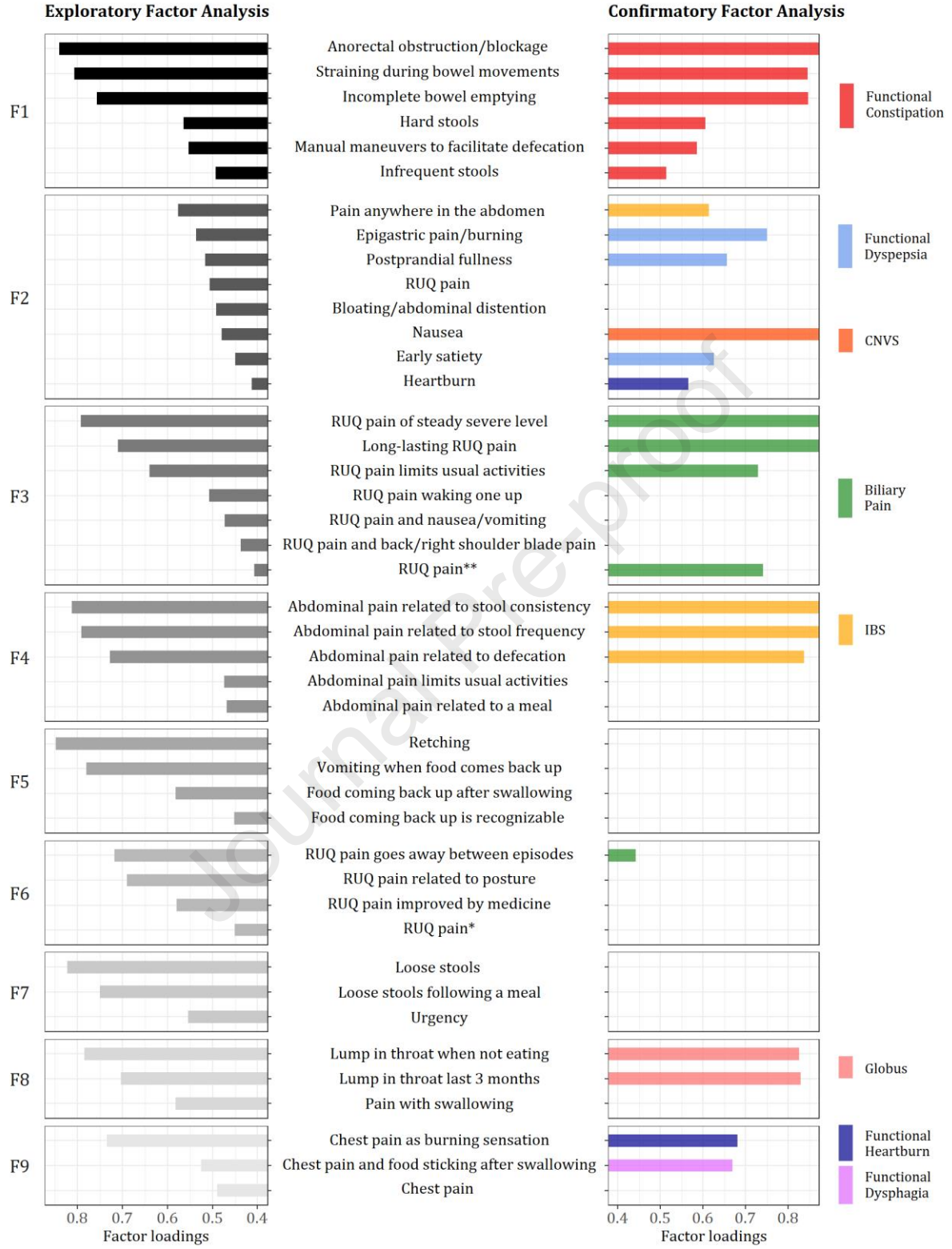
Item	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lump in throat last 3 months	0.08	0.11	0.14	0.08	0.24	0.07	0.068	**0.75**	0.11
Lump in throat when not eating	0.14	0.15	0.21	0.13	0.14	0.11	0.069	**0.86**	0.18
Chest pain as burning sensation	0.2	0.13	0.2	0.12	0.16	0.09	0.089	0.18	**0.68**
Heartburn	0.09	0.11	0.23	0.13	**0.45**	0.09	0.16	0.13	0.2
Chest pain and food sticking after swallowing	0.15	0.11	0.25	0.16	0.09	0.1	0.1	0.16	**0.55**
Food stuck in chest	0.13	0.15	0.24	0.11	0.37	0.1	0.12	0.29	0.27
Postprandial fullness	0.15	0.21	0.21	0.17	**0.54**	0.13	0.11	0.14	0.12
Early satiety	0.2	0.2	0.21	0.16	**0.48**	0.12	0.063	0.12	0.12
Nausea	0.28	0.14	0.37	0.12	0.38	0.09	0.016	0.15	0.16
Vomiting	0.22	0.11	**0.45**	0.07	0.21	0.1	0.004	0.1	0.11
Pain anywhere in the abdomen	0.25	0.17	0.14	**0.46**	**0.59**	0.08	0.19	0.11	0.066
Abdominal pain related to defecation	0.17	0.2	0.14	**0.73**	0.21	0.15	0.17	0.1	0.1
Abdominal pain related to stool consistency	0.14	0.22	0.14	**0.81**	0.17	0.21	0.17	0.09	0.09
Abdominal pain related to stool frequency	0.17	0.23	0.15	**0.79**	0.16	0.2	0.14	0.09	0.1
Hard stools	0.11	**0.57**	0.11	0.13	0.1	0.02	0.07	0.06	0.058
Infrequent stools	0.1	**0.51**	0.1	0.08	0.08	0.05	0.077	0.05	0.038
Straining during bowel movements	0.11	**0.85**	0.11	0.15	0.14	0.06	0.094	0.06	0.067
Incomplete bowel emptying	0.11	**0.65**	0.11	0.18	0.17	0.18	0.13	0.09	0.064
Anorectal obstruction/blockage	0.15	**0.84**	0.13	0.15	0.16	0.09	0.093	0.09	0.084
Manual maneuvers to facilitate defecation	0.15	**0.47**	0.12	0.02	0.07	0.07	0.007	0.06	0.083
RUQ pain	**0.46**	0.2	0.11	0.19	**0.45**	0.11	**0.45**	0.12	0.05
Long-lasting RUQ pain	**0.67**	0.22	0.15	0.22	0.23	0.13	0.31	0.09	0.034
RUQ pain of steady severe level	**0.78**	0.22	0.16	0.18	0.2	0.12	0.16	0.09	0.071
RUQ pain goes away between episodes	0.19	0.14	0.07	0.16	0.11	0.09	**0.74**	0.05	0.064
RUQ pain limits usual activities	**0.69**	0.17	0.2	0.15	0.16	0.14	0.14	0.1	0.15
Pain with swallowing	0.19	0.16	0.24	0.15	0.11	0.09	0.06	**0.52**	0.27
Chest pain	0.11	0.13	0.12	0.11	0.32	0.08	0.1	0.18	**0.55**
Epigastric pain/burning	0.32	0.15	0.24	0.22	**0.56**	0.1	0.11	0.11	0.16
Epigastric pain/burning improved by defecation	0.2	0.13	0.21	0.34	0.28	0.12	0.17	0.09	0.16
Self-induced vomiting	0.14	0.08	0.35	0.08	0.04	0.08	0.023	0.06	0.09
Food coming back up after swallowing	0.07	0.14	**0.63**	0.07	0.33	0.09	0.12	0.12	0.036
Retching	0.15	0.17	**0.78**	0.14	0.15	0.11	0.089	0.11	0.11
Vomiting when food comes back up	0.16	0.14	**0.76**	0.14	0.14	0.11	0.087	0.1	0.12
Food coming back up is recognizable	0.09	0.12	**0.57**	0.08	0.1	0.08	0.1	0.09	0.085
Belching	0.16	0.14	0.24	0.1	0.35	0.11	0.043	0.06	0.089
Abdominal pain related to a meal	0.29	0.18	0.17	**0.58**	0.29	0.16	0.12	0.09	0.12
Abdominal pain limits usual activities	0.38	0.18	0.21	**0.5**	0.26	0.15	0.066	0.11	0.16
Loose stools	0.1	0.1	0.11	0.14	0.12	**0.81**	0.097	0.05	0.042
Loose stools following a meal	0.12	0.09	0.12	0.21	0.09	**0.77**	0.096	0.06	0.052
Urgency	0.2	0.18	0.15	0.16	0.11	**0.54**	0.073	0.07	0.095
Bloating/abdominal distention	0.15	0.36	0.09	0.21	**0.5**	0.17	0.17	0.1	0.002
RUQ pain related to defecation	**0.45**	0.25	0.17	0.29	0.13	0.16	0.35	0.08	0.11
RUQ pain related to posture	0.33	0.17	0.11	0.17	0.14	0.08	**0.63**	0.07	0.1
RUQ pain improved by medicine	0.28	0.11	0.16	0.13	0.16	0.09	**0.53**	0.06	0.12
RUQ pain and nausea/vomiting	**0.56**	0.16	0.3	0.13	0.14	0.12	0.13	0.09	0.13
RUQ pain and back/right shoulder blade pain	**0.53**	0.2	0.16	0.15	0.22	0.13	0.26	0.11	0.14
RUQ pain waking one up	**0.62**	0.17	0.21	0.14	0.17	0.16	0.19	0.08	0.15
Fecal incontinence	0.13	0.06	0.16	0.06	0.16	0.29	0.022	0.09	0.089
Anorectal pain	0.18	**0.41**	0.15	0.15	0.31	0.1	0.098	0.08	0.083

