The Russian Multicenter Observational Program

Obtaining of data on the impact of different treatment modalities on the quality of life of the patients with acute and chronic hemorrhoid disease (EQUALISER)

PROTOCOL

NCT03743311

Protocol № IC4 -05682-058-RUS

Data of report: 1/03/2019

Introduction

Any long-term morbid condition associated severe physical discomfort, including hemorrhoids, is a powerful stress factor that affects psychological and physiological components of a person's health.

As of today, about 10% of adults in total population suffer from hemorrhoids, and this disease accounts for more than 40% of all cases of coloproctological diseases [1, 2, 3]. The prevalence of hemorrhoids is about 130-145 cases per 1,000 adult population, and in the group of middle-aged and elderly adults it reaches 210-240 cases per 1,000 population [2, 4].

The main method of treating chronic hemorrhoids of grade III-IV is surgical one [2, 3]. At the same time, the symptoms of hemorrhoids in grade 1-2 are successfully relieved with conservative treatment.

Criteria for assessing the treatment efficacy in acute and chronic hemorrhoids are the rates of complications and relapse of the major clinical manifestations of the disease. In addition to quantitative indicators of treatment efficacy, qualitative methods are becoming increasingly important, and one of them is an assessment of the quality of life (QoL) of patients [5, 7,6]. The purpose of this program is to obtain data on the effect of different treatment approaches in acute and chronic hemorrhoids in a broad cohort of patients in routine clinical practice.

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Aims and goals of the program:

The program is aimed at obtaining data on the impact of the method and type of treatment on the quality of life of patients with acute or chronic hemorrhoids.

Primary endpoints:

- Changes in the quality of life of patients suffering from acute or chronic hemorrhoids within 1 month after presenting to a doctor, in general population and in specific demographic and clinical groups.

Secondary endpoints:

- Scores for different health status dimensions of the SF36 questionnaire in patients suffering from acute or chronic hemorrhoids, and their association with demographic and clinical parameters, as well as the chosen treatment strategies (surgical, minimally invasive, or conservative).
- Changes in the QoL of patients suffering from acute or chronic hemorrhoids, who underwent surgical intervention, within 1 month after presenting to a doctor.
- Changes in the QoL of patients suffering from acute or chronic hemorrhoids, who received conserative treatment, within 1 month after presenting to a doctor.
- Changes in the QoL of patients suffering from acute or chronic hemorrhoids, who received combination treatment, within 1 month after presenting to a doctor.
- Changes in the QoL of patients suffering from acute or chronic hemorrhoids, who underwent minimally invasive interventions, within 1 month after presenting to a doctor.
- Changes in clinical manifestations in patients suffering from acute or chronic hemorrhoids, and their association with demographic and clinical parameters, as well as the chosen treatment strategies (surgical, minimally invasive, or conservative).
- Patient's compliance with recommendations of a doctor.

Design:

The EQUALISER program is a Russian, multicenter, observational program.
In Russia, the program is scheduled for 2018-2019. It is expected that 90 doctors will take part in the program in 60 cities of the Russian Federation. The planned number of patients is 900. Each participating doctor includes at least 10 patients and fills out an electronic case report form (CRF). All treatment is carried out in accordance with the instructions for medical use and routine clinical practice.

First visit of the first patient	02\2019
Last visit of the last patient	05\2019
Completion of statistical analysis	08\2019
Preliminary report	12\2019
Final report	03\2020

Methods:

During the program, at each visit the leading clinical symptoms of hemorrhoids will be assessed.

The quality of life assessment will be carried out using the validated questionnaire SF36 (in Russian) (**Appendix 2**)

Inclusion visit (V0)

Patients who meet the inclusion criteria will be included in the program, and for them the CRF will be completed.

Visit 1 (V1) Surgical intervention (if applicable).

Visit 2 (V2) in 5-7 days after surgical intervention or 5-7 days after the Inclusion Visit (V0), if intervention was not performed.

Visit 3 (V3) in 25-30 days after surgical intervention or 25-30 days after Inclusion Visit (V0), if intervention was not performed.

