

The DOMINO trial

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On behalf of

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IBS: Rome IV Criteria

Recurrent abdominal
pain

>1 day/week in the last 3 months
+ 2 or more of

A

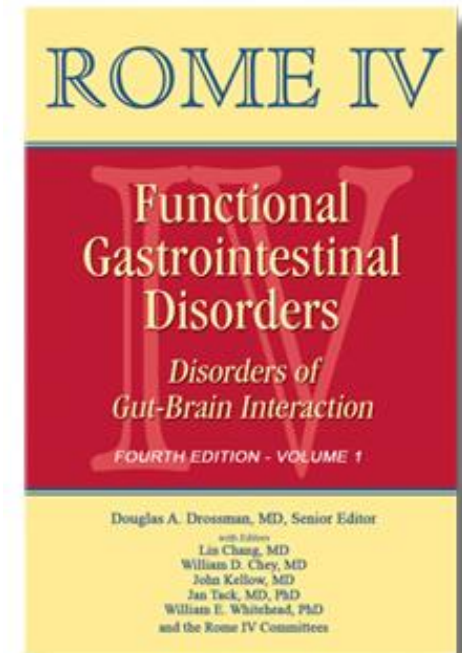
Related to defecation

B

Associated with change
in frequency of stool

C

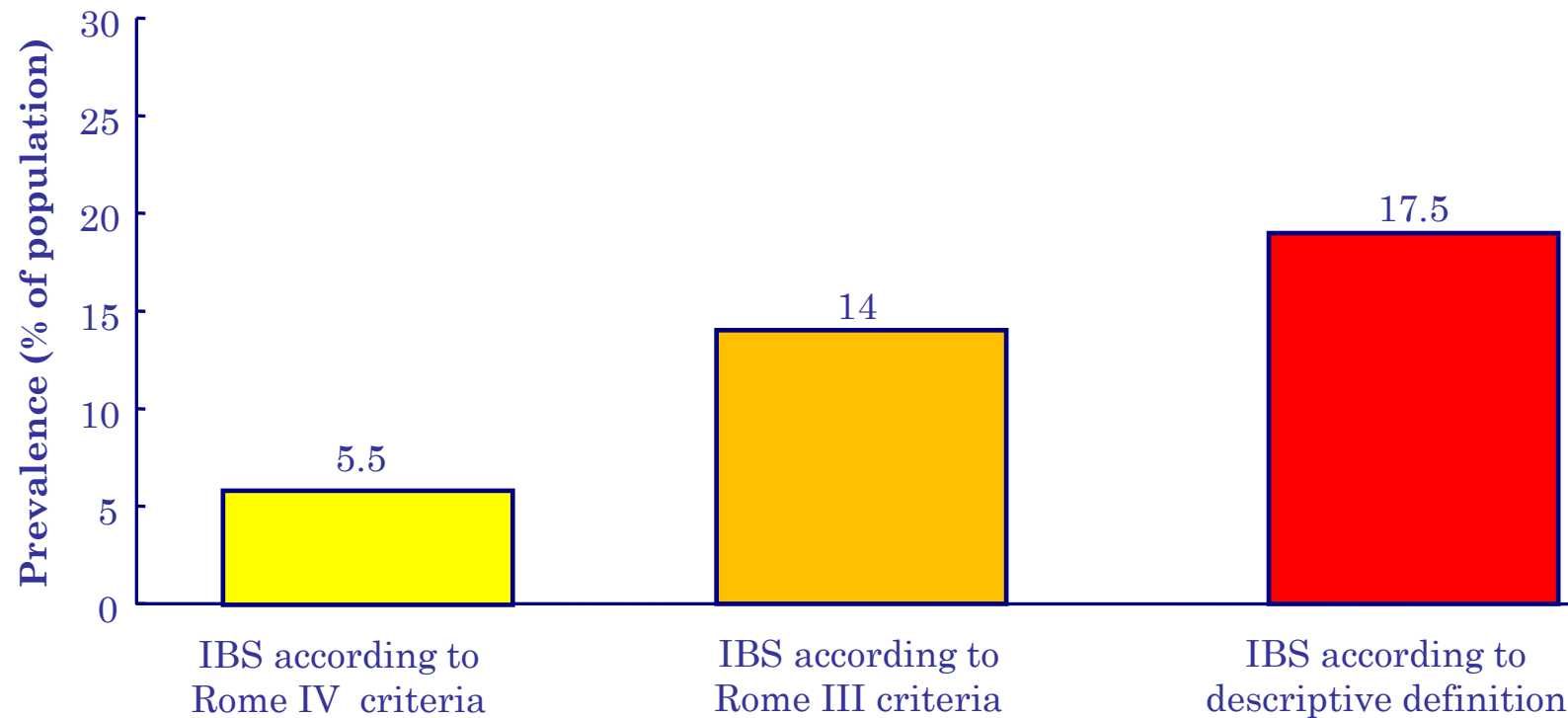
Associated with change
in form of stool



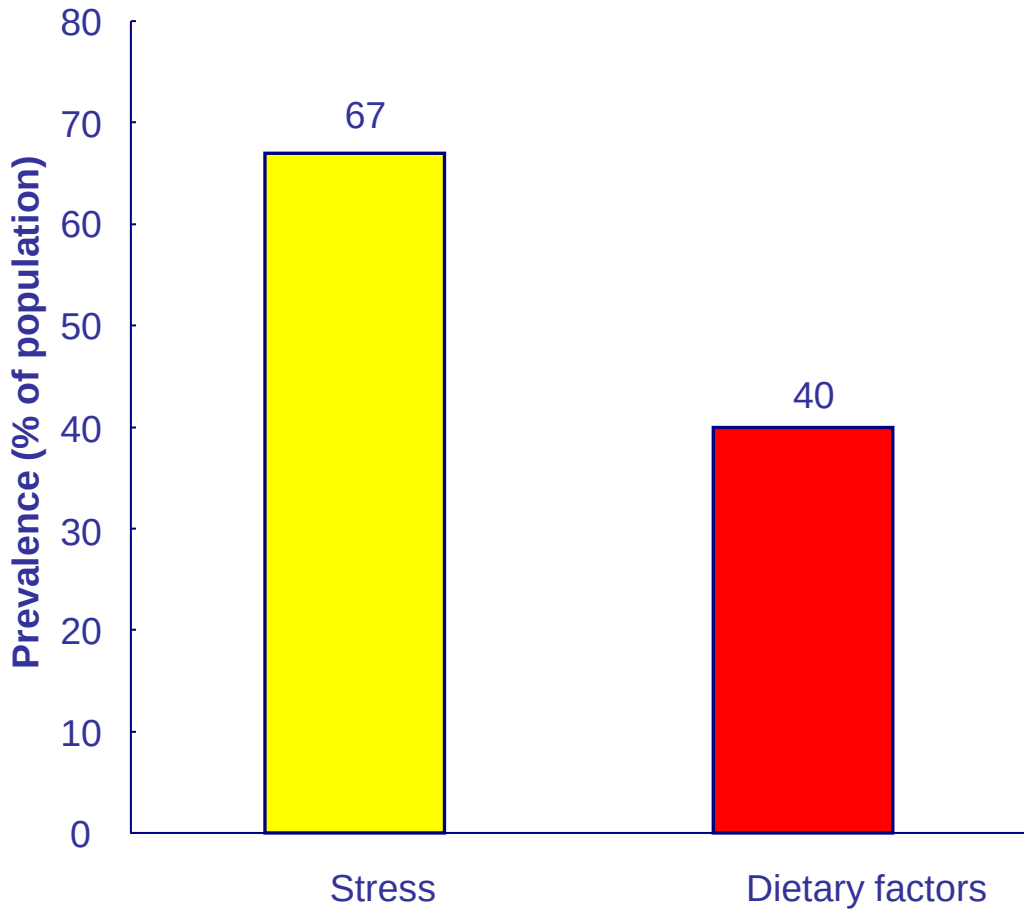
- Criteria present for the last 3 months
- Onset at least 6 months prior to diagnosis
- Absence of obvious anatomical or physiological abnormalities identified by routine diagnostic examinations

