Development, dIagnostic and prevention of gender-related Somatic and mental COmorbitiEs in iRritable bowel syndrome In Europe

Published: 28-12-2021
Last updated: 07-09-2024

Primary Objective: The overarching goal of the multicentre trial is to characterize the overlap between mental and non-mental comorbid conditions of IBS. In IBS and patient control groups we will characterize depression, anxiety, fibromyalgia and...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal conditions NEC
Study type	Observational invasive

Summary

ID

NL-OMON51010

Source
ToetsingOnline

Brief title
DISCOvERIE

Condition

- Gastrointestinal conditions NEC
- Mood disorders and disturbances NEC

Synonym
bowel disorder, intestinal complaints

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: EU

Intervention

Keyword: comorbidities, Irritable Bowel Syndrome

Outcome measures

Primary outcome

Physical symptoms using scores on the IBS Severity Scoring System (IBS-SSS), Patient Health Questionnaire-15 (PHQ-15), Multidimensional Fatigue Inventory (MFI) and mental symptoms using scores on the Generalized Anxiety Disorder 7-Item Scale (GAD-7) and Patient Health Questionnaire-9 (PHQ-9). All measures used are identical across all study sites.

Secondary outcome

Biological materials: gut microbial profile through sequencing of bacterial DNA in faecal sample, intestinal permeability measured trough passage of ingested sugars in urine, bacterial products in blood.

Study description

Background summary

Irritable Bowel Syndrome (IBS) is extremely common in Europe: IBS is a condition marked by altered defecation, abdominal pain, and/or bloating, being the most frequent of the multiple recognized functional gastrointestinal disorders (FGIDs). Current data indicate that IBS afflicts up to 85 million European citizens.
IBS is characterized by several co-morbid diagnoses and complaints. For example, patients with IBS have 40% to 80% higher prevalence odds of suffering from chronic fatigue, fibromyalgia compared to control population without IBS. Chronic fatigue syndrome and fibromyalgia are chronic pain/disabling

somatic/mental disorders that also afflict millions of people (17-24 million by chronic fatigue syndrome and about 10 million fibromyalgia) across Europe. Large cohort studies show that the prevalence of chronic fatigue syndrome in IBS patients is 6-25% compared to 2.2% in healthy controls3 and of 32.5% for fibromyalgia (28%-65%).
Epidemiological evidence has also consistently demonstrated a link between IBS and mood and anxiety disorders, as adult patients with IBS display a nearly 3.6-fold increased risk of developing psychiatric disorders. Specifically, in studies that have administered structured clinical interviews to establish the rate of psychiatric comorbidity per criteria as specified in the American Psychiatric Association*s Diagnostic and Statistical Manual of Mental Disorders, approximately 60% of treatments seeking IBS patients have a diagnosable psychiatric condition, such as generalized anxiety disorder and depression, being the most common disorders affecting 25 to 44% of IBS. Mood and anxiety disorders also represent the most prevalent psychiatric conditions in the EU, affecting over 60 million people and this is expected to nearly double by 2030.

Despite these alarming figures, to date, comorbidities in IBS are treated mostly as a separate condition by a variety of drugs, mainly analgesics and antidepressants, on a *trial-and error* basis because prediction of treatment response is currently not possible. This strategy often renders poor results and has failed to a large extent, as it does not consider in full the potential role of brain- gut interactions in symptom generation. Consequently, treatments are unsatisfactory for patients and doctors. For instance, with current antidepressant treatments, only half of the patients achieve a 50% reduction in depressive symptoms, remission is achieved in around 20-30% of patients, and many patients inadequately respond to any therapy and develop treatment-resistant depression. Similarly, the majority of IBS patients categorized their healthcare as unsatisfactory (73.3%) and this was partially related to the coexistence of psychological traits and psychological disorders and to an average therapeutic gain over placebo of only 5% to 15% for most available treatments. For chronic fatigue syndrome sufferers, available therapies only provide moderate satisfaction, and same applies to fibromyalgia patients.

Different patients with IBS may show resiliency or susceptibility to develop mental and somatic comorbidities. The reasons and mechanisms explaining the association of IBS with mental and somatic comorbidities are, unfortunately, far from being established. Therefore, the overarching aim of the multicentre DISCOvERIE trial is to understand similarities and differences among patients with IBS with and without comorbidities, and to demonstrate mechanisms underlying these differences and similarities . In order to achieve this, patients with IBS with and without these comorbidities, as well as a small group of healthy control patients without these conditions, and a group of patients with the comorbid conditions but without IBS, will be included in this

pan-European project, with the aim to compare the following measures within and between the groups:

· Demographic, clinical and psychosocial characteristics, as well as lifestyle factors (e.g. sleep, physical activity, nutrition, stress and social interaction)
· Mechanisms of intestinal and central nervous system function, and their interaction with the peripheral microbiota-gut-brain axis. Specifically, we will look at epithelial barrier function and neuro-immune function in the intestine and in the neuroendocrine stress system, as well as the function of nociceptive and affective-cognitive neuro-circuits in the brain.
· Disease-specific genetic and epigenetic signatures.