Visit	Actions
V0	• Signing the Informed Consent Form

	• Checking of fulfilment of inclusion/non-inclusion criteria. • Obtaining the data: - Disease duration - Clinical manifestations of haemorrhoids - клинические проявления геморроя: • prolapse of hemorrhoids (Appendix 4) • pain, itching, dyscomfort (Appendix 6) • bleeding - The Rome III criteria for constipation (Appendix 3) - Conservative treatment (systemic venotonic drug, topical agents, analgetics) - Diagnosis according to the National guidelines on coloproctology, 2015 (Appendix 5) - The surgical treatment scheduled - QoL assessment using the SF36 scale (Appendix 2)
V1	• Surgical treatment (if performed)
V2	• **5-7 days after intervention** or after V0, if intervention was not performed • Clinical manifestations of haemorrhoids at the day of visit • Patient's compliance with doctor recommendations • Recording the adverse events (Appendix 1). • Assessment of pain, itching, and discomfort using VAS (Appendix 5)
V3	• **25-30 days after intervention** or after V0, if intervention was not performed • Clinical manifestations of haemorrhoids at the day of visit • Patient's compliance with doctor recommendations • Patient's satisfaction with the treatment • Recording the adverse events • Clinical manifestations of haemorrhoids at the day of visit • QoL assessment using the SF36 scale

Inclusion criteria

Patients fulfilment of the criteria of the inclusion in the program will be determined by the following parameters:

1) Age over 18 years;
2) Providing written information to a patient about inclusion in the program, and his/her consent to participate in it,
3) Absence of conditions requiring urgent medical care and not related to hemorrhoids;
4) The patient was diagnosed with:

- Acute hemorrhoids (with thrombosis of hemorrhoids);
- Exacerbation of chronic hemorrhoids (pain, bleeding, oedema (swelling) of hemorrhoids);
- Chronic hemorrhoids (prolapsed hemorrhoids, bleeding events, anal discomfort).

Exclusion criteria

1) The patient is consulting for an urgent issue not related to hemorrhoids;
2) The presence of severe systemic diseases;
3) Pregnancy;

4) Inability to understand the meaning of the Program and follow the doctor's recommendations
5) Patients with inflammatory bowel diseases (Crohn's disease, non-specific ulcerative colitis);
6) Patients with concomitant diseases of the anal canal (fissure, fistulas, paraproctitis, etc.);
7) Patients taking anticoagulants;
8) Patients with previous anorectal surgeries, including hemorrhoidectomy or excision of anal fistula.

Treatment

The observational nature of program presumes that all examinations, procedures and changes in the treatment of patients, including changes in the dosing regimen, should be carried out only on the basis of judgment of the treating physician and in full compliance with the guidelines on the treatment of patients of the analysed population, instructions for medical use of drugs, and in the settings of daily routine practice.

Therapy is conducted in full accordance with existing guidelines. The patient's participation in the program, as well as his/her refusal to continue such participation, should not affect the current treatment, the availability of diagnostic procedures or the volume and quality of other necessary medical care.

Safety considerations

1. Definitions

1.1 Pharmacovigilance information

Pharmacovigilance data include any unintended or adverse event associated with the use of a medicinal product in humans, whether or not considered drug related, including the following special situations (situations where no adverse event occurred but information needs to be collected):

- exposure during pregnancy or breastfeeding;
- overdose, abuse, misuse, off-label uses, medication error, occupational exposure (including professional one);
- lack of the treatment efficacy of drug.

1.2. Adverse Event (AE)

Adverse event is any untoward medical occurrence in a patient or a clinical-trial subject who received the medicinal product, which does not necessarily have a causal relationship with the use of this medicinal product.

An adverse event can therefore be any unfavourable and unintended sign (e.g. an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

1.3. Adverse (drug) reaction (ADR)

Adverse reaction (synonyms: Adverse drug reaction, Suspected adverse (drug) reaction, Adverse effect, Undesirable effect) is a response to a medicinal product which is noxious and unintended.

“Response” in this context means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility.

Adverse reactions may arise from use of the product within or outside the terms of the marketing authorization or from occupational exposure. Conditions of use outside the marketing authorization include off-label use, overdose, misuse, abuse and medication errors.

1.4. Serious adverse (drug) reaction (SADR)

Serious adverse reaction is an adverse reaction, which results in death, is life-threatening, requires in-patient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly/birth defect.

“Life threatening” in this context refers to a reaction in which the patient was at risk of death at the time of the reaction; it does not refer to a reaction that hypothetically might have caused death if more severe.