Prevalence IBS in Belgium

- Internet survey in 1012 subjects reflecting the national adult population



Triggering factors



Treatment

Medication

- 43% of subjects use analgesics
- 49% use spasmolytics (otilonium bromide #1)
- 21% use neuromodulators
- 21% use medical fibre supplements
- 18% use laxatives
- 11% antidiarrheals

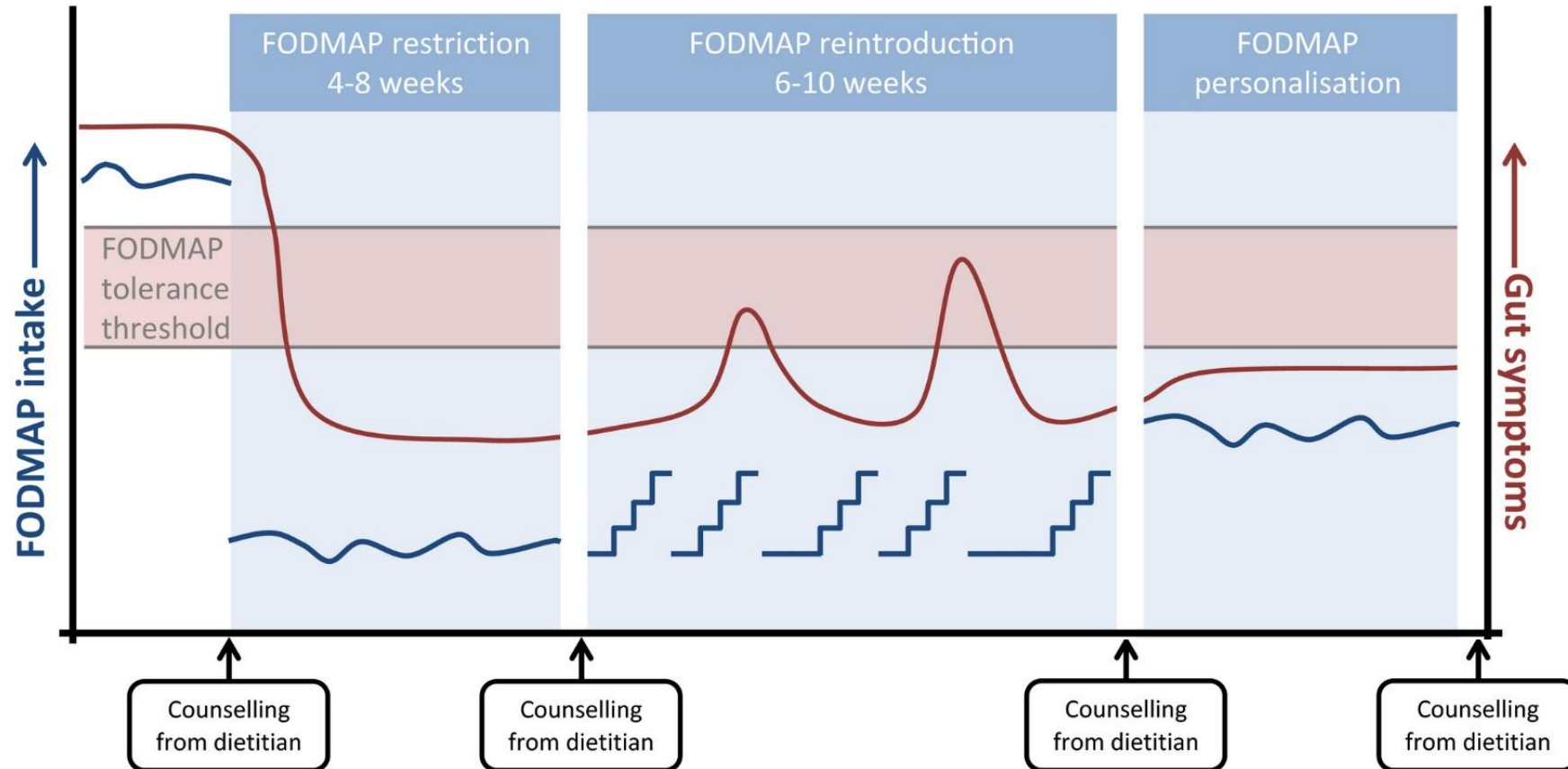
Diet

- 86% of subjects self-adjust the diet
 - Extra intake of water: 50%
 - Avoiding fatty meals: 50%
 - Increasing fiber intake: 43%
 - Smaller size meals: 21%

IBS treatment: The low FODMAP diet

Restriction
max. 8 weeks

Reintroduction: Long
process, Individual tolerance



Limitations:

- Very strict diet difficult to follow
→ **Weight loss!**
- Specialized experienced dietitian
→ **Availability, cost!**