Supplementary Figure and Table 4 - Western Europe



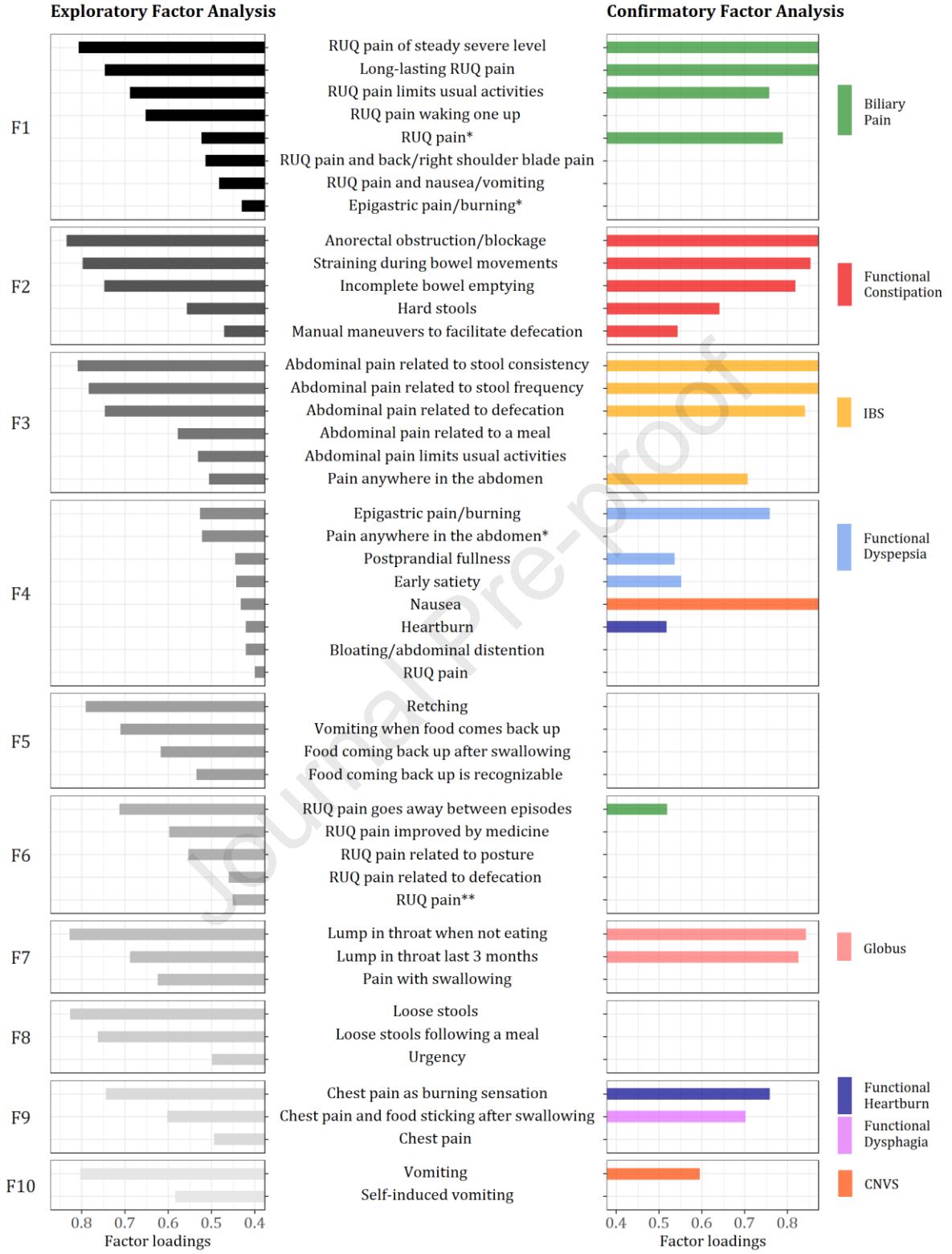
Item	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Lump in throat last 3 months	0.13	0.09	0.08	0.14	0.23	0.08	0.071	**0.77**	0.13	-0.01
Lump in throat when not eating	0.14	0.11	0.12	0.14	0.11	0.08	0.069	**0.8**	0.15	0.024
Chest pain as burning sensation	0.11	0.14	0.14	0.17	0.16	0.1	0.093	0.15	**0.73**	0.0085
Heartburn	0.11	0.13	0.1	0.2	0.38	0.14	0.11	0.18	0.26	-0.016
Chest pain and food sticking after swallowing	0.11	0.11	0.15	0.24	0.12	0.1	0.077	0.17	**0.58**	0.1
Food stuck in chest	0.17	0.11	0.11	0.29	0.32	0.11	0.089	0.27	0.26	0.047
Postprandial fullness	0.2	0.14	0.12	0.23	**0.43**	0.1	0.13	0.18	0.13	0.042
Early satiety	0.2	0.14	0.14	0.23	**0.4**	0.08	0.12	0.15	0.12	0.09
Nausea	0.16	0.16	0.26	0.33	**0.44**	0.06	0.12	0.16	0.09	0.21
Vomiting	0.09	0.06	0.17	**0.44**	0.27	0.02	0.1	0.11	0.05	0.31
Pain anywhere in the abdomen	0.19	**0.5**	0.29	0.12	**0.49**	0.2	0.12	0.09	0.08	-0.14
Abdominal pain related to defecation	0.18	**0.78**	0.1	0.09	0.1	0.19	0.14	0.09	0.09	0.011
Abdominal pain related to stool consistency	0.21	**0.84**	0.11	0.11	0.1	0.15	0.19	0.09	0.09	0.029
Abdominal pain related to stool frequency	0.21	**0.8**	0.14	0.13	0.11	0.14	0.19	0.08	0.11	0.055
Hard stools	**0.6**	0.13	0.08	0.07	0.07	0.07	-0.003	0.09	0.05	0.03
Infrequent stools	**0.48**	0.06	0.09	0.07	0.06	0.05	0.048	0.04	0.04	0.035
Straining during bowel movements	**0.79**	0.16	0.08	0.09	0.07	0.07	0.033	0.07	0.05	-0.009
Incomplete bowel emptying	**0.73**	0.2	0.1	0.1	0.15	0.11	0.18	0.09	0.07	-0.045
Anorectal obstruction/blockage	**0.82**	0.15	0.15	0.12	0.13	0.1	0.065	0.09	0.08	0.0059
Manual maneuvers to facilitate defecation	**0.52**	0.04	0.13	0.13	0.09	0.06	0.055	0.06	0.08	0.11
RUQ pain	0.21	0.24	**0.49**	0.12	0.4	**0.47**	0.13	0.09	0.09	-0.15
Long-lasting RUQ pain	0.21	0.22	**0.74**	0.11	0.18	0.27	0.11	0.09	0.08	-0.16
RUQ pain of steady severe level	0.22	0.2	**0.79**	0.14	0.14	0.18	0.12	0.1	0.12	-0.054
RUQ pain goes away between episodes	0.13	0.21	0.17	0.04	0.09	**0.73**	0.064	0.08	0.03	-0.09
RUQ pain limits usual activities	0.18	0.17	**0.66**	0.18	0.16	0.16	0.13	0.1	0.12	0.15
Pain with swallowing	0.15	0.11	0.14	0.25	0.1	0.07	0.078	**0.52**	0.23	0.11
Chest pain	0.15	0.13	0.14	0.15	0.31	0.11	0.1	0.21	**0.51**	-0.05
Epigastric pain/burning	0.14	0.19	0.36	0.22	**0.54**	0.13	0.1	0.11	0.22	0.079
Epigastric pain/burning improved by defecation	0.11	0.27	0.2	0.18	0.31	0.19	0.097	0.09	0.2	0.1
Self-induced vomiting	0.09	0.04	0.09	0.31	0.09	0.03	0.069	0.08	0.06	0.26
Food coming back up after swallowing	0.14	0.09	0.1	**0.65**	0.3	0.09	0.11	0.13	0.12	-0.047
Retching	0.12	0.11	0.14	**0.77**	0.09	0.07	0.094	0.11	0.13	0.0012
Vomiting when food comes back up	0.12	0.13	0.15	**0.76**	0.12	0.06	0.096	0.08	0.1	0.051
Food coming back up is recognizable	0.1	0.08	0.06	**0.5**	0.09	0.09	0.073	0.09	0.11	-0.029
Belching	0.12	0.09	0.16	0.29	0.39	0.07	0.1	0.1	0.14	0.1
Abdominal pain related to a meal	0.17	**0.57**	0.25	0.15	0.24	0.14	0.17	0.07	0.12	0.015
Abdominal pain limits usual activities	0.18	**0.55**	0.36	0.16	0.25	0.07	0.15	0.1	0.09	0.061
Loose stools	0.07	0.18	0.11	0.1	0.11	0.08	**0.84**	0.06	0.06	-0.011
Loose stools following a meal	0.08	0.21	0.1	0.12	0.08	0.07	**0.76**	0.07	0.08	0.013
Urgency	0.18	0.21	0.15	0.15	0.15	0.08	**0.58**	0.08	0.08	0.049
Bloating/abdominal distention	0.38	0.21	0.15	0.1	0.39	0.19	0.18	0.1	0.06	-0.14
RUQ pain related to defecation	0.22	0.34	0.33	0.13	0.08	**0.43**	0.15	0.08	0.09	0.064
RUQ pain related to posture	0.16	0.18	0.3	0.1	0.11	**0.64**	0.069	0.09	0.11	0.051
RUQ pain improved by medicine	0.1	0.1	0.24	0.14	0.15	**0.48**	0.078	0.05	0.15	0.16
RUQ pain and nausea/vomiting	0.16	0.13	**0.49**	0.28	0.2	0.2	0.12	0.1	0.1	0.3
RUQ pain and back/right shoulder blade pain	0.19	0.11	**0.44**	0.17	0.2	0.3	0.1	0.09	0.15	0.12
RUQ pain waking one up	0.16	0.13	**0.52**	0.21	0.17	0.24	0.14	0.1	0.16	0.19
Fecal incontinence	0.08	0.06	0.13	0.19	0.2	0.05	0.28	0.04	0.09	0.12
Anorectal pain	0.35	0.17	0.17	0.16	0.32	0.12	0.13	0.08	0.11	0.025

Supplementary Figure and Table 5 - Eastern Europe



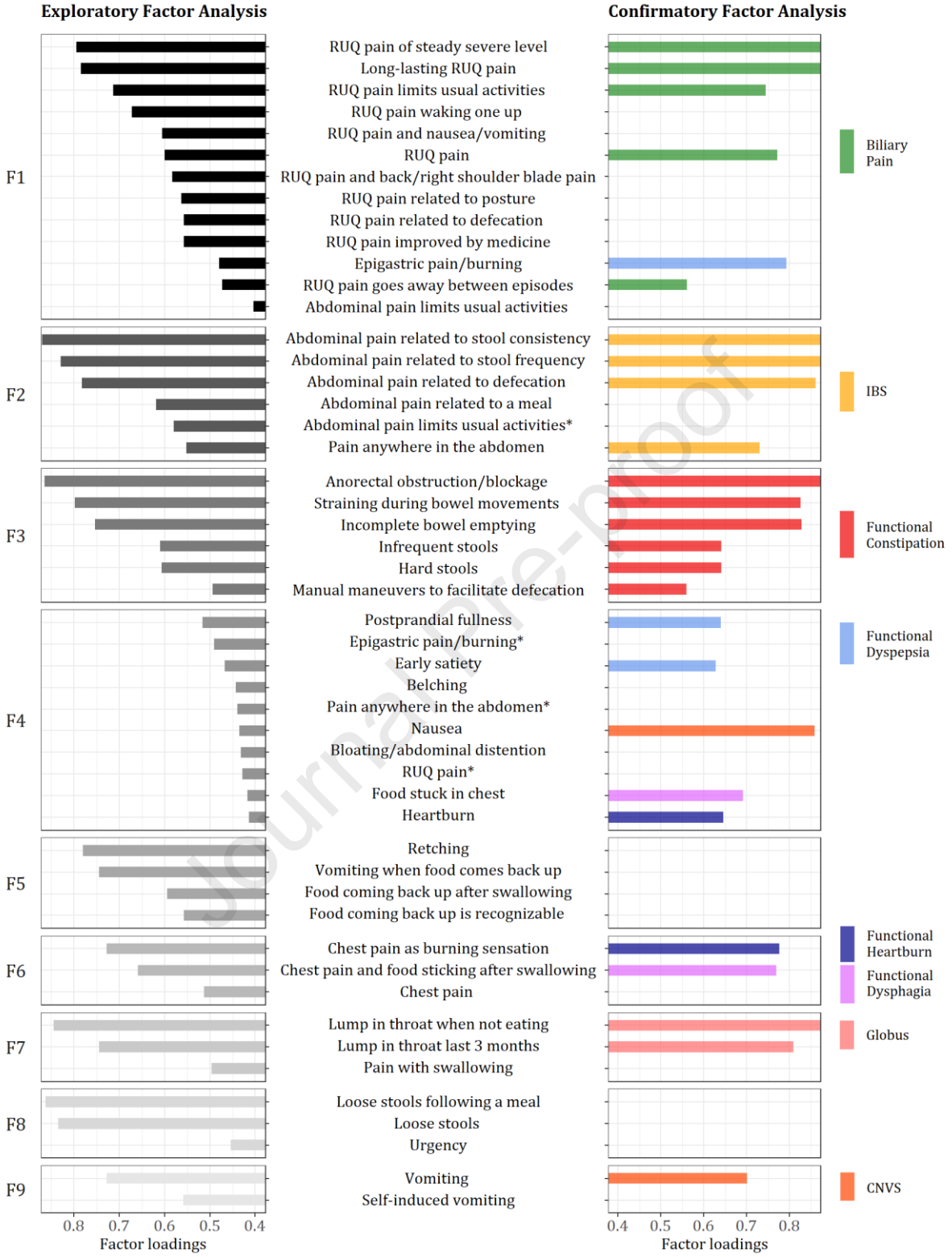
Item	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Lump in throat last 3 months	0.11	0.31	0.09	0.07	0.12	0.083	0.053	**0.7**	0.12	0.0066
Lump in throat when not eating	0.14	0.15	0.11	0.15	0.14	0.081	0.085	**0.78**	0.16	0.0071
Chest pain as burning sensation	0.13	0.19	0.17	0.11	0.18	0.094	0.087	0.2	**0.73**	-0.006
Heartburn	0.09	**0.41**	0.1	0.11	0.18	0.14	0.08	0.14	0.24	-0.003
Chest pain and food sticking after swallowing	0.12	0.17	0.15	0.12	0.24	0.11	0.093	0.22	**0.53**	0.12
Food stuck in chest	0.17	0.37	0.14	0.1	0.24	0.1	0.088	0.29	0.24	0.059
Postprandial fullness	0.21	**0.52**	0.11	0.15	0.16	0.073	0.11	0.17	0.1	0.052
Early satiety	0.17	**0.45**	0.16	0.12	0.19	0.064	0.1	0.15	0.09	0.11
Nausea	0.13	**0.48**	0.23	0.15	0.3	0.048	0.099	0.16	0.12	0.23
Vomiting	0.09	0.25	0.16	0.06	0.39	0.009	0.11	0.08	0.04	0.28
Pain anywhere in the abdomen	0.18	**0.58**	0.25	0.36	0.11	0.22	0.11	0.09	0.06	-0.087
Abdominal pain related to defecation	0.21	0.2	0.11	**0.73**	0.13	0.16	0.13	0.1	0.08	0.028
Abdominal pain related to stool consistency	0.22	0.16	0.12	**0.81**	0.13	0.14	0.19	0.11	0.07	0.0065
Abdominal pain related to stool frequency	0.21	0.16	0.15	**0.79**	0.15	0.13	0.19	0.11	0.09	0.043
Hard stools	**0.56**	0.08	0.1	0.15	0.08	0.057	0.009	0.06	0.07	0.014
Infrequent stools	**0.49**	0.07	0.09	0.05	0.09	0.036	0.014	0.05	0.05	0.028
Straining during bowel movements	**0.81**	0.14	0.09	0.15	0.07	0.073	0.07	0.08	0.05	-0.026
Incomplete bowel emptying	**0.76**	0.22	0.09	0.18	0.1	0.11	0.18	0.09	0.05	-0.053
Anorectal obstruction/blockage	**0.84**	0.19	0.12	0.14	0.11	0.085	0.1	0.08	0.06	0.0039
Manual maneuvers to facilitate defecation	**0.55**	0.09	0.13	0.04	0.1	0.054	0.047	0.06	0.08	0.14
RUQ pain	0.16	**0.51**	**0.41**	0.16	0.09	**0.45**	0.1	0.08	0.08	-0.13
Long-lasting RUQ pain	0.18	0.23	**0.71**	0.18	0.09	0.28	0.13	0.11	0.08	-0.19
RUQ pain of steady severe level	0.2	0.2	**0.79**	0.17	0.14	0.16	0.12	0.1	0.11	-0.082
RUQ pain goes away between episodes	0.09	0.13	0.13	0.14	0.03	**0.72**	0.072	0.05	0.02	-0.046
RUQ pain limits usual activities	0.17	0.17	**0.64**	0.15	0.16	0.17	0.14	0.09	0.12	0.15
Pain with swallowing	0.16	0.15	0.18	0.15	0.21	0.062	0.096	**0.58**	0.26	0.093
Chest pain	0.12	0.36	0.15	0.08	0.12	0.095	0.11	0.21	**0.49**	-0.036
Epigastric pain/burning	0.12	**0.54**	0.35	0.17	0.21	0.13	0.067	0.1	0.24	0.13
Epigastric pain/burning improved by defecation	0.12	0.32	0.2	0.29	0.17	0.19	0.065	0.11	0.22	0.14
Self-induced vomiting	0.07	0.08	0.13	0.08	0.29	0.038	0.095	0.06	0.04	0.22
Food coming back up after swallowing	0.12	0.35	0.07	0.07	**0.58**	0.088	0.083	0.1	0.1	-0.029
Retching	0.12	0.12	0.14	0.13	**0.85**	0.069	0.099	0.12	0.11	-0.032
Vomiting when food comes back up	0.13	0.12	0.16	0.12	**0.78**	0.056	0.087	0.11	0.1	0.053
Food coming back up is recognizable	0.09	0.1	0.06	0.11	**0.45**	0.051	0.076	0.06	0.1	-0.012
Belching	0.14	0.4	0.13	0.1	0.29	0.047	0.11	0.12	0.14	0.093
Abdominal pain related to a meal	0.16	0.29	0.29	**0.47**	0.17	0.15	0.16	0.08	0.12	0.016
Abdominal pain limits usual activities	0.2	0.28	0.35	**0.47**	0.17	0.075	0.17	0.09	0.07	0.062
Loose stools	0.07	0.13	0.12	0.16	0.1	0.066	**0.82**	0.05	0.07	-0.006
Loose stools following a meal	0.06	0.1	0.11	0.2	0.13	0.073	**0.75**	0.07	0.06	0.018
Urgency	0.19	0.18	0.16	0.15	0.17	0.095	**0.55**	0.09	0.09	0.065
Bloating/abdominal distention	0.29	**0.49**	0.09	0.16	0.09	0.2	0.17	0.09	0.04	-0.073
RUQ pain related to defecation	0.23	0.15	0.35	0.33	0.15	0.29	0.15	0.1	0.07	0.11
RUQ pain related to posture	0.14	0.13	0.22	0.15	0.07	**0.69**	0.076	0.09	0.07	0.04
RUQ pain improved by medicine	0.07	0.14	0.23	0.1	0.12	**0.58**	0.055	0.05	0.14	0.1
RUQ pain and nausea/vomiting	0.13	0.18	**0.47**	0.11	0.3	0.19	0.15	0.1	0.08	0.25
RUQ pain and back/right shoulder blade pain	0.2	0.21	**0.44**	0.09	0.16	0.24	0.087	0.11	0.17	0.16
RUQ pain waking one up	0.17	0.17	**0.51**	0.14	0.23	0.17	0.13	0.09	0.15	0.21
Fecal incontinence	0.1	0.15	0.12	0.05	0.17	0.052	0.23	0.04	0.05	0.14
Anorectal pain	0.34	0.36	0.15	0.14	0.14	0.12	0.14	0.09	0.04	0.053

