Güncel koşullarda Fonksiyonel bağırsak hastalığı

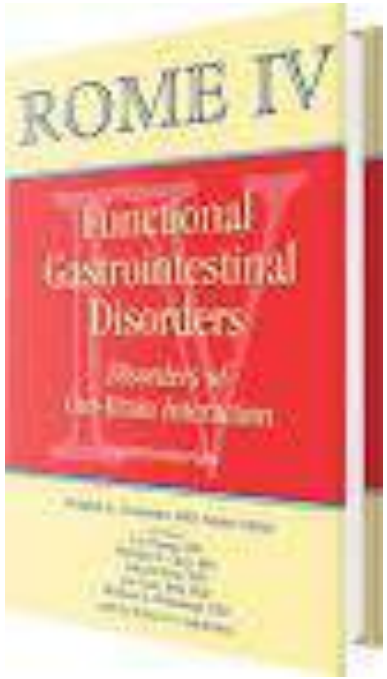
giderek artıyor mu?….

Güncel yönetim nasıl olmalı?

Prof.Dr.Filiz Akyüz
İstanbul Tıp Fakültesi Gastroenteroloji BD

Fonksiyonel barsak hastalıkları artıyor mu?

ARTIK POZİTİF BİR TANI…..



<u>Fonksiyonel barsak hastalıkları</u>

IBS (kabız, ishal, mikst, sınıflanamayan)

Şişkinlik (Gaz)

Kabızlık

İshal

Sınıflandırılamayan

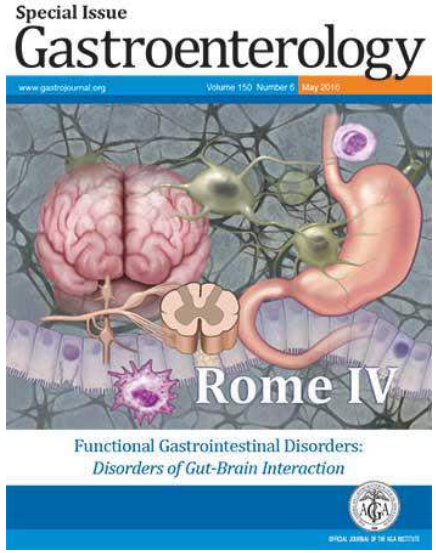
Opioid ilişkili kabızlık

<u>Fonksiyonel anorektal hastalıklar</u>

Fekal inkontinans

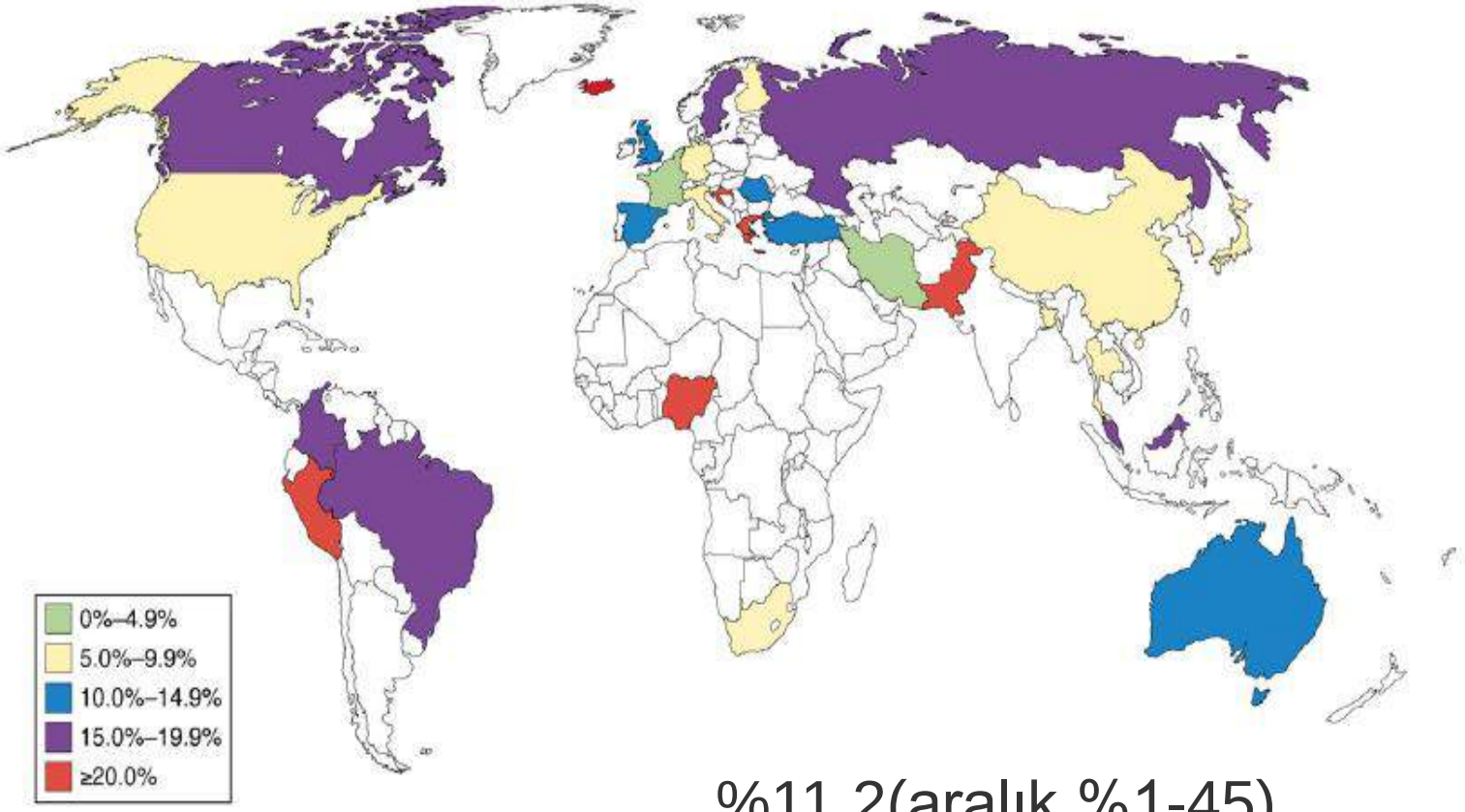
Anorektal ağrı (levator ani sendromu, sınıflanamayan, Proctalgia fugax)

Fonksiyonel dışkılama problemleri



Lacy BE, et al. Gastroenterology 2016;150:1393–1407

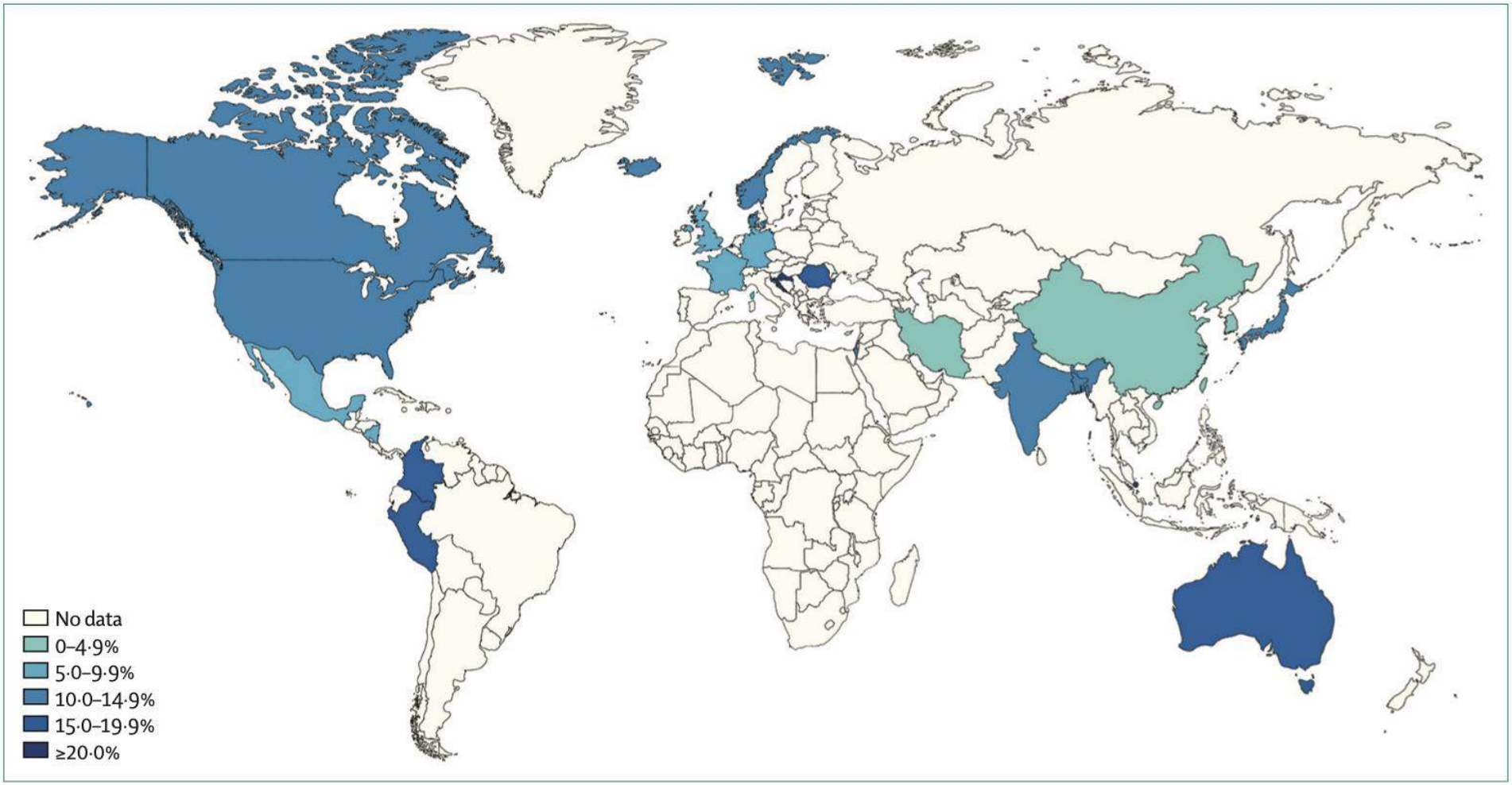
IBS SIKLIĞI



%11.2(aralık %1-45)

Lovell & Ford, Clin Gastroenterol Hepatol 2012;10:712-21

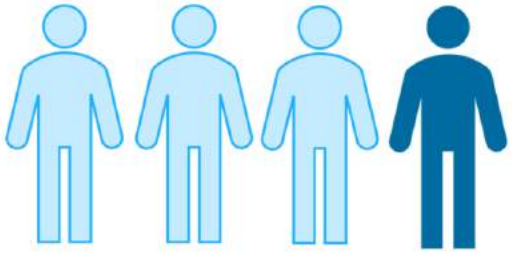
IBS SIKLIĞI



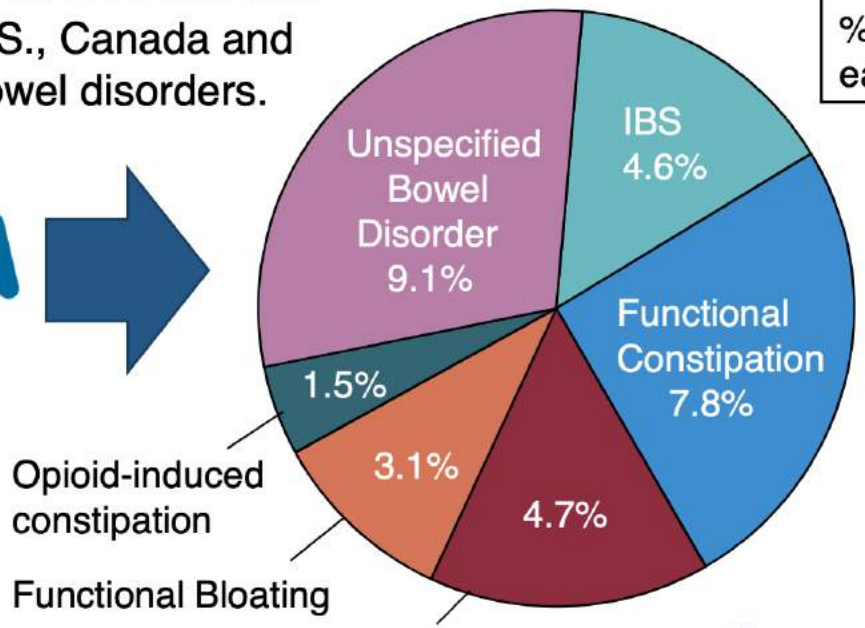
Ford A, et al. Lancet 2020

Prevalence of Functional Bowel Disorders

More than **1 in every 4 adults** in the U.S., Canada and the U.K. has one of the six functional bowel disorders.

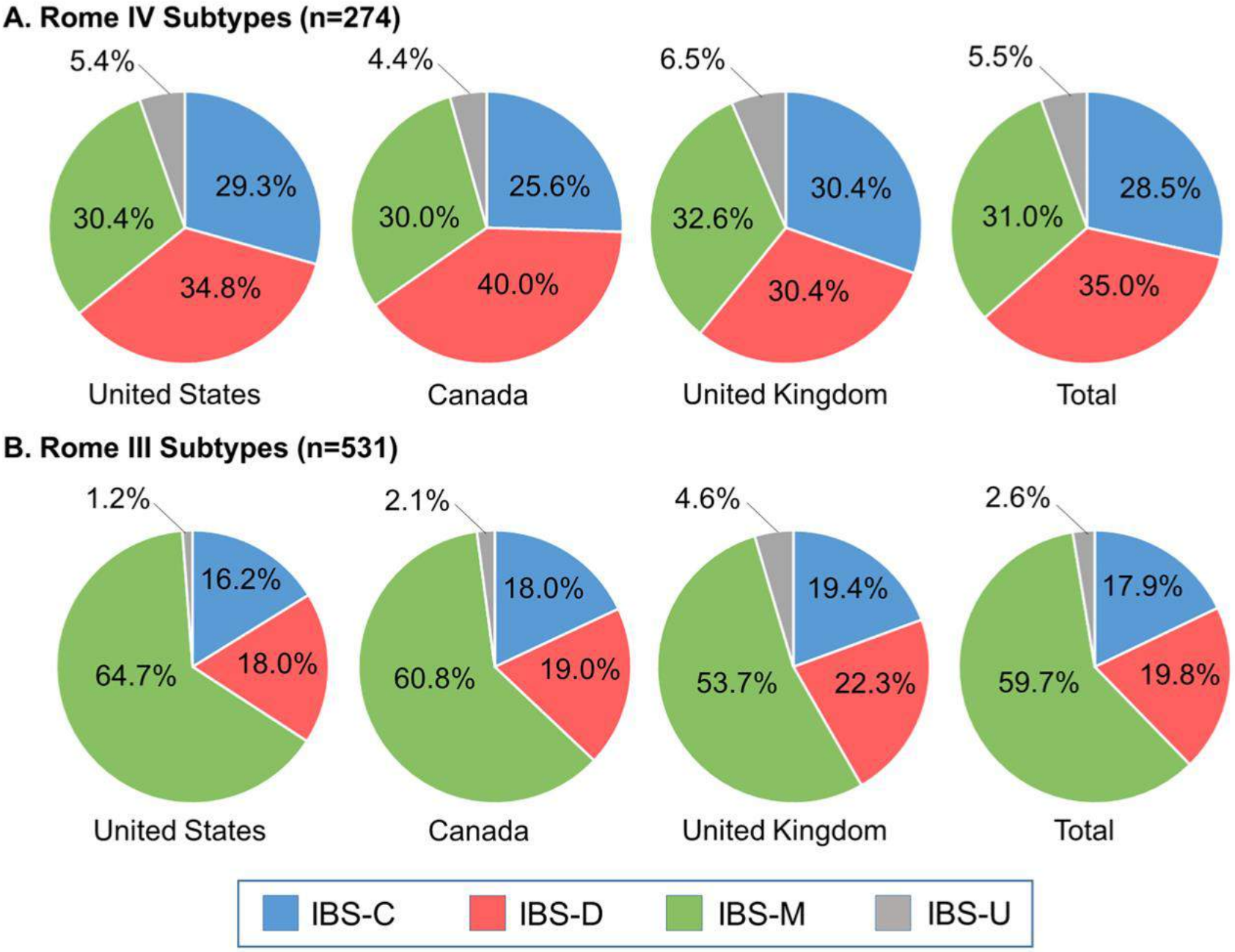


- ✓ Functional bowel disorders are more common in women than men
- ✓ They become less common after mid-life

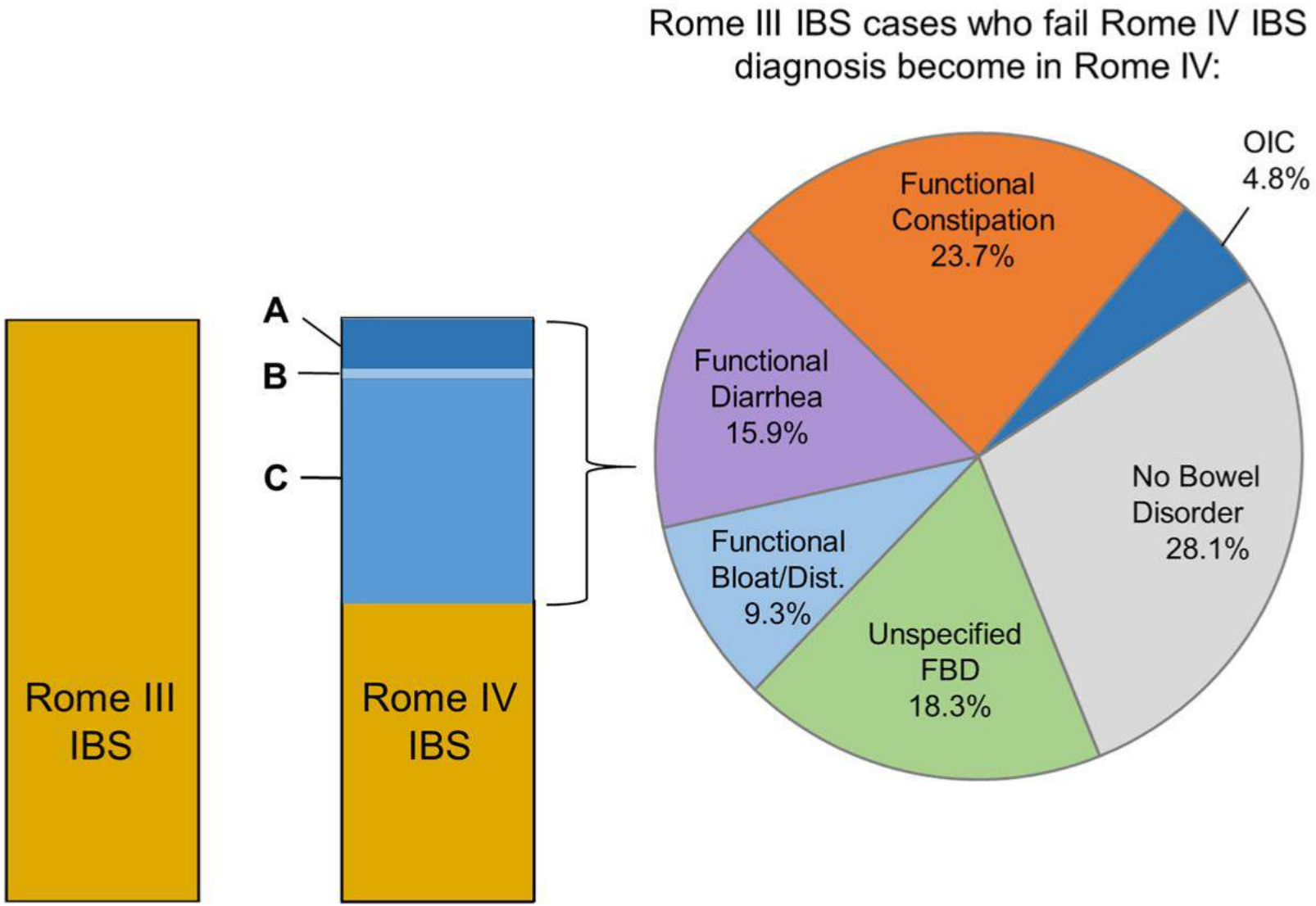


Gastroenterology

Palsson OS, et al. Gastroenterology (2020),



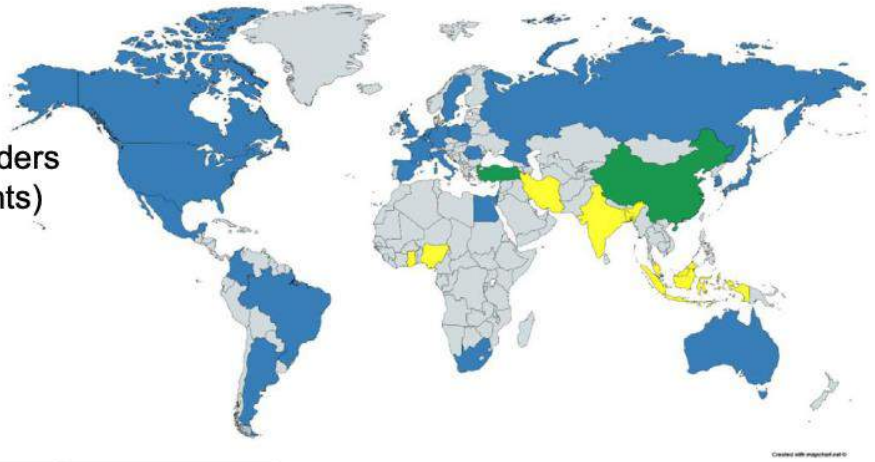
Palsson OS, et al. Gastroenterology (2020),



Palsson OS, et al. Gastroenterology (2020),

A global epidemiological study of functional GI disorders

- 73,076 adults surveyed (33 countries, 6 continents)
- Data collection: By Internet (24 countries, blue), by household interview (7 countries, yellow), or both methods (China and Turkey, green).