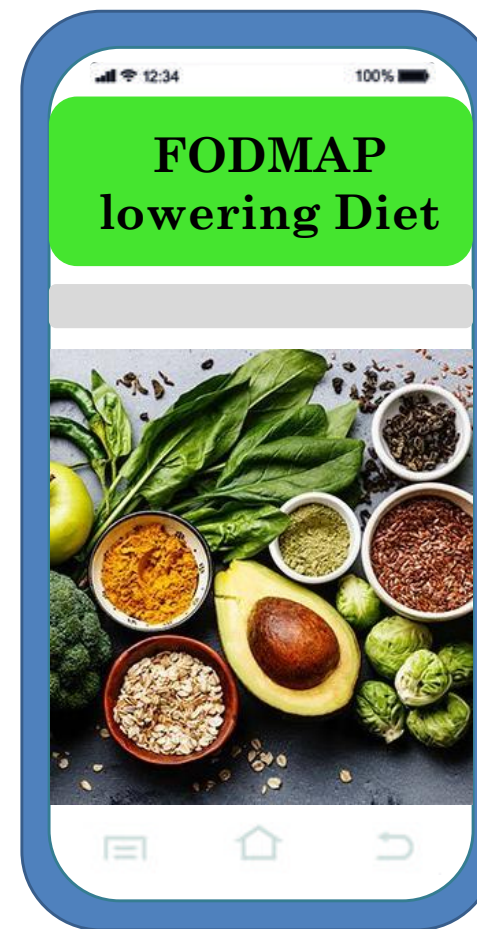
Aim

Classical therapy

Spasmolytic agent:
Otilonium Bromide



New approach



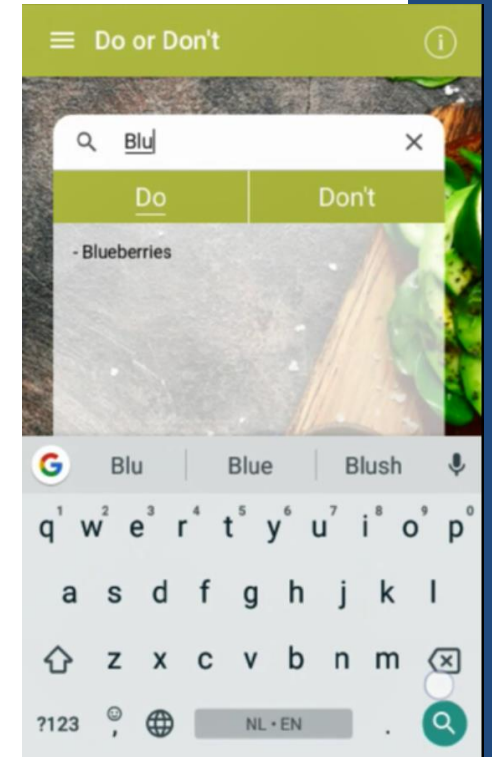
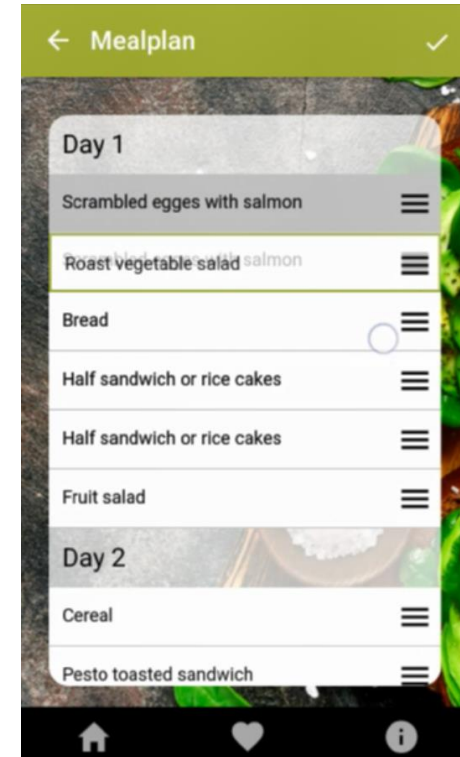
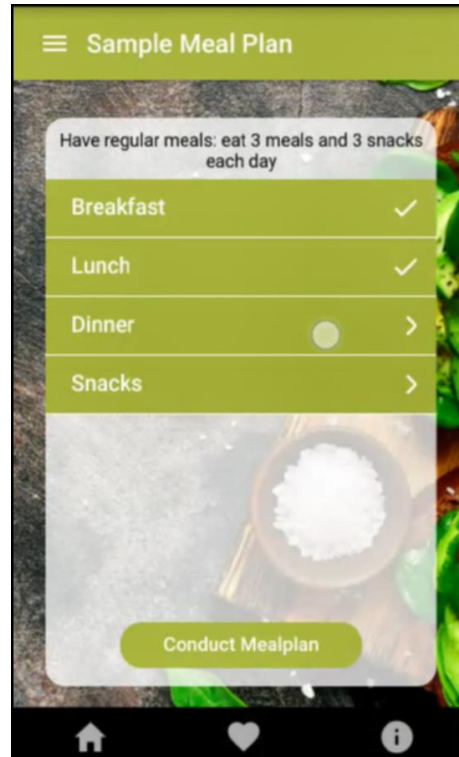
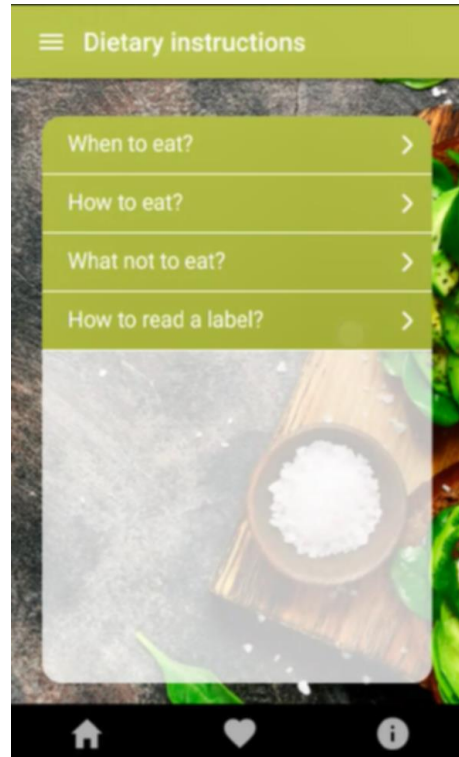
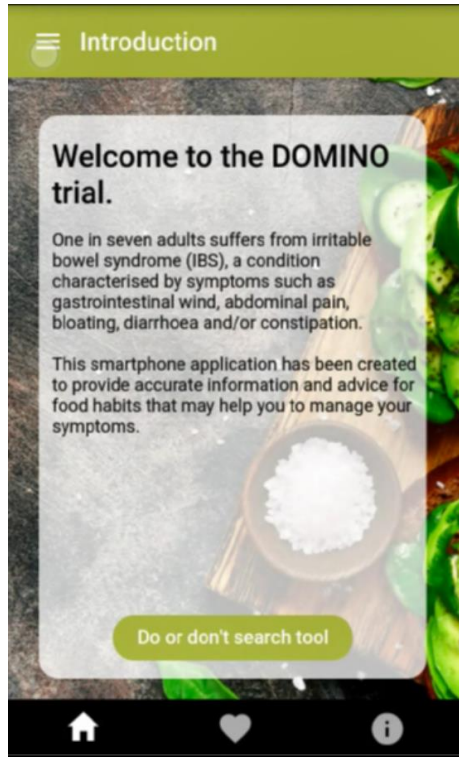
TREATMENT EFFICACY