Medical and scientific judgement should be exercised in deciding whether other situations should be considered serious reactions, such as important medical events that might not be immediately life threatening or result in death or hospitalisation but might jeopardise the patient or might require intervention to prevent one of the other outcomes listed above.

Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation or development of dependency or abuse.

Any suspected transmission via a medicinal product of an infectious agent is also considered a serious adverse reaction.

2. Responsibilities

2.1. Events to be reported

All available information about the following reported events occurring during the study will be recorded:

- All serious adverse drug reactions related to the use to Detralex
- All non-serious adverse drug reactions related to the use to Detralex
- All reports about special situations (see 1.1)
- All adverse events

2.2. Responsibilities of the investigator

In prospective studies, at medical visits, the investigator will ask the participating patient to indicate whether or not an adverse event (serious or not) has occurred.

The investigator has to assess the causal relationship between an adverse event and the investigated drug intake, as well as the seriousness criteria and later on the outcome of the event.

In case of Adverse Events, Adverse Drug Reactions or special situations that occurs during the study (both serious and non-serious), the investigator must complete the “Adverse event / Adverse drug reaction / Special Situation Reporting Form” (Appendix 1) without waiting for the clinical outcome or the results of additional investigations.

When assessing the quality of life using the EQ-5D, the investigator should evaluate data (patient's answers), their clinical relevance, and fill out the " Adverse event / Adverse drug reaction / Special Situation Reporting Form” if he/she considers these data as AE, ADR or a special situation.

If the event is serious, it will be notified immediately (same or next working day at the latest) to Servier company in Russia via e-mail to address pvmail.rus@servier.com or by fax to number (495) 937-47-66. The anonymized copies of all the available and relevant laboratory findings, hospitalisation reports or other investigation results performed in connection with the adverse event should be attached to the form.

All other events should be reported by investigator within 2 working days.

The same rules apply for the transferring of additional information about the event.

The investigator must ensure the appropriate follow-up of the patient depending on the nature of event, until it resolves.

The investigator will continue to notify follow up data according to timeframes defined above.

If investigator does not follow-up a patients anymore (i.e. in case of hospitalisation followed by the treatment by specialist or the participant's general practitioner,…), he/she will do every effort to contact the specialist or department in charge of follow-up of the patient, so as to have additional information and report it to Servier company in Russia.

2.3. Responsibilities of the Sponsor/Marketing Authorisation Holder

Independently of the regulatory obligations of investigator, the sponsor/MAH must report the pharmacovigilance data to the appropriate authorities in accordance with the Good Vigilance Practice and local regulations.

Cases are closed when an adverse event has recovered or patient's condition was stabilised and the report is deemed sufficiently detailed for adequate medical analysis of the case.

Ethical considerations

The study will be conducted in accordance with the principles set out in the Declaration of Helsinki (version adopted in Fortaleza, Brazil, in 2013).
The protocol of the program was reviewed and approved in accordance with the legislation of the Russian Federation and will be followed by the sponsor, in particular, with regard to data collection. Participants will be fully informed and provide their written consent to participate in the program. Investigator is obliged to indicate in the CRF that the informed consent was obtained from the patient, as well as to keep the signed Form in the clinical file for the participant. The "informed consent" also means that individual discussion with participant concerning the nature of the program and the necessary investigations. Sponsor will not have access to the data allowing identification of participants. Documents relating to the study will be reviewed by Ethical committee.

Organizational structure and responsibilities

Investigators
Investigators will receive informed consent forms and enroll participants, ensure data collection in accordance with the protocol, fill in case report forms and verify the accuracy of information in these case report forms, as much as possible. The patient will be provided with all information to obtain informed consent. At the same time, participants will be asked to consent to the use of their personal data. The data of the participants will remain completely confidential.

Sponsor
The sponsor will be responsible for all stages of the program, for providing the resources necessary to initiate and run the program in accordance with local regulations, as well as for the validity of the recorded data.