Supplementary Figure and Table 6 - Middle East



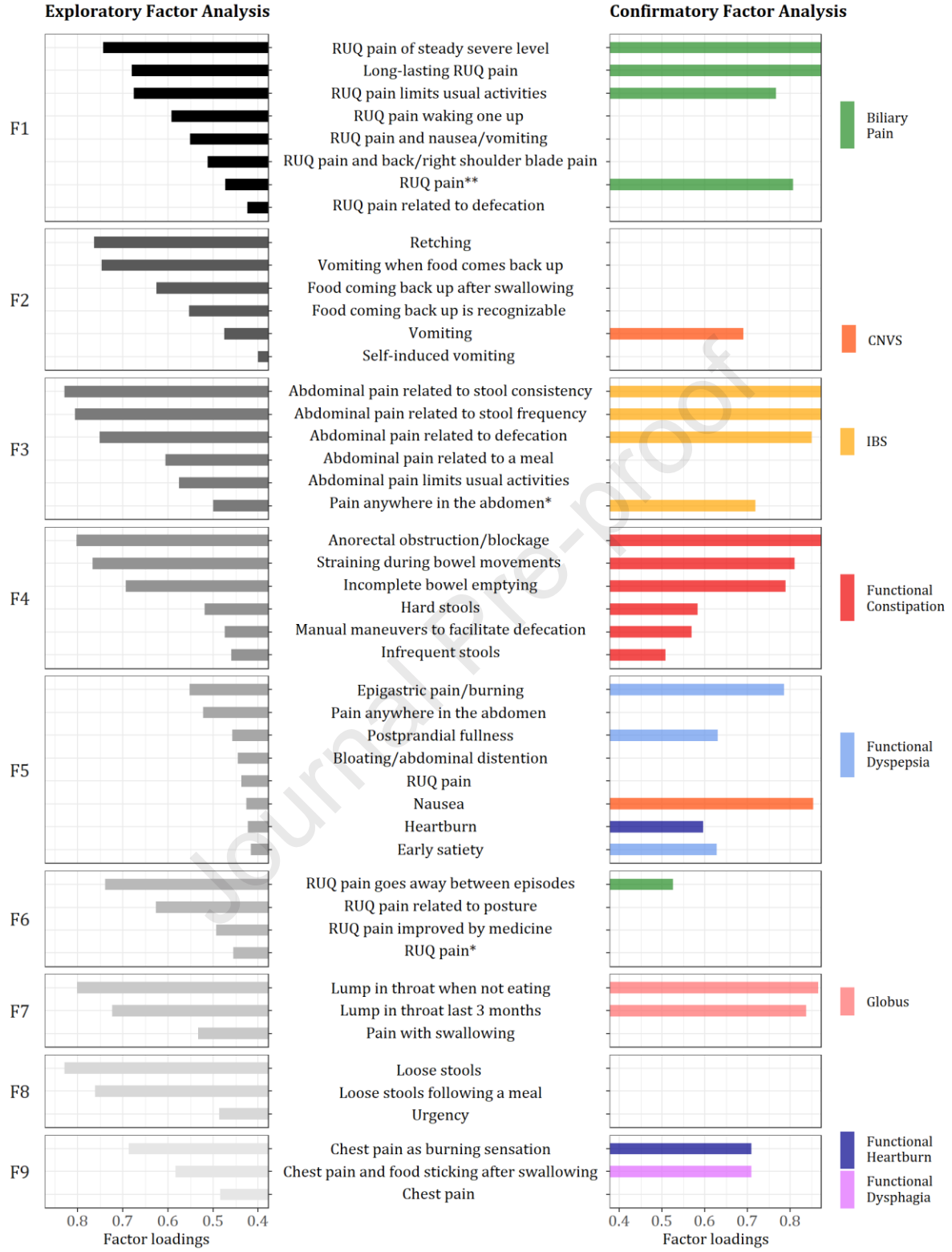
Item	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Lump in throat last 3 months	0.09	0.12	0.07	0.29	0.11	0.1	**0.69**	0.07	0.11	0.08
Lump in throat when not eating	0.11	0.11	0.14	0.13	0.16	0.08	**0.83**	0.07	0.14	0.07
Chest pain as burning sensation	0.21	0.15	0.13	0.22	0.17	0.07	0.19	0.07	**0.74**	0.06
Heartburn	0.07	0.12	0.12	**0.42**	0.11	0.09	0.07	0.07	0.26	0.09
Chest pain and food sticking after swallowing	0.17	0.1	0.11	0.15	0.19	0.06	0.23	0.09	**0.6**	0.1
Food stuck in chest	0.16	0.16	0.13	0.36	0.2	0.1	0.25	0.07	0.22	0.11
Postprandial fullness	0.12	0.16	0.11	**0.45**	0.12	0.06	0.13	0.07	0.093	0.06
Early satiety	0.11	0.18	0.1	**0.44**	0.14	0.05	0.13	0.07	0.095	0.1
Nausea	0.24	0.14	0.17	**0.43**	0.23	0.07	0.15	0.09	0.091	0.36
Vomiting	0.14	0.1	0.04	0.23	0.22	0.05	0.09	0.06	0.055	**0.8**
Pain anywhere in the abdomen	0.25	0.21	**0.51**	**0.52**	0.05	0.2	0.06	0.1	0.055	0.05
Abdominal pain related to defecation	0.12	0.2	**0.75**	0.16	0.11	0.19	0.1	0.12	0.095	0.04
Abdominal pain related to stool consistency	0.12	0.26	**0.81**	0.14	0.1	0.18	0.09	0.18	0.076	0.06
Abdominal pain related to stool frequency	0.14	0.26	**0.78**	0.14	0.12	0.15	0.08	0.18	0.098	0.06
Hard stools	0.18	**0.56**	0.16	0.12	0.1	0.08	0.07	0.04	0.061	0.08
Infrequent stools	0.11	0.4	0.11	0.1	0.08	0.06	0.04	0.1	0.054	0.08
Straining during bowel movements	0.11	**0.8**	0.19	0.15	0.09	0.11	0.08	0.04	0.064	0.04
Incomplete bowel emptying	0.12	**0.75**	0.16	0.2	0.08	0.1	0.08	0.11	0.063	0.02
Anorectal obstruction/blockage	0.15	**0.83**	0.16	0.17	0.1	0.09	0.08	0.08	0.086	0.05
Manual maneuvers to facilitate defecation	0.18	**0.47**	0.07	0.07	0.14	0.09	0.07	0.08	0.077	0.08
RUQ pain	**0.52**	0.2	0.17	**0.4**	0.08	**0.45**	0.1	0.07	0.063	0.05
Long-lasting RUQ pain	**0.75**	0.22	0.18	0.2	0.08	0.27	0.09	0.09	0.063	0.04
RUQ pain of steady severe level	**0.81**	0.23	0.16	0.17	0.11	0.16	0.09	0.12	0.075	0.05
RUQ pain goes away between episodes	0.22	0.13	0.19	0.1	0.06	**0.71**	0.07	0.09	0.057	0.02
RUQ pain limits usual activities	**0.69**	0.17	0.15	0.14	0.13	0.17	0.1	0.1	0.15	0.1
Pain with swallowing	0.17	0.14	0.12	0.13	0.17	0.05	**0.62**	0.1	0.23	0.12
Chest pain	0.15	0.13	0.1	0.39	0.09	0.09	0.14	0.06	**0.5**	0.08
Epigastric pain/burning	**0.43**	0.15	0.2	**0.53**	0.19	0.1	0.09	0.09	0.12	0.09
Epigastric pain/burning improved by defecation	0.3	0.15	0.29	0.32	0.21	0.13	0.1	0.08	0.13	0.04
Self-induced vomiting	0.12	0.12	0.06	0.07	0.23	0.05	0.11	0.09	0.1	**0.58**
Food coming back up after swallowing	0.12	0.15	0.1	0.36	**0.62**	0.09	0.12	0.08	0.064	0.09
Retching	0.19	0.14	0.13	0.13	**0.79**	0.08	0.15	0.09	0.14	0.16
Vomiting when food comes back up	0.2	0.15	0.14	0.15	**0.71**	0.08	0.13	0.08	0.098	0.23
Food coming back up is recognizable	0.11	0.15	0.09	0.13	**0.54**	0.07	0.08	0.11	0.12	0.13
Belching	0.18	0.17	0.1	0.32	0.27	0.05	0.11	0.09	0.11	0.07
Abdominal pain related to a meal	0.27	0.18	**0.58**	0.22	0.15	0.13	0.11	0.16	0.11	0.05
Abdominal pain limits usual activities	0.37	0.22	**0.53**	0.25	0.13	0.08	0.13	0.15	0.078	0.08
Loose stools	0.11	0.12	0.14	0.11	0.09	0.07	0.07	**0.83**	0.05	0.06
Loose stools following a meal	0.1	0.09	0.21	0.08	0.1	0.1	0.07	**0.76**	0.047	0.06
Urgency	0.19	0.25	0.21	0.16	0.12	0.07	0.08	**0.5**	0.094	0.05
Bloating/abdominal distention	0.19	0.36	0.19	**0.42**	0.09	0.18	0.1	0.12	0.009	0.01
RUQ pain related to defecation	0.38	0.24	0.3	0.13	0.15	**0.46**	0.09	0.13	0.081	0.08
RUQ pain related to posture	0.33	0.18	0.15	0.11	0.12	**0.55**	0.09	0.09	0.084	0.04
RUQ pain improved by medicine	0.21	0.09	0.14	0.11	0.06	**0.6**	0.05	0.05	0.032	0.05
RUQ pain and nausea/vomiting	**0.48**	0.16	0.11	0.16	0.22	0.21	0.08	0.12	0.13	0.26
RUQ pain and back/right shoulder blade pain	**0.51**	0.2	0.11	0.2	0.16	0.23	0.11	0.1	0.16	0.1
RUQ pain waking one up	**0.65**	0.16	0.14	0.14	0.18	0.17	0.08	0.09	0.15	0.14
Fecal incontinence	0.12	0.06	0.07	0.22	0.09	0.07	0.07	0.21	0.096	0.15
Anorectal pain	0.21	0.33	0.17	0.34	0.12	0.11	0.1	0.08	0.085	0.07