This approach should allow us to identify specific-disease diagnostic biomarkers for comorbid IBS and to further develop novel and efficient predictive and therapeutic strategies. Within this multicentre study, the Radboudumc will not contribute to the IBS patient group (and its control group) but will recruit patient control groups: patients with depression or anxiety, chronic fatigue syndrome or fibromyalgia, or both a mental and somatic diagnosis.

Study objective

Primary Objective: The overarching goal of the multicentre trial is to characterize the overlap between mental and non-mental comorbid conditions of IBS. In IBS and patient control groups we will characterize depression, anxiety, fibromyalgia and chronic fatigue syndrome with a particular focus on age and gender-related differences, infections, life style and nutrition.

Secondary Objective(s): Locally, three patient control groups 1) patients with a depression or anxiety diagnosis, 2) patients with chronic fatigue syndrome or fibromyalgia, or 3) patients with both a mental and somatic diagnosis will be assessed. For these patient groups, three objectives are determined:

1. A thorough clinical and psychosocial characterization. We will look for depression, anxiety, fibromyalgia and chronic fatigue syndrome.
2. Assessment of epithelial barrier function via sugar excretion in urine, bacterial products in blood and gut microbial profile through sequencing of bacterial DNA in faecal sample.
3. Determining the influence of lifestyle (sleep, physical activity, nutrition, stress and social interaction) on disease symptoms through eHealth monitoring tools.

Study design

This is a prospective, cross-sectional, longitudinal cohort study lasting 24

months in a regular care setting. This cross-sectional cohort will be followed up for a maximum of 3 years. During this time we will record clinical symptoms using a digital platform and collect blood (annually) and urine and faeces (twice) to unravel shared mechanisms of brain-gut-microbiota axis dysfunction.

The data collection in the DISCOvERIE study at the Radboudumc/StMaartenskliniek is part of a large multi-centre effort characterizing the overlap between gastrointestinal and mental and non-mental comorbid conditions. In other centres, IBS patients, with and without mental and non-mental comorbidities, as well as different combinations of disease controls and health will be recruited. At the Radboudumc/StMaartenskliniek we will recruit patients with a psychiatric and/or somatic diagnosis, though no IBD patients and no healthy controls. To assess the study objectives data will be pooled across centres.

Study burden and risks

The frequency of the blood draws has been reduced to minimise burden. Blood samples will be collected by experienced members of the study team. Local anaesthetics (e.g. Emla band-aid) can be provided for minimising pain. If the participant will report resistance or discomfort, the procedure will be stopped immediately. No examination will be performed against the will of the participant or the caregiver. Where needed, appropriate therapeutic care will be provided in the best interest of the participant.
Faeces and urine donation are non-invasive and have a low burden on the participant.

The participant may benefit directly from participation by receiving detailed characterization of their symptoms, both mental and somatic, as well as the ecological measures. On the long term patient care will improve by increased understanding of co-morbidity in IBS and generally the underlying mechanisms driving somatic complaints in mental disorders and vice versa.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 10
Nijmegen 6525 GA
NL
Scientific
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 10

Nijmegen 6525 GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

* Signed written informed consent
* Age at least 18 years at baseline visit
* Fulfilling criteria for at least one of the comorbid conditions (checklists in CRF):
* The psychiatric patient group (1):
* anxiety and/or depression during the MINI interview
* The somatic patient group (2) should (also) have:
* chronic fatigue syndrome according to 2015 IOM/SEID or
* fibromyalgia according to ACR criteria (2011)
* The psychiatric patient group with somatic comorbidities (3) should fulfil both of the above diagnoses
* Ability to understand and willingness to comply with the study procedures, and to give consent.

Exclusion criteria

* Participation in another clinical study 1 month prior to screening visit and throughout the study
* Abnormal results on the screening laboratory tests, clinically relevant for study participation
* Other gastrointestinal disease(s) explaining the patient*s symptoms, as judged by the investigator
* Other severe disease(s) such as malignancy, severe heart disease, kidney disease or neurological disease, interfering with study evaluations
* Symptoms indicating other severe disease(s) such as gastrointestinal

bleeding, weight loss or fever
* Severe psychiatric disease, other than the comorbid conditions explicitly studied, with necessary additional psychopharmacotherapy or psychiatric intervention involving day-care/ inpatient treatment at start of study or during the study, especially a diagnosis of bipolar disorder, schizophrenia, autism spectrum disorder, schizoaffective disorder or organic psychiatric disorder (current OR lifetime).
* Previous history of drug or alcohol abuse 6 months prior to screening
* Consumption of antibiotics 3 months prior to the baseline visit
* Pregnant or lactating at the baseline visit
* Use of probiotics in the last three months

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-03-2022
Enrollment:	39
Type:	Actual

Ethics review

Approved WMO

Date:	28-12-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL77873.091.21