Statistical parameters

Variables:

- Change in the mean score of the EQ-5D index in patients suffering from acute or chronic hemorrhoids within 1 month after presenting a doctor, in general population and in specific demographic and clinical groups.
- Rates (in %) of different variables of health profile according to the EQ-5D in patients suffering from acute or chronic hemorrhoids, and their relationship to demographic, clinical parameters and the chosen treatment strategies (surgical, minimally invasive, and conservative).
- Change in the mean score of the EQ-5D index in patients suffering from acute or chronic hemorrhoids, who underwent surgical intervention, within 1 month after presenting to a doctor
- Change in the mean score of the EQ-5D index in patients suffering from acute or chronic hemorrhoids, who received conservative treatment, within 1 month after presenting to a doctor
- Change in the mean score of the EQ-5D index in patients suffering from acute or chronic hemorrhoids, who received combination treatment, within 1 month after presenting to a doctor
- Change in the mean score of the EQ-5D index in patients suffering from acute or chronic hemorrhoids, who underwent minimally invasive intervention, within 1 month after presenting to a doctor

- Change in the mean score by VAS (in mm) scale from SF36 questionnaire in patients suffering from acute or chronic hemorrhoids, who underwent surgical intervention, within 1 month after presenting a doctor, in general population and in specific demographic groups
- Change in the mean score by VAS (in mm) scale from SF36 questionnaire in patients suffering from acute or chronic hemorrhoids, who received conservative treatment, within 1 month after presenting to a doctor
- Change in the mean score by VAS (in mm) scale from SF36 questionnaire in patients suffering from acute or chronic hemorrhoids, who received combination treatment, within 1 month after presenting to a doctor
- Change in the mean score by VAS (in mm) scale from SF36 questionnaire in patients suffering from acute or chronic hemorrhoids, who underwent minimally invasive intervention, within 1 month after presenting to a doctor
- Change in the mean score by VAS (in mm) scale from CRF for pain, itching, and discomfort in patients suffering from acute or chronic hemorrhoids, within 1 month after presenting to a doctor, and their relationship to demographic, clinical parameters and the chosen treatment strategies (surgical, minimally invasive, and conservative).
- Change in the proportion (in %) of patients with bleeding events or prolapse of hemorrhoids among patients suffering from acute or chronic hemorrhoids, within 1 month after presenting a doctor, and its relationship to demographic, clinical parameters and the chosen treatment strategies (surgical, minimally invasive, and conservative).
- Proportion (%) of patients compliant with recommendations on lifestyle changes
- Proportion (%) of patients compliant with recommendations on medical therapy.

Statistical analysis:

Baseline characteristics will be analyzed in all included patients despite adherence to the protocol. Analysis of the results of program will be performed using the SPSS 12.0 software package (SPSS Inc., USA). The data entry errors will be corrected before the statistical processing. Quantitative parameters will be presented depending on the distribution of primary data as arithmetic mean ± standard deviation for parametric variables, or as median (25; 75 percentiles) for nonparametric variables. Multiple comparisons will include adjustments for continuity.

Changes in the quantitative parameters during the follow-up period will be evaluated using the Student's t-test for paired samples or its nonparametric analogue, Wilcoxon test. Differences on the quantitative parameters, both between the independent groups and during the follow-up, will be evaluated as the mean difference with the corresponding 95% confidence interval.

Comparisons of changes on the VAS scales and the Rome III constipation scale will be carried out using two-factor analysis of variance (ANOVA) with repeated measures to compare the scores before and after the treatment.

Adverse events will be recorded and analyzed in patients with the reporting of all the AEs, SAEs, ADRs, SADRs and special situations.

Administrative considerations

The right to own the documentation, data and results of the program.

The sponsor reserves the exclusive rights for all materials, information, unpublished documentation, results and information received during the program. The sponsor reserves the right to send data on the program (case report forms, results of analyses, and reports) to health authorities.

No unpublished documentation or information transmitted to investigators can be transferred to unauthorized persons without the prior written consent of the Sponsor.

Publication and communication

Sponsor is responsible for communication and publication of data on the program. No aspect of the results of this program or other data may be published, presented, or distributed without the explicit written permission of Sponsor. Participants of the program fully transfer to the Sponsor the authority for the first presentation, communication and publication of the results on behalf of all employees. No other communication or publication is permitted before this first publication. Any subsequent communication or publication must first be considered and approved by the Sponsor and must refer to the program and the first publication.