Supplementary Figure and Table 7 - Asia



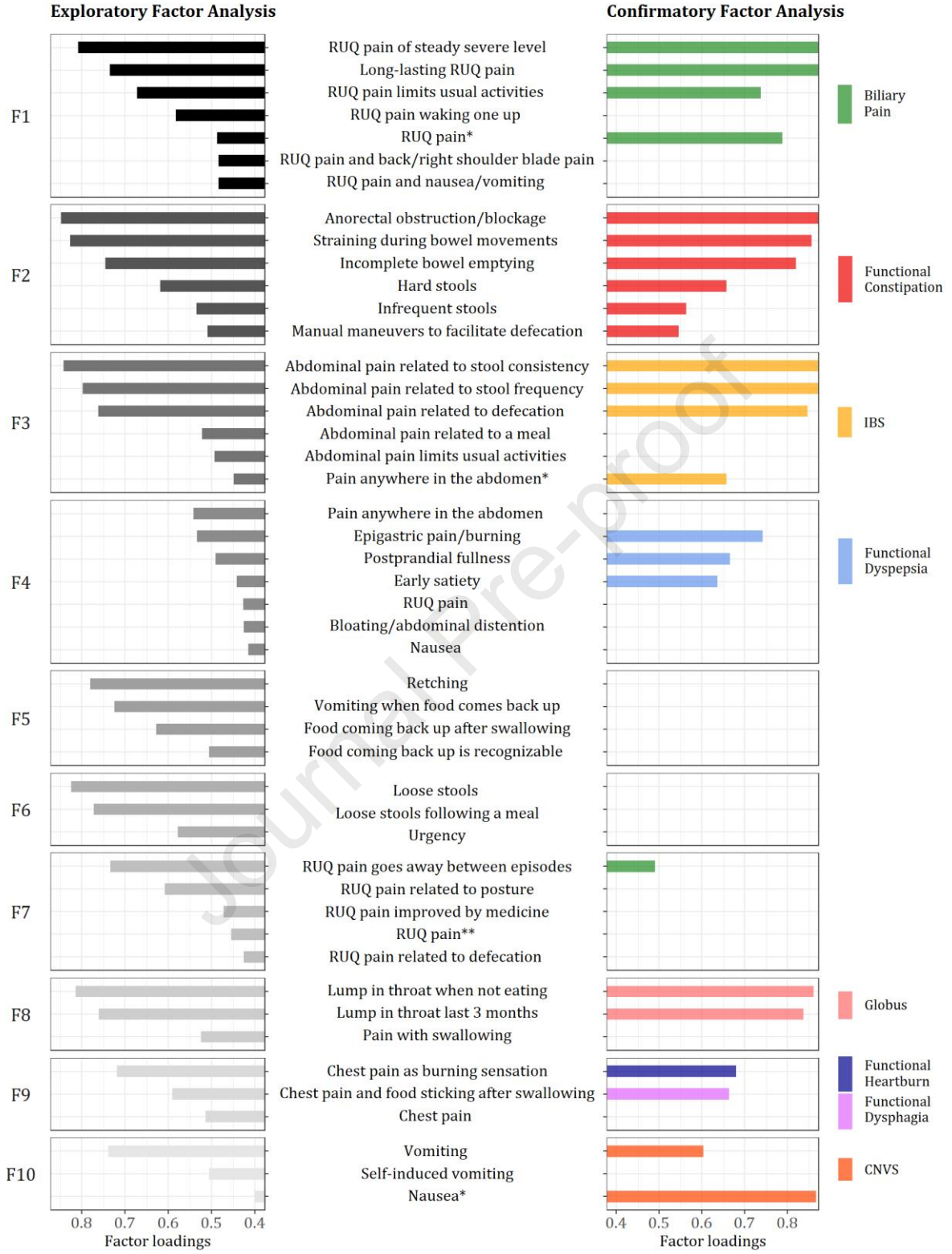
Item	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lump in throat last 3 months	0.11	0.09	0.08	0.28	0.1	0.09	**0.74**	0.06	0.048
Lump in throat when not eating	0.17	0.13	0.13	0.14	0.14	0.18	**0.84**	0.08	0.069
Chest pain as burning sensation	0.28	0.14	0.13	0.2	0.19	**0.73**	0.15	0.08	0.11
Heartburn	0.21	0.17	0.12	**0.41**	0.18	0.34	0.15	0.09	0.084
Chest pain and food sticking after swallowing	0.29	0.13	0.13	0.18	0.21	**0.66**	0.19	0.06	0.13
Food stuck in chest	0.23	0.14	0.13	**0.42**	0.2	0.31	0.27	0.08	0.13
Postprandial fullness	0.19	0.16	0.18	**0.52**	0.19	0.12	0.15	0.09	0.09
Early satiety	0.19	0.15	0.18	**0.47**	0.18	0.11	0.13	0.07	0.13
Nausea	0.28	0.15	0.13	**0.43**	0.23	0.18	0.16	0.07	0.4
Vomiting	0.22	0.08	0.11	0.29	0.24	0.13	0.1	0.05	**0.73**
Pain anywhere in the abdomen	0.36	**0.55**	0.14	**0.44**	0.11	0.07	0.08	0.09	0.062
Abdominal pain related to defecation	0.23	**0.78**	0.16	0.15	0.09	0.08	0.06	0.1	0.067
Abdominal pain related to stool consistency	0.2	**0.87**	0.16	0.11	0.09	0.07	0.08	0.12	0.062
Abdominal pain related to stool frequency	0.23	**0.83**	0.16	0.11	0.12	0.09	0.08	0.13	0.073
Hard stools	0.14	0.1	**0.61**	0.07	0.07	0.07	0.06	0.01	0.051
Infrequent stools	0.15	0.07	**0.61**	0.07	0.04	0.06	0.03	0.06	0.058
Straining during bowel movements	0.11	0.15	**0.8**	0.1	0.06	0.03	0.07	0.06	0.048
Incomplete bowel emptying	0.14	0.18	**0.75**	0.19	0.11	0.04	0.08	0.18	-0.0028
Anorectal obstruction/blockage	0.17	0.16	**0.86**	0.13	0.09	0.05	0.05	0.08	0.039
Manual maneuvers to facilitate defecation	0.23	0.02	**0.49**	0.07	0.12	0.11	0.06	0.06	0.11
RUQ pain	**0.6**	0.27	0.17	**0.43**	0.1	0.09	0.11	0.11	0.029
Long-lasting RUQ pain	**0.8**	0.22	0.19	0.16	0.1	0.06	0.09	0.11	0.044
RUQ pain of steady severe level	**0.8**	0.21	0.21	0.12	0.12	0.1	0.1	0.12	0.089
RUQ pain goes away between episodes	**0.5**	0.31	0.12	0.2	0.06	0.03	0.04	0.08	-0.033
RUQ pain limits usual activities	**0.7**	0.1	0.16	0.08	0.14	0.14	0.08	0.09	0.16
Pain with swallowing	0.25	0.13	0.15	0.15	0.21	0.33	**0.5**	0.06	0.13
Chest pain	0.23	0.14	0.1	0.4	0.12	**0.51**	0.19	0.06	0.11
Epigastric pain/burning	**0.5**	0.2	0.09	**0.49**	0.16	0.25	0.11	0.06	0.15
Epigastric pain/burning improved by defecation	0.38	0.32	0.08	0.31	0.14	0.23	0.1	0.05	0.066
Self-induced vomiting	0.17	0.12	0.11	0.08	0.23	0.1	0.06	0.08	**0.56**
Food coming back up after swallowing	0.17	0.08	0.11	0.37	**0.59**	0.11	0.12	0.08	0.16
Retching	0.25	0.14	0.14	0.14	**0.78**	0.17	0.11	0.07	0.16
Vomiting when food comes back up	0.23	0.18	0.14	0.15	**0.74**	0.16	0.1	0.07	0.17
Food coming back up is recognizable	0.14	0.13	0.11	0.19	**0.56**	0.09	0.1	0.06	0.098
Belching	0.21	0.1	0.11	**0.44**	0.24	0.13	0.19	0.05	0.11
Abdominal pain related to a meal	0.35	**0.62**	0.16	0.15	0.15	0.14	0.1	0.13	0.084
Abdominal pain limits usual activities	**0.4**	**0.58**	0.17	0.15	0.15	0.14	0.08	0.11	0.095
Loose stools	0.16	0.13	0.13	0.11	0.07	0.05	0.06	**0.83**	0.051
Loose stools following a meal	0.18	0.17	0.11	0.09	0.08	0.06	0.06	**0.86**	0.059
Urgency	0.24	0.23	0.27	0.13	0.1	0.09	0.06	**0.45**	0.079
Bloating/abdominal distention	0.22	0.21	0.36	**0.43**	0.11	0.03	0.09	0.15	0.0009
RUQ pain related to defecation	**0.6**	0.37	0.19	0.16	0.12	0.06	0.12	0.13	0.056
RUQ pain related to posture	**0.6**	0.24	0.16	0.2	0.1	0.09	0.09	0.07	0.03
RUQ pain improved by medicine	**0.6**	0.19	0.1	0.19	0.1	0.11	0.06	0.06	0.023
RUQ pain and nausea/vomiting	**0.6**	0.14	0.17	0.14	0.23	0.2	0.09	0.1	0.25
RUQ pain and back/right shoulder blade pain	**0.6**	0.11	0.19	0.14	0.17	0.21	0.11	0.09	0.19
RUQ pain waking one up	**0.7**	0.12	0.16	0.1	0.17	0.18	0.08	0.11	0.16
Fecal incontinence	0.24	0.04	0.09	0.22	0.16	0.16	0.05	0.13	0.17
Anorectal pain	0.31	0.21	0.23	0.35	0.17	0.15	0.09	0.1	0.13