HEALTH ECONOMIC IMPACT

SCIENTIFIC ASPECTS

DOMINO smartphone app



- Dietary instructions
 - What to eat?
 - When to eat?
 - What to avoid?
 -
- 27 Recipes Breakfast
- 27 Recipes Lunch
- 27 Recipes Dinner
- Snacks and Desserts
- Search function
- Supermarket list
- Manage a week menu (meal plan)

Recruitment of GPs in Belgium

- ± 2000 Invitation letters
- ± 1000 Phone calls
- Advertising via: Artsenkrant, Medipresse
- Contacted Domus medica, Intego, ~~Association des Médecins Généralistes~~
- Organizing 14 educational and investigator meetings for GPs (Bruges, Gent, Genk, Leuven, Antwerp, La Hulpe-Rixensart, ...)

**105 General practitioners
agreed to participate**



105 Contracts with UZLeuven
(3 copies, 315 signatures)

Treatment Efficacy



470 IBS
patients

Randomized

Treatment period

FODMAP lowering diet
N=235

Otilonium Bromide (Spasmomen®)
N=235

8 weeks

Visit 1

Visit 2

IBS-SSS

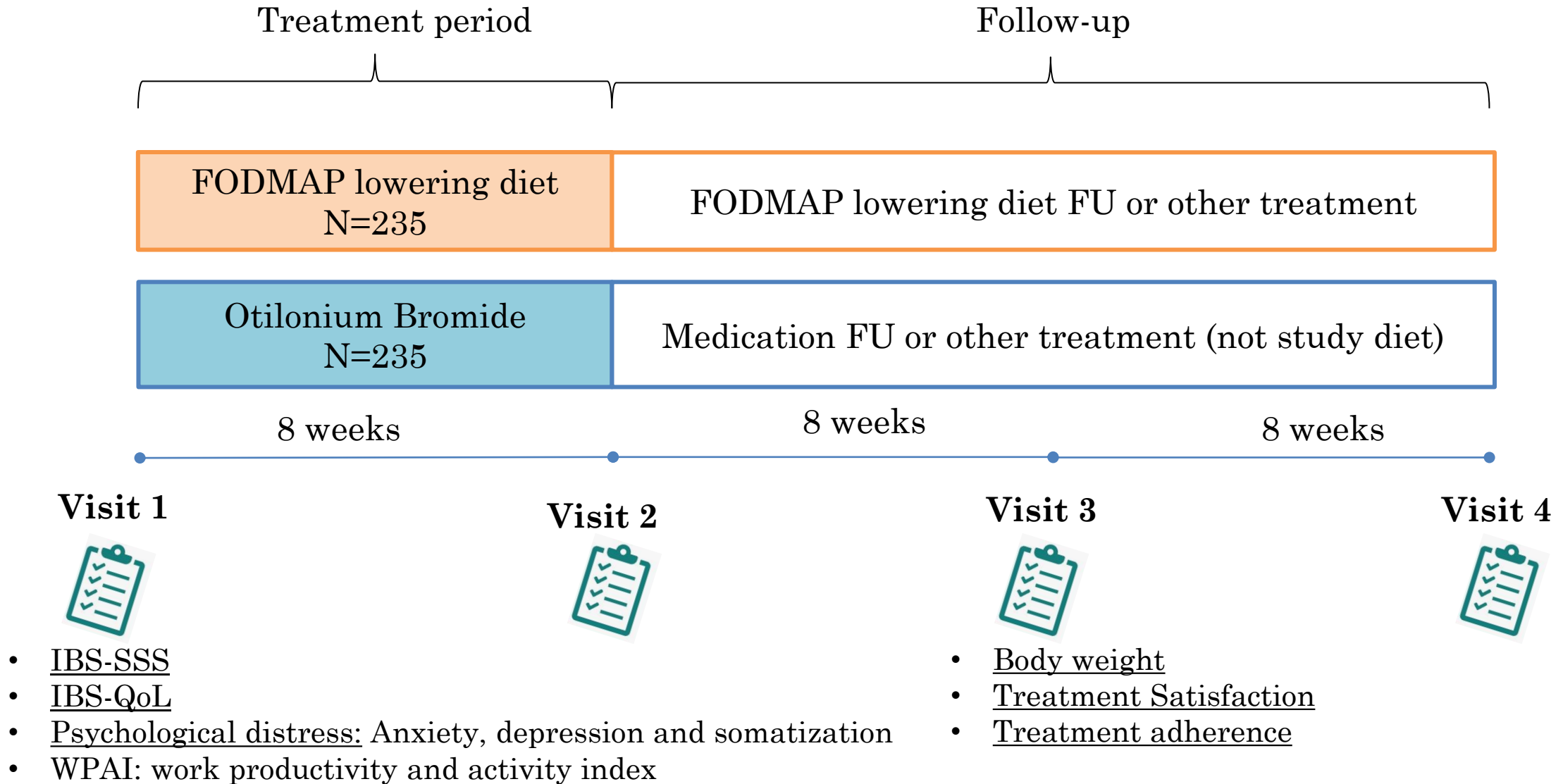
IBS-SSS

Inclusion criteria:

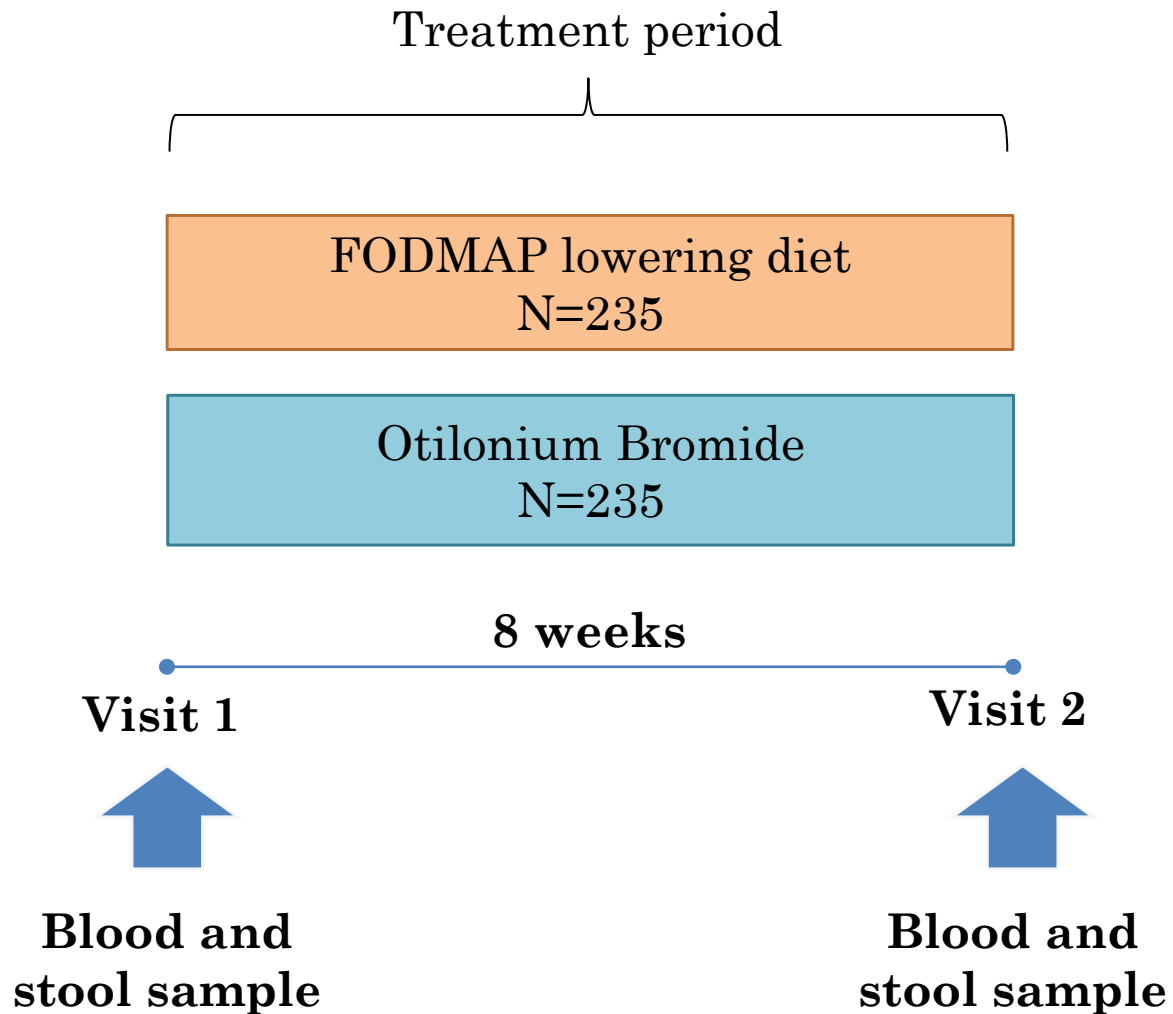
- IBS diagnosis by general practitioner
- Newly diagnosed or newly treated IBS patient
- No current or prior long-term (> 3 weeks) treatment with Otilonium Bromide, no diet

Long term treatment impact

Health economic impact



Scientific aim



Blood sample: **Genetic research**

- Genetic predisposition
- IBS genetic polymorphisms
- Relationship to treatment response



Stool sample: **Microbiome**

- Changes in gut microbiome
- Relationship to treatment response



Kits for biological samples



3 x EDTA



1 x Fluoride
(By GP during visit)



1 x SST

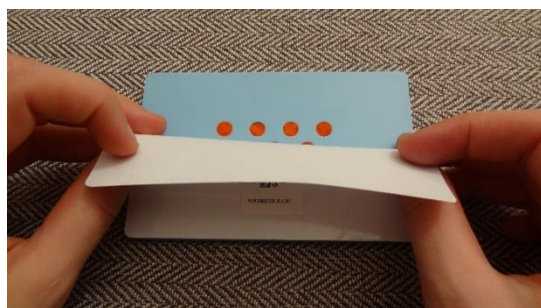
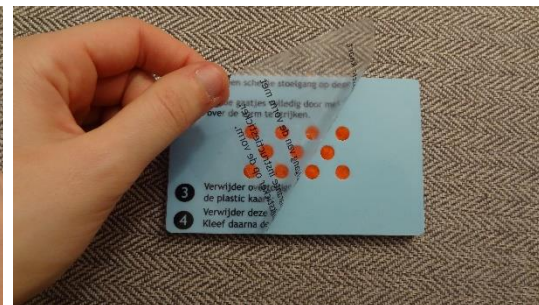


Stool sample
(By patient at home)

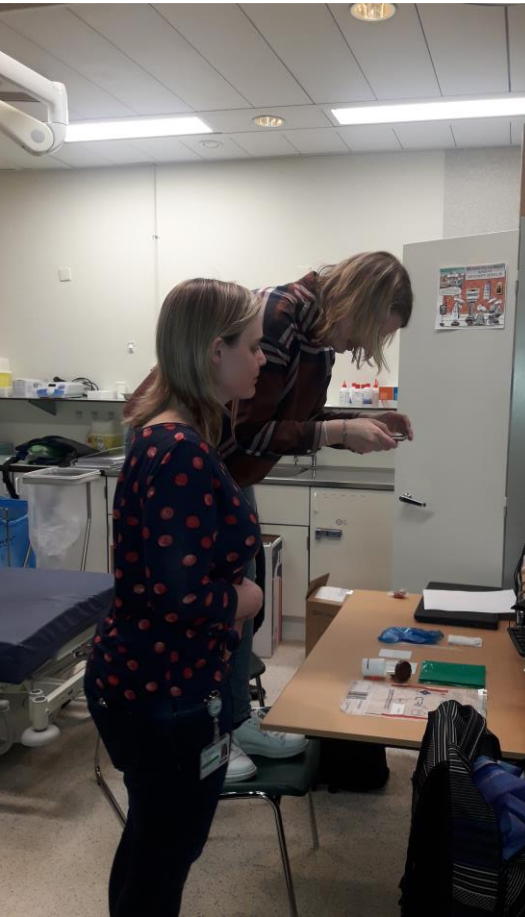
- The DOMINO team provided Kits to GPs
- CRI labo collected blood and stool samples from the different sites
- CRI performed standard clinical analyses on samples
- Complex genetic and microbiome analysis
 - Prof D'Amato (Monash Uni, Australia) and Prof Raes (KU Leuven)