APPENDIX 1

Adverse event / Adverse drug reaction / Special Situation Reporting Form*

IC4-05682-058-RUS *Please send this form immediately by fax (495) 937-47-66 or by email to pvmail.rus@servier.com, or pass to the associate of the company.*

Year of birth or **Age**	**Gender**	**Height**	**Weight**	**Patient's ID:**
____ or ___	M / F	___	___	_____

Description of adverse event/reaction/special situation:	**Date of event onset**	**Date of event termination (in case of recovery)**
	__ __ ____	__ __ ____

Criteria of seriousness: ☐ NO
☐ YES (please, specify from stated below)
- ☐ Death
- ☐ Life threatening
- ☐ Hospitalization or prolongation of existing hospitalisation
- ☐ Persistent or significant disability or incapacity
- ☐ Congenital anomaly/birth defect
- ☐ Medically important event

Outcome:
- ☐ Recovered
- ☐ Recovered with consequences (persistent structural or functional impairment)
- ☐ Not yet recovered
- ☐ No recovery
- ☐ Death
- ☐ Unknown

General disease(s) / Concomitant disease(s) (please indicate year when first diagnosed).

Course adverse event/reaction/special situation (please enclose relevant findings, e.g. laboratory, hospital reports, histology, etc.):

Causal relationship with intake of investigational drug: ☐☐
☐ NO ☐ YES ☐ NOT APPLICABLE

***If «Yes»**, please indicate dates of the use of investigational drug in the first line of the table below:*

***If «No» or «Not applicable»**, please specify whether the adverse event/special situation is related to the medication of Servier company (which is specified in the table below)*:
☐ NO ☐ YES *Please indicate the name of the medication of Servier company: ……*

List of current medications	**Daily dose / route of administration**	**Dates of intake: from to**	**Indication**
		-	
		-	
		-	

Name (last, first, patronymic) of doctor:
Speciality:
Work address:
Phone number: _____
(city code)

Date:

Signature:

Stamp (whenever possible)

**Special situations are cases when adverse event was not observed, but the information should be collected: the impact of the drug during pregnancy/breastfeeding, abuse, misuse, medication error, overdose, off-label use, occupational exposure, or treatment failure…*

APPENDIX 2 SF36 Questionnaire

SF-36 QUESTIONNAIRE

Name:_____ Ref. Dr:_____ Date: _____

ID#: _____ Age: _____ Gender: M / F

Please answer the 36 questions of the **Health Survey** completely, honestly, and without interruptions.

GENERAL HEALTH:

In general, would you say your health is:

◯ Excellent ◯ Very Good ◯ Good ◯ Fair ◯ Poor

Compared to one year ago, how would you rate your health in general now?

◯ Much better now than one year ago
◯ Somewhat better now than one year ago
◯ About the same
◯ Somewhat worse now than one year ago
◯ Much worse than one year ago

LIMITATIONS OF ACTIVITIES:

The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports.

◯ Yes, Limited a lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf

◯ Yes, Limited a Lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Lifting or carrying groceries

◯ Yes, Limited a Lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Climbing several flights of stairs

◯ Yes, Limited a Lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Climbing one flight of stairs

◯ Yes, Limited a Lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Bending, kneeling, or stooping

◯ Yes, Limited a Lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Walking more than a mile

◯ Yes, Limited a Lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Walking several blocks

◯ Yes, Limited a Lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Walking one block

◯ Yes, Limited a Lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Have you felt downhearted and blue?

- ○ All of the time
- ○ Most of the time
- ○ A good Bit of the Time
- ○ Some of the time
- ○ A little bit of the time
- ○ None of the Time

Did you feel worn out?

- ○ All of the time
- ○ Most of the time
- ○ A good Bit of the Time
- ○ Some of the time
- ○ A little bit of the time
- ○ None of the Time

Have you been a happy person?

- ○ All of the time
- ○ Most of the time
- ○ A good Bit of the Time
- ○ Some of the time
- ○ A little bit of the time
- ○ None of the Time

Did you feel tired?

- ○ All of the time
- ○ Most of the time
- ○ A good Bit of the Time
- ○ Some of the time
- ○ A little bit of the time
- ○ None of the Time

SOCIAL ACTIVITIES:
During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

- ○ All of the time
- ○ Most of the time
- ○ Some of the time
- ○ A little bit of the time
- ○ None of the Time

ENERGY AND EMOTIONS:
These questions are about how you feel and how things have been with you during the last 4 weeks. For each question, please give the answer that comes closest to the way you have been feeling.