Supplementary Figure and Table 8 - Males



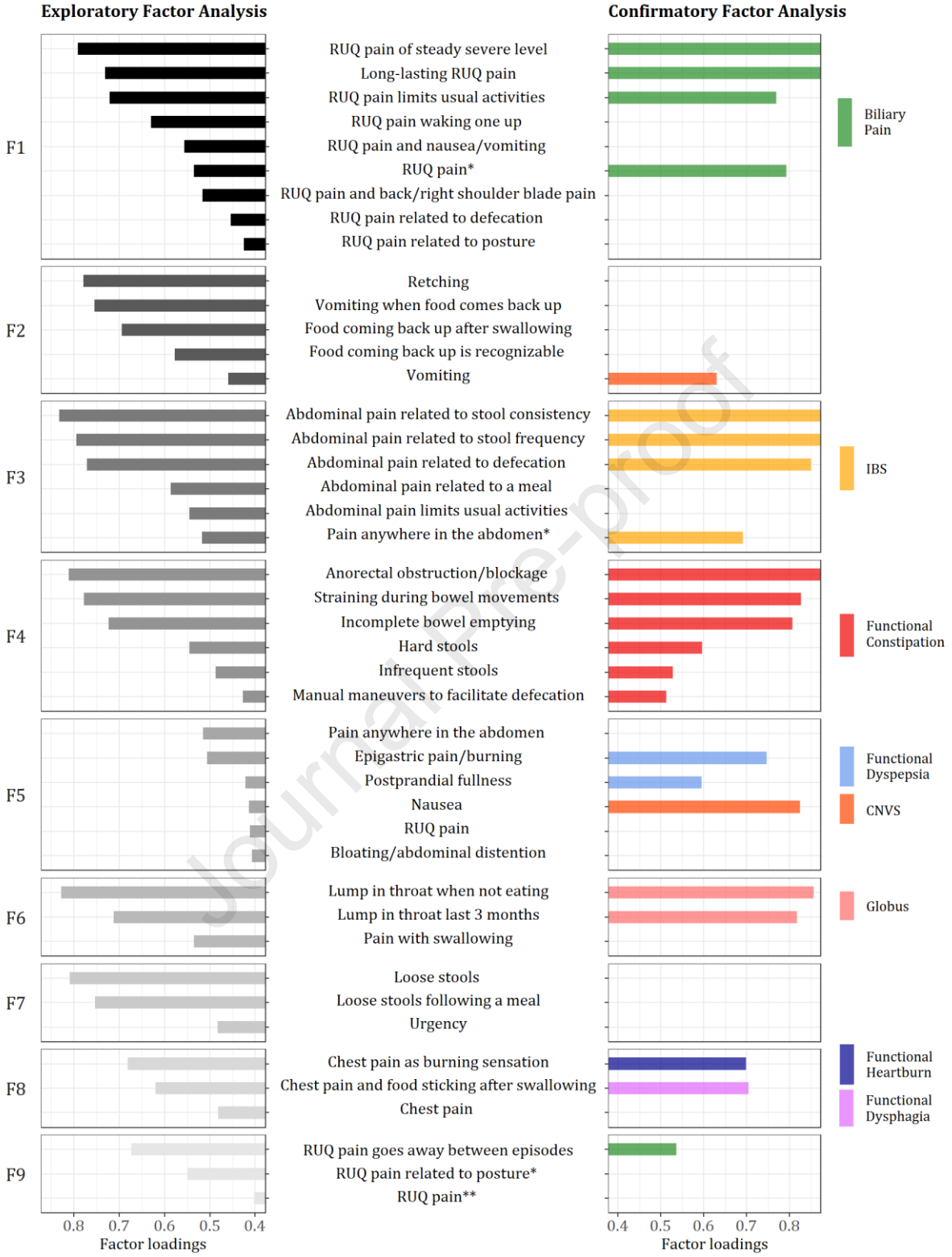
Item	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lump in throat last 3 months	0.09	0.17	0.09	0.13	0.28	0.086	**0.72**	0.06	0.1
Lump in throat when not eating	0.14	0.2	0.14	0.15	0.14	0.081	**0.8**	0.08	0.14
Chest pain as burning sensation	0.19	0.22	0.16	0.16	0.21	0.11	0.17	0.09	**0.69**
Heartburn	0.09	0.2	0.16	0.12	**0.42**	0.16	0.13	0.1	0.24
Chest pain and food sticking after swallowing	0.19	0.29	0.15	0.15	0.16	0.09	0.19	0.08	**0.58**
Food stuck in chest	0.14	0.31	0.13	0.18	0.38	0.1	0.27	0.08	0.25
Postprandial fullness	0.11	0.22	0.16	0.21	**0.46**	0.12	0.16	0.1	0.11
Early satiety	0.14	0.26	0.14	0.2	**0.42**	0.083	0.15	0.1	0.1
Nausea	0.28	0.4	0.16	0.15	**0.43**	0.035	0.17	0.09	0.14
Vomiting	0.25	**0.48**	0.08	0.11	0.29	0.005	0.12	0.1	0.11
Pain anywhere in the abdomen	0.26	0.13	**0.5**	0.16	**0.52**	0.22	0.09	0.09	0.07
Abdominal pain related to defecation	0.13	0.14	**0.75**	0.18	0.15	0.19	0.1	0.12	0.1
Abdominal pain related to stool consistency	0.12	0.13	**0.83**	0.21	0.15	0.18	0.1	0.17	0.09
Abdominal pain related to stool frequency	0.16	0.16	**0.81**	0.21	0.15	0.15	0.09	0.16	0.09
Hard stools	0.13	0.13	0.12	**0.52**	0.09	0.059	0.07	0.05	0.08
Infrequent stools	0.12	0.1	0.07	**0.46**	0.08	0.05	0.05	0.07	0.06
Straining during bowel movements	0.1	0.11	0.17	**0.77**	0.13	0.096	0.08	0.06	0.05
Incomplete bowel emptying	0.1	0.11	0.19	**0.69**	0.19	0.12	0.1	0.18	0.05
Anorectal obstruction/blockage	0.16	0.14	0.16	**0.8**	0.17	0.096	0.09	0.09	0.08
Manual maneuvers to facilitate defecation	0.24	0.23	0.06	**0.47**	0.08	0.026	0.08	0.09	0.09
RUQ pain	**0.47**	0.13	0.23	0.18	**0.44**	**0.46**	0.11	0.11	0.07
Long-lasting RUQ pain	**0.68**	0.12	0.23	0.2	0.23	0.3	0.1	0.11	0.07
RUQ pain of steady severe level	**0.74**	0.18	0.21	0.22	0.19	0.19	0.11	0.12	0.09
RUQ pain goes away between episodes	0.19	0.04	0.21	0.1	0.12	**0.74**	0.06	0.08	0.05
RUQ pain limits usual activities	**0.68**	0.23	0.18	0.2	0.16	0.15	0.1	0.11	0.12
Pain with swallowing	0.2	0.28	0.15	0.19	0.14	0.062	**0.53**	0.08	0.24
Chest pain	0.16	0.16	0.14	0.14	0.4	0.12	0.19	0.08	**0.48**
Epigastric pain/burning	0.38	0.28	0.23	0.14	**0.55**	0.1	0.12	0.07	0.17
Epigastric pain/burning improved by defecation	0.24	0.23	0.32	0.14	0.33	0.16	0.1	0.06	0.17
Self-induced vomiting	0.18	**0.4**	0.08	0.1	0.09	0.008	0.09	0.09	0.09
Food coming back up after swallowing	0.1	**0.63**	0.1	0.15	0.34	0.13	0.13	0.09	0.07
Retching	0.18	**0.76**	0.15	0.18	0.12	0.1	0.12	0.09	0.12
Vomiting when food comes back up	0.2	**0.75**	0.16	0.16	0.13	0.094	0.1	0.09	0.12
Food coming back up is recognizable	0.07	**0.55**	0.11	0.14	0.12	0.11	0.09	0.08	0.08
Belching	0.19	0.32	0.14	0.18	0.39	0.052	0.12	0.08	0.09
Abdominal pain related to a meal	0.28	0.2	**0.61**	0.19	0.23	0.12	0.1	0.13	0.12
Abdominal pain limits usual activities	0.37	0.21	**0.58**	0.2	0.23	0.073	0.11	0.13	0.11
Loose stools	0.12	0.13	0.15	0.14	0.13	0.085	0.06	**0.83**	0.05
Loose stools following a meal	0.13	0.15	0.19	0.13	0.1	0.084	0.07	**0.76**	0.06
Urgency	0.2	0.19	0.19	0.27	0.16	0.071	0.08	**0.49**	0.09
Bloating/abdominal distention	0.15	0.11	0.2	0.31	**0.45**	0.2	0.11	0.18	0.04
RUQ pain related to defecation	**0.42**	0.2	0.33	0.22	0.13	0.36	0.11	0.13	0.09
RUQ pain related to posture	0.33	0.13	0.19	0.16	0.14	**0.63**	0.08	0.07	0.1
RUQ pain improved by medicine	0.3	0.18	0.16	0.11	0.15	**0.49**	0.06	0.07	0.12
RUQ pain and nausea/vomiting	**0.55**	0.37	0.13	0.18	0.15	0.14	0.12	0.12	0.14
RUQ pain and back/right shoulder blade pain	**0.51**	0.23	0.13	0.21	0.19	0.24	0.11	0.11	0.15
RUQ pain waking one up	**0.59**	0.26	0.17	0.19	0.17	0.2	0.09	0.12	0.14
Fecal incontinence	0.19	0.25	0.08	0.13	0.25	0.025	0.06	0.2	0.09
Anorectal pain	0.24	0.21	0.18	0.32	0.36	0.11	0.1	0.12	0.08

Supplementary Figure and Table 9 - Females



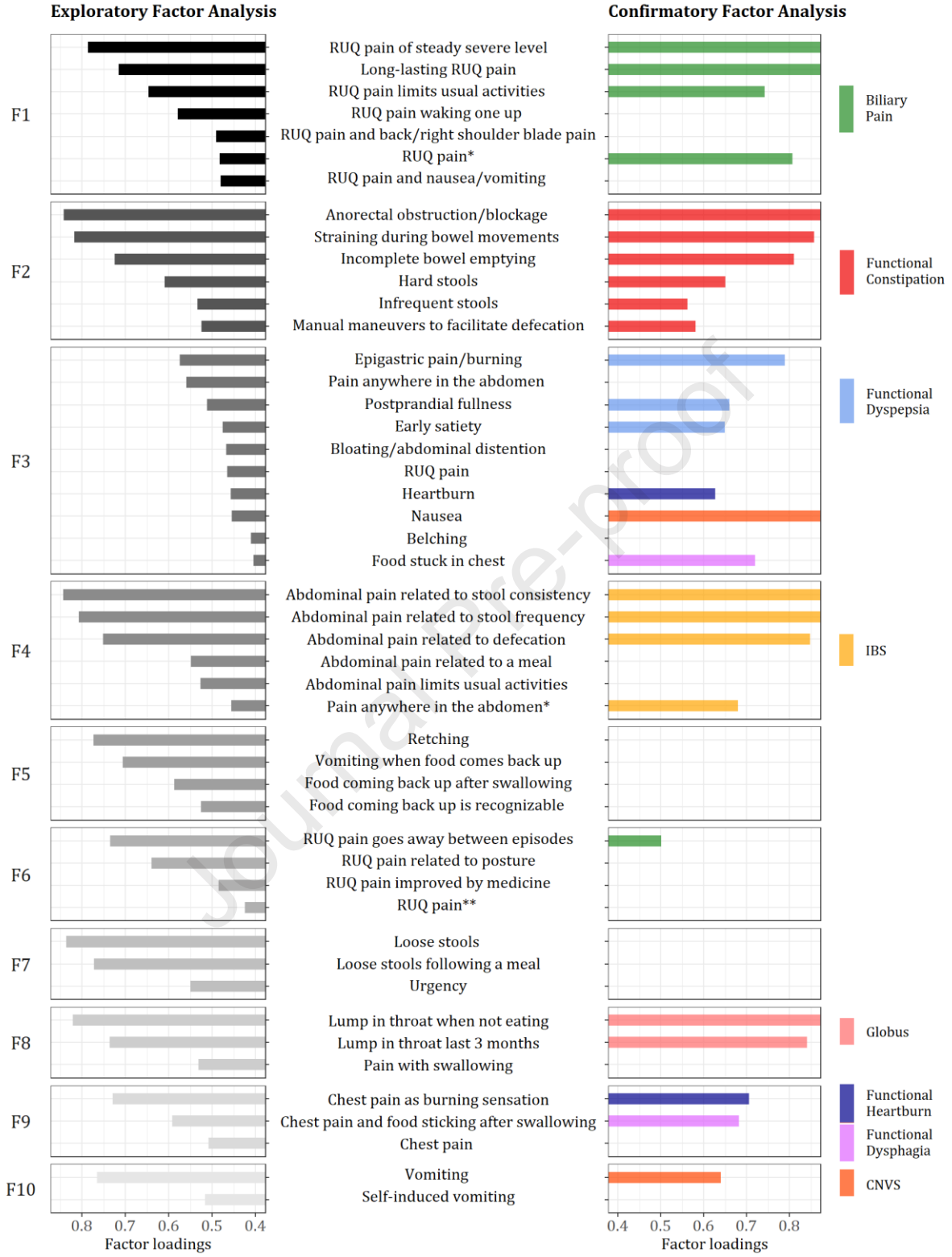
Item	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Lump in throat last 3 months	0.07	0.1	0.062	0.23	0.11	0.069	0.067	**0.76**	0.11	0.064
Lump in throat when not eating	0.11	0.12	0.11	0.12	0.12	0.076	0.076	**0.81**	0.16	0.062
Chest pain as burning sensation	0.18	0.12	0.11	0.18	0.14	0.084	0.081	0.15	**0.72**	0.07
Heartburn	0.11	0.11	0.11	0.4	0.17	0.094	0.13	0.13	0.27	0.056
Chest pain and food sticking after swallowing	0.16	0.1	0.1	0.13	0.19	0.083	0.084	0.17	**0.59**	0.11
Food stuck in chest	0.13	0.15	0.11	0.34	0.23	0.094	0.11	0.28	0.29	0.091
Postprandial fullness	0.15	0.19	0.13	**0.49**	0.16	0.11	0.079	0.15	0.13	0.11
Early satiety	0.15	0.17	0.12	**0.44**	0.15	0.12	0.057	0.13	0.13	0.15
Nausea	0.24	0.13	0.14	**0.42**	0.21	0.11	0.049	0.15	0.12	**0.4**
Vomiting	0.14	0.082	0.042	0.21	0.25	0.092	0.027	0.088	0.067	**0.74**
Pain anywhere in the abdomen	0.29	0.17	**0.45**	**0.54**	0.09	0.12	0.2	0.095	0.063	0.038
Abdominal pain related to defecation	0.11	0.18	**0.76**	0.15	0.092	0.15	0.19	0.077	0.094	0.038
Abdominal pain related to stool consistency	0.12	0.21	**0.84**	0.12	0.099	0.2	0.16	0.082	0.077	0.059
Abdominal pain related to stool frequency	0.15	0.21	**0.8**	0.12	0.11	0.2	0.14	0.082	0.097	0.07
Hard stools	0.11	**0.62**	0.12	0.089	0.072	-0.02	0.07	0.072	0.06	0.047
Infrequent stools	0.098	**0.53**	0.063	0.072	0.066	0.048	0.057	0.031	0.04	0.049
Straining during bowel movements	0.093	**0.83**	0.15	0.1	0.066	0.046	0.078	0.061	0.046	0.041
Incomplete bowel emptying	0.11	**0.75**	0.17	0.17	0.082	0.16	0.11	0.078	0.048	0.022
Anorectal obstruction/blockage	0.14	**0.85**	0.13	0.14	0.091	0.08	0.082	0.068	0.069	0.042
Manual maneuvers to facilitate defecation	0.13	**0.51**	0.029	0.068	0.083	0.042	0.053	0.055	0.1	0.082
RUQ pain	**0.49**	0.2	0.18	**0.43**	0.088	0.12	**0.45**	0.099	0.072	0.024
Long-lasting RUQ pain	**0.73**	0.2	0.18	0.21	0.086	0.12	0.28	0.091	0.046	0.015
RUQ pain of steady severe level	**0.81**	0.21	0.17	0.17	0.11	0.13	0.16	0.092	0.09	0.043
RUQ pain goes away between episodes	0.18	0.12	0.18	0.088	0.036	0.081	**0.73**	0.056	0.036	0.021
RUQ pain limits usual activities	**0.67**	0.15	0.14	0.15	0.12	0.13	0.14	0.085	0.13	0.12
Pain with swallowing	0.17	0.13	0.11	0.12	0.19	0.081	0.05	**0.53**	0.27	0.13
Chest pain	0.14	0.13	0.094	0.32	0.095	0.09	0.11	0.2	**0.51**	0.08
Epigastric pain/burning	0.38	0.13	0.16	**0.53**	0.2	0.11	0.1	0.089	0.22	0.086
Epigastric pain/burning improved by defecation	0.23	0.11	0.27	0.31	0.18	0.11	0.17	0.071	0.22	0.029
Self-induced vomiting	0.083	0.094	0.06	0.036	0.18	0.08	0.049	0.064	0.088	**0.51**
Food coming back up after swallowing	0.1	0.13	0.077	0.34	**0.63**	0.1	0.081	0.12	0.11	0.13
Retching	0.16	0.13	0.11	0.14	**0.78**	0.1	0.057	0.12	0.13	0.16
Vomiting when food comes back up	0.17	0.12	0.12	0.14	**0.72**	0.11	0.059	0.099	0.11	0.23
Food coming back up is recognizable	0.092	0.098	0.08	0.11	**0.51**	0.074	0.076	0.081	0.1	0.085
Belching	0.15	0.12	0.079	0.36	0.25	0.095	0.036	0.11	0.12	0.1
Abdominal pain related to a meal	0.29	0.16	**0.52**	0.28	0.13	0.19	0.14	0.075	0.11	0.053
Abdominal pain limits usual activities	0.38	0.17	**0.49**	0.28	0.12	0.16	0.07	0.1	0.098	0.1
Loose stools	0.12	0.067	0.16	0.12	0.073	**0.82**	0.076	0.055	0.042	0.054
Loose stools following a meal	0.12	0.064	0.21	0.082	0.086	**0.77**	0.077	0.058	0.06	0.053
Urgency	0.17	0.17	0.2	0.14	0.11	**0.58**	0.09	0.072	0.083	0.06
Bloating/abdominal distention	0.15	0.35	0.18	**0.43**	0.086	0.16	0.2	0.098	0.034	0.0031
RUQ pain related to defecation	0.35	0.22	0.32	0.084	0.11	0.16	**0.43**	0.075	0.088	0.066
RUQ pain related to posture	0.3	0.16	0.16	0.11	0.085	0.081	**0.61**	0.073	0.099	0.051
RUQ pain improved by medicine	0.26	0.097	0.11	0.14	0.11	0.065	**0.47**	0.043	0.13	0.052
RUQ pain and nausea/vomiting	**0.48**	0.14	0.12	0.16	0.21	0.13	0.19	0.079	0.13	0.27
RUQ pain and back/right shoulder blade pain	**0.48**	0.18	0.1	0.19	0.14	0.1	0.25	0.093	0.19	0.091
RUQ pain waking one up	**0.58**	0.16	0.12	0.15	0.17	0.14	0.17	0.081	0.18	0.13
Fecal incontinence	0.12	0.053	0.059	0.14	0.13	0.29	0.052	0.054	0.099	0.12
Anorectal pain	0.17	0.34	0.16	0.32	0.14	0.12	0.1	0.089	0.11	0.055