Stool sample collection

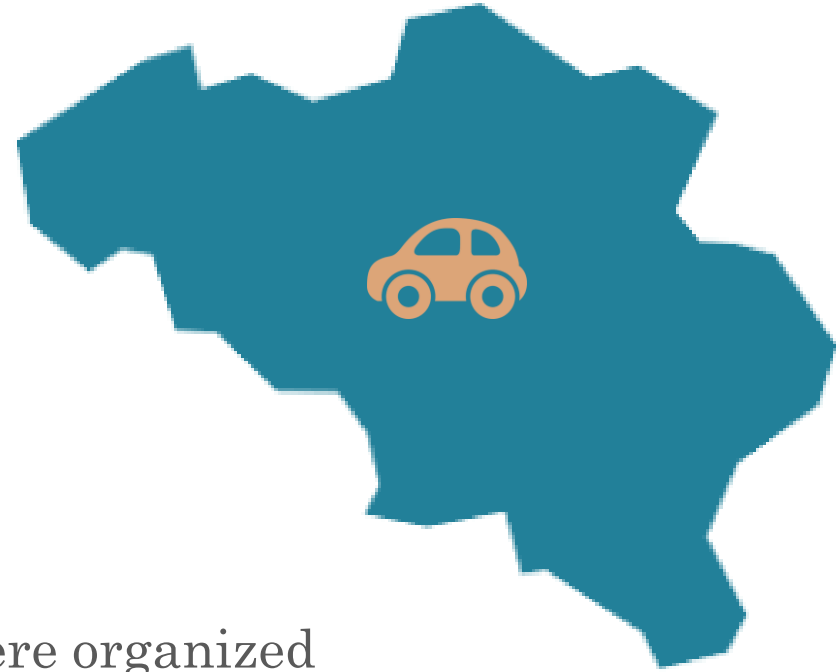


Kits



Monitoring

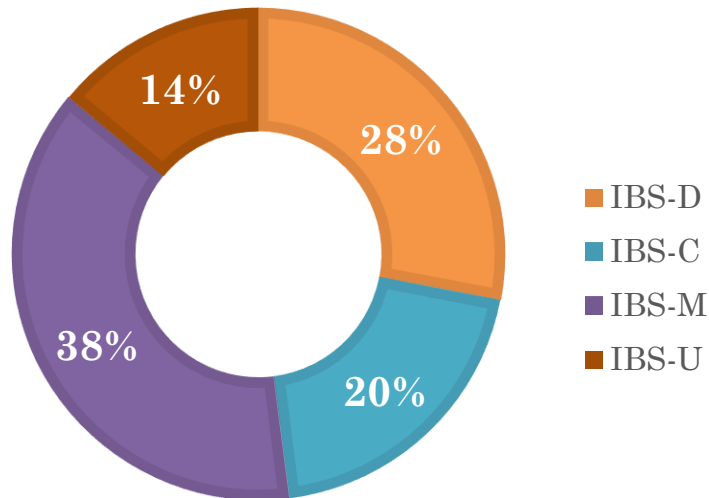
- Remote: via eCRF
- On-site: visit to GPs
- Throughout the study: 75 monitoring visits
- At the end of the study, 103 close-out visits were organized



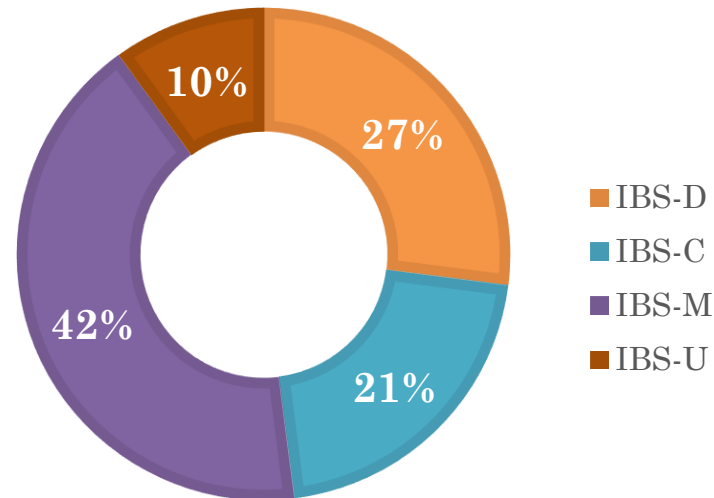
Study arm characteristics

	Diet	Medication	P-value
Average <u>age</u> (SD)	40.6 (14.5)	41.2 (14.9)	0.61
Gender (Female)	168 (75.7%)	175 (75.8%)	0.98
Weight	69.7 (13.8)	71.1 (14.3)	0.3
Average <u>BMI</u> (SD)	24.3 (4.4)	24.9 (4.6)	0.16