Prevalence of meeting criteria for at least one of 22 functional GI disorders (%):

	All Participants	Females	Males
Internet surveys	40.3	46.5	34.2
Household surveys	20.7	23.1	18.3

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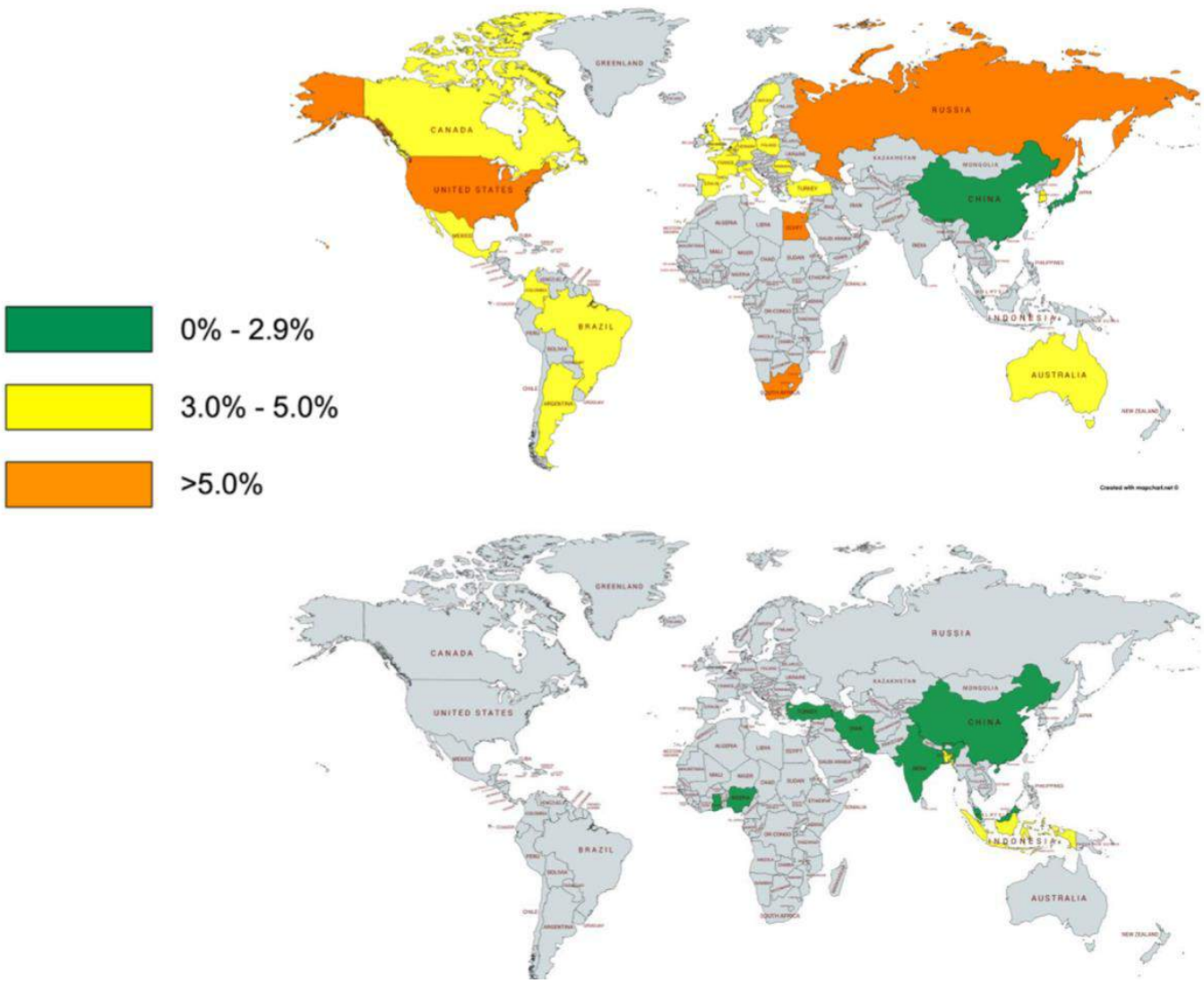
IBS



Internet

Household

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FGID	Overall N = 54,127	Sex		Age group (y)		
		Female n = 26,578	Male n = 27,549	18–39 n = 23,003	40–64 n = 22,281	65+ n = 8843
Internet						
Any FGID	40.3 (39.9–40.7)	46.5 (45.9–47.1)	34.2 (33.7–34.8)	44.3 (43.7–44.9)	39.4 (38.8–40.1)	31.9 (30.9–32.8)
A. Esophageal Disorders						
Functional chest pain	1.4 (1.3–1.5)	1.5 (1.3–1.6)	1.3 (1.1–1.4)	1.4 (1.3–1.6)	1.5 (1.3–1.6)	1.0 (0.8–1.3)
Functional heartburn	1.1 (1.0–1.2)	1.3 (1.1–1.4)	1.0 (0.9–1.1)	1.3 (1.1–1.4)	1.2 (1.0–1.3)	0.7 (0.5–0.8)
Reflux hypersensitivity	0.8 (0.8–0.9)	0.9 (0.8–1.0)	0.8 (0.7–0.9)	0.9 (0.7–1.0)	1.0 (0.8–1.1)	0.5 (0.4–0.6)
Globus	0.8 (0.7–0.8)	0.9 (0.7–1.0)	0.7 (0.6–0.8)	0.8 (0.6–0.9)	0.9 (0.7–1.0)	0.5 (0.4–0.7)
Functional dysphagia	3.2 (3.0–3.3)	3.5 (3.3–3.7)	2.9 (2.7–3.1)	3.3 (3.1–3.5)	3.2 (3.0–3.4)	2.7 (2.4–3.0)
Any esophageal disorder	6.0 (5.8–6.2)	6.6 (6.3–6.9)	5.4 (5.1–5.6)	6.2 (5.9–6.5)	6.3 (6.0–6.6)	4.6 (4.2–5.0)
B. Gastroduodenal Disorders						
Functional dyspepsia	7.2 (7.0–7.4)	8.7 (8.4–9.1)	5.8 (5.5–6.0)	9.2 (8.8–9.5)	6.6 (6.2–6.9)	3.8 (3.4–4.2)
PDS	6.1 (5.9–6.3)	7.5 (7.2–7.8)	4.8 (4.6–5.1)	7.8 (7.5–8.2)	5.5 (5.2–5.8)	3.3 (2.9–3.6)
EPS	2.4 (2.3–2.5)	2.8 (2.6–3.0)	2.0 (1.8–2.2)	2.9 (2.7–3.1)	2.4 (2.2–2.6)	1.2 (0.9–1.4)
Belching disorder	1.0 (0.9–1.1)	1.1 (1.0–1.2)	0.9 (0.7–1.0)	1.1 (1.0–1.2)	1.0 (0.8–1.1)	0.7 (0.5–0.8)
Rumination syndrome	2.8 (2.7–2.9)	3.1 (2.9–3.3)	2.5 (2.3–2.7)	2.7 (2.5–2.9)	3.0 (2.8–3.2)	2.4 (2.1–2.7)
Chronic nausea vomiting syndrome	0.9 (0.8–1.0)	1.2 (1.0–1.3)	0.7 (0.6–0.8)	1.3 (1.2–1.5)	0.7 (0.6–0.8)	0.4 (0.3–0.5)
Cyclic vomiting syndrome	1.2 (1.1–1.2)	1.2 (1.1–1.3)	1.1 (1.0–1.2)	1.6 (1.4–1.8)	0.9 (0.8–1.0)	0.6 (0.5–0.8)
Cannabinoid hyperemesis syndrome	0.05 (0.03–0.07)	0.02 (0.01–0.04)	0.08 (0.05–0.11)	0.11 (.07–15)	0.010(.00–0.02)	0.01 (0.00–0.03)
Any gastroduodenal disorder	10.6 (10.4–10.9)	12.4 (12.0–12.8)	8.9 (8.6–9.2)	13.0 (12.5–13.4)	9.8 (9.4,10.2)	6.6 (6.1–7.2)
C. Bowel Disorders						
Rome-IV IBS	4.1 (3.9–4.2)	5.2 (5.0–5.5)	2.9 (2.7–3.1)	5.3 (5.0–5.6)	3.7 (3.5–4.0)	1.7 (1.4–1.9)
IBS-C	1.3 (1.2–1.4)	1.8 (1.7–2.0)	0.8 (0.7–0.9)	1.8 (1.6–2.0)	1.1 (1.0–1.2)	0.6 (0.4–0.8)
IBS-D	1.2 (1.1–1.3)	1.3 (1.2–1.5)	1.0 (0.9–1.1)	1.1 (0.9–1.2)	0.5 (0.3–0.6)	0.5 (0.3–0.6)
IBS-U	0.3 (0.2–0.3)	0.3 (0.2–0.4)	0.2 (0.2–0.3)	0.3 (0.2–0.4)	0.3 (0.2–0.3)	0.1 (0.0–0.2)
IBS-M	1.3 (1.2–1.4)	1.8 (1.6–1.9)	0.9 (0.8–1.0)	1.6 (1.5–1.8)	1.3 (1.2–1.5)	0.5 (0.3–0.6)
Functional Constipation	11.7 (11.4–12.0)	15.2 (14.8–15.7)	8.3 (8.0–8.6)	13.2 (12.8–13.7)	11.0 (10.6–11.4)	9.4 (8.8–10.0)
Opioid-induced constipation	1.6 (1.5–1.7)	1.8 (1.6–1.9)	1.4 (1.2–1.5)	1.5 (1.3–1.7)	1.6 (1.5–1.8)	1.5 (1.3–1.8)
Functional diarrhea	4.7 (4.5–4.9)	4.1 (3.8–4.3)	5.3 (5.1–5.6)	4.6 (4.3–4.9)	5.1 (4.8–5.3)	4.1 (3.7–4.5)
Functional bloating/distention	3.5 (3.3–3.6)	4.6 (4.3–4.8)	2.4 (2.2–2.5)	3.4 (3.2–3.7)	3.9 (3.6–4.1)	2.4 (2.1–2.7)
Unspecified functional bowel disorder	8.8 (8.6–9.0)	9.5 (9.1–9.8)	8.1 (7.8–8.5)	9.5 (9.1–9.9)	8.7 (8.3–9.1)	7.2 (6.7–7.7)
Any bowel disorder	33.4 (33.0–33.8)	39.3 (38.7–39.9)	27.7 (27.2–28.2)	36.7 (36.1–37.3)	33.0 (32.4–33.6)	25.9 (24.9–26.8)
D. Central Nervous System Disorders of GI Pain						
Centrally mediated abdominal pain syndrome	0.02 (0.01–03)	0.03 (0.01–0.06)	0.00[a]	0.03 (0.01–0.05)	0.01(0.00–0.02)	0.01 (0.00–0.03)
E. Biliary Disorders						
Functional biliary pain	0.08 (0.06–0.11)	0.14 (0.09–0.18)	0.03 (0.01–0.04)	0.13 (0.08–0.18)	0.05 (0.02–0.08)	0.02 (0.00–0.05)
F. Anorectal Disorders						
Fecal incontinence	1.6 (1.5–1.7)	1.5 (1.4–1.7)	1.6 (1.5–1.8)	1.1 (1.0–1.3)	1.7 (1.6–1.9)	2.3 (2.0–2.7)
Levator ani syndrome	1.1 (1.1–1.2)	1.4 (1.2–1.5)	0.9 (0.8–1.0)	1.3 (1.2–1.5)	1.2 (1.1–1.4)	0.6 (0.4–0.7)
Proctalgia fugax	5.6 (5.4–5.8)	6.4 (6.1–6.7)	4.7 (4.5–5.0)	6.1 (5.8–6.4)	5.7 (5.4–6.0)	3.9 (3.5–4.3)
Any anorectal disorder	7.7 (7.5–8.0)	8.8 (8.5–9.2)	6.7 (6.4–7.0)	8.0 (7.6–8.3)	8.0 (7.6–8.3)	6.4 (5.9–6.9)
Household						

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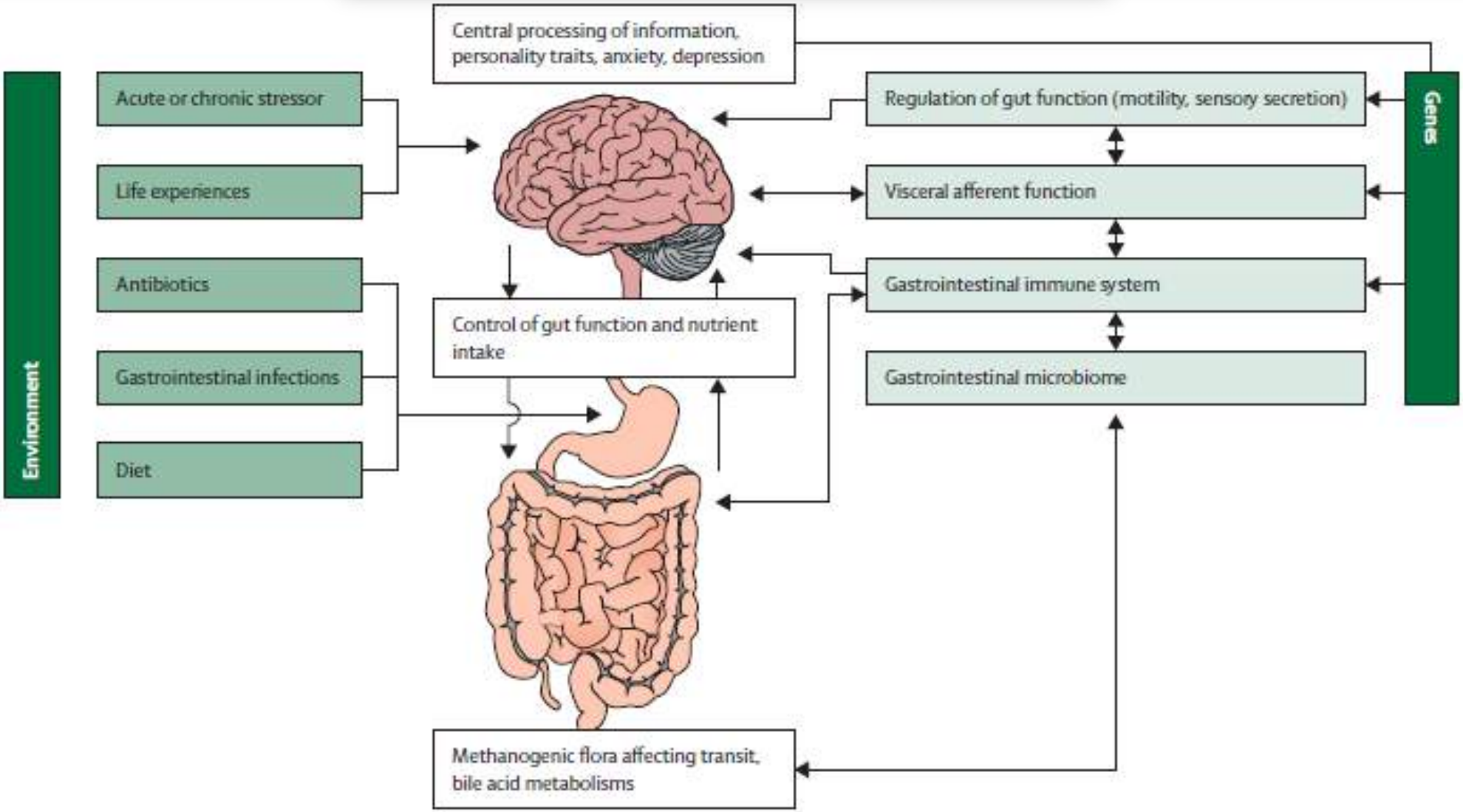
Table 2. Prevalence Rates (% and 95% CI) for 5 Selected Major Functional Gastrointestinal Diagnoses (Rome IV)– for Any FGID (26 Countries) and Rome III IBS (14 Countries) in the Internet Survey and for All 9 Countries in the Household Survey

	N	Any FGID	Functional Dyspepsia	IBS (Rome IV)	IBS (Rome III) (N=14)	Functional Constipation	Functional Diarrhea	Functional bloating/distention
INTERNET								
Argentina	2057	43.9 (41.8–46.1)	6.9 (5.8–8.0)	3.5 (2.7–4.3)	N/A	12.2 (10.7–13.6)	6.3 (5.2–7.3)	5.2 (4.2–6.1)
Australia	2036	37.6 (35.5–39.7)	7.2 (6.0–8.3)	3.5 (2.7–4.3)	N/A	7.7 (6.6–8.9)	5.1 (4.1–6.0)	4.2 (3.3–5.0)
Belgium	2021	35.6 (33.5–37.7)	5.0 (4.0–5.9)	3.3 (2.5–4.0)	7.5 (6.4–8.7)	11.0 (9.7–12.4)	4.0 (3.2–4.9)	2.4 (1.7–3.0)
Brazil	2004	43.6 (41.4–45.8)	10.6 (9.2–11.9)	4.7 (3.8–5.6)	8.3 (7.1–9.5)	11.9 (10.5–13.3)	4.8 (3.9–5.7)	2.7 (2.0–3.5)
Canada	2029	41.3 (39.1–43.4)	7.8 (6.7–9.0)	4.2 (3.3–5.1)	10.12 (8.8–11.4)	9.3 (8.0–10.5)	7.6 (6.4–8.7)	3.3 (2.5–4.1)
China	2914	34.4 (32.7–36.1)	5.9 (5.0–6.7)	2.3 (1.8–2.9)	7.4 (6.5–8.4)	10.6 (9.5–11.7)	5.6 (4.8–6.5)	0.7 (0.4–1.0)
Colombia	2007	42.5 (40.3–44.7)	7.2 (6.0–8.3)	4.3 (3.4–5.2)	N/A	12.8 (11.3–14.2)	4.1 (3.2–5.0)	4.5 (3.6–5.4)
Egypt	2020	47.7 (45.5–49.9)	12.3 (10.8–13.7)	7.6 (6.4–8.7)	14.0 (12.4–15.59)	14.1 (12.6–15.6)	2.2 (1.6–2.9)	3.2 (2.4–3.9)
France	2019	47.3 (45.1–49.5)	8.5 (7.3–9.7)	4.2 (3.3–5.0)	9.8 (8.5–11.1)	14.5 (12.6–16.1)	6.1 (5.1–7.2)	6.0 (5.0–7.0)
Germany	2020	36.5 (34.4–38.6)	6.9 (5.8–8.0)	3.7 (2.8–4.5)	11.1 (9.8–12.5)	9.8 (7.9–10.5)	5.4 (4.4–6.4)	2.8 (2.1–3.5)
Holland	2008	30.6 (28.6–32.6)	4.1 (3.2–5.0)	3.8 (2.9–4.6)	9.7 (8.4–11.0)	9.2 (7.9–10.5)	3.2 (2.5–4.0)	1.5 (1.0–2.0)
Israel	2012	36.4 (34.3–38.5)	3.6 (2.8–4.4)	3.2 (2.5–4.0)	12.8 (11.4–14.3)	13.1 (11.6–14.6)	2.4 (1.8–3.1)	2.1 (1.5–2.7)
Italy	2063	47.2 (45.1–49.4)	9.1 (7.8–10.3)	5.0 (4.1–5.9)	N/A	14.4 (12.7–15.8)	3.2 (2.5–4.0)	8.2 (7.1–9.4)
Japan	2504	39.4 (37.5–41.3)	2.4 (1.8–3.0)	2.2 (1.6–2.7)	9.3 (8.2–10.4)	16.6 (15.1–18.0)	5.2 (4.3–6.0)	1.2 (0.8–1.6)
South Korea	2022	39.3 (37.2–41.4)	4.9 (4.0–5.9)	4.7 (3.8–5.6)	N/A	12.5 (11.0–13.9)	5.8 (4.8–6.8)	2.1 (1.5–2.8)
Mexico	2001	40.2 (38.0–42.3)	6.6 (5.5–7.7)	4.0 (3.2–4.9)	12.6 (11.1–14.0)	11.5 10.1–12.9)	4.4 (3.5–5.3)	3.4 (2.6–4.2)
Poland	2057	46.0 (43.9–48.2)	8.3 (7.1–9.5)	4.4 (3.5–5.3)	N/A	14.2 (12.7–15.8)	4.5 (3.6–5.4)	5.3 (4.3–6.3)
Romania	2049	40.1 (38.1–42.2)	7.4 (6.3–8.6)	3.5 (2.7–4.3)	N/A	11.7 (10.3–13.1)	2.6 (1.9–3.3)	6.7 (5.6–7.8)
Russia	2000	44.6 (42.4–46.8)	10.3 (9.0–11.6)	5.9 (4.8–6.9)	16.5 (14.9–18.1)	11.6 (10.1–13.0)	7.1 (6.0–8.2)	2.6 (1.9–3.2)
Singapore	2047	31.1 (29.1–33.1)	5.9 (4.9–6.9)	1.3 (0.8–1.8)	4.3 (3.4–5.1)	9.5 (8.2–10.7)	4.3 (3.4–5.1)	3.6 (2.8–4.4)
South Africa	2021	45.2 (43.0–47.3)	11.0 (9.7–12.4)	5.9 (4.9–7.0)	N/A	11.1 (9.7–12.5)	5.1 (4.2–6.1)	4.2 (3.3–5.1)
Spain	2072	43.7 (41.6–45.9)	7.4 (6.3–8.5)	4.2 (3.4–5.1)	N/A	12.8 (11.4–14.3)	4.8 (3.9–5.7)	3.4 (2.6–4.2)
Sweden	2084	39.0 (36.9–41.1)	8.2 (7.0–9.4)	4.0 (3.1–4.8)	N/A	10.3 (9.0–11.6)	5.9 (4.8–6.9)	3.1 (2.4–3.9)
Turkey	2010	39.7 (37.6–41.8)	5.3 (4.3–6.3)	3.9 (3.1–4.8)	9.8 (8.5–11.1)	14.1 (12.6–15.6)	2.5 (1.8–3.2)	3.0 (2.2–3.7)
USA	2023	39.9 (37.8–42.0)	10.1 (8.8–11.4)	5.3 (4.4–6.3)	N/A	8.7 (7.5–10.0)	5.0 (4.1–6.0)	2.0 (1.4–2.6)
UK	2027	36.7 (34.6–38.8)	6.6 (5.5–7.6)	4.0 (3.1–4.8)	N/A	8.6 (7.4–9.8)	4.5 (3.6–5.4)	3.8 (3.0–4.7)
Pooled overall prevalence	**54127**	**40.3 (39.9–40.7)**	**7.2 (7.0–7.4)**	**4.1 (3.9–4.2)**	**10.1 (9.8–10.5)**	**10.1 (11.4–12.0)**	**4.7 (4.5–4.9)**	**3.5 (3.3–3.6)**
HOUSEHOLD								
Bangladesh	2018	40.0 (37.9–42.2)	19.4 (17.7–21.2)	4.6 (3.7–5.5)	10.7 (9.3–12.0)	11.8 (10.4–13.2)	2.1 (1.5–2.8)	2.2 (1.6–2.9)
China	2710	22.7 (21.1–24.2)	4.3 (3.6–5.1)	1.4 (1.0–1.8)	3.8 (3.1–4.5)	6.2 (5.3–7.1)	2.6 (2.0–3.2)	1.3 (0.8–1.7)
Ghana	1190	45.0 (42.2–47.9)	7.2 (5.8–8.7)	0.3 (0.0–0.7)	0.4 (0.1–0.8)	26.1 (23.6–28.6)	0.7 (0.2–1.1)	0.0
India	4592	7.2 (6.5–8.0)	0.7 (0.5–1.0)	0.2 (0.1–0.3)	0.4 (0.2–0.6)	1.8 (1.4–2.2)	0.2 (0.1–0.4)	0.2 (0.1–0.3)
Indonesia	1231	19.0 (16.8–21.2)	4.4 (3.2–5.5)	3.5 (2.5–4.5)	6.2 (4.8–7.5)	3.5 (2.5–4.5)	1.1 (0.5–1.6)	1.1 (0.5–1.6)
Iran	1840	27.2 (25.2–29.3)	2.9 (2.1–3.6)	2.1 (1.4–2.7)	4.6 (3.6–5.5)	11.0 (9.5–12.4)	1.3 (0.7–1.8)	5.1 (4.1–6.1)
Malaysia	1976	19.7 (18.0–21.5)	3.3 (2.5–4.1)	0.7 (0.3–1.1)	3.9 (3.1–4.8)	5.4 (4.4–6.4)	1.7 (1.1–2.3)	0.9 (0.5–1.3)
Nigeria	1442	25.1 (22.9–27.3)	6.0 (4.8–7.3)	2.7 (1.9–3.5)	5.1 (3.8–6.4)	4.3 (3.3–5.3)	0.9 (0.4–1.4)	0.3 (0.0–0.7)
Turkey	1950	7.6 (6.5–8.8)	1.1 (0.6–1.5)	0.4 (0.1–0.7)	0.9 (0.5–1.3)	1.9 (1.3–2.6)	0.4 (0.1–0.6)	0.5 (0.2–0.8)
Pooled overall prevalence	**18949**	**20.7 (20.2–21.3)**	**4.8 (4.5–5.1)**	**1.5 (1.3–1.7)**	**3.5 (3.3–3.8)**	**6.6 (6.3–6.9)**	**1.2 (1.0–1.3)**	**1.2 (1.0–1.3)**

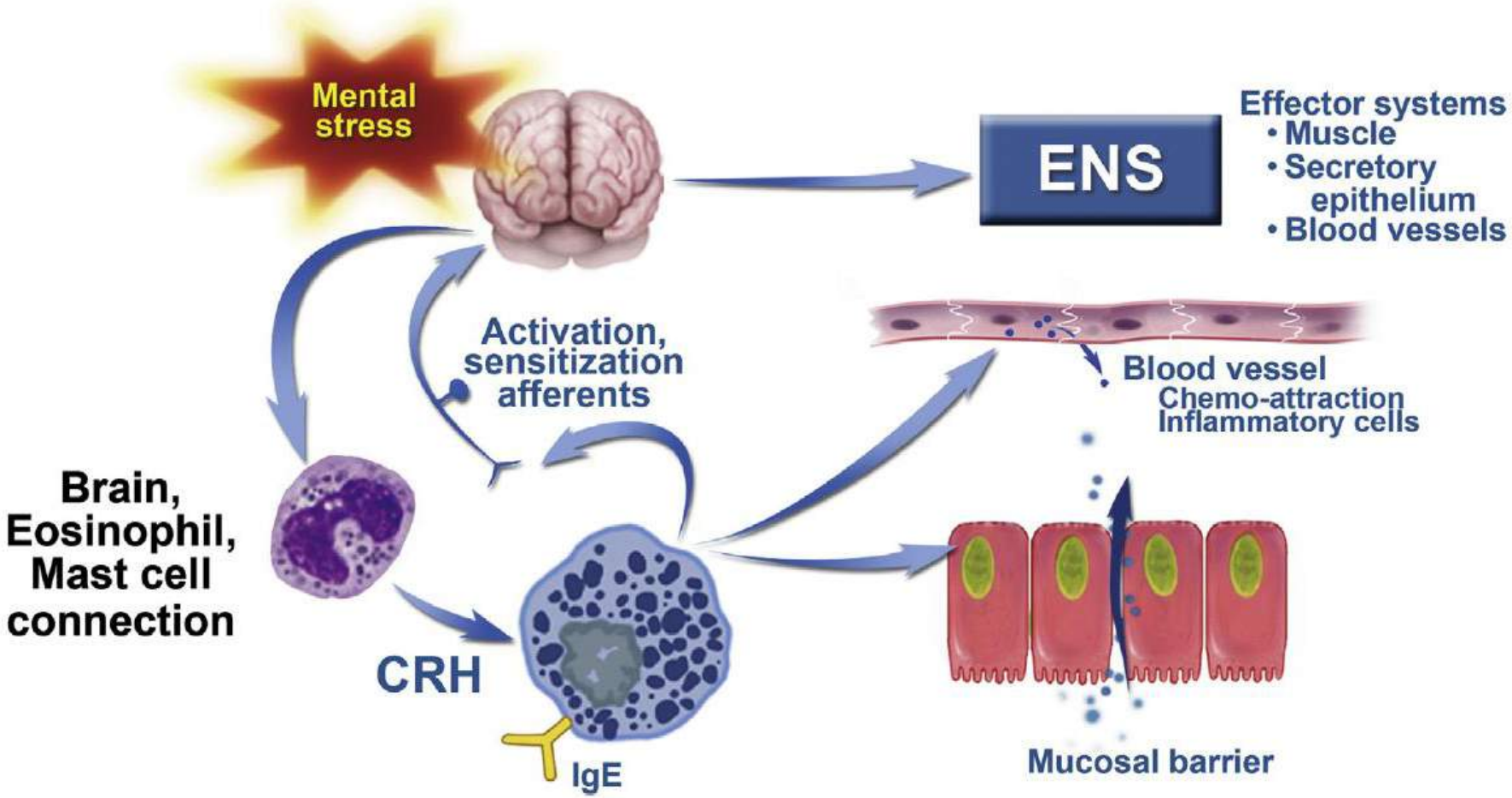
Ami D. Sperber et al. Gastroenterology 2021;160:99–114

Risk faktörleri nelerdir?