Supplementary Figure and Table 10 - Age 18-34



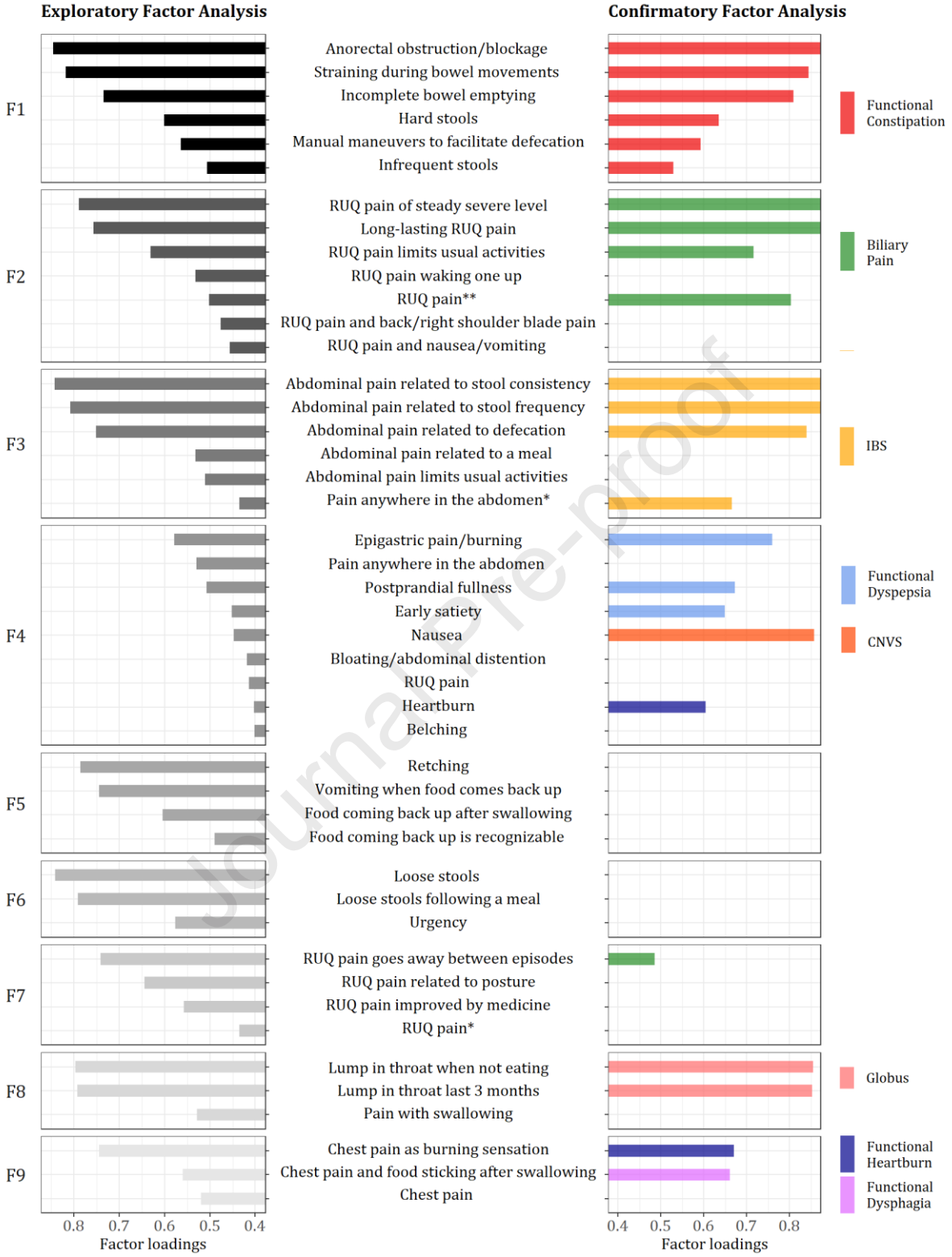
Item	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lump in throat last 3 months	0.087	0.17	0.063	0.094	0.24	**0.71**	0.063	0.11	0.061
Lump in throat when not eating	0.12	0.18	0.13	0.12	0.1	**0.83**	0.07	0.15	0.064
Chest pain as burning sensation	0.2	0.23	0.12	0.14	0.17	0.18	0.078	**0.68**	0.072
Heartburn	0.13	0.22	0.15	0.12	0.38	0.13	0.093	0.26	0.12
Chest pain and food sticking after swallowing	0.19	0.27	0.12	0.1	0.11	0.18	0.084	**0.62**	0.061
Food stuck in chest	0.16	0.31	0.12	0.15	0.32	0.24	0.064	0.3	0.081
Postprandial fullness	0.13	0.22	0.13	0.19	**0.42**	0.12	0.084	0.12	0.071
Early satiety	0.14	0.23	0.13	0.19	0.39	0.13	0.069	0.11	0.04
Nausea	0.24	0.36	0.16	0.14	**0.41**	0.15	0.082	0.11	0.0019
Vomiting	0.19	**0.46**	0.049	0.089	0.25	0.099	0.094	0.1	-0.022
Pain anywhere in the abdomen	0.27	0.13	**0.52**	0.18	**0.52**	0.074	0.077	0.044	0.15
Abdominal pain related to defecation	0.13	0.12	**0.77**	0.19	0.13	0.082	0.12	0.084	0.15
Abdominal pain related to stool consistency	0.12	0.12	**0.83**	0.22	0.097	0.073	0.16	0.066	0.14
Abdominal pain related to stool frequency	0.16	0.14	**0.79**	0.22	0.1	0.072	0.16	0.094	0.11
Hard stools	0.13	0.11	0.13	**0.54**	0.082	0.073	0.0001	0.063	0.053
Infrequent stools	0.11	0.091	0.075	**0.49**	0.082	0.029	0.065	0.062	0.053
Straining during bowel movements	0.12	0.11	0.19	**0.78**	0.11	0.064	0.065	0.044	0.07
Incomplete bowel emptying	0.12	0.12	0.19	**0.72**	0.16	0.079	0.15	0.041	0.099
Anorectal obstruction/blockage	0.16	0.14	0.16	**0.81**	0.14	0.073	0.089	0.072	0.068
Manual maneuvers to facilitate defecation	0.22	0.2	0.04	**0.43**	0.073	0.072	0.083	0.12	0.016
RUQ pain	**0.54**	0.14	0.21	0.2	**0.41**	0.093	0.08	0.062	**0.4**
Long-lasting RUQ pain	**0.73**	0.12	0.22	0.19	0.2	0.093	0.087	0.043	0.21
RUQ pain of steady severe level	**0.79**	0.15	0.19	0.21	0.17	0.099	0.1	0.083	0.11
RUQ pain goes away between episodes	0.3	0.046	0.21	0.12	0.095	0.06	0.074	0.047	**0.67**
RUQ pain limits usual activities	**0.72**	0.2	0.15	0.17	0.13	0.1	0.096	0.13	0.081
Pain with swallowing	0.18	0.24	0.11	0.13	0.085	**0.54**	0.065	0.25	0.029
Chest pain	0.17	0.18	0.097	0.13	0.35	0.19	0.063	**0.48**	0.09
Epigastric pain/burning	0.39	0.28	0.2	0.13	**0.51**	0.11	0.064	0.21	0.045
Epigastric pain/burning improved by defecation	0.26	0.22	0.31	0.1	0.27	0.1	0.076	0.21	0.1
Self-induced vomiting	0.13	0.35	0.061	0.091	0.069	0.082	0.092	0.1	-0.005
Food coming back up after swallowing	0.1	**0.69**	0.097	0.14	0.27	0.1	0.072	0.067	0.1
Retching	0.16	**0.78**	0.12	0.15	0.078	0.12	0.061	0.1	0.082
Vomiting when food comes back up	0.17	**0.75**	0.15	0.14	0.1	0.099	0.065	0.096	0.063
Food coming back up is recognizable	0.086	**0.58**	0.099	0.12	0.07	0.068	0.07	0.11	0.091
Belching	0.16	0.34	0.088	0.15	0.31	0.11	0.081	0.12	0.03
Abdominal pain related to a meal	0.28	0.17	**0.59**	0.17	0.21	0.085	0.15	0.12	0.085
Abdominal pain limits usual activities	0.36	0.16	**0.54**	0.18	0.24	0.1	0.12	0.087	0.018
Loose stools	0.13	0.15	0.17	0.12	0.11	0.069	**0.81**	0.054	0.068
Loose stools following a meal	0.13	0.14	0.21	0.11	0.081	0.054	**0.75**	0.069	0.068
Urgency	0.21	0.18	0.21	0.25	0.14	0.082	**0.48**	0.1	0.052
Bloating/abdominal distention	0.17	0.12	0.22	0.35	**0.41**	0.074	0.15	0.022	0.17
RUQ pain related to defecation	**0.45**	0.16	0.32	0.23	0.093	0.066	0.13	0.092	0.37
RUQ pain related to posture	**0.43**	0.11	0.19	0.17	0.1	0.079	0.064	0.11	**0.55**
RUQ pain improved by medicine	0.38	0.15	0.15	0.11	0.11	0.056	0.072	0.14	0.37
RUQ pain and nausea/vomiting	**0.56**	0.31	0.12	0.15	0.15	0.097	0.12	0.14	0.12
RUQ pain and back/right shoulder blade pain	**0.52**	0.21	0.1	0.2	0.18	0.099	0.098	0.19	0.2
RUQ pain waking one up	**0.63**	0.25	0.13	0.17	0.13	0.082	0.13	0.16	0.095
Fecal incontinence	0.21	0.3	0.043	0.089	0.2	0.091	0.19	0.15	0.0076
Anorectal pain	0.21	0.22	0.17	0.31	0.34	0.09	0.12	0.1	0.076