Stool type: Diet

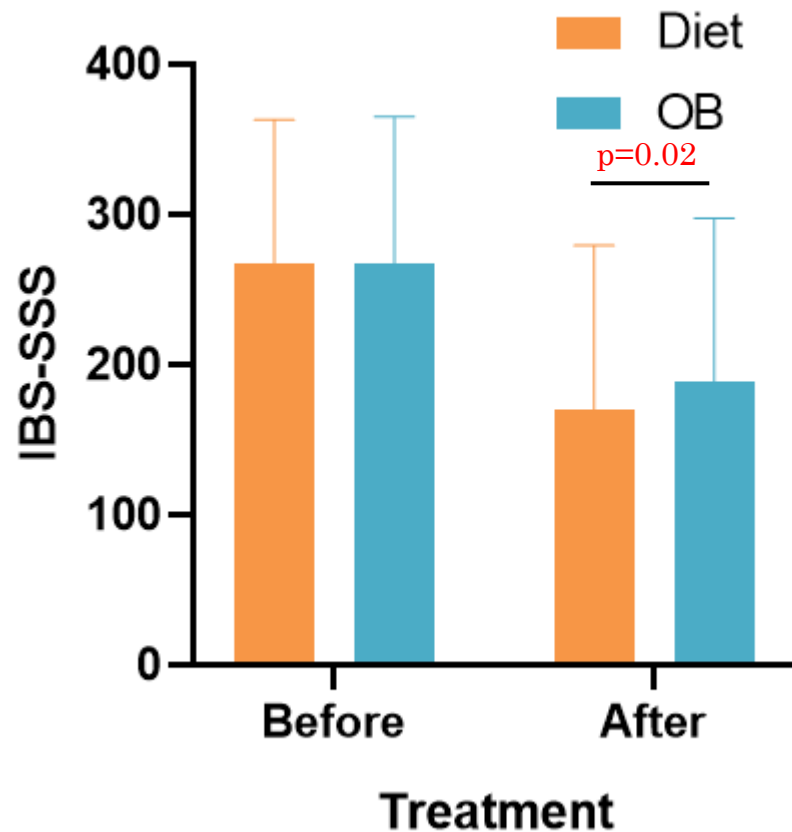


Stool type: Medication



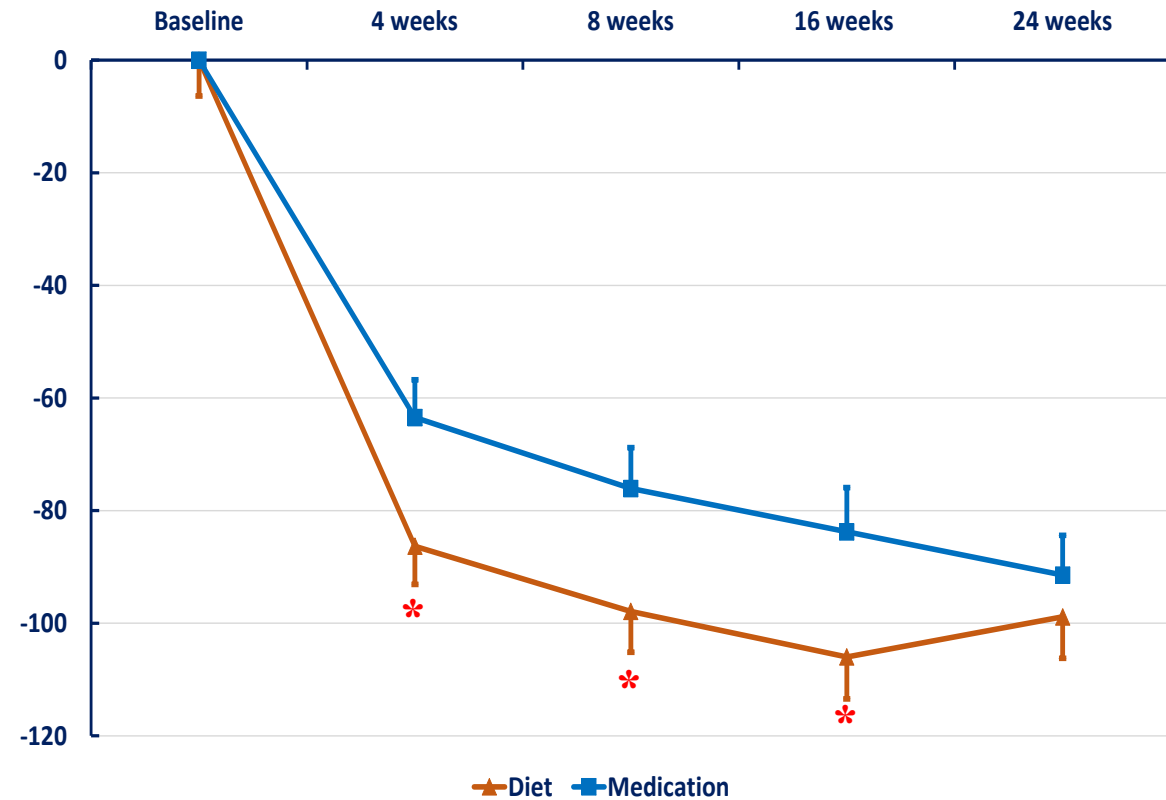
Results

Evolution of IBS-SSS at 8 weeks



IBS-SSS: Irritable Bowel Syndrome Symptom severity scale
OB: otilonium bromide

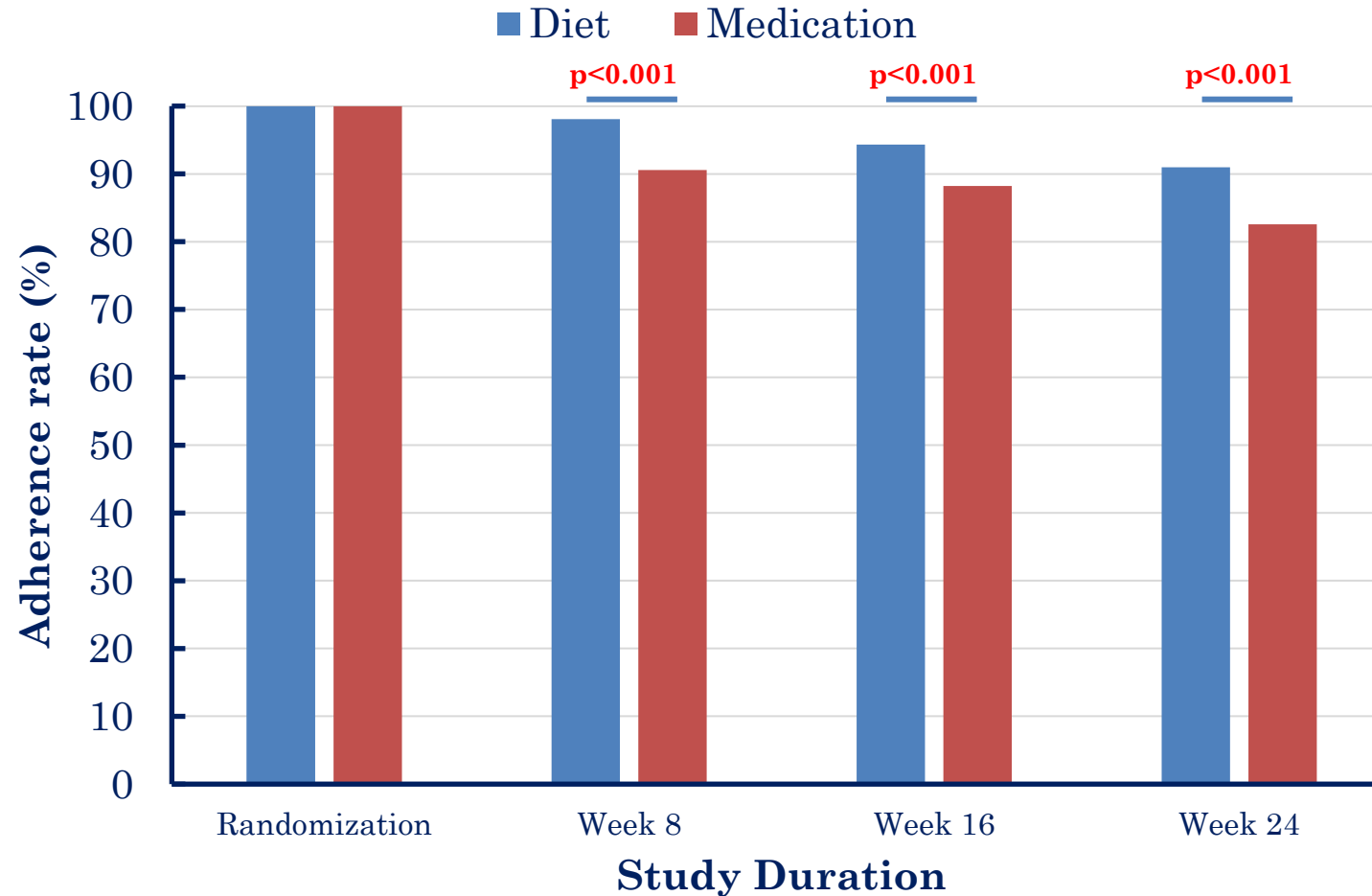
Change from baseline with time



* Significantly different (p<0.05)

Van Den Houte K, Carbone F, Tack J et al. Gut 2022

Treatment adherence



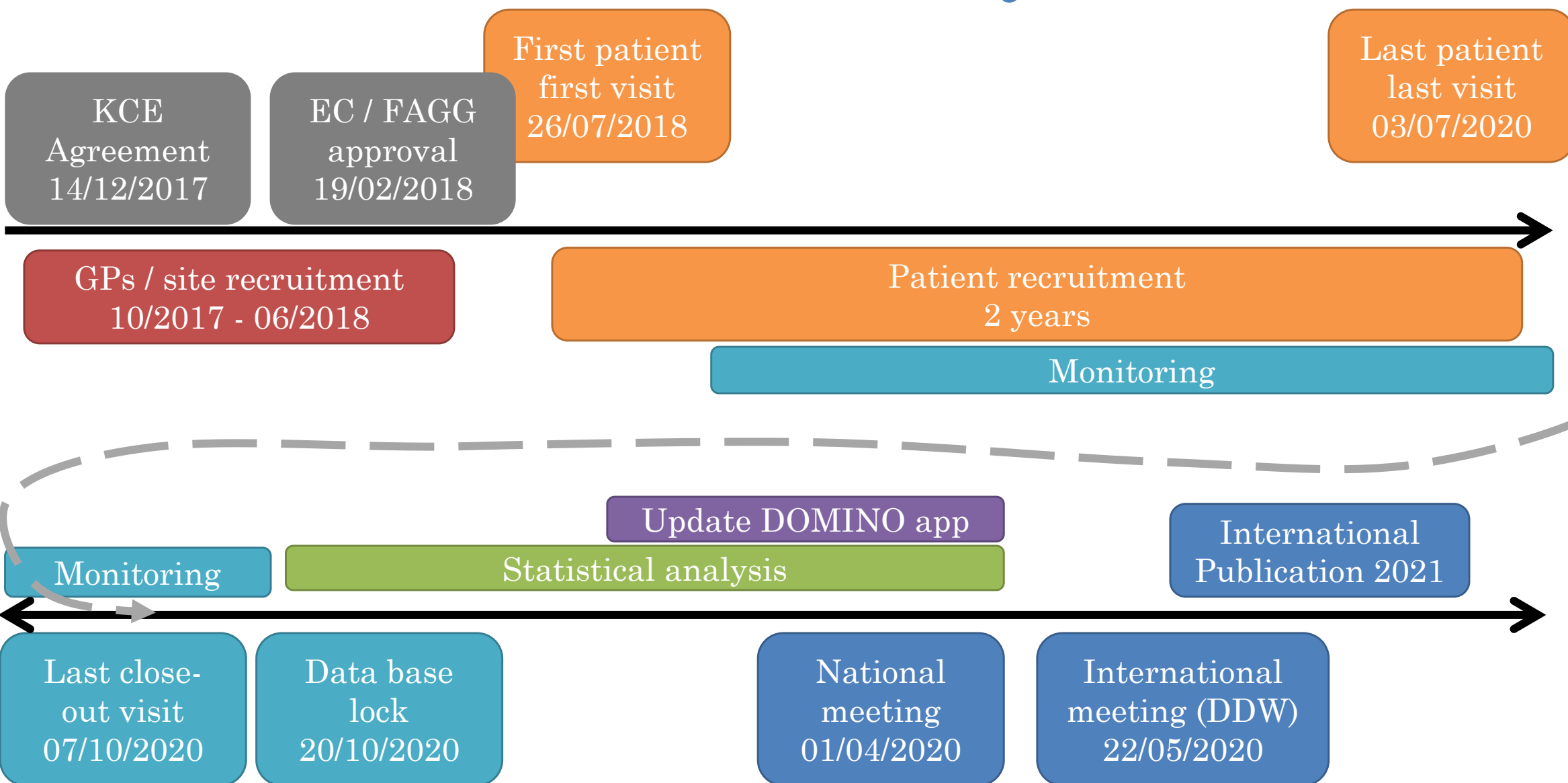
Genotype Association to response

- Response to Diet
 - Gene *CCR3*: chemokine receptor
 - SNP variant rs7617872, Allele “A”
 - Associated with increased response
 - eQTL: Associated with increased mRNA expression in whole blood
- Response to Medication
 - Gene *SLC6A4*: Serotonin reuptake transporter
 - SNP variant rs2020934, Allele “G”
 - Associated with increased response
 - eQTL: Associated with increased expression mRNA expression in aorta, breast, esophagus and adipose tissues

Conclusion

- **A FODMAP lowering diet administered through a smartphone application is superior to standard medical therapy in primary care IBS**
- **Response and treatment adherence are maintained for up to 6 months during follow-up**
- **This is associated with significant improvement in quality of life, anxiety, depression and somatization, compared to baseline**
- **Female gender is a predictor of response to diet**
- **Somatization score is a predictor of response to medication**
- **Genetic polymorphisms determine response to therapy in primary care IBS**

Timeline DOMINO study





The DOMINO trial

DOMINO TEAM:

Karen Van den Houte

Linde Besard

Jan Tack

Florencia Carbone



Thank you!



KU LEUVEN