Did you feel full of pep?
- ◯ All of the time
- ◯ Most of the time
- ◯ A good Bit of the Time
- ◯ Some of the time
- ◯ A little bit of the time
- ◯ None of the Time

Have you been a very nervous person?
- ◯ All of the time
- ◯ Most of the time
- ◯ A good Bit of the Time
- ◯ Some of the time
- ◯ A little bit of the time
- ◯ None of the Time

Have you felt so down in the dumps that nothing could cheer you up?
- ◯ All of the time
- ◯ Most of the time
- ◯ A good Bit of the Time
- ◯ Some of the time
- ◯ A little bit of the time
- ◯ None of the Time

Have you felt calm and peaceful?
- ◯ All of the time
- ◯ Most of the time
- ◯ A good Bit of the Time
- ◯ Some of the time
- ◯ A little bit of the time
- ◯ None of the Time

Did you have a lot of energy?
- ◯ All of the time
- ◯ Most of the time
- ◯ A good Bit of the Time
- ◯ Some of the time
- ◯ A little bit of the time
- ◯ None of the Time

Bathing or dressing yourself

◯Yes, Limited a Lot ◯Yes, Limited a Little ◯No, Not Limited at all

PHYSICAL HEALTH PROBLEMS:

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

Cut down the amount of time you spent on work or other activities

◯Yes ◯No

Accomplished less than you would like

◯Yes ◯No

Were limited in the kind of work or other activities

◯Yes ◯No

Had difficulty performing the work or other activities (for example, it took extra effort)

◯Yes ◯No

EMOTIONAL HEALTH PROBLEMS:

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

Cut down the amount of time you spent on work or other activities

◯Yes ◯No

Accomplished less than you would like

◯Yes ◯No

Didn't do work or other activities as carefully as usual

◯Yes ◯No

SOCIAL ACTIVITIES:

Emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

◯Not at all ◯Slightly ◯Moderately ◯Severe ◯Very Severe

PAIN:

How much bodily pain have you had during the past 4 weeks?

◯None ◯Very Mild ◯Mild ◯Moderate ◯Severe ◯Very Severe

During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

◯Not at all ◯A little bit ◯Moderately ◯Quite a bit ◯Extremely

GENERAL HEALTH:
How true or false is each of the following statements for you?

I seem to get sick a little easier than other people
○ Definitely true ○ Mostly true ○ Don't know ○ Mostly false ○ Definitely false

I am as healthy as anybody I know
○ Definitely true ○ Mostly true ○ Don't know ○ Mostly false ○ Definitely false

I expect my health to get worse
○ Definitely true ○ Mostly true ○ Don't know ○ Mostly false ○ Definitely false

My health is excellent
○ Definitely true ○ Mostly true ○ Don't know ○ Mostly false ○ Definitely false

APPENDIX 3. The Rome III diagnostic criteria for the constipation

Symptoms	Characteristics of the symptoms
1. Straining during at least 25% of defecations	Symptoms should be observed within 12 weeks (not necessarily consecutive) during the previous year. Syndrome must include two or more of the symptoms listed in this table.
2. Lumpy or hard stools in at least 25% of defecations	
3. Sensation of incomplete evacuation for at least 25% of defecations	

4. Sensation of anorectal obstruction/blockage for at least 25% of defecations	
5. Manual maneuvers to facilitate at least 25% of defecations (e.g., digital evacuation, support of the pelvic floor)	
6. Fewer than three defecations per week	

APPENDIX 4

Classification of internal hemorrhoids (Goligher's classification)

*Assessment criteria:

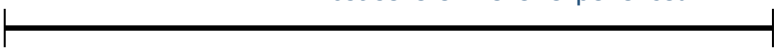
Grade I	Hemorrhoids are prolapsed only into the anal canal.
Grade II	Bleeding and prolapse of hemorrhoids. Hemorrhoids spontaneously reduce after defecation.
Grade III	Prolapse of hemorrhoids after defecation requires their manual reduction.
Grade IV	Prolapse of hemorrhoids that cannot be reduced into the anal canal.

APPENDIX 5.
Example of wording of the diagnosis statement (National guidelines on coloproctology, 2015)

- Internal hemorrhoids (II- 3, III- 7, II-11)
- External (3A, 7B) and internal hemorrhoids (II- 3, III- 7, II-11)
- External hemorrhoids, complicated by an acute thrombosis of grade 2 (7 o`clock).

APPENDIX 6.
Visual analogue scale (VAS)

«Not at all» «Most severe ... ever experienced»



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