Supplementary Figure and Table 11 - Age 35-49



Item	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Lump in throat last 3 months	0.08	0.11	0.27	0.08	0.1	0.08	0.067	**0.74**	0.12	0.08
Lump in throat when not eating	0.12	0.14	0.16	0.13	0.14	0.08	0.08	**0.82**	0.16	0.072
Chest pain as burning sensation	0.18	0.13	0.23	0.13	0.16	0.09	0.082	0.17	**0.73**	0.086
Heartburn	0.12	0.12	**0.46**	0.14	0.15	0.13	0.1	0.13	0.27	0.081
Chest pain and food sticking after swallowing	0.15	0.13	0.16	0.13	0.22	0.1	0.079	0.19	**0.59**	0.13
Food stuck in chest	0.16	0.17	**0.41**	0.13	0.23	0.11	0.094	0.27	0.27	0.14
Postprandial fullness	0.14	0.2	**0.51**	0.13	0.15	0.1	0.11	0.16	0.12	0.078
Early satiety	0.15	0.18	**0.48**	0.12	0.15	0.09	0.11	0.13	0.12	0.14
Nausea	0.24	0.14	**0.45**	0.15	0.21	0.06	0.096	0.16	0.13	0.4
Vomiting	0.14	0.1	0.25	0.06	0.22	0.04	0.089	0.09	0.08	**0.77**
Pain anywhere in the abdomen	0.29	0.17	**0.56**	**0.46**	0.08	0.19	0.1	0.09	0.07	0.047
Abdominal pain related to defecation	0.12	0.19	0.17	**0.75**	0.11	0.19	0.14	0.09	0.1	0.048
Abdominal pain related to stool consistency	0.13	0.2	0.15	**0.84**	0.1	0.17	0.19	0.09	0.09	0.066
Abdominal pain related to stool frequency	0.16	0.21	0.15	**0.81**	0.12	0.15	0.18	0.09	0.1	0.073
Hard stools	0.12	**0.61**	0.09	0.11	0.08	0.07	0.002	0.06	0.07	0.054
Infrequent stools	0.1	**0.53**	0.09	0.06	0.06	0.05	0.037	0.04	0.05	0.051
Straining during bowel movements	0.1	**0.82**	0.12	0.16	0.07	0.09	0.051	0.07	0.05	0.036
Incomplete bowel emptying	0.11	**0.72**	0.2	0.18	0.09	0.12	0.17	0.08	0.05	0.013
Anorectal obstruction/blockage	0.15	**0.84**	0.17	0.14	0.09	0.1	0.084	0.07	0.07	0.042
Manual maneuvers to facilitate defecation	0.16	**0.52**	0.09	0.05	0.12	0.04	0.062	0.08	0.09	0.12
RUQ pain	**0.48**	0.2	**0.47**	0.2	0.09	**0.43**	0.12	0.11	0.06	0.044
Long-lasting RUQ pain	**0.72**	0.21	0.24	0.21	0.09	0.28	0.12	0.1	0.05	0.028
RUQ pain of steady severe level	**0.79**	0.22	0.2	0.19	0.12	0.17	0.13	0.1	0.09	0.067
RUQ pain goes away between episodes	0.18	0.11	0.11	0.19	0.03	**0.73**	0.077	0.06	0.05	0.019
RUQ pain limits usual activities	**0.65**	0.19	0.18	0.15	0.15	0.15	0.13	0.08	0.14	0.13
Pain with swallowing	0.17	0.17	0.16	0.13	0.21	0.07	0.077	**0.53**	0.27	0.14
Chest pain	0.14	0.11	0.39	0.12	0.09	0.11	0.096	0.21	**0.51**	0.092
Epigastric pain/burning	0.38	0.15	**0.58**	0.2	0.2	0.1	0.085	0.1	0.19	0.11
Epigastric pain/burning improved by defecation	0.23	0.14	0.34	0.29	0.19	0.17	0.082	0.1	0.21	0.06
Self-induced vomiting	0.1	0.1	0.05	0.06	0.21	0.05	0.092	0.08	0.09	**0.52**
Food coming back up after swallowing	0.12	0.14	0.39	0.09	**0.59**	0.09	0.098	0.13	0.09	0.15
Retching	0.18	0.15	0.17	0.13	**0.77**	0.07	0.11	0.12	0.14	0.17
Vomiting when food comes back up	0.19	0.14	0.17	0.15	**0.71**	0.08	0.11	0.1	0.13	0.24
Food coming back up is recognizable	0.11	0.12	0.14	0.09	**0.53**	0.09	0.08	0.1	0.1	0.1
Belching	0.18	0.14	**0.41**	0.11	0.24	0.03	0.087	0.13	0.11	0.13
Abdominal pain related to a meal	0.29	0.18	0.28	**0.55**	0.16	0.13	0.15	0.09	0.13	0.06
Abdominal pain limits usual activities	0.39	0.19	0.27	**0.53**	0.14	0.07	0.14	0.1	0.11	0.098
Loose stools	0.13	0.08	0.13	0.15	0.08	0.07	**0.84**	0.06	0.05	0.068
Loose stools following a meal	0.12	0.07	0.1	0.19	0.1	0.08	**0.77**	0.06	0.06	0.061
Urgency	0.18	0.2	0.16	0.19	0.12	0.09	**0.55**	0.07	0.1	0.094
Bloating/abdominal distention	0.16	0.36	**0.47**	0.19	0.07	0.19	0.16	0.09	0.01	0.003
RUQ pain related to defecation	0.35	0.23	0.12	0.33	0.14	0.4	0.15	0.11	0.08	0.075
RUQ pain related to posture	0.28	0.16	0.15	0.16	0.1	**0.64**	0.078	0.08	0.1	0.052
RUQ pain improved by medicine	0.27	0.11	0.16	0.14	0.13	**0.49**	0.062	0.06	0.13	0.075
RUQ pain and nausea/vomiting	**0.48**	0.17	0.19	0.13	0.24	0.18	0.13	0.1	0.13	0.27
RUQ pain and back/right shoulder blade pain	**0.49**	0.2	0.23	0.12	0.16	0.25	0.11	0.1	0.15	0.1
RUQ pain waking one up	**0.58**	0.17	0.19	0.15	0.19	0.18	0.14	0.08	0.16	0.15
Fecal incontinence	0.14	0.08	0.22	0.07	0.14	0.05	0.24	0.07	0.11	0.19
Anorectal pain	0.19	0.35	0.36	0.16	0.14	0.11	0.12	0.1	0.09	0.097

Supplementary Figure and Table 12 - Age 50-64

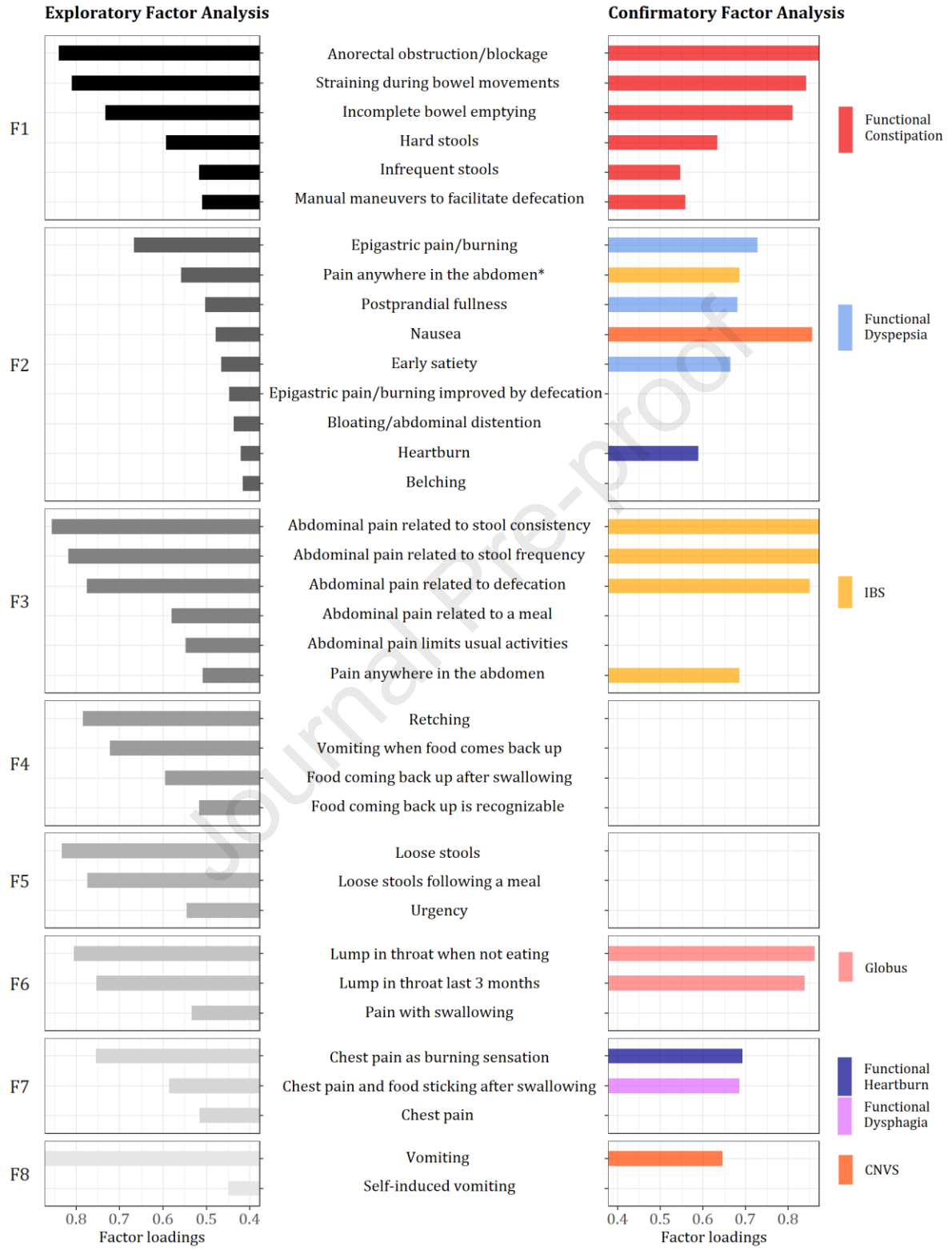


Item	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Lump in throat last 3 months	0.12	0.06	0.07	0.23	0.12	0.06	0.06	**0.79**	0.09	0.014
Lump in throat when not eating	0.13	0.12	0.11	0.12	0.12	0.07	0.07	**0.8**	0.15	0.045
Chest pain as burning sensation	0.11	0.18	0.14	0.18	0.18	0.09	0.08	0.13	**0.74**	0.025
Heartburn	0.11	0.08	0.13	**0.4**	0.19	0.1	0.15	0.15	0.27	-0.015
Chest pain and food sticking after swallowing	0.11	0.15	0.1	0.15	0.22	0.08	0.08	0.18	**0.56**	0.15
Food stuck in chest	0.15	0.09	0.11	0.36	0.25	0.09	0.1	0.3	0.24	0.061
Postprandial fullness	0.19	0.13	0.14	**0.51**	0.19	0.13	0.11	0.15	0.12	0.055
Early satiety	0.18	0.15	0.13	**0.45**	0.19	0.13	0.09	0.12	0.11	0.12
Nausea	0.14	0.26	0.12	**0.45**	0.25	0.12	0.07	0.17	0.1	0.31
Vomiting	0.08	0.17	0.05	0.25	0.38	0.11	0.05	0.11	0.04	0.37
Pain anywhere in the abdomen	0.16	0.32	**0.44**	**0.53**	0.11	0.12	0.22	0.11	0.09	-0.1
Abdominal pain related to defecation	0.17	0.12	**0.75**	0.15	0.1	0.14	0.2	0.08	0.1	0.013
Abdominal pain related to stool consistency	0.21	0.14	**0.84**	0.14	0.11	0.2	0.18	0.09	0.1	0.034
Abdominal pain related to stool frequency	0.2	0.16	**0.81**	0.15	0.12	0.2	0.14	0.09	0.1	0.074
Hard stools	**0.6**	0.09	0.11	0.09	0.07	0.01	0.06	0.06	0.06	0.021
Infrequent stools	**0.51**	0.11	0.04	0.05	0.09	0.05	0.06	0.02	0.03	0.059
Straining during bowel movements	**0.82**	0.08	0.13	0.11	0.09	0.04	0.07	0.07	0.06	-0.009
Incomplete bowel emptying	**0.73**	0.09	0.17	0.17	0.09	0.19	0.1	0.1	0.07	-0.029
Anorectal obstruction/blockage	**0.85**	0.13	0.13	0.15	0.1	0.07	0.08	0.09	0.08	0.03
Manual maneuvers to facilitate defecation	**0.56**	0.11	0.06	0.07	0.06	0.04	0.06	0.06	0.05	0.11
RUQ pain	0.19	**0.5**	0.21	**0.41**	0.11	0.14	**0.43**	0.12	0.08	-0.13
Long-lasting RUQ pain	0.2	**0.76**	0.19	0.2	0.13	0.13	0.25	0.09	0.08	-0.1
RUQ pain of steady severe level	0.22	**0.79**	0.18	0.18	0.14	0.13	0.15	0.08	0.11	0.011
RUQ pain goes away between episodes	0.13	0.15	0.2	0.11	0.05	0.07	**0.74**	0.07	0.04	-0.065
RUQ pain limits usual activities	0.14	**0.63**	0.17	0.18	0.14	0.14	0.12	0.09	0.13	0.19
Pain with swallowing	0.14	0.15	0.1	0.15	0.23	0.1	0.05	**0.53**	0.25	0.16
Chest pain	0.12	0.14	0.12	0.34	0.1	0.1	0.11	0.2	**0.52**	-0.016
Epigastric pain/burning	0.13	0.36	0.16	**0.58**	0.19	0.12	0.12	0.1	0.18	0.14
Epigastric pain/burning improved by defecation	0.12	0.2	0.27	0.36	0.16	0.09	0.19	0.06	0.15	0.14
Self-induced vomiting	0.08	0.11	0.07	0.06	0.26	0.07	0.06	0.08	0.07	0.32
Food coming back up after swallowing	0.13	0.1	0.09	0.35	**0.6**	0.11	0.09	0.12	0.13	-0.025
Retching	0.13	0.16	0.1	0.15	**0.79**	0.11	0.06	0.11	0.12	0.14
Vomiting when food comes back up	0.12	0.15	0.11	0.15	**0.74**	0.1	0.06	0.1	0.08	0.17
Food coming back up is recognizable	0.08	0.06	0.09	0.11	**0.49**	0.08	0.06	0.07	0.11	-0.016
Belching	0.11	0.15	0.1	**0.4**	0.25	0.11	0.06	0.1	0.12	0.12
Abdominal pain related to a meal	0.16	0.3	**0.53**	0.29	0.15	0.19	0.14	0.07	0.1	0.071
Abdominal pain limits usual activities	0.17	0.37	**0.51**	0.29	0.15	0.17	0.07	0.1	0.1	0.14
Loose stools	0.06	0.11	0.13	0.11	0.09	**0.84**	0.08	0.05	0.07	-0.003
Loose stools following a meal	0.06	0.11	0.18	0.08	0.11	**0.79**	0.08	0.05	0.07	0.043
Urgency	0.17	0.16	0.18	0.17	0.14	**0.58**	0.08	0.07	0.07	0.062
Bloating/abdominal distention	0.35	0.16	0.19	**0.42**	0.11	0.18	0.19	0.13	0.06	-0.099
RUQ pain related to defecation	0.22	0.34	0.35	0.1	0.12	0.17	0.37	0.08	0.08	0.079
RUQ pain related to posture	0.14	0.25	0.16	0.13	0.07	0.08	**0.64**	0.07	0.09	0.093
RUQ pain improved by medicine	0.1	0.2	0.12	0.18	0.11	0.06	**0.56**	0.03	0.1	0.14
RUQ pain and nausea/vomiting	0.14	**0.46**	0.11	0.17	0.25	0.13	0.16	0.09	0.11	0.37
RUQ pain and back/right shoulder blade pain	0.18	**0.48**	0.13	0.21	0.11	0.1	0.24	0.11	0.15	0.16
RUQ pain waking one up	0.16	**0.53**	0.16	0.19	0.17	0.13	0.21	0.09	0.17	0.23
Fecal incontinence	0.11	0.12	0.13	0.17	0.12	0.33	0.03	0.07	0.05	0.11
Anorectal pain	0.35	0.2	0.18	0.33	0.1	0.13	0.11	0.1	0.1	0.037