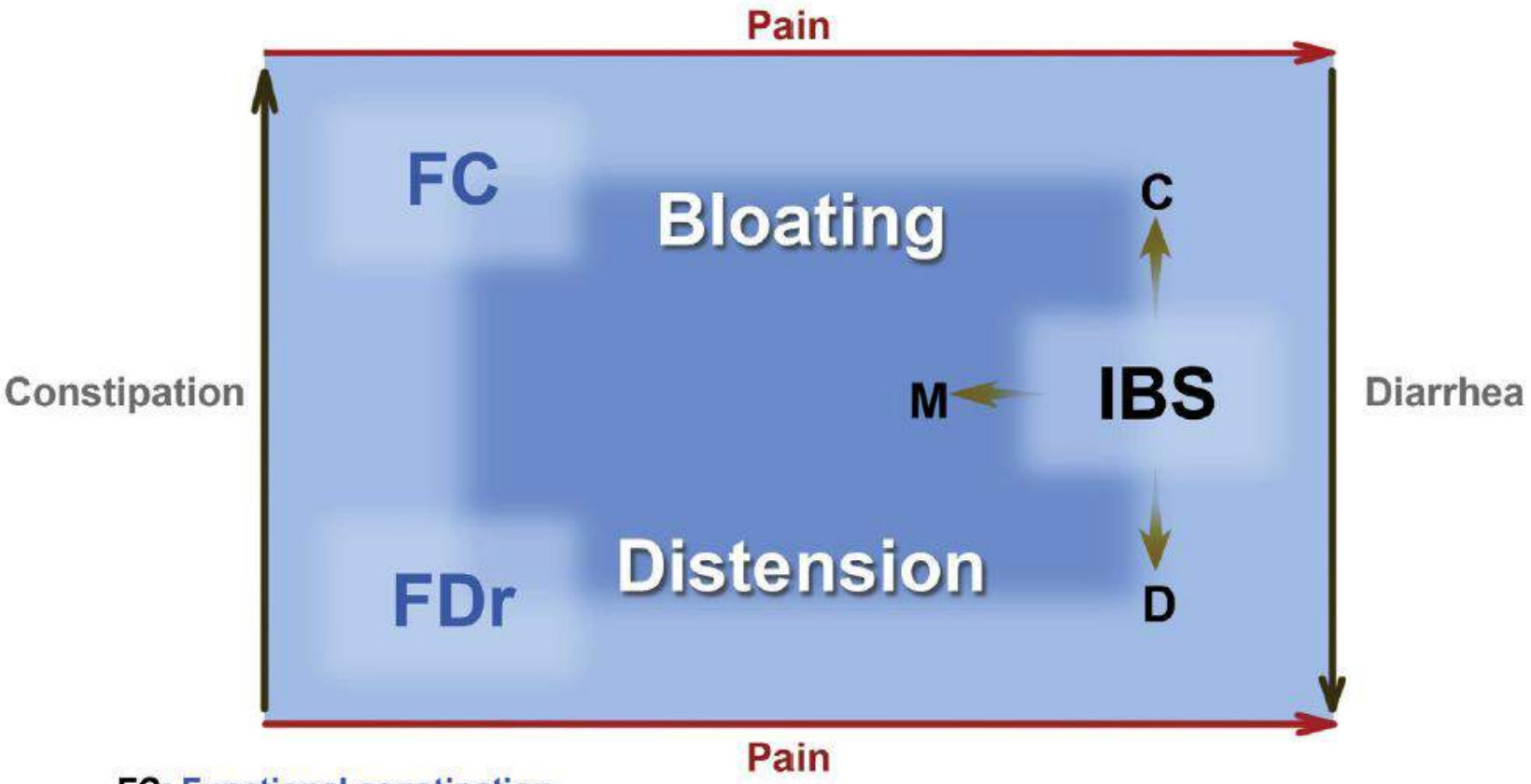
IBS heterojen bir hastalık



Holtmann GJ, Ford AC, Talley. NJ. Lancet 2016

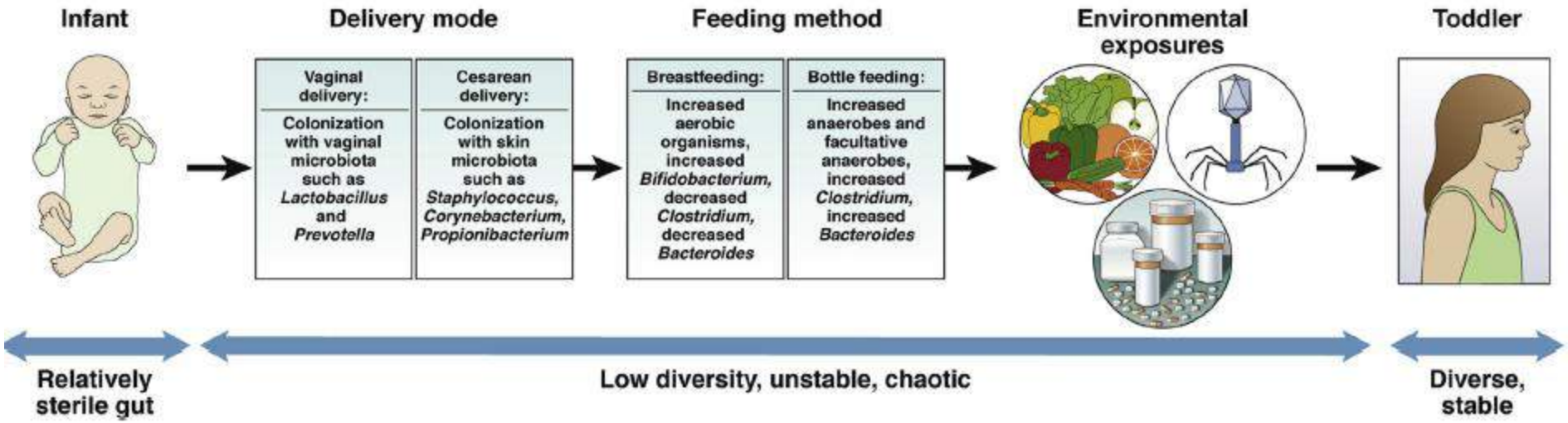


Guy Boeckxstaens, et al. Gastroenterology 2016;150:1292–1304



FC: Functional constipation
FDr: Functional diarrhea
IBS-C: Irritable bowel syndrome with predominant constipation
IBS-D: Irritable bowel syndrome with predominant diarrhea
IBS-M: Irritable bowel syndrome with predominant irregular bowel habits (mixed D/C)

Lacy BE, et al. Gastroenterology 2016;150:1393–1407



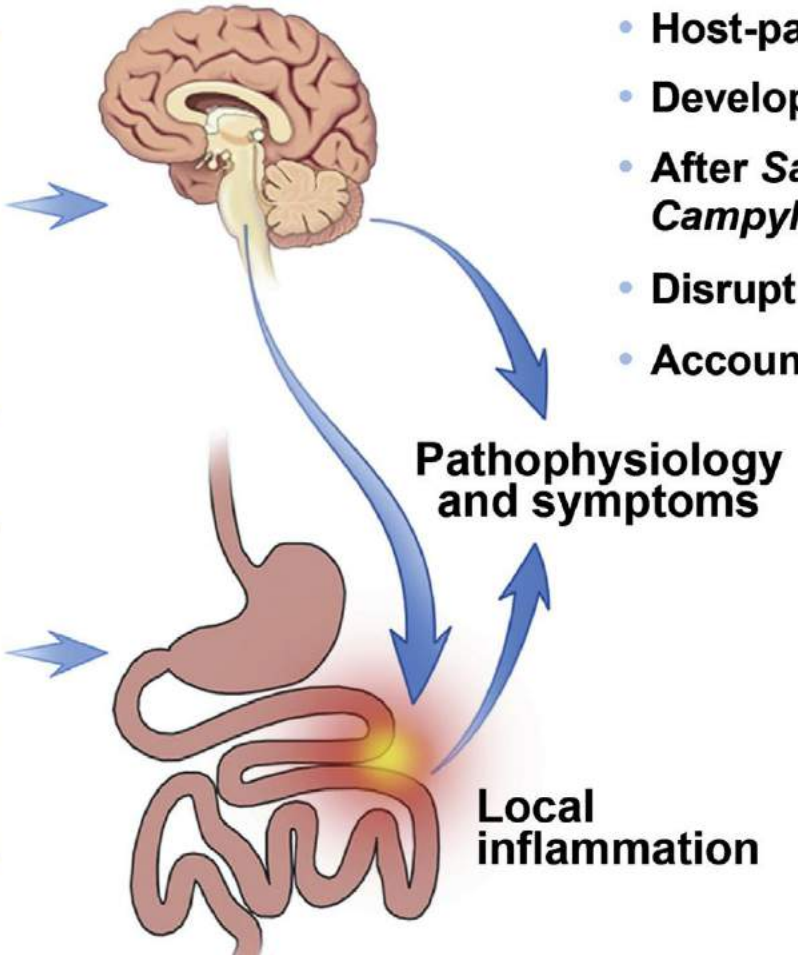
Albenberg LG, Wu GD. Gastroenterology 2014;146:1564–1572

Post infeksiyöz IBS

➢Mukozal inflamasyon viseral duyarlılığa neden olur

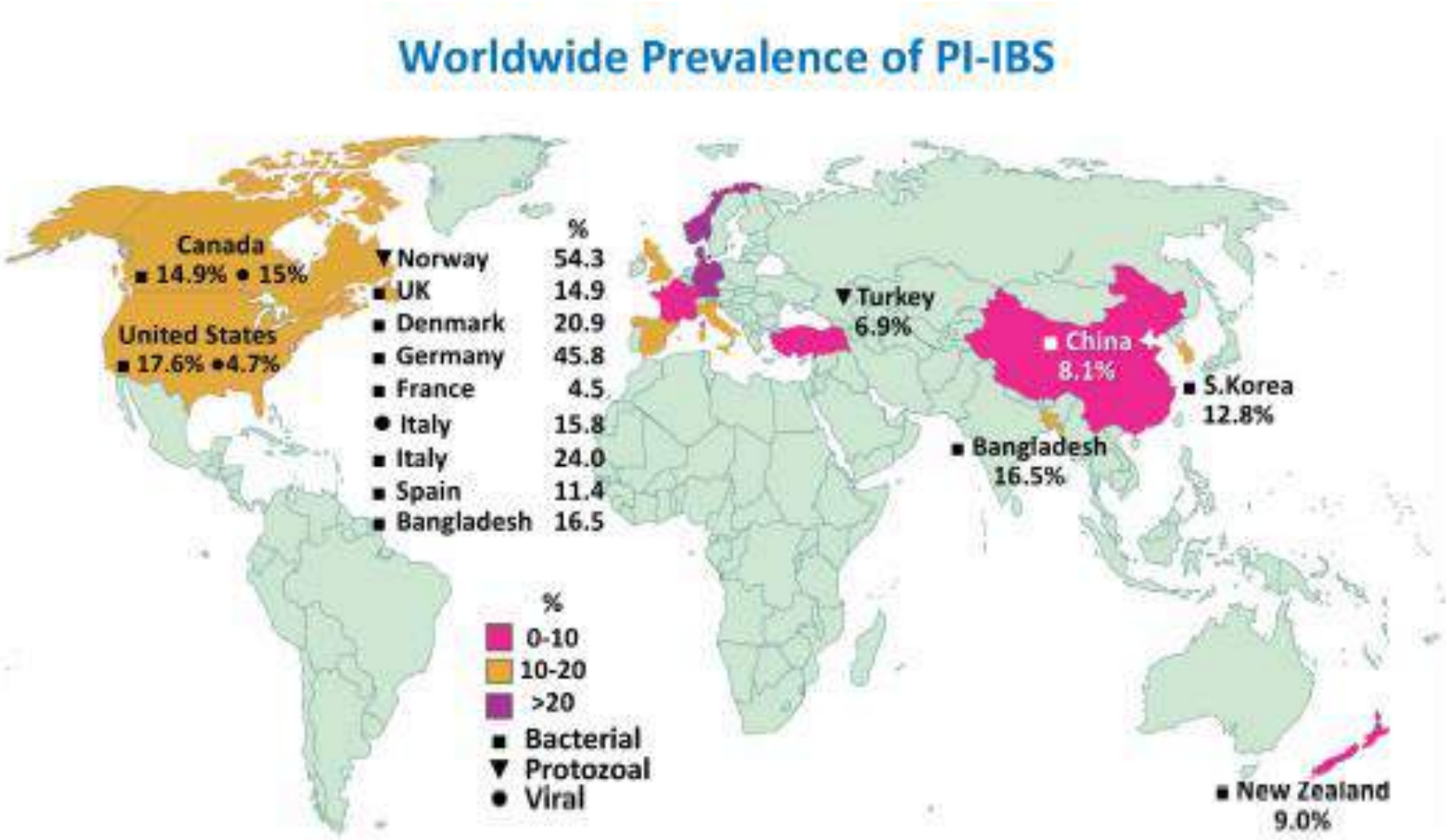
Adverse life events	RR 2.0
Depression	RR 3.2
Hypochrondriasis	RR 2.0
Age >60	RR 0.4
Female	RR 3.0
Smoking	RR 4.8

Lymphocytosis	RR 3.2
EC hyperplasia	RR 3.8
Elongating toxin	RR 12.8
Duration of initial illness	RR 11.5



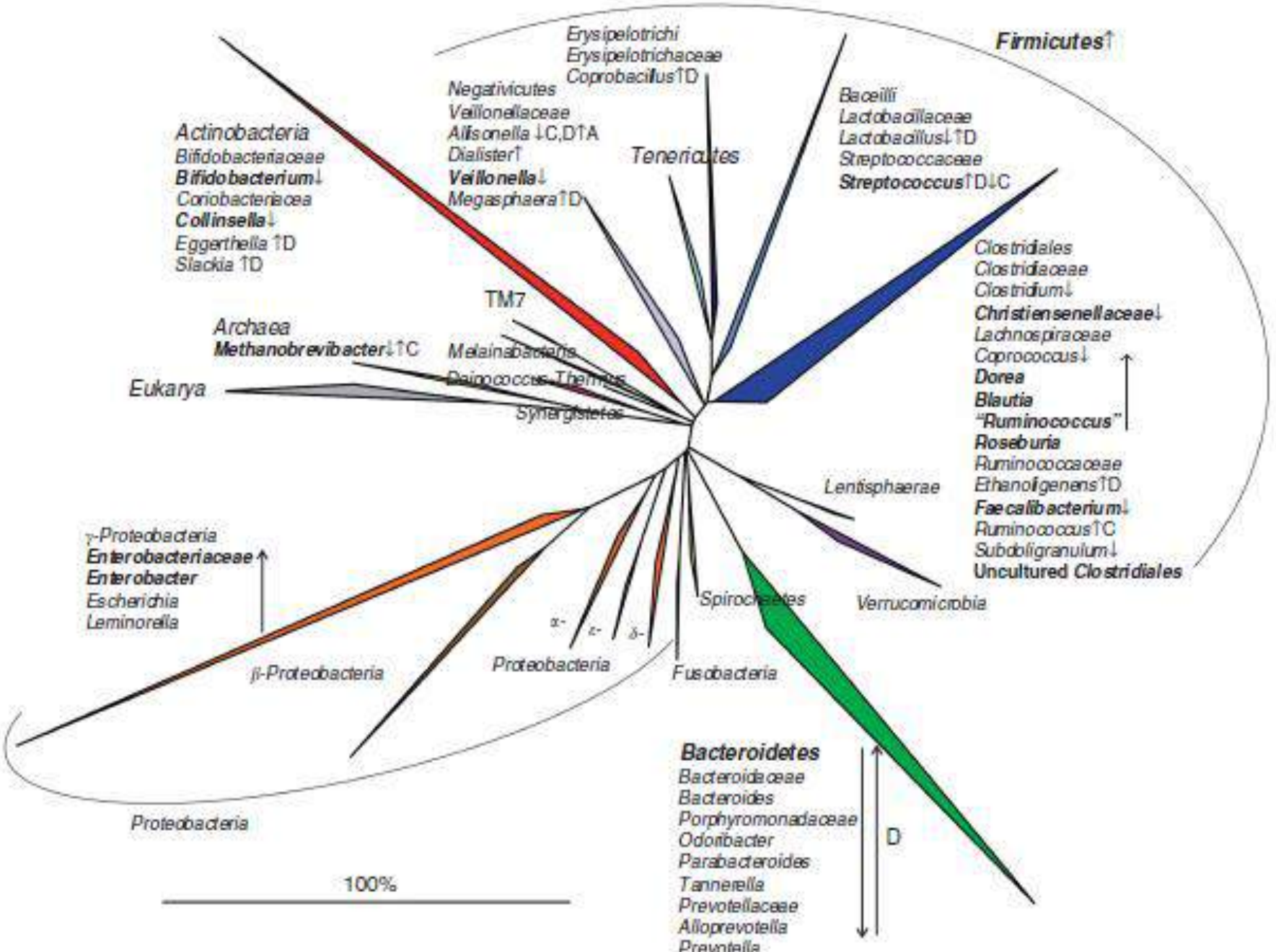
- Host-pathogen interactions
- Develops in ~10% of subjects
- After *Salmonella, Shigella, Campylobacter*
- Disrupt intestinal ecosystem
- Accounts for 6–17% of all IBS

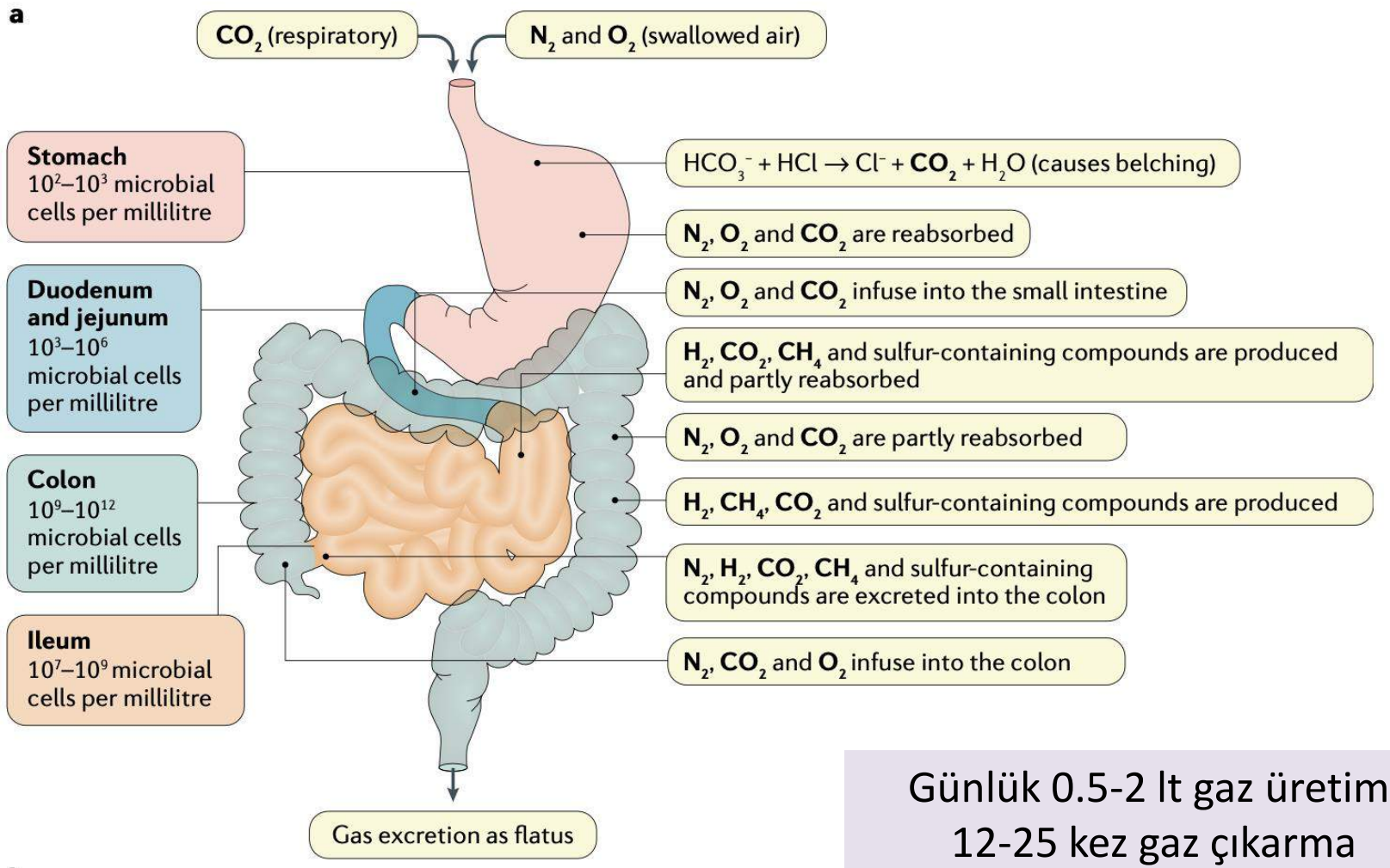
Barbara G. Gastroenterology 2016



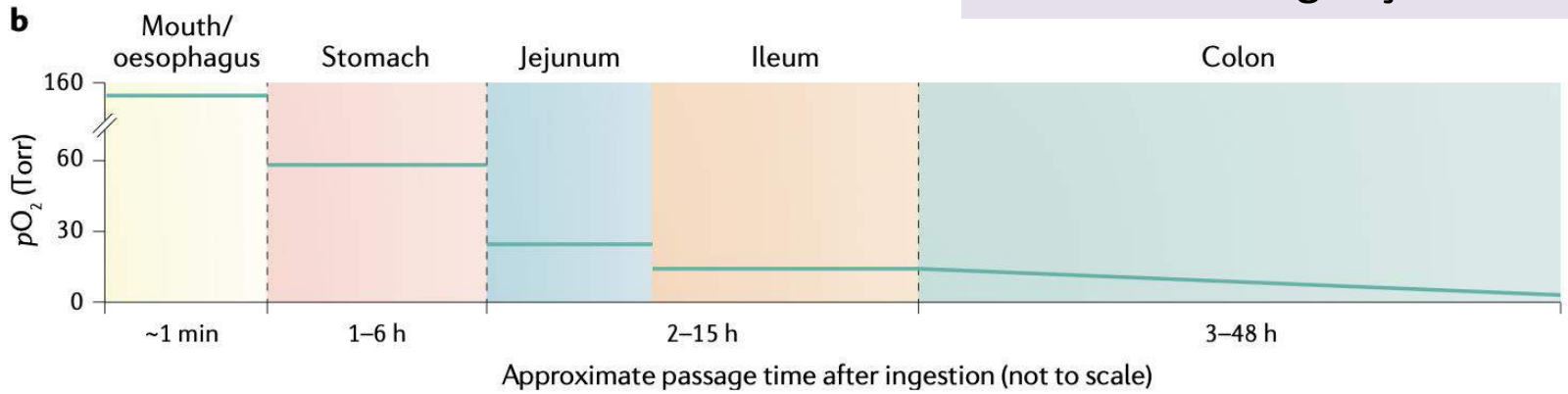
Barbara G, et al. Gastroenterology 2018

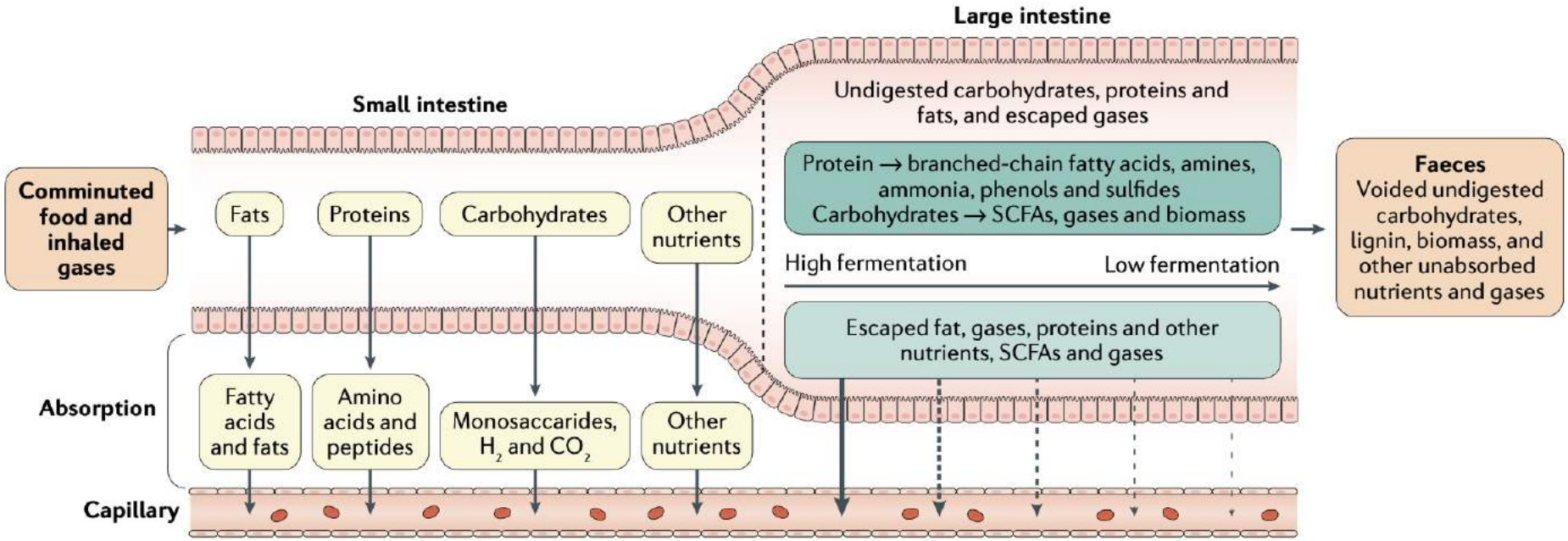
Mirjana Rajilić-Stojanović, et al *Am J Gastroenterol 2015; 110:278–287;*



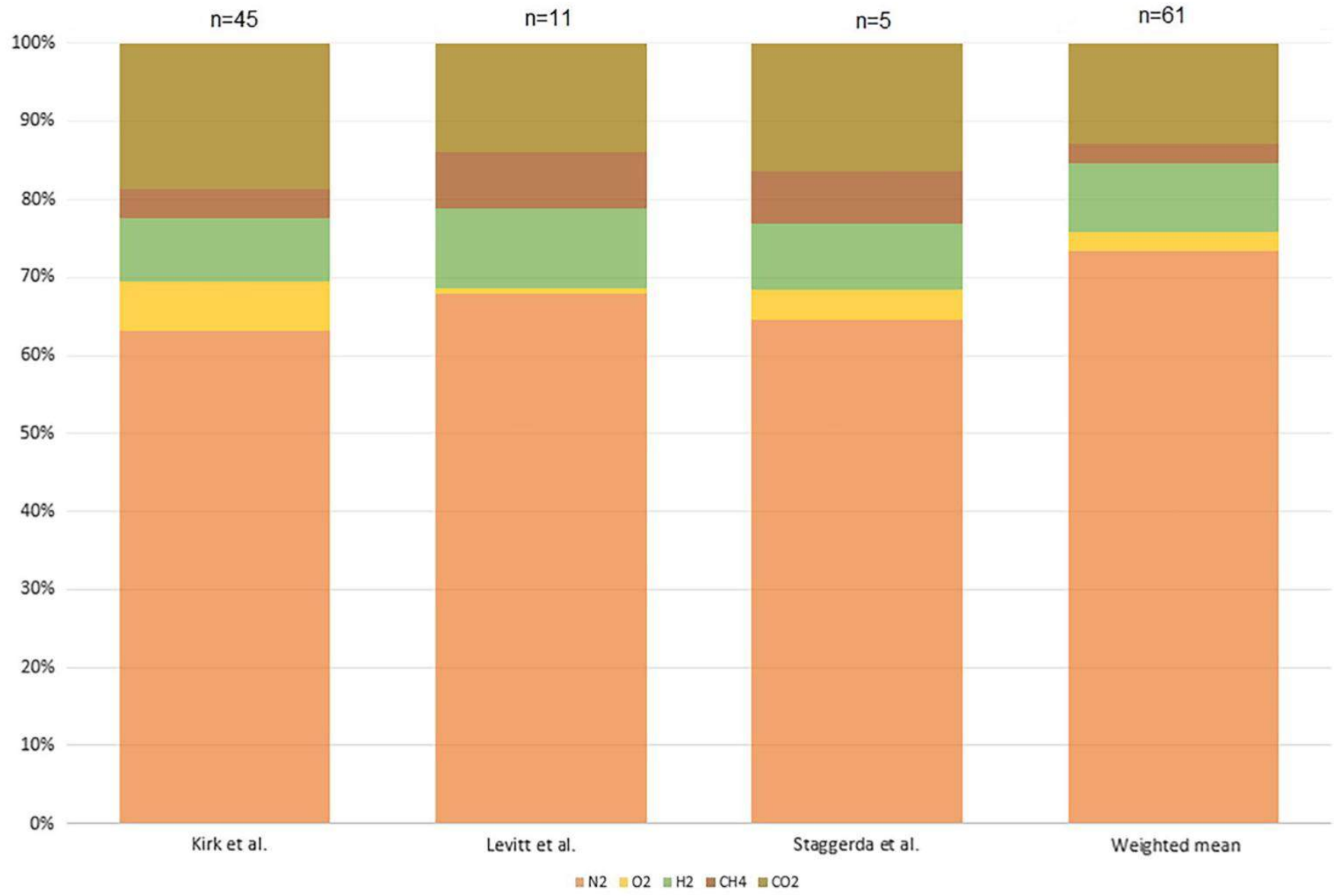


Günlük 0.5-2 lt gaz üretimi
12-25 kez gaz çıkarma

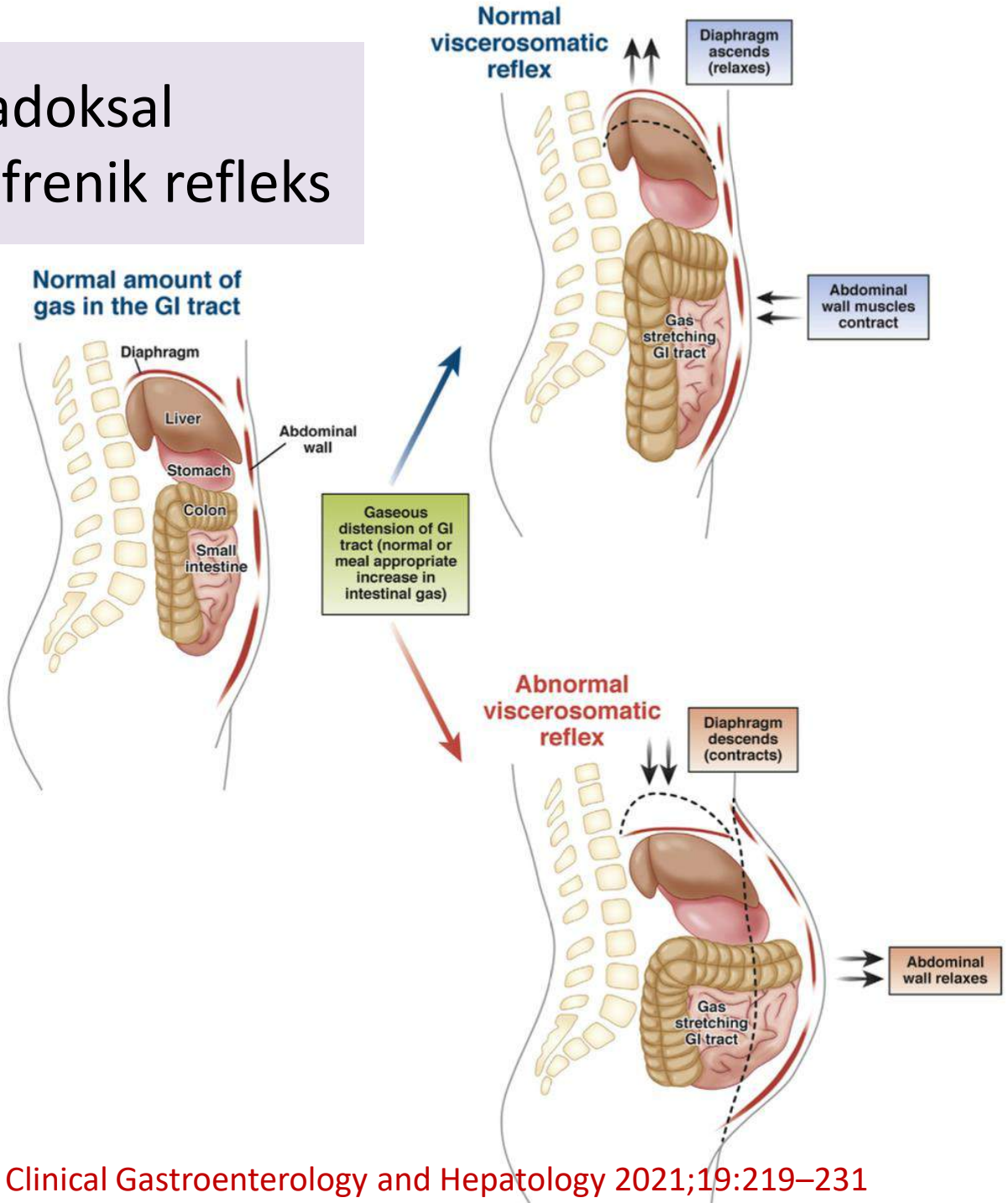




Kourosh Kalantar-Zadeh et al. NatuRe RevIeWS **GASTroEnTEroloGy & HEPATOloGy 2019**


n=45
n=11
n=5
n=61
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Kirk et al.
Levitt et al.
Staggerda et al.
Weighted mean
N2
O2
H2
CH4
CO2

Paradoksal abdominofrenik refleks



Brian E. Lacy et al. Clinical Gastroenterology and Hepatology 2021;19:219–231

Organic/pathologic etiologies

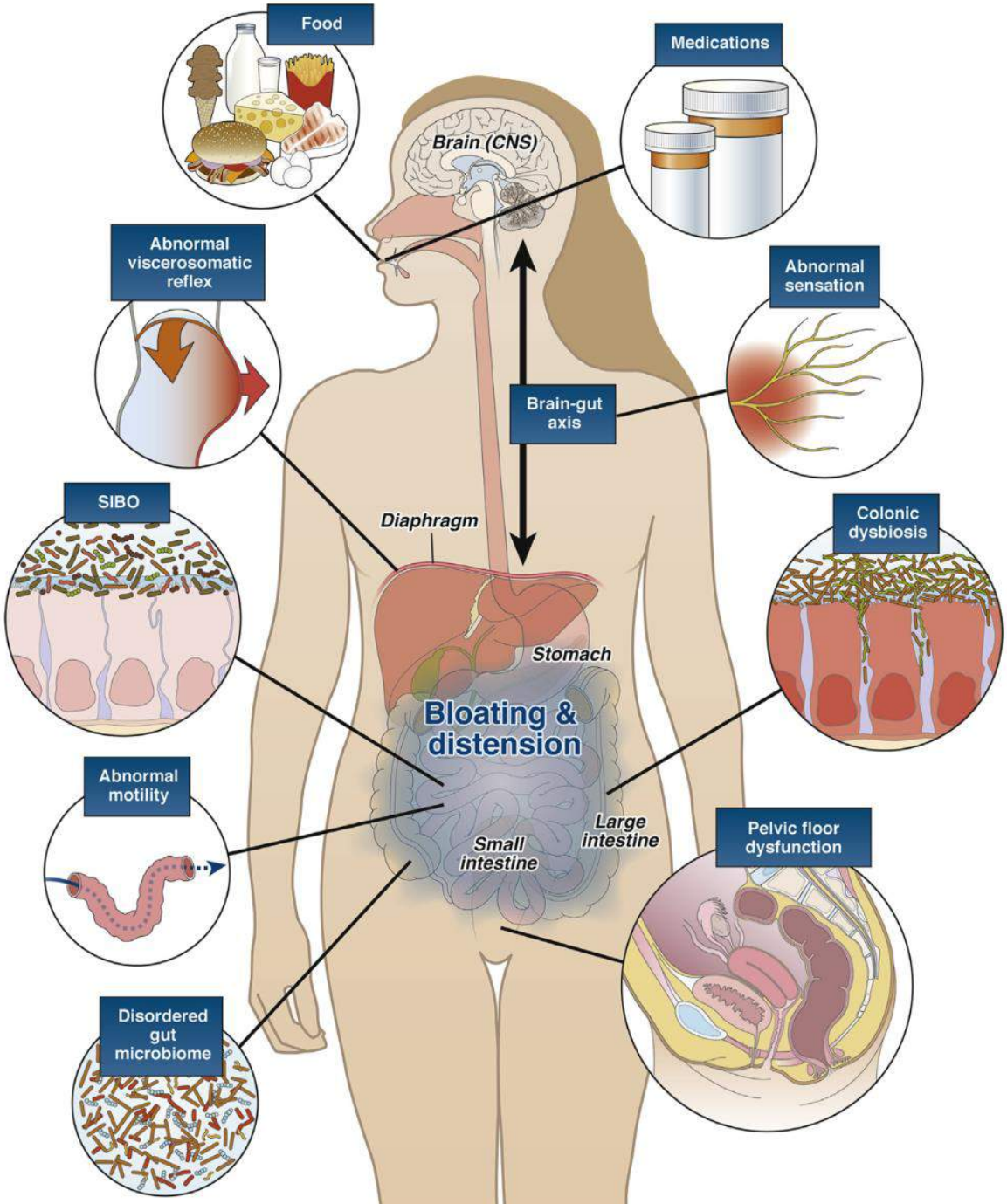
- Small intestinal bacterial overgrowth
- Lactose, fructose, and other carbohydrate intolerances
- Celiac disease
- Pancreatic insufficiency
- Prior gastroesophageal surgery (eg, fundoplication, bariatric surgery)
- Gastric outlet obstruction
- Gastroparesis
- Ascites
- Gastrointestinal or gynecologic malignancy
- Hypothyroidism
- Adiposity
- Small intestine diverticulosis
- Chronic intestinal pseudo-obstruction

Disorders of gut-brain interaction

- Irritable bowel syndrome
- Chronic idiopathic constipation
- Pelvic floor dysfunction
- Functional dyspepsia
- Functional bloating

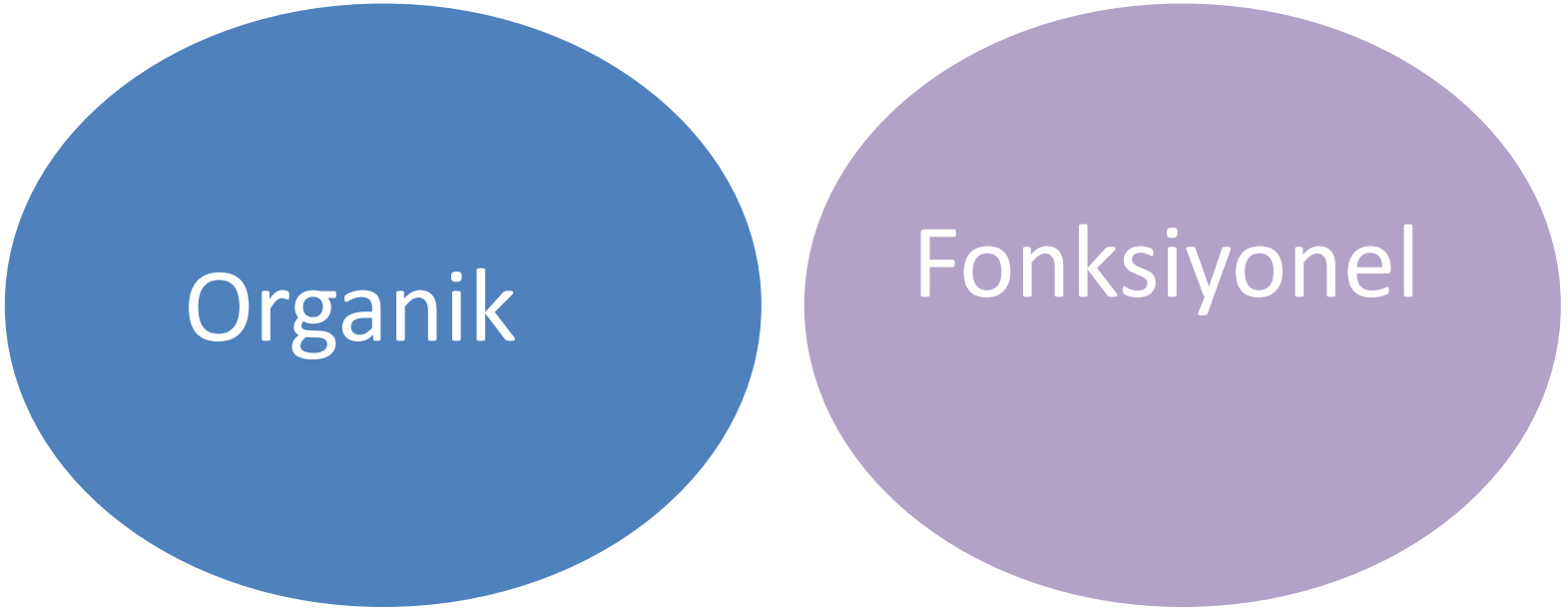
Brian E. Lacy et al. Clinical Gastroenterology and Hepatology 2021;19:219–231

Nedenleri
•**Aerofaji**
•Anoreksi, bulimia
•Gastroparezi
•Mide çıkış yolu obstrüksiyonu
•**Fonksiyonel şişkinlik (gaz)**
•**Fonksiyonel dispepsi**
•Diyet (laktoz intoleransı, Fruktoz intoleransı, Fruktan tüketimi, Sorbitol tüketimi, Gluten duyarlılığı)
•Çölyak
•**Kronik kabızlık**
•**IBS**
•SIBO
•Dismotilite
•Kolon geçiş süresinde bozulma

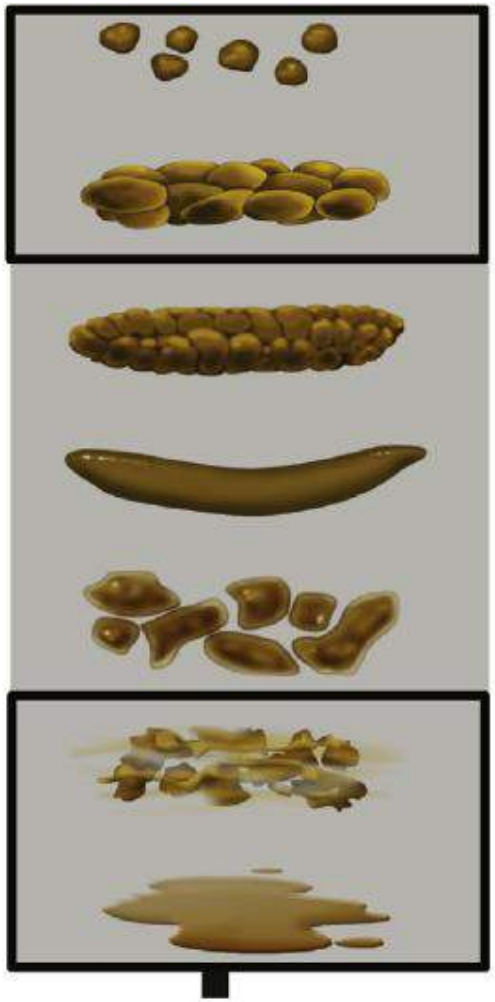


Brian E. Lacy et al. Clinical Gastroenterology and Hepatology 2021;19:219–231

Tanı nasıl konulur?


Organik
Fonksiyonel

Bristol skalası

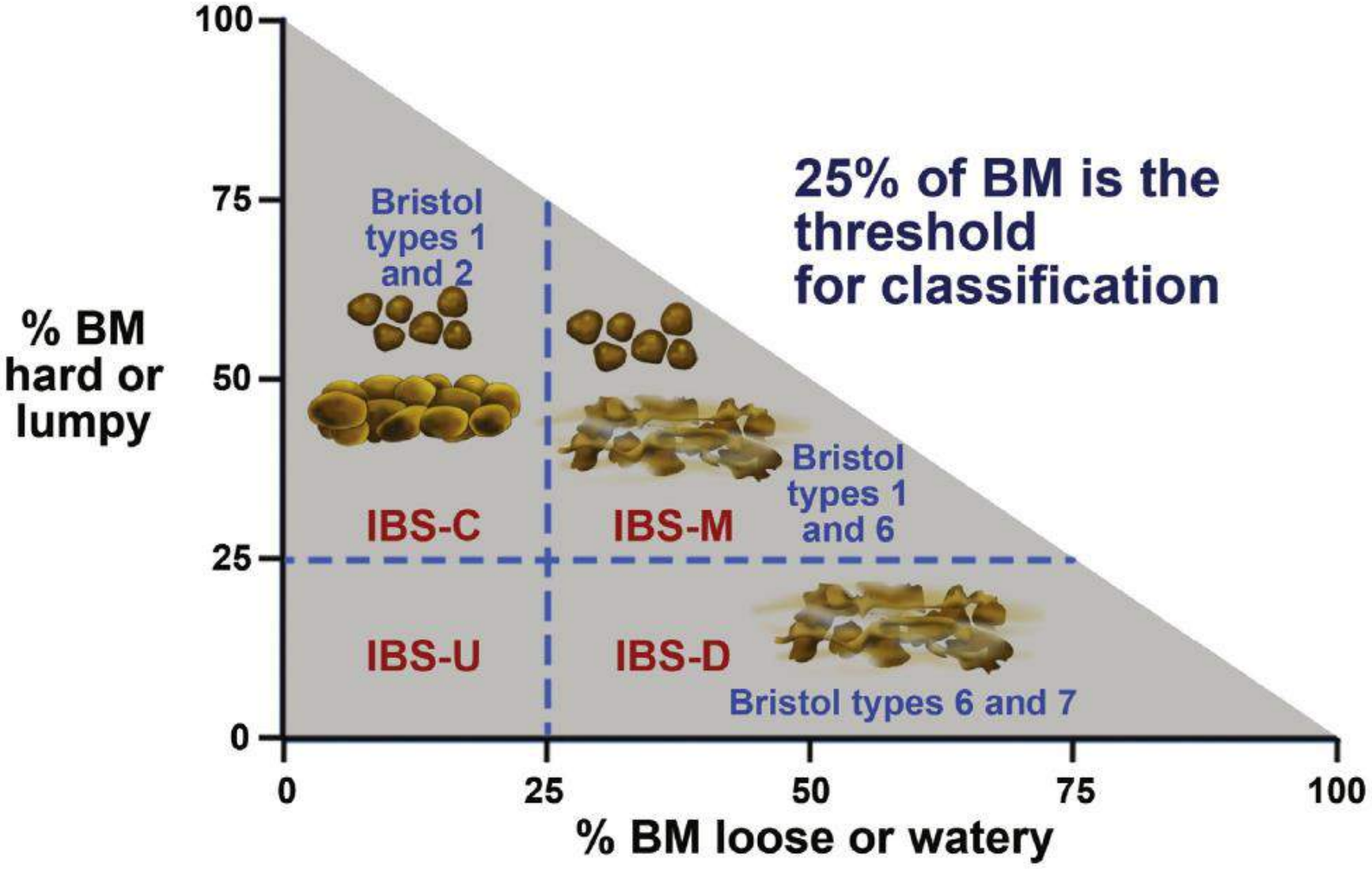


Type 1	Separate hard lumps, like nuts (hard to pass)
Type 2	Sausage-shaped but lumpy
Type 3	Like a sausage but with cracks on the surface
Type 4	Like a sausage or snake, smooth and soft
Type 5	Soft blobs with clear-cut edges
Type 6	Fluffy pieces with ragged edges, a mushy stool
Type 7	Watery, no solid pieces, entirely liquid

IBS de Roma IV kriterleri-2016

Şikayetlerin tanıdan en az 6 ay önce başlamış olması gerekir ve son 3 ayda kriterleri doldurmalıdır.

- **Son 3 ayda, haftada en az 1 gün tekrarlayan karın ağrısı** (aşağıdaki kriterlerden 2 veya daha fazlası eşlik etmeli)
- **Defekasyon ile ilişkili**
- **Dışkılama sıklığında değişme**
- **Dışkı şeklinde değişme**


100
75
50
25
0
% BM hard or lumpy
Bristol types 1 and 2
25% of BM is the threshold for classification
Bristol types 1 and 6
IBS-C
IBS-M
IBS-U
IBS-D
Bristol types 6 and 7
0
25
50
75
100
% BM loose or watery

Fonksiyonel ishalde Roma IV kriterleri

- Fonksiyonel ishal için;

- **<u>Ağrı veya şişkinlik olmadan</u>** dışkılamanın %25'inde sulu veya yumuşak olması
- Son 3 ayda kriterleri doldurmalı, en az 6 ay önce başlamalı
- IBS-ishal den ayırdedilmeli

Lacy BE, et al. Gastroenterology 2016;150:1393–1407

Fonksiyonel kabızlık ve defekasyon problemleri

Functional constipation (Chronic idiopathic constipation [CIC])

Criteria fulfilled for the last 3 mo with symptom onset at least 6 mo prior to diagnosis

1. Must include two or more of the following:
   - Straining during more than one fourth (25%) of defecations
   - Lumpy or hard stools (BSFS 1-2) more than one fourth (25%) of defecations
   - Sensation of incomplete evacuation more than one fourth (25%) of defecations
   - Sensation of anorectal obstruction/blockage more than one fourth (25%) of defecations
   - Manual manoeuvres to facilitate more than one fourth (25%) of defecations (eg, digital evacuation, support of the pelvic floor)
   - Fewer than three spontaneous bowel movements per week
2. Loose stools are rarely present without the use of laxatives
3. Insufficient criteria for IBS-C

Functional defecation disorders

Criteria fulfilled for the last 3 mo with symptom onset at least 6 mo prior to diagnosis

1. The patient must satisfy diagnostic criteria for functional constipation and/or IBS-C
2. During repeated attempts to defecate, there must be features of impaired evacuation, as demonstrated by two of the following three tests:
   - Abnormal balloon expulsion test
   - Abnormal anorectal evacuation pattern with manometry or anal surface electromyography
   - Impaired rectal evacuation by imaging
3. Subcategories F3a and F3b apply to patients who satisfy criteria for a functional defecation disorderF3a. Diagnostic criteria for inadequate defecatory propulsion

Inadequate propulsive forces as measured with manometry with or without inappropriate contraction of the anal sphincter and/or pelvic floor muscles[b]

F3b. Diagnostic criteria for dyssynergic defecation

Inappropriate contraction of the pelvic floor as measured with anal surface electromyography or manometry with adequate propulsive forces during attempted defecation[b]

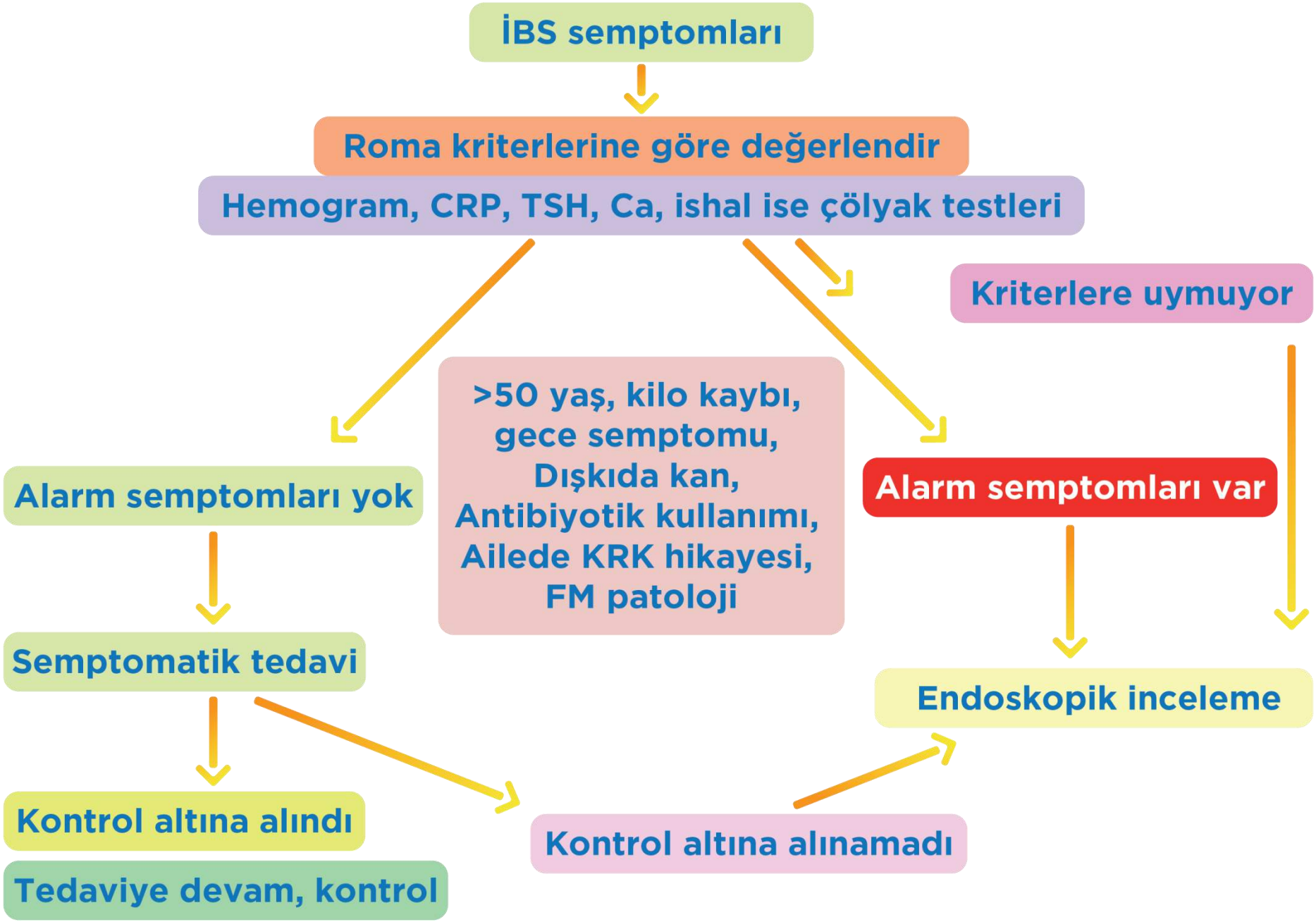
Fonksiyonel Gaz

Diagnostic criteria for functional abdominal bloating and/or distension include:

- Recurrent bloating and/or distention occurring at least 1 d/wk on average;
- Bloating and distension should be the predominant gastrointestinal symptom;
- Patients should not meet criteria for irritable bowel syndrome, functional constipation, functional diarrhea, or postprandial distress syndrome;
- Symptom onset should have occurred at least 6 months prior to diagnosis;
- Symptoms should be active within the preceding 3 months.

Brian E. Lacy et al. Clinical Gastroenterology and Hepatology 2021;19:219–231

Ne zaman tetkik yapalım?


İBS semptomları
Roma kriterlerine göre değerlendir
Hemogram, CRP, TSH, Ca, ishal ise çölyak testleri
Kriterlere uymuyor
>50 yaş, kilo kaybı,
gece semptomu,
Dışkıda kan,
Antibiyotik kullanımı,
Ailede KRK hikayesi,
FM patoloji
Alarm semptomları yok
Alarm semptomları var
Semptomatik tedavi
Endoskopik inceleme
Kontrol altına alındı
Kontrol altına alınamadı
Tedaviye devam, kontrol

Tedavi yönetimi nasıl olmalıdır?

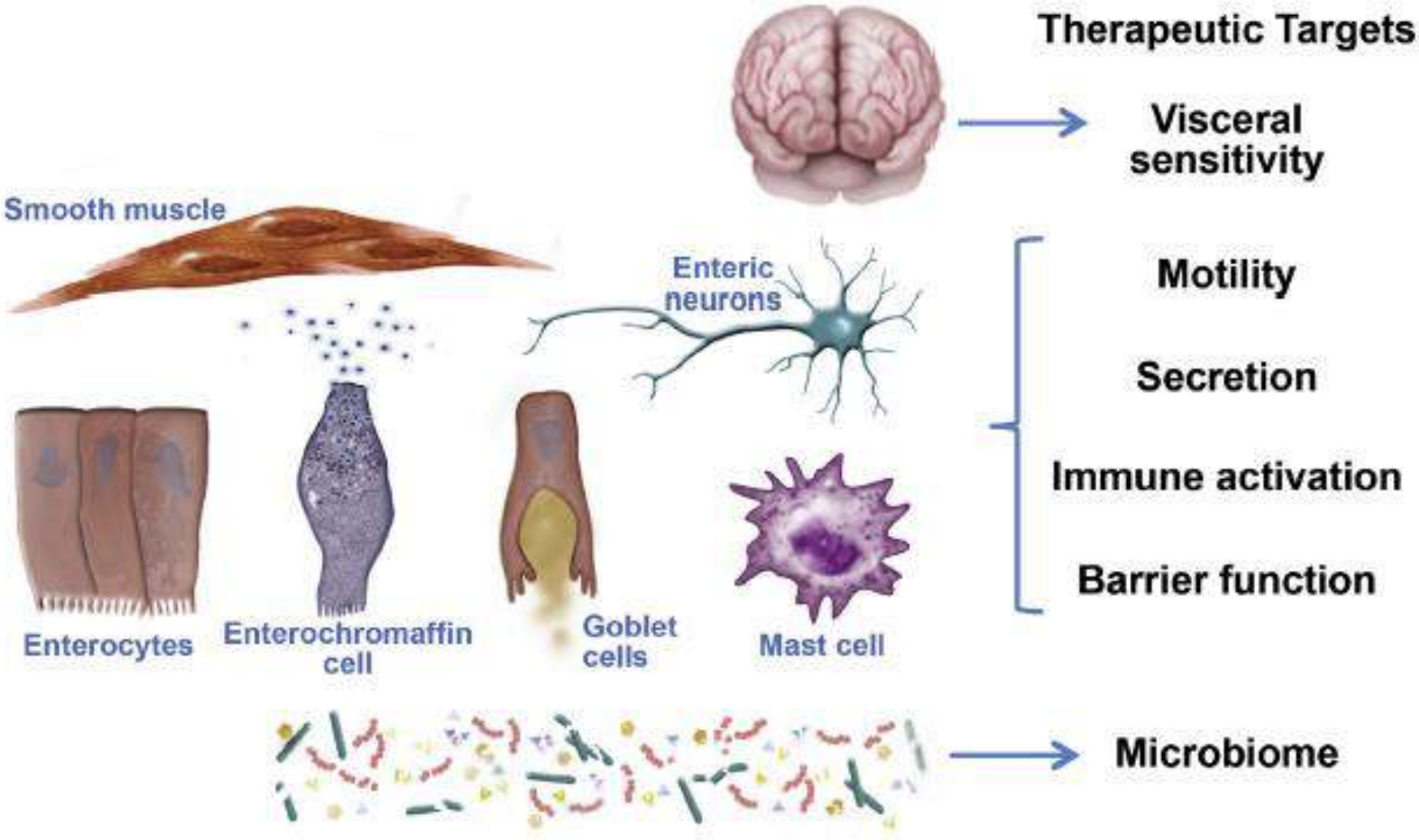
İyi Tedavi Cevabı

Fonksiyonel hastalıklarda

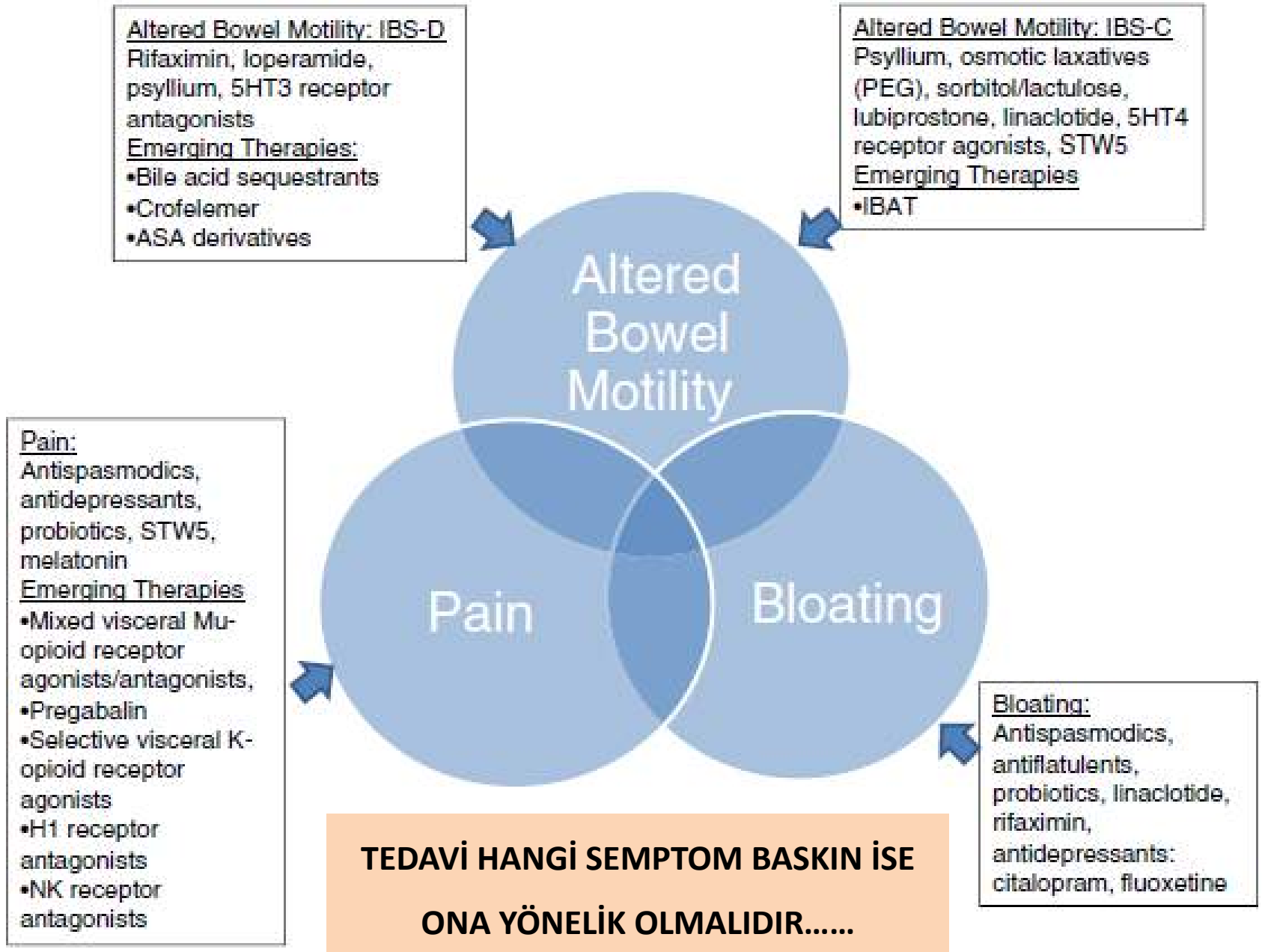
tedavi

semptoma yöneliktir

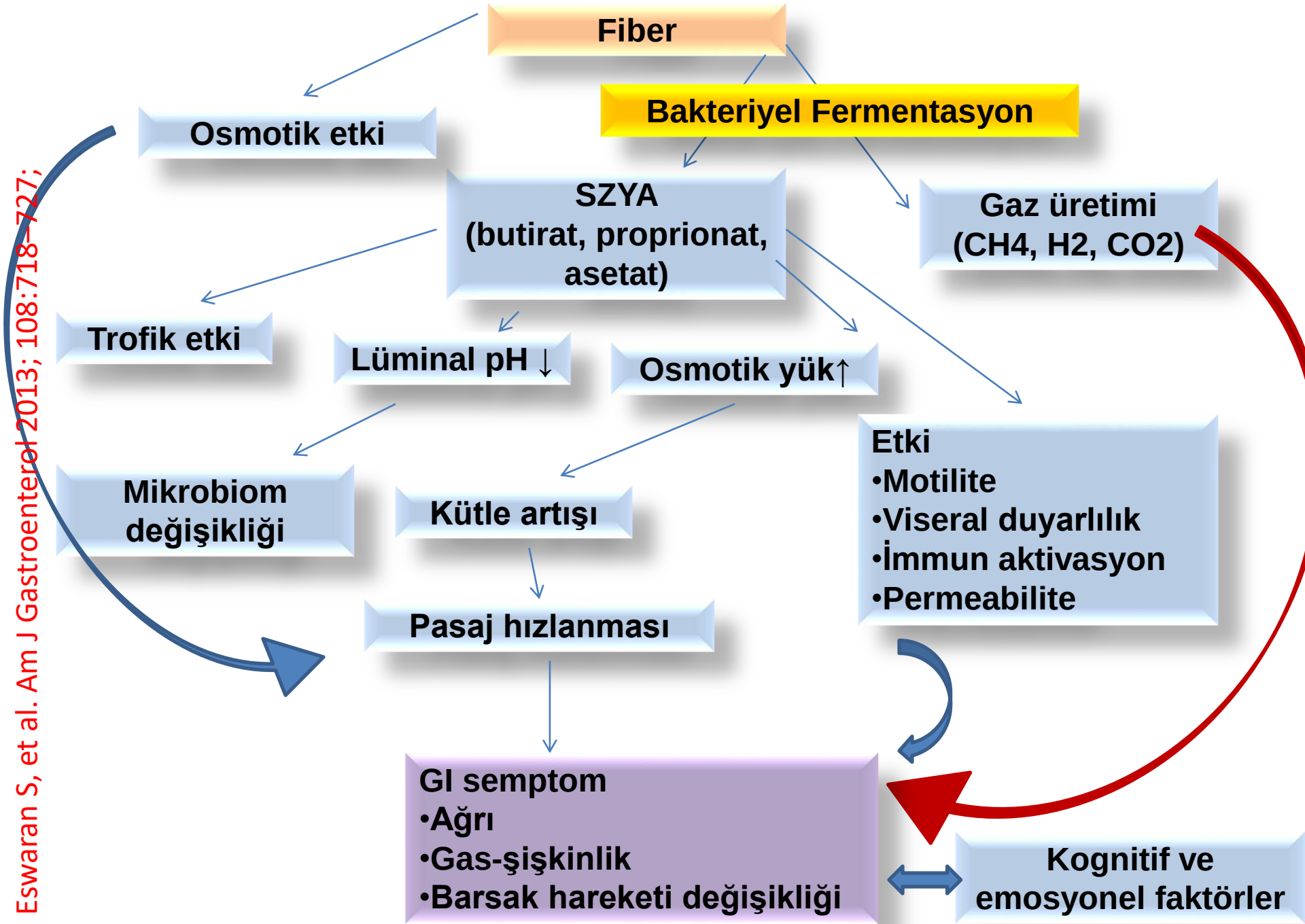
TEDAVİ HEDEFLERİ



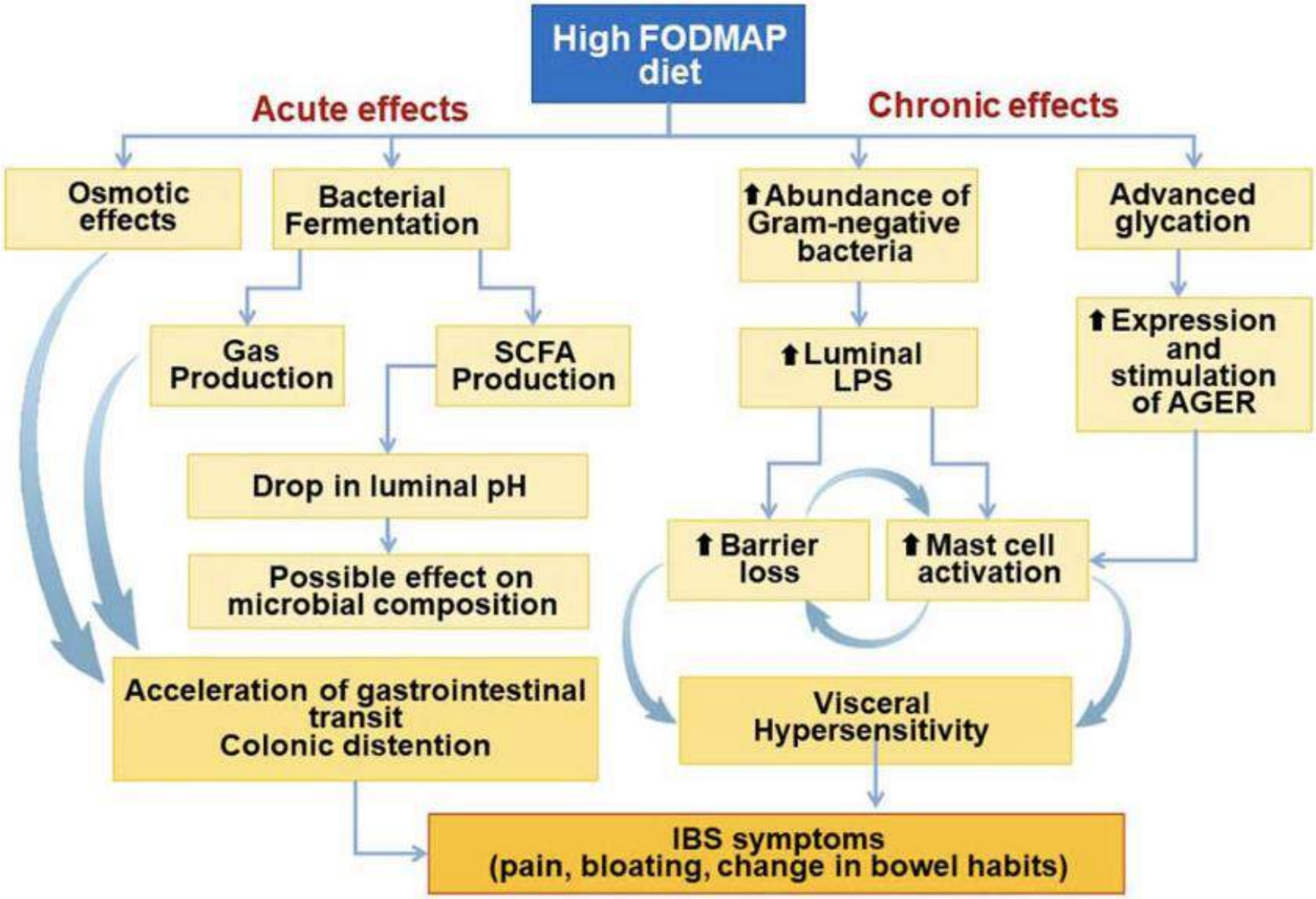
Camilleri M, et al. Gastroenterology 2016;150:1319–1331



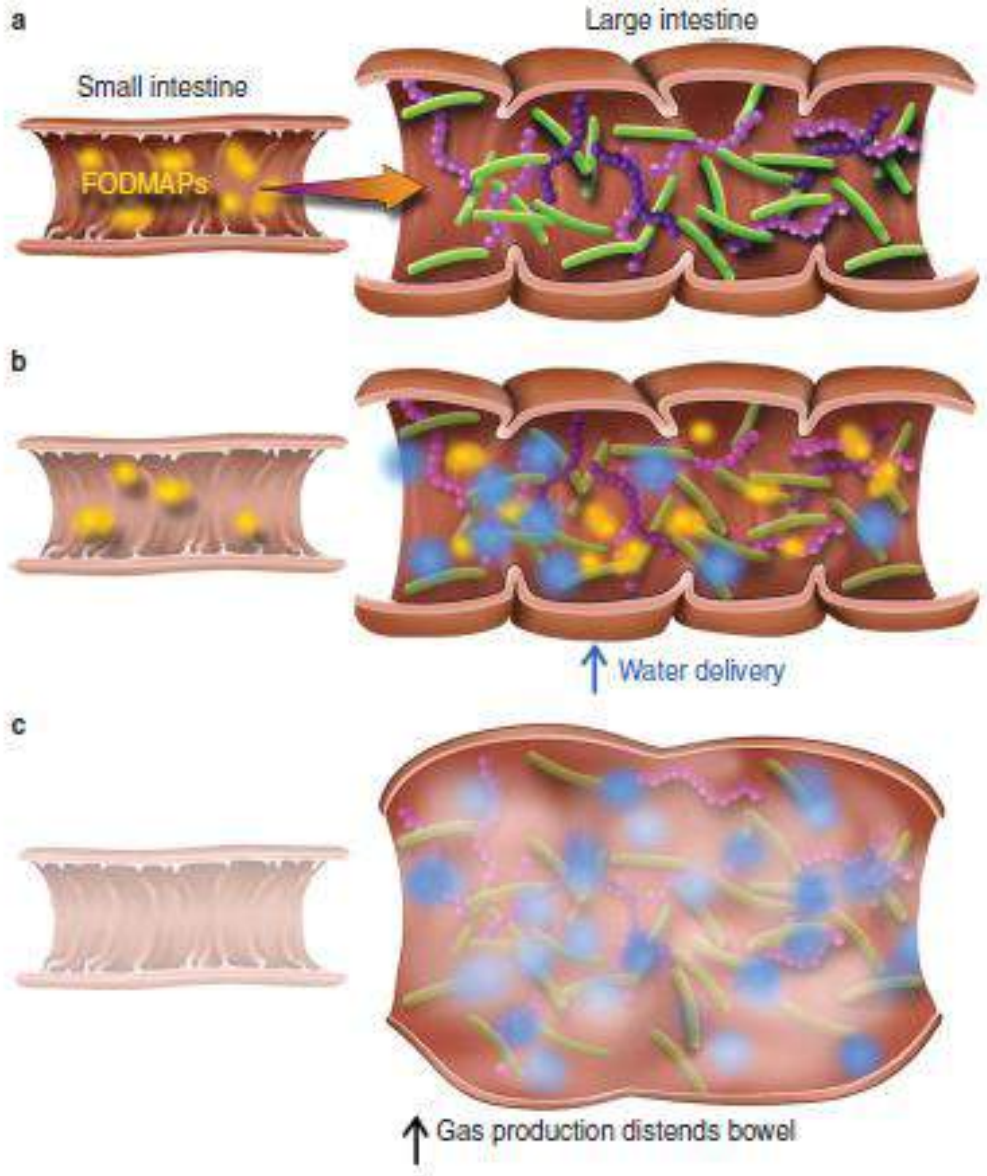
Barboza JL, et al. Drugs (2014) 74:1849–1870



Eswaran S, et al. Am J Gastroenterol 2013; 108:718–727;



Singh et al. Am J Gastroenterol 2022;117:947–957.



FODMAP diyet

(oligo-di-mono-poli

sakkaridlerin

kısıtlaması)

Diyetten fruktoz ve

laktozu kaldırmak

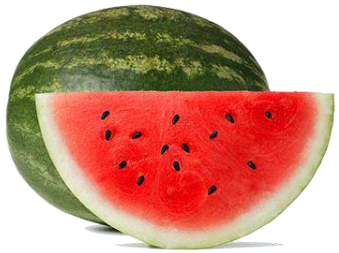
Shepherd SJ, et al. Am J Gastroenterol 2013; 108:707–717

Fodmap Diyet **Nedir?**

Barsak bakterileri tarafından Fermente edilebilen
Oligo**D**i**M**onos**A**kkarid ve **P**oliyollerin diyetten uzaklaştırılması

Monosakkarid: Glikoz, fruktoz, galaktoz, ksiloz, arabinoz
Disakkarid: Sukroz, laktoz, maltoz, izomaltoz, trehaloz
Poliyol: sorbitol, mannitol, isomalt, laktitol, mannitol
Oligosakkarid: Maltodekstrin, rafine şekerler, frukto-oligosakkarid, soya

O ligosakkaridleri içeren gıdalar:
Buğday, arpa, çavdar, soğan, pırasa, sarımsak, enginar,
pancar, rezene, bezelye, hindiba, fıstık, kaju, mercimek, nohut



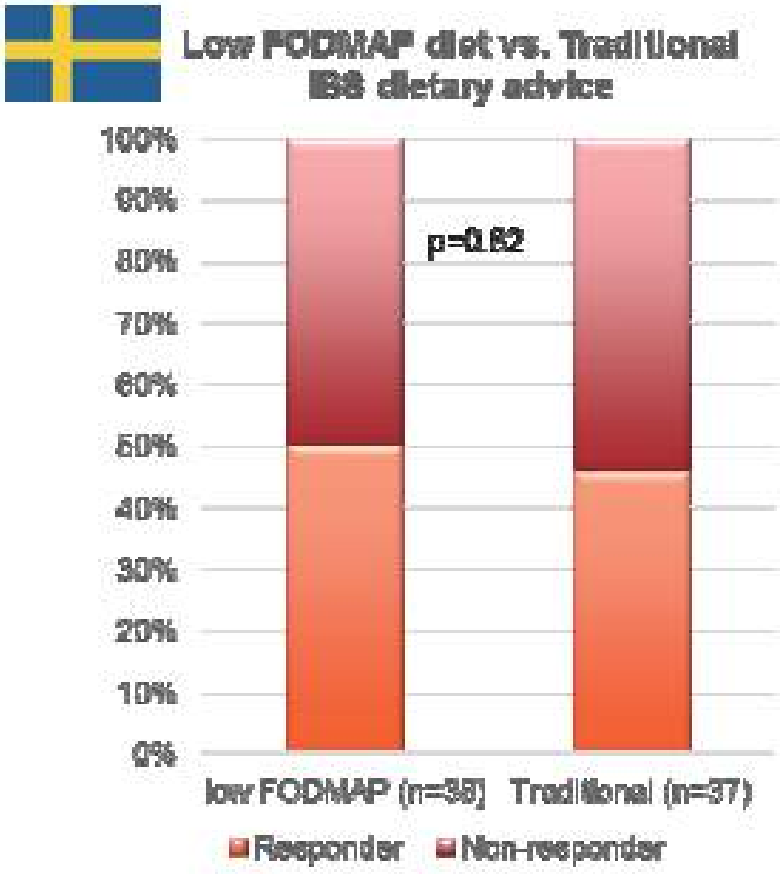
D isakkaridleri içeren gıdalar:
Süt, dondurma, yoğurt, krema

M onosakkaridleri içeren gıdalar:
Elma, mango, bal, yüksek fruktoz içeren mısır şurubu, armut, karpuz, kuşkonmaz

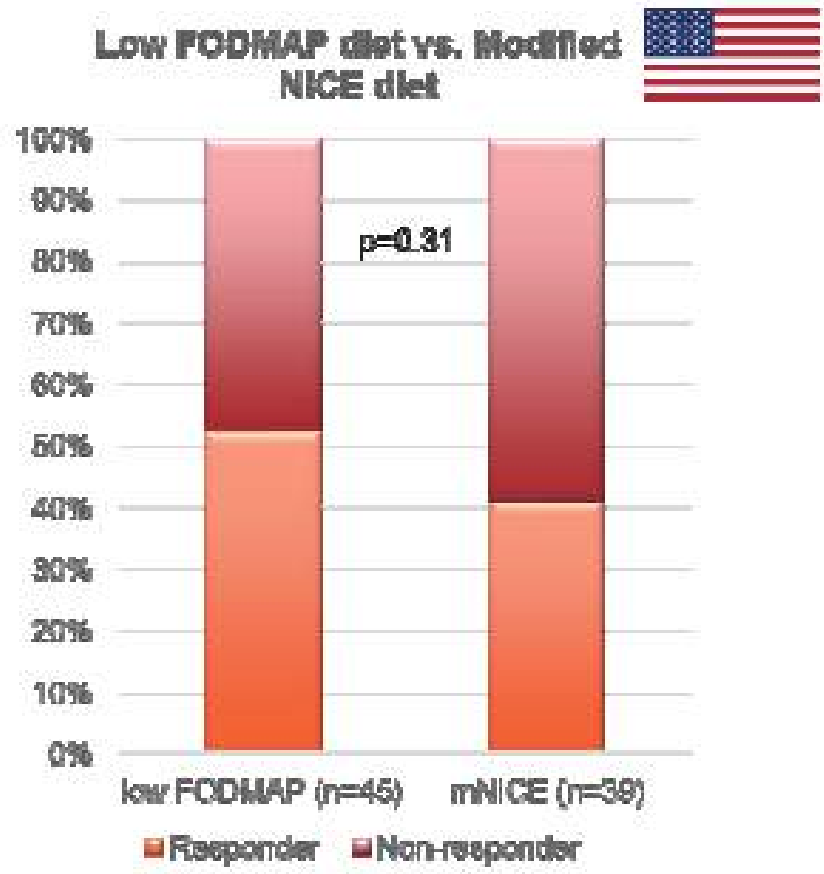
P oliyolleri içeren gıdalar:
Elma, armut, nektarin, karpuz, mantar, tatlandırıcılı sakızlar, kayısı, şeftali, karnıbahar, erik

Shepherd SJ, et al. Am J Gastroenterol 2013; 108:707–717

Geleneksel önerilen diyet de semptomları düzeltmede etkili



Böhn et al Gastroenterology 2015

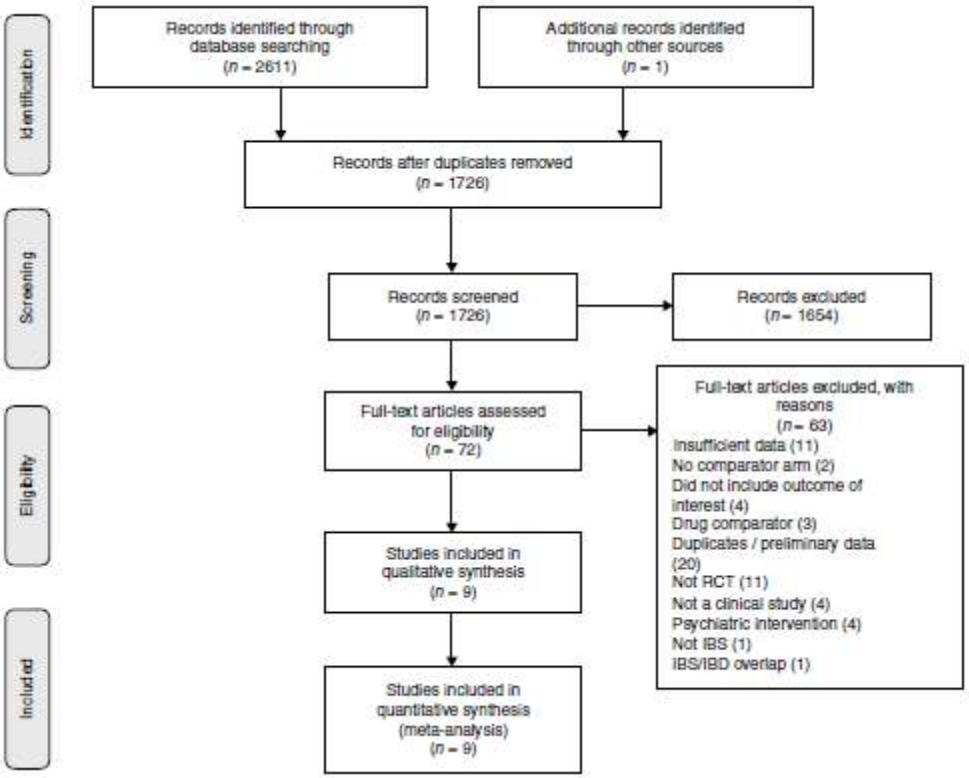


Eswaran et al Am J Gastroenterol 2016

A Systematic Review and Meta-Analysis Evaluating the Efficacy of a Gluten-Free Diet and a Low FODMAPs Diet in Treating Symptoms of Irritable Bowel Syndrome

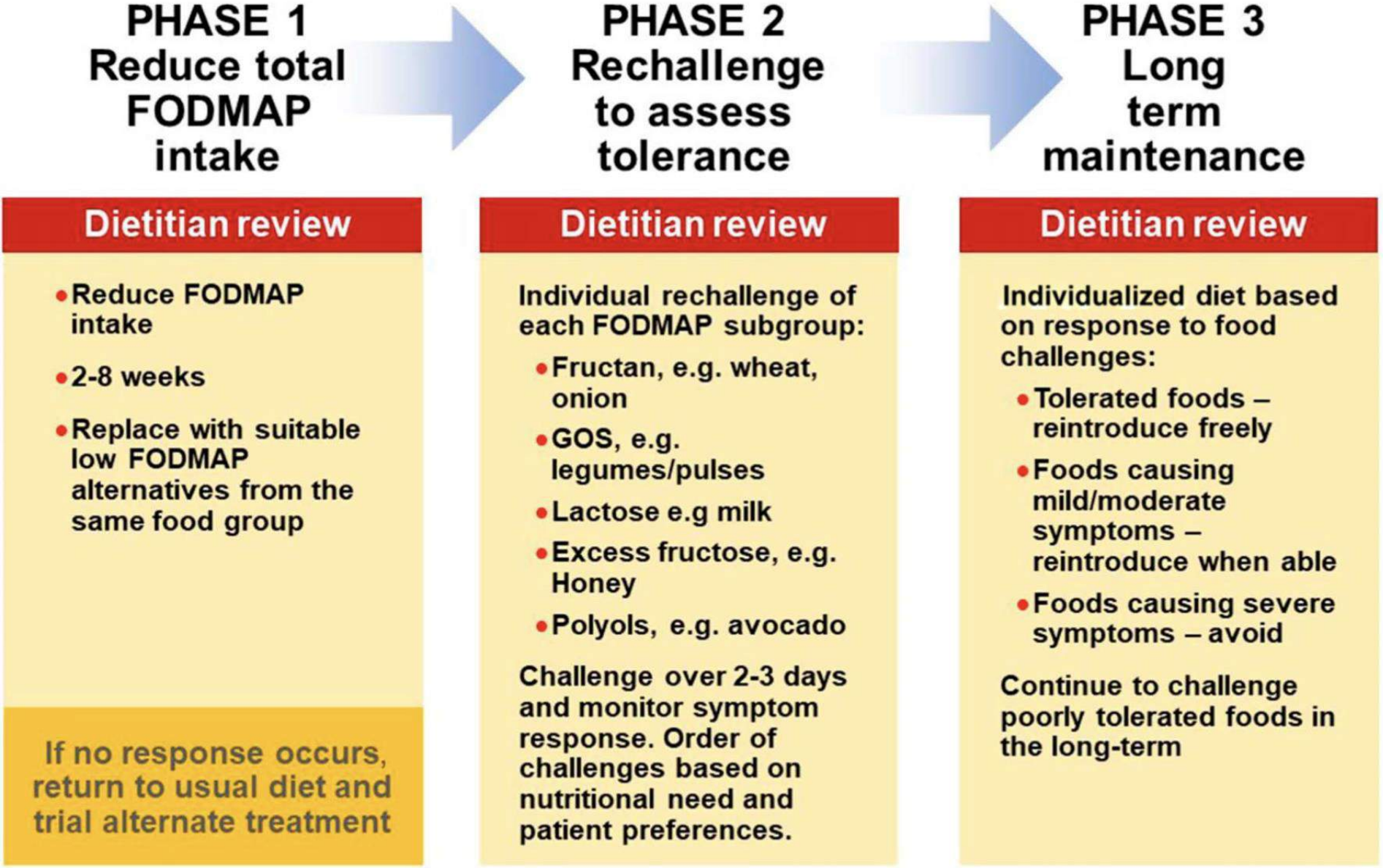
Joanna Dionne, MD, MSc, FRCP, PhD[1], Alexander C. Ford, MB, ChB, FRCP[2,3], Yuhong Yuan, MD[1], William D. Chey, MD, FACG[4], Brian E. Lacy, MD, PhD, FACG[5], Yuri A. Saito, MD, MPH[6], Eamonn M. M. Quigley, MD, FRCP, FACP, MACG, FRCPI[7] and Paul Moayyedi, MB, ChB, PhD, FACG[1,8]

The findings of this review demonstrate that, at present, there is insufficient evidence to recommend a GFD to reduce global IBS symptoms. There is very low quality evidence that a low FODMAP diet is effective in reducing global symptoms in IBS patients. More data are needed, but of the available dietary interventions, a low FODMAP diet currently has the greatest evidence for efficacy in IBS.

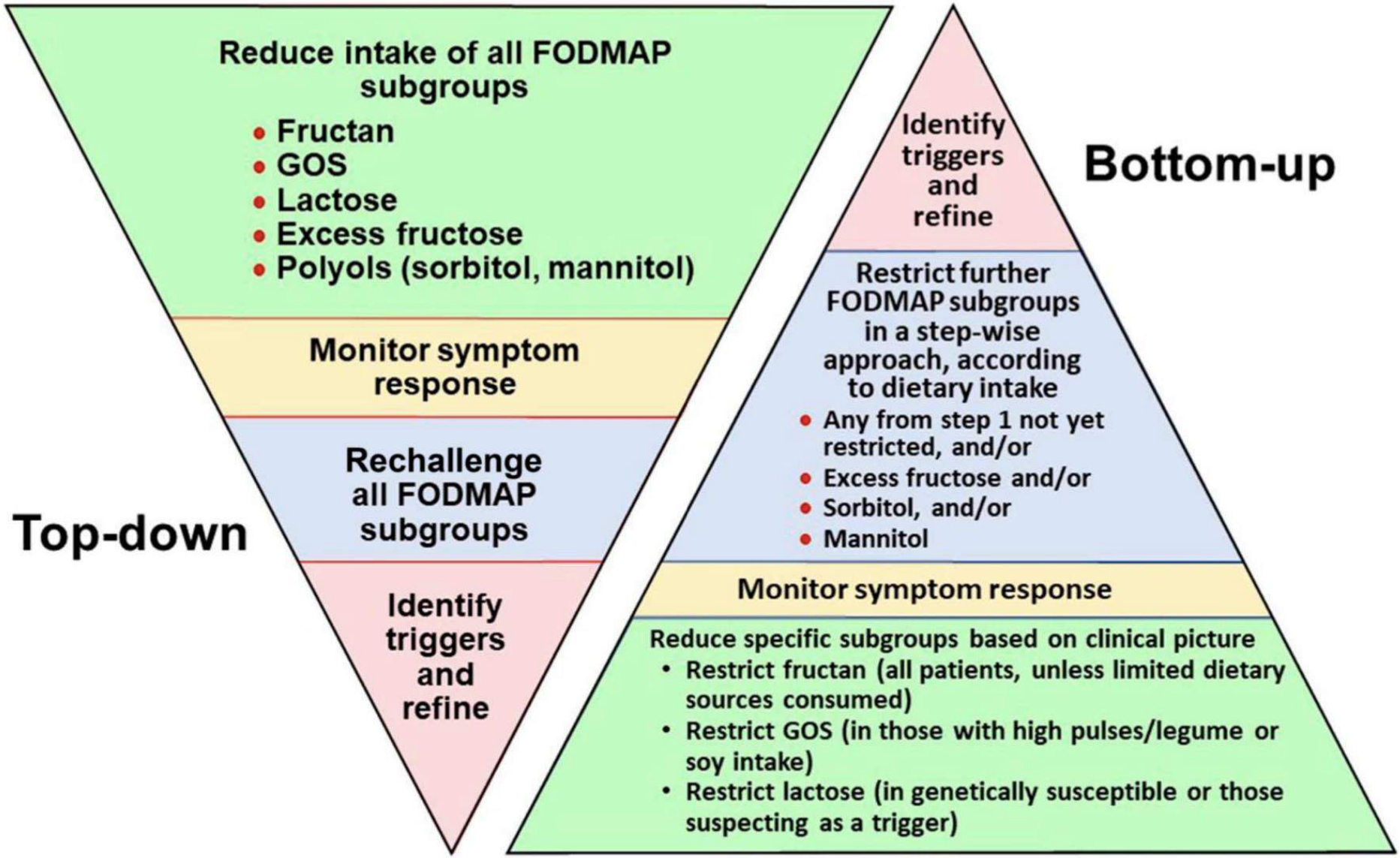


CONCLUSIONS: **There is insufficient evidence to recommend a GFD to reduce IBS symptoms. There is very low quality evidence that a low FODMAP diet is effective in reducing symptoms in IBS patients.**

Dionne et al. *Am J Gastroenterol 2018*



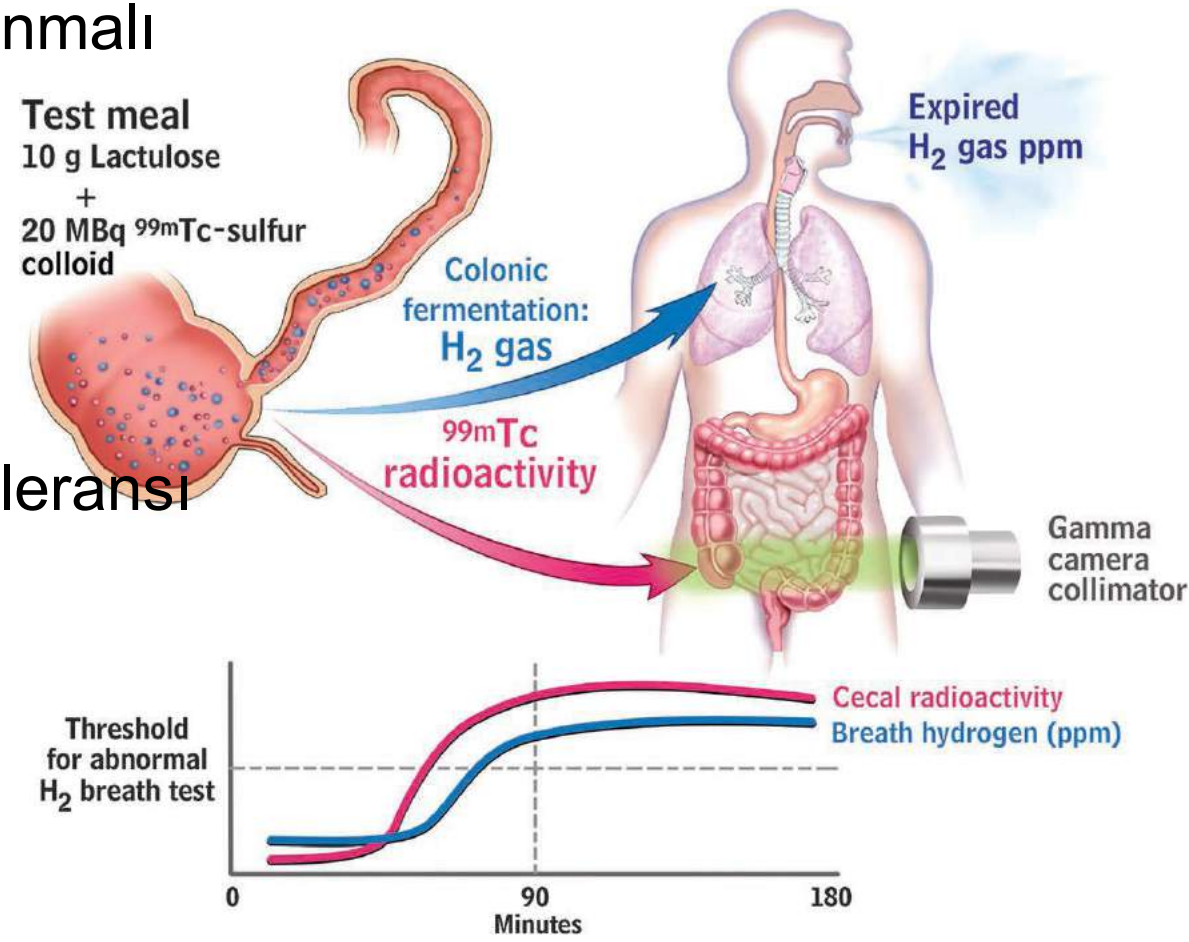
Singh et al. Am J Gastroenterol 2022;117:947–957.



Singh et al. Am J Gastroenterol 2022;117:947–957.

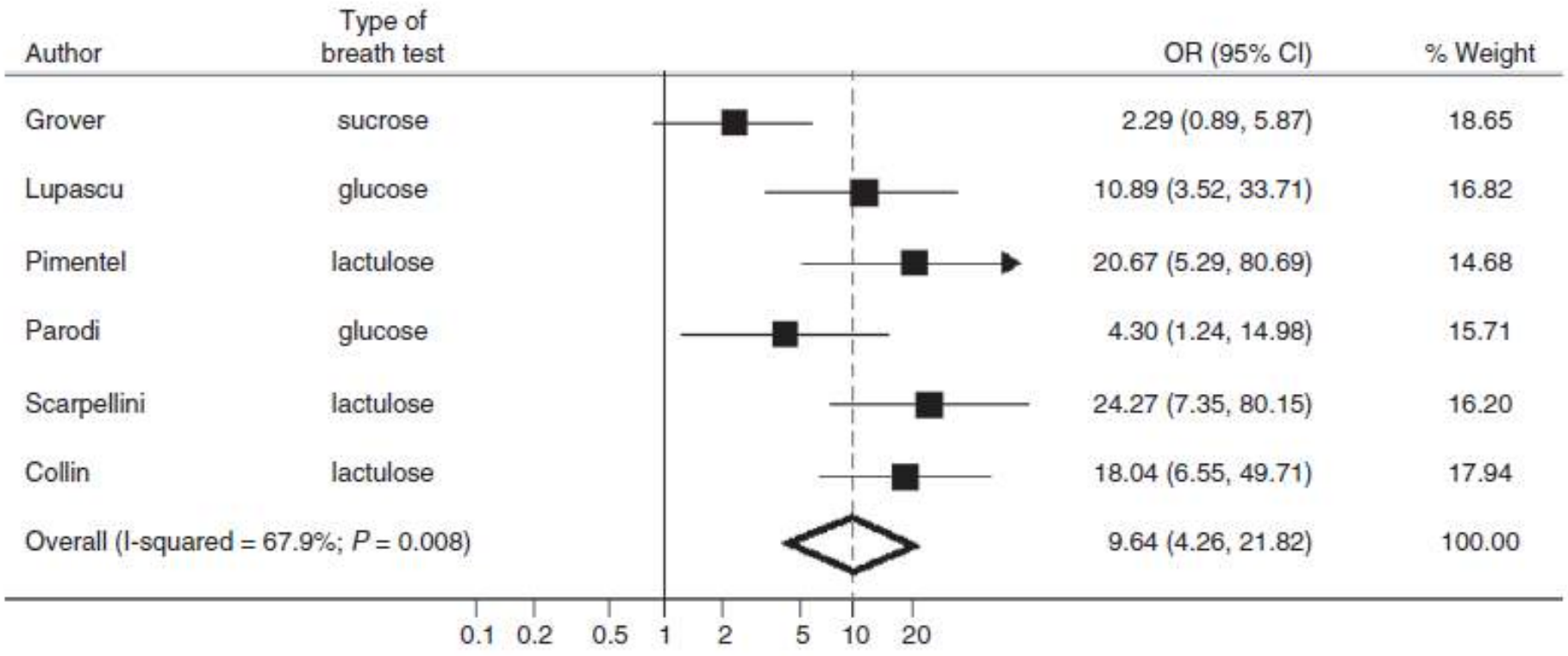
Gaz

- Diyet ile ilişkisi sorgulanmalı
- Laktoz ve fruktoz intoleransı değerlendirilmeli



Laktuloz alımından 90 dk sonra Hidrojen konsantrasyonu >20ppm SIBO yu işaret eder.

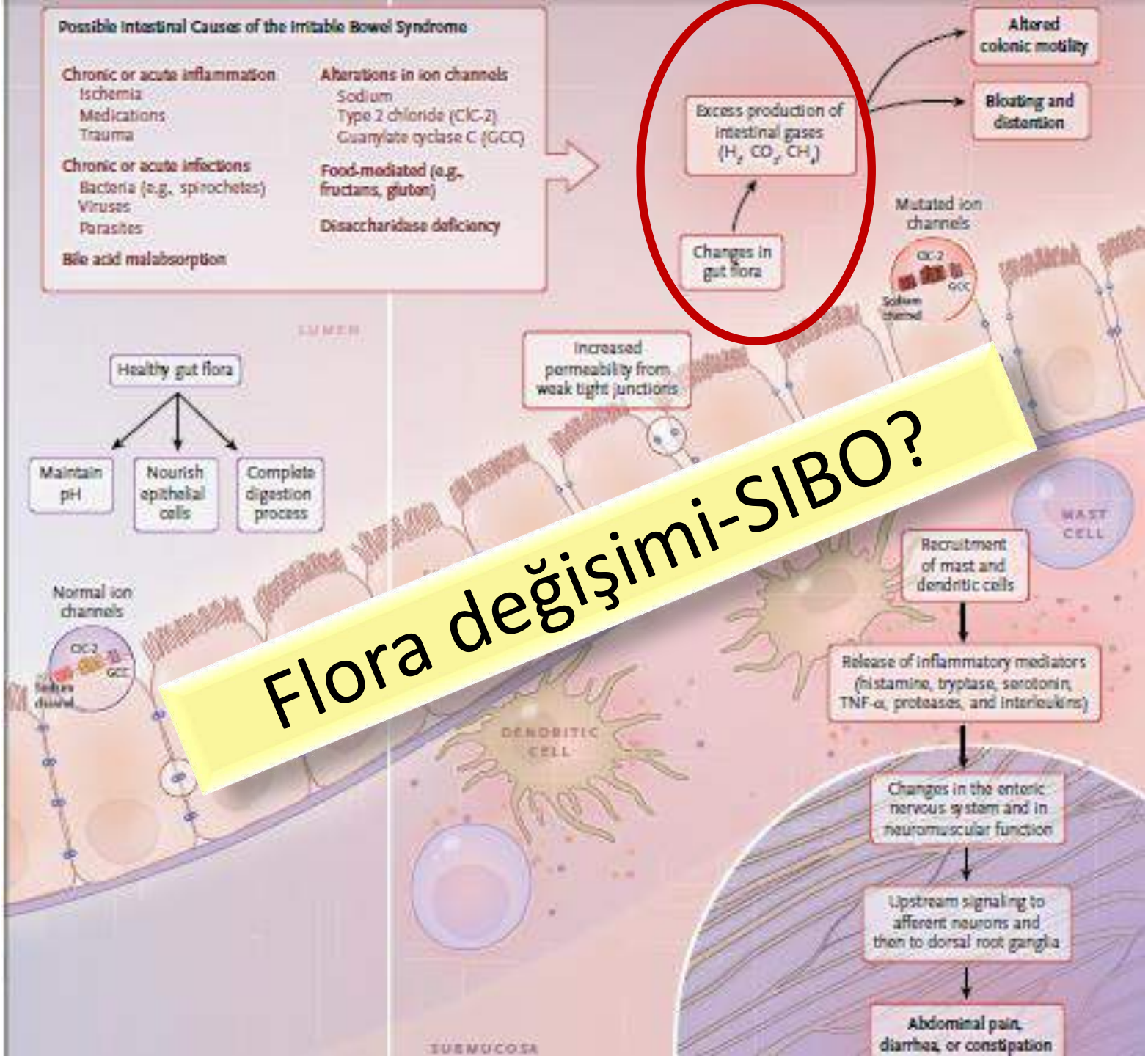
Pek çok çalışmada nefes testi İBS de patolojik



Pimentel M. Aliment Pharmacol Ther 2016; 43 (Suppl 1): 37–49

First author	Year	Country	Number of IBS cases vs. healthy controls	Test used to diagnose SIBO	SIBO prevalence: IBS vs. healthy controls
Pimentel [21]	2003	USA	111 vs. 15	LHBT	84 vs. 20%*
Walters [25]	2005	Canada	39 vs. 20	LHBT: double peak	10 vs. 10%
				LHBT: >20 ppm H2-rise within 90 min	28 vs. 30%
				LHBT: >20 ppm H2-rise within 180 min	69 vs. 75%
Lupascu [26]	2005	Italy	65 vs. 102	GHBT	31 vs. 4%*
Posserud [27]	2006	Sweden	162 vs. 26	Jejunal aspirate >10^5 CFU/ml (colonic bacteria)	4 vs. 4%
				Jejunal aspirate ≥5 × 10^3 CFU/ml (any bacteria)	43 vs. 12%*
				Jejunal aspirate ≥5 × 10^3 CFU/ml (colonic bacteria)	11 vs. 4%
			54 vs. 20	GHBT	2 vs. 0%
			46 vs. 21	LHBT: double peak	15 vs. 20%
				LHBT: >20 ppm H2-rise within 90 min	35 vs. 45%
				LHBT: >20 ppm H2-rise within 180 min	78 vs. 70%
Bratten [28]	2008	USA	180 vs. 34	LHBT	74 vs. 85%
Rana [29]	2008	India	225 vs. 100	GHBT	11 vs. 1%*
Parodi [30]	2009	Italy	130 vs. 70	GHBT	16 vs. 4.3%*
Ghoshal [31]	2010	India	192 vs. 51	GHBT	8.5 vs. 2%
Lombardo [32]	2010	Italy	200 vs. 50	GHBT	24.5 vs. 6%
Rana [33]	2012	India	175 vs. 150	LHBT	34 vs. 30%
				GHBT	6.2 vs. 0.7%*
Park [34]	2010	Korea	76 vs. 40	LHBT	44.7 vs.40%
Sachdeva [35]	2011	India	59 vs. 37	GHBT	23.7 vs. 2.7%*
Morariu [36]	2014	Romania	331 vs. 105	GHBT	31.6 vs. 6.6%*
Abbasi [37]	2015	Iran	107 vs. 107	GHBT	37.4 vs. 12.1%*
Chu [38]	2016	China	89 vs. 13	LHBT: double peak	44 vs. 38%
				LHBT: >20 ppm H2-rise within 90 min	31 vs. 30%
				LHBT: >20 ppm H2-rise within 180 min	75 vs. 70%

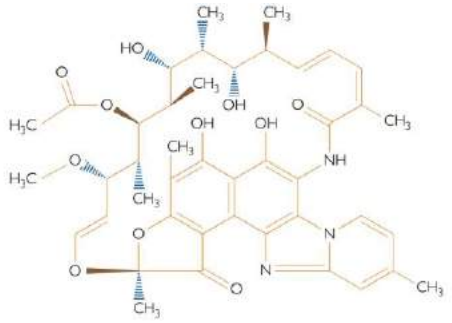
Aziz I, et al. Curr Opin Gastroenterol 2017, 33:196–202



Flora değişimi-SIBO?

Ford AC, Talley NJ. NEGM 2017

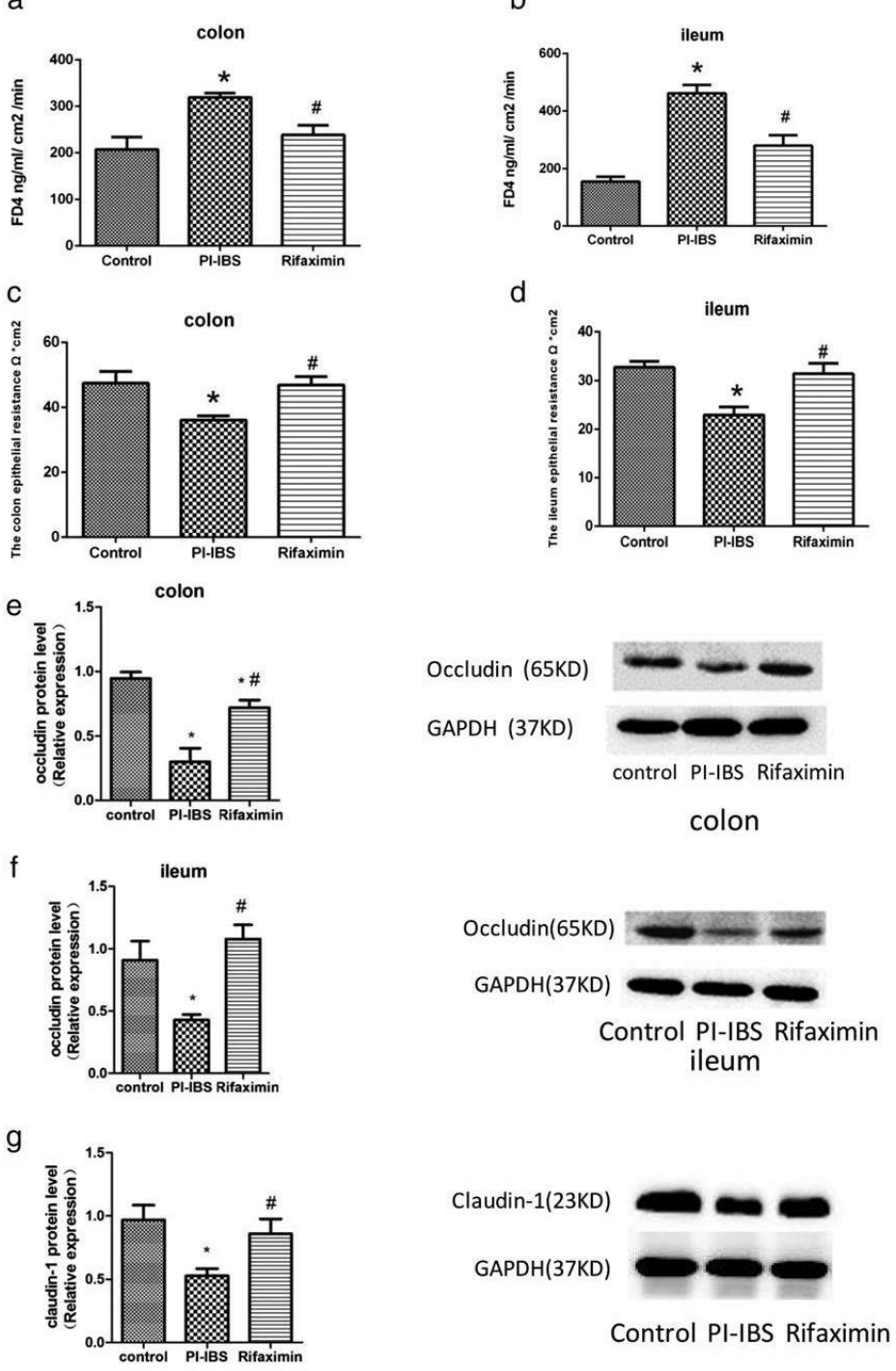
oral emilmeyen rifaximin olası etki mekanizmaları…



- florayı değiştirerek mikrobiotadaki çeşitliliği azaltır
- Kolonik Fermentasyon azalır
- İleumda da flora değişir mukozal inflamasyonu önler, geçirgenlik değiştirir ve hiperaljeziyi azaltır

Aziz I, et al. Curr Opin Gastroenterol 2017, 33:196–202

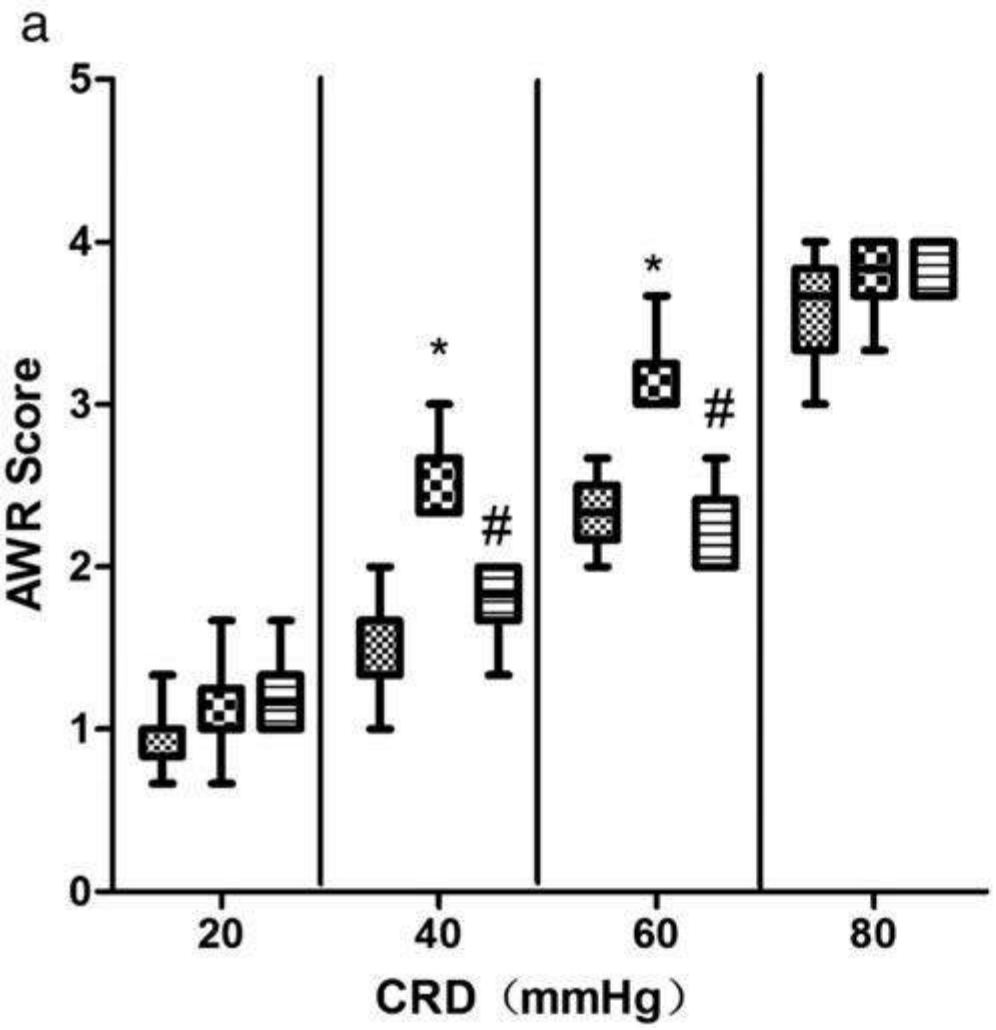
Xu D, et al. Gastroenterol 2014; 146:484-496.

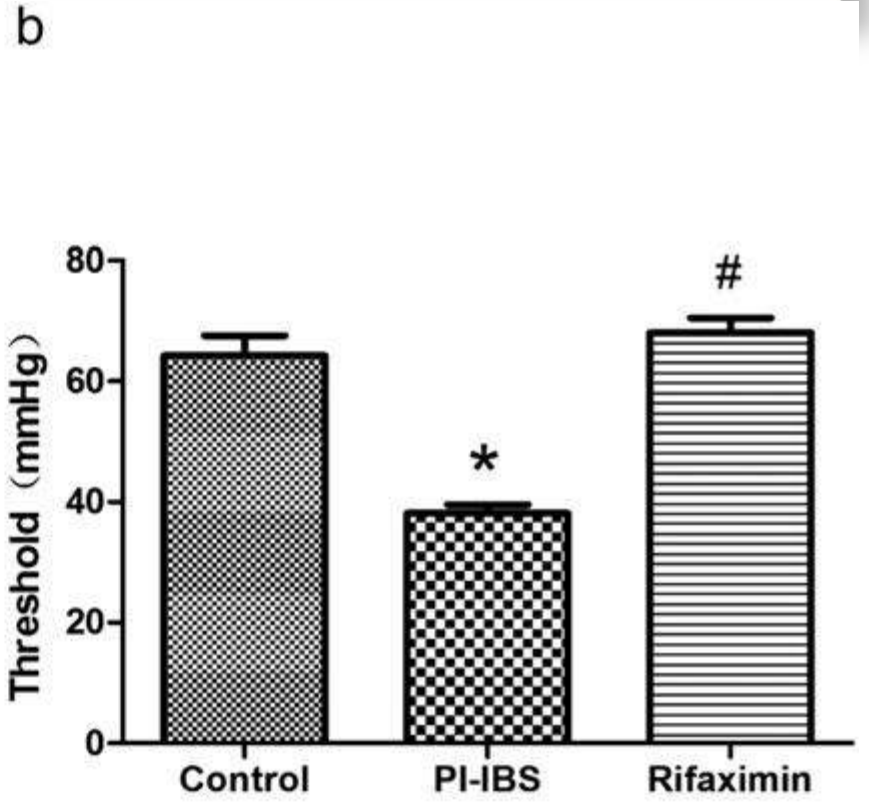


- Rifaximin
- post infeksiyöz İBS de
- İleum ve kolonda geçirgenliği azaltır
- Florada anlamlı değişiklik olmamış
- Tight-junction proteinlerinde up-regülasyon

Jin J, et al. Journal of Gastroenterology and Hepatology 33 (2018) 443–452

Post infeksiyöz IBS' de sıçan çalışmasında rifaximin viseral duyarlılığı azaltır





Jin J, et al. Journal of Gastroenterology and Hepatology 33 (2018) 443–452

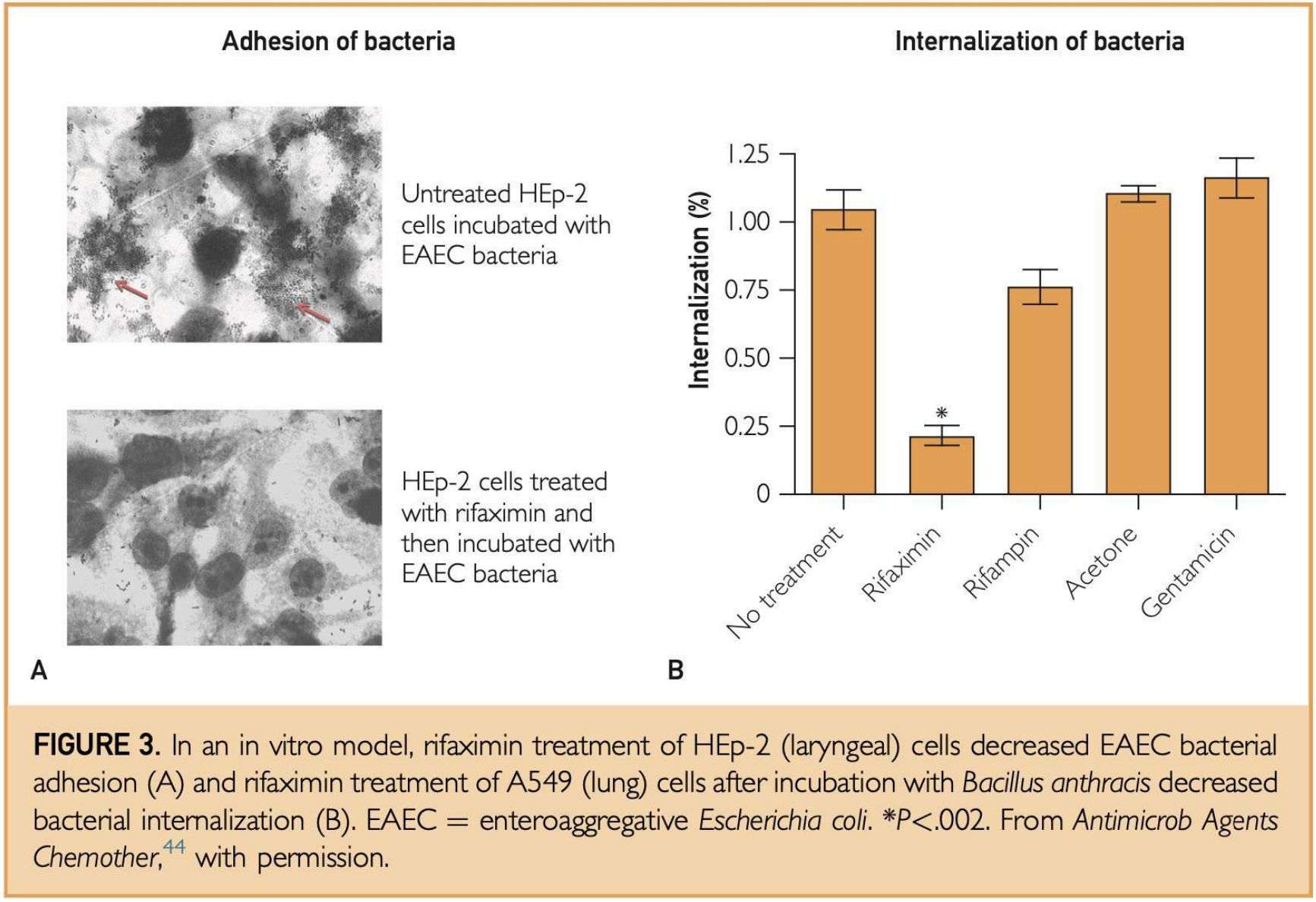


FIGURE 3. In an in vitro model, rifaximin treatment of HEp-2 (laryngeal) cells decreased EAEC bacterial adhesion (A) and rifaximin treatment of A549 (lung) cells after incubation with *Bacillus anthracis* decreased bacterial internalization (B). EAEC = enteroaggregative *Escherichia coli*. *$P<.002$. From *Antimicrob Agents Chemother*,[44] with permission.

DuPont et al. Mayo Clin Proc. 2015;90(8):1116-1124
Brown EL, et al. Antimicrob Agents Chemother. 2010;54(1):388-396.

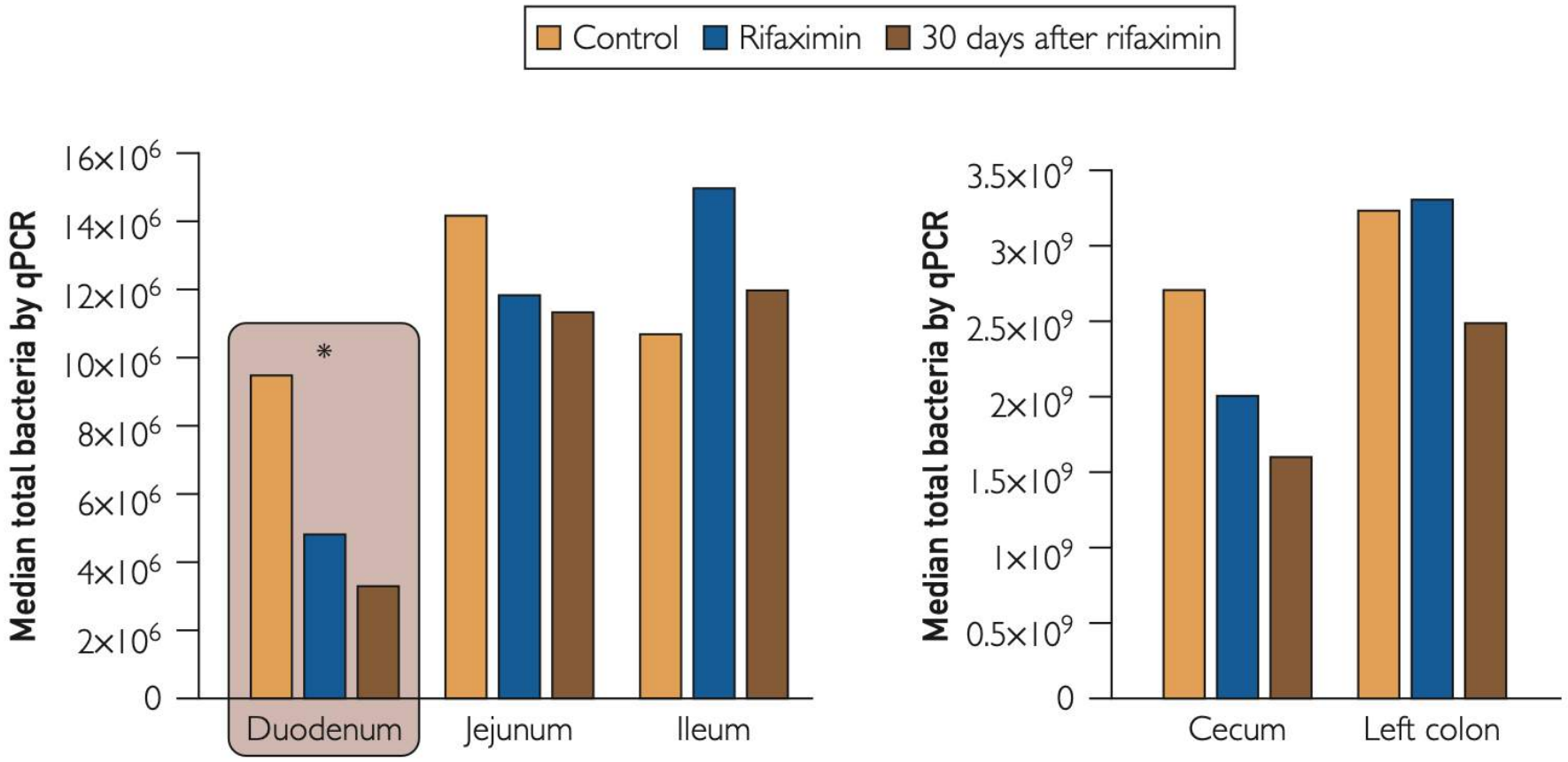
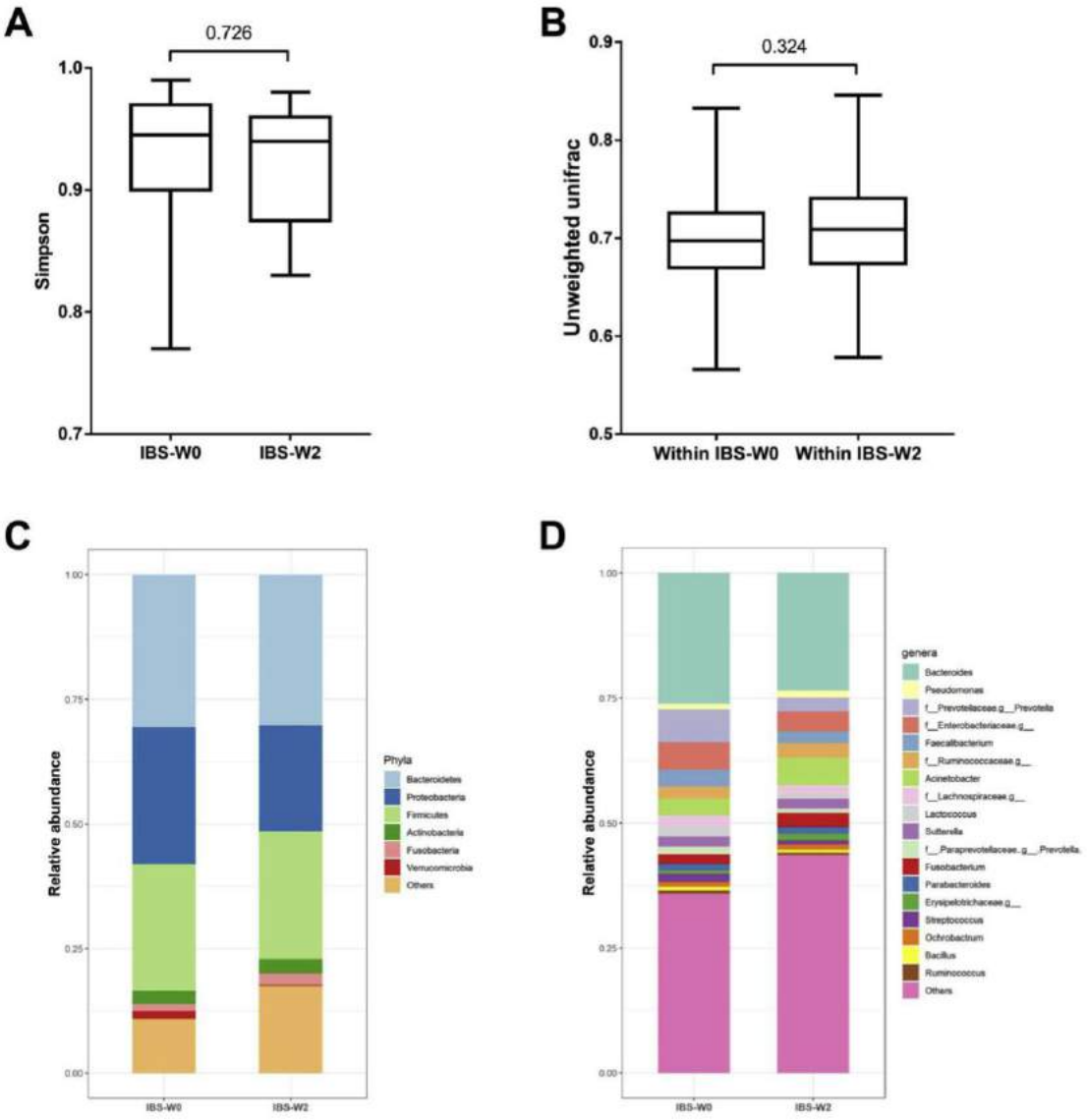


FIGURE 2. In an animal model, treatment with rifaximin for 10 days and subsequent assessment 30 days posttreatment indicated a decrease in bacterial counts as measured by qPCR, but a long-term effect was restricted to the duodenum. qPCR = quantitative polymerase chain reaction. *P=.08. From *Dig Dis Sci*,[45] with permission.

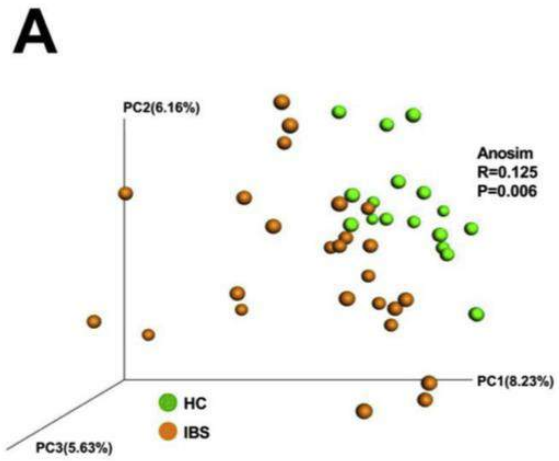
DuPont et al. Mayo Clin Proc. 2015;90(8):1116-1124
Kim MS, et al. Dig Dis Sci. 2013;58(6): 1676-1682.

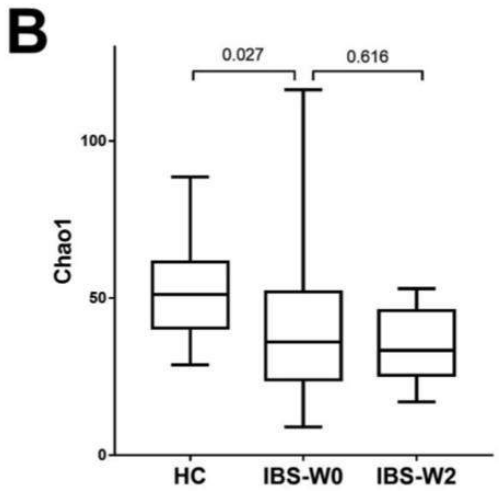
Rektumda florayı değiştirmiyor

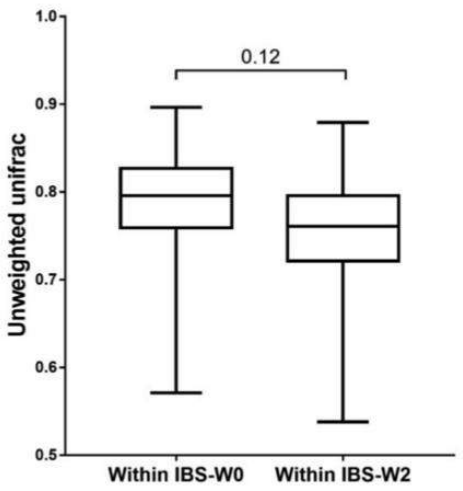


Li et al. Pharmacological Research 159 (2020) 104936

Fungal florayı değiştirmiyor







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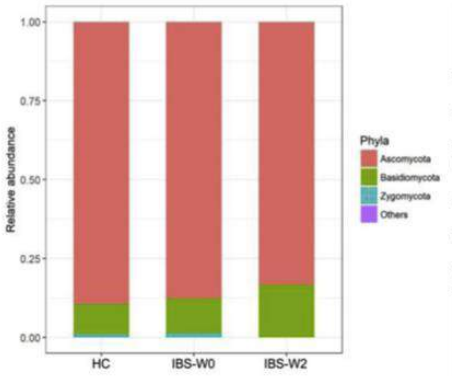
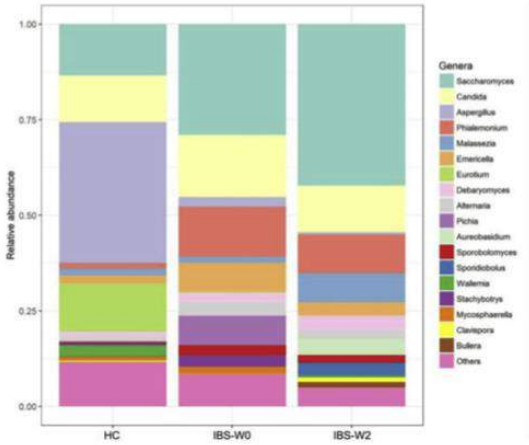


Phyla	P (HC VS. IBS-W0)	P (IBS-W0 VS. IBS-W2)
Ascomycota	0.279	0.527
Basidiomycota	0.362	0.867
Zygomycota	**0.005****	0.109
Others	0.092	0.317

E



Genera	P (HC VS. IBS-W0)	P (IBS-W0 VS. IBS-W2)
Saccharomyces	0.74	0.102
Candida	0.487	0.661
Aspergillus	**<0.001*****	0.691
Phialemonium	0.139	0.853
Malassezia	0.07	0.158
Emericella	0.707	0.836
Eurotium	0.319	0.109
Debaryomyces	0.092	0.646
Alternaria	0.204	0.569
Pichia	0.972	0.08
Aureobasidium	0.396	0.273
Sporobolomyces	0.84	1
Sporidiobolus	**0.006****	0.18
Wallemia	0.157	0.593
Stachybotrys	0.717	0.18
Mycosphaerella	**0.014***	0.465
Clavispora	0.714	0.854
Bullera	1	0.317
Others	0.214	0.581

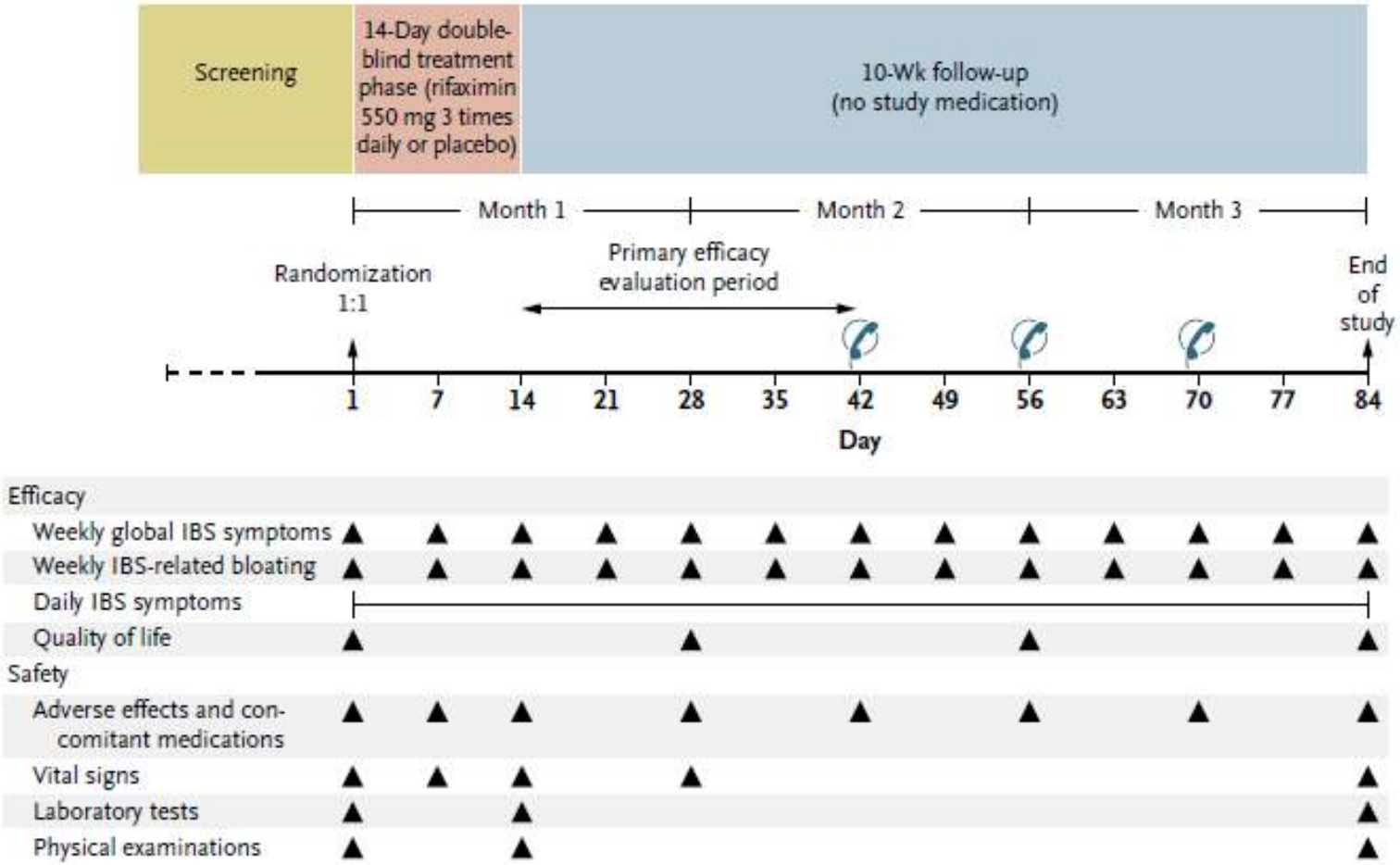
Li et al. Pharmacological Research 159 (2020) 104936

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Rifaximin Therapy for Patients with Irritable Bowel Syndrome without Constipation

Mark Pimentel, M.D., Anthony Lembo, M.D., William D. Chey, M.D., Salam Zakko, M.D., Yehuda Ringel, M.D., Jing Yu, Ph.D., Shadreck M. Mareya, Ph.D., Audrey L. Shaw, Ph.D., Enoch Bortey, Ph.D., and William P. Forbes, Pharm.D., for the TARGET Study Group*

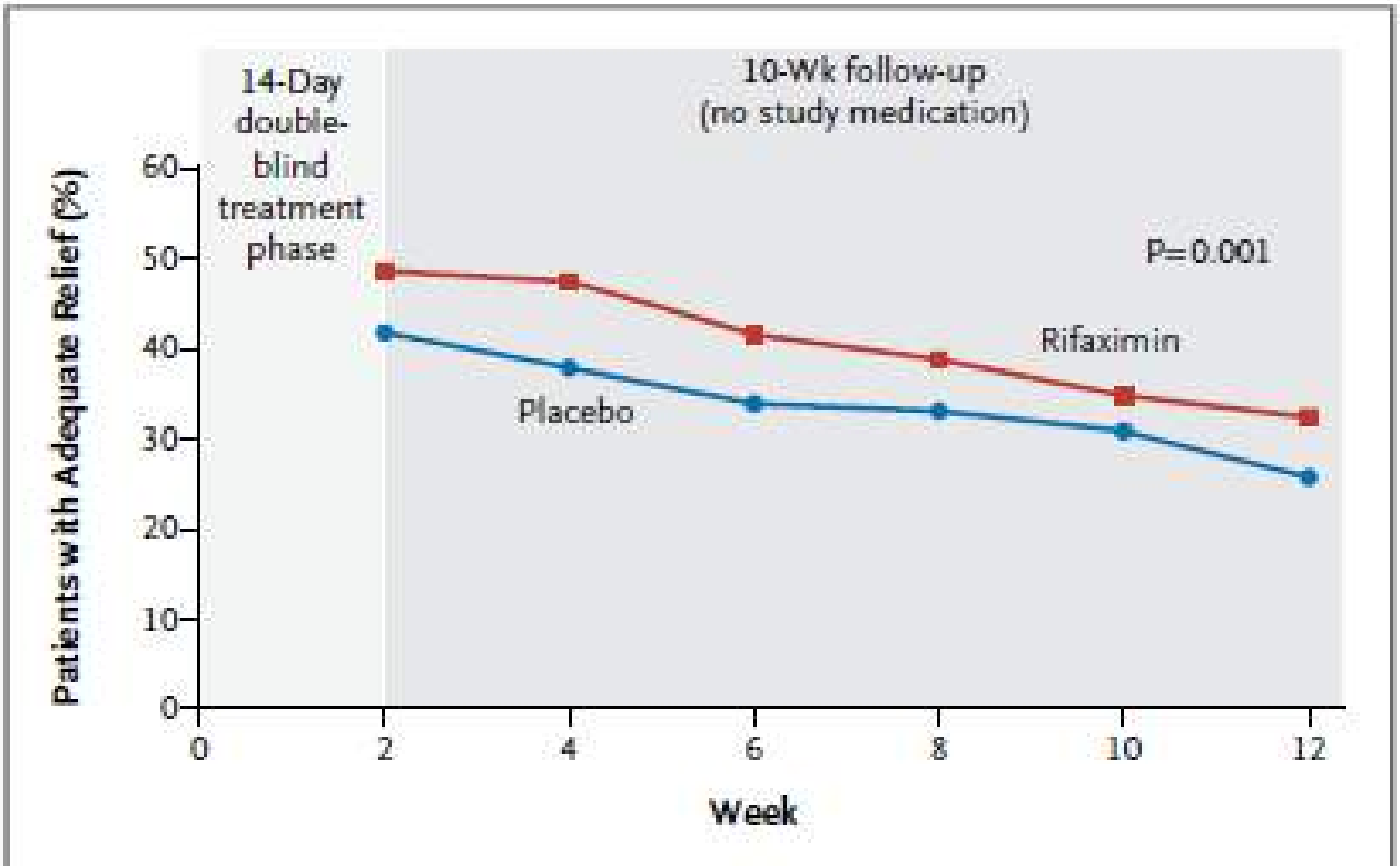


N Engl J Med 2011;364:22-32.

Efficacy Outcome	Proportion of Patients with a Response		Odds Ratio (95% CI)	Treatment Effect
	Placebo	Rifaximin		
	no./total no.			
Primary end point				
Weekly global IBS symptoms				
TARGET 1	98/314	126/309	1.53	0.01
TARGET 2	103/320	128/315	1.45	0.03
Combined	201/634	254/624	1.49	<0.001
Key secondary end point				
Weekly IBS-related bloating				
TARGET 1	90/314	122/309	1.62	0.005
TARGET 2	102/320	129/315	1.49	0.02
Combined	192/634	251/624	1.56	<0.001
Secondary end points				
Daily global IBS symptoms				
TARGET 1	96/314	132/309	1.76	<0.001
TARGET 2	91/320	119/315	1.59	0.007
Combined	187/634	251/624	1.61	<0.001
Daily IBS-related bloating				
TARGET 1	102/314	121/309	1.41	0.05
TARGET 2	99/320	137/315	1.76	<0.001
Combined	201/634	258/624	1.52	<0.001
Daily IBS-related abdominal pain				
TARGET 1	114/314	137/309	1.45	0.03
TARGET 2	110/320	135/315	1.46	0.02
Combined	224/634	272/624	1.42	0.003
Daily abdominal pain and stool consistency				
TARGET 1	121/314	144/309	1.40	0.04
TARGET 2	116/320	147/315	1.55	0.008
Combined	237/634	291/624	1.47	<0.001
Daily abdominal pain				
TARGET 1	132/314	159/309	1.48	0.02
TARGET 2	138/320	165/315	1.46	0.02
Combined	270/634	324/624	1.46	<0.001
Daily stool consistency				
TARGET 1	212/314	244/309	1.80	0.002
TARGET 2	206/320	233/315	1.57	0.01
Combined	418/634	477/624	1.67	<0.001

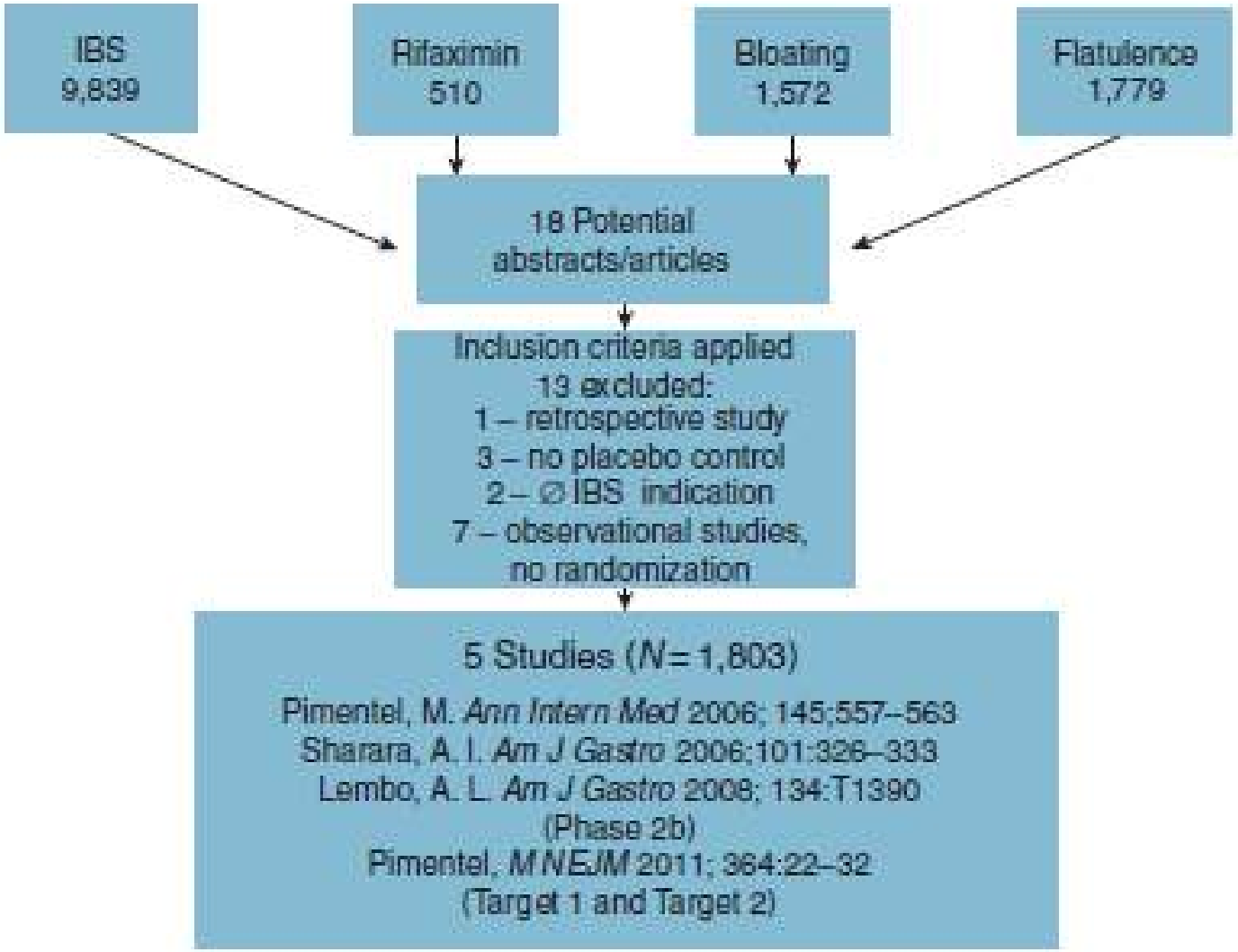
N Engl J Med 2011;364:22-32.

%40.7 vs %31.7
NNT: 11



N Engl J Med 2011;364:22-32.

Metaanaliz



Menees SB, et al. Am J Gastroenterol 2012; 107:28–35;

IBS genel semptomlar ve gaz/şişkinlik iyileşmesinde placebo'ya üstün

Table 2. Primary outcome: global improvement of IBS symptoms, rifaximin vs. placebo

Study	Dose duration	Response rate, % (response/*N*)		Therapeutic Gain, %	NNT	OR
		Rifaximin	Placebo			
Sharara *et al.*	400 mg b.i.d., 10 days	27.0 (10/37)	9.1 (3/33)	17.9	5.6	3.70
Pimentel *et al.*	400 mg t.i.d., 10 days	32.6 (14/43)	9.1 (4/44)	23.5	4.3	4.83
Lembo *et al.*	550 mg b.i.d., 14 days	52.3 (100/191)	44.2 (87/197)	8.1	12.3	1.39
Target 1	550 mg t.i.d., 14 days	40.8 (126/309)	31.2 (98/314)	9.6	10.4	1.52
Target 2	550 mg t.i.d., 14 days	40.6 (128/315)	32.2 (103/320)	8.4	11.9	1.44
Pooled OR	—	42.2 (378/895)	32.4 (295/908)	9.8	10.2	1.57

IBS, irritable bowel syndrome; NNT, number needed to treat; OR, odds ratio.

Table 3. Secondary outcome: improvement of bloating, rifaximin vs. placebo

Study	Response rate, % (response /N)		Therapeutic Gain, %	NNT	OR
	Rifaximin