Supplementary Figure and Table 13 - Age 65+

Item	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lump in throat last 3 months	0.08	0.18	0.13	0.08	0.08	0.06	0.19	**0.8**	0.1
Lump in throat when not eating	0.14	0.18	0.12	0.1	0.07	0.08	0.11	**0.75**	0.17
Chest pain as burning sensation	0.18	0.18	0.11	0.13	0.11	0.08	0.13	0.16	**0.61**
Heartburn	0.09	0.21	0.11	0.1	0.17	0.07	0.35	0.13	0.2
Chest pain and food sticking after swallowing	0.18	0.27	0.11	0.12	0.08	0.07	0.1	0.19	**0.59**
Food stuck in chest	0.1	0.29	0.17	0.1	0.12	0.12	0.27	0.37	0.27
Postprandial fullness	0.11	0.28	0.17	0.15	0.09	0.12	**0.49**	0.2	0.13
Early satiety	0.14	0.27	0.17	0.12	0.06	0.13	**0.43**	0.17	0.14
Nausea	0.28	**0.45**	0.13	0.13	0.04	0.1	0.33	0.12	0.25
Vomiting	0.21	**0.57**	0.1	0.06	0.02	0.07	0.2	0.06	0.2
Pain anywhere in the abdomen	0.31	0.13	0.18	**0.46**	0.28	0.12	**0.46**	0.09	0.073
Abdominal pain related to defecation	0.14	0.1	0.17	**0.76**	0.19	0.16	0.12	0.08	0.1
Abdominal pain related to stool consistency	0.15	0.12	0.2	**0.84**	0.16	0.21	0.09	0.1	0.092
Abdominal pain related to stool frequency	0.18	0.15	0.19	**0.81**	0.14	0.21	0.09	0.09	0.097
Hard stools	0.1	0.11	**0.59**	0.11	0.06	0.04	0.06	0.07	0.059
Infrequent stools	0.11	0.08	**0.5**	0.09	0.04	0.07	0.06	0.04	0.047
Straining during bowel movements	0.07	0.07	**0.81**	0.11	0.09	0.03	0.08	0.08	0.043
Incomplete bowel emptying	0.09	0.09	**0.71**	0.17	0.11	0.18	0.14	0.09	0.072
Anorectal obstruction/blockage	0.13	0.11	**0.85**	0.12	0.08	0.08	0.1	0.07	0.058
Manual maneuvers to facilitate defecation	0.14	0.13	**0.57**	0.02	0.03	0.03	0.05	0.06	0.086
RUQ pain	**0.49**	0.11	0.19	0.21	**0.5**	0.11	0.35	0.12	0.086
Long-lasting RUQ pain	**0.73**	0.11	0.18	0.2	0.3	0.12	0.17	0.08	0.018
RUQ pain of steady severe level	**0.79**	0.18	0.21	0.17	0.16	0.11	0.14	0.11	0.055
RUQ pain goes away between episodes	0.18	0.05	0.1	0.19	**0.77**	0.09	0.08	0.05	0.042
RUQ pain limits usual activities	**0.65**	0.21	0.15	0.13	0.11	0.14	0.11	0.09	0.13
Pain with swallowing	0.2	0.27	0.16	0.1	0.06	0.09	0.11	**0.52**	0.3
Chest pain	0.14	0.18	0.15	0.12	0.14	0.07	0.24	0.21	**0.51**
Epigastric pain/burning	**0.41**	0.29	0.13	0.21	0.13	0.11	**0.47**	0.09	0.23
Epigastric pain/burning improved by defecation	0.26	0.2	0.11	0.28	0.19	0.1	0.28	0.06	0.2
Self-induced vomiting	0.13	**0.42**	0.04	0.06	0.03	0.04	0.05	0.02	0.13
Food coming back up after swallowing	0.07	**0.61**	0.14	0.08	0.11	0.09	0.25	0.19	0.038
Retching	0.15	**0.8**	0.14	0.11	0.08	0.1	0.06	0.13	0.1
Vomiting when food comes back up	0.17	**0.79**	0.13	0.12	0.08	0.11	0.05	0.09	0.086
Food coming back up is recognizable	0.07	**0.46**	0.1	0.08	0.09	0.07	0.09	0.12	0.01
Belching	0.19	0.31	0.16	0.12	0.04	0.09	0.33	0.15	0.13
Abdominal pain related to a meal	0.28	0.2	0.16	**0.53**	0.15	0.18	0.24	0.05	0.13
Abdominal pain limits usual activities	0.38	0.22	0.16	**0.51**	0.1	0.18	0.21	0.09	0.12
Loose stools	0.08	0.08	0.09	0.14	0.08	**0.82**	0.07	0.04	0.033
Loose stools following a meal	0.12	0.1	0.08	0.19	0.07	**0.79**	0.06	0.08	0.058
Urgency	0.16	0.13	0.17	0.18	0.09	**0.59**	0.11	0.08	0.053
Bloating/abdominal distention	0.15	0.1	0.34	0.17	0.2	0.18	**0.42**	0.14	0.024
RUQ pain related to defecation	0.39	0.19	0.19	0.31	0.36	0.15	0.07	0.11	0.11
RUQ pain related to posture	0.29	0.11	0.13	0.16	**0.65**	0.08	0.09	0.07	0.11
RUQ pain improved by medicine	0.27	0.13	0.09	0.13	**0.56**	0.09	0.14	0.07	0.14
RUQ pain and nausea/vomiting	**0.51**	0.36	0.14	0.12	0.1	0.09	0.08	0.08	0.21
RUQ pain and back/right shoulder blade pain	**0.53**	0.22	0.17	0.14	0.23	0.08	0.09	0.08	0.19
RUQ pain waking one up	**0.57**	0.21	0.17	0.14	0.21	0.11	0.09	0.11	0.15
Fecal incontinence	0.11	0.17	0.1	0.11	0.05	0.31	0.14	0.05	0.089
Anorectal pain	0.2	0.22	0.37	0.17	0.1	0.1	0.23	0.09	0.12

Supplementary Figure and Table 14 - Global analysis with exclusion of right upper quadrant pain



Item	F1	F2	F3	F4	F5	F6	F7	F8
Lump in throat last 3 months	0.12	0.25	0.083	0.11	0.07	**0.75**	0.11	0.073
Lump in throat when not eating	0.14	0.16	0.14	0.14	0.084	**0.81**	0.17	0.068
Chest pain as burning sensation	0.14	0.23	0.15	0.16	0.095	0.16	**0.75**	0.081
Heartburn	0.13	**0.42**	0.15	0.15	0.1	0.14	0.26	0.078
Chest pain and food sticking after swallowing	0.12	0.2	0.14	0.22	0.093	0.19	**0.59**	0.1
Food stuck in chest	0.17	0.39	0.13	0.23	0.096	0.29	0.26	0.11
Postprandial fullness	0.21	**0.5**	0.15	0.16	0.12	0.17	0.11	0.079
Early satiety	0.2	**0.47**	0.14	0.16	0.11	0.15	0.1	0.13
Nausea	0.16	**0.48**	0.17	0.24	0.11	0.17	0.13	0.34
Vomiting	0.11	0.25	0.068	0.24	0.094	0.099	0.087	**0.9**
Pain anywhere in the abdomen	0.21	**0.56**	**0.51**	0.093	0.12	0.1	0.093	0.069
Abdominal pain related to defecation	0.2	0.19	**0.78**	0.1	0.14	0.092	0.1	0.046
Abdominal pain related to stool consistency	0.22	0.15	**0.86**	0.1	0.19	0.097	0.089	0.062
Abdominal pain related to stool frequency	0.22	0.17	**0.82**	0.12	0.19	0.094	0.1	0.068
Hard stools	**0.59**	0.12	0.14	0.086	0.017	0.076	0.07	0.054
Infrequent stools	**0.52**	0.11	0.082	0.073	0.061	0.041	0.053	0.052
Straining during bowel movements	**0.81**	0.12	0.17	0.078	0.056	0.077	0.059	0.04
Incomplete bowel emptying	**0.73**	0.19	0.2	0.088	0.18	0.095	0.061	0.026
Anorectal obstruction/blockage	**0.84**	0.18	0.16	0.1	0.094	0.085	0.08	0.05
Manual maneuvers to facilitate defecation	**0.51**	0.13	0.058	0.13	0.071	0.074	0.1	0.082
Pain with swallowing	0.16	0.19	0.13	0.22	0.091	**0.53**	0.26	0.11
Chest pain	0.15	0.36	0.13	0.1	0.093	0.21	**0.52**	0.094
Epigastric pain/burning	0.16	**0.67**	0.22	0.21	0.11	0.11	0.21	0.1
Epigastric pain/burning improved by defecation	0.14	**0.45**	0.31	0.19	0.1	0.089	0.19	0.03
Self-induced vomiting	0.1	0.086	0.081	0.24	0.09	0.085	0.11	**0.45**
Food coming back up after swallowing	0.15	0.36	0.099	**0.59**	0.11	0.14	0.1	0.14
Retching	0.16	0.2	0.13	**0.78**	0.11	0.13	0.15	0.15
Vomiting when food comes back up	0.15	0.2	0.15	**0.72**	0.11	0.11	0.13	0.21
Food coming back up is recognizable	0.12	0.16	0.1	**0.52**	0.089	0.097	0.11	0.086
Belching	0.15	**0.42**	0.11	0.26	0.1	0.13	0.12	0.091
Abdominal pain related to a meal	0.19	0.35	**0.58**	0.16	0.18	0.088	0.13	0.062
Abdominal pain limits usual activities	0.21	0.38	**0.55**	0.15	0.16	0.11	0.12	0.09
Loose stools	0.1	0.13	0.17	0.088	**0.83**	0.062	0.06	0.061
Loose stools following a meal	0.096	0.12	0.21	0.1	**0.77**	0.066	0.069	0.055
Urgency	0.22	0.2	0.22	0.13	**0.55**	0.085	0.094	0.068
Bloating/abdominal distention	0.37	**0.44**	0.23	0.077	0.18	0.11	0.049	0.028
Fecal incontinence	0.091	0.22	0.079	0.15	0.25	0.071	0.11	0.14
Anorectal pain	0.35	0.37	0.19	0.15	0.13	0.11	0.11	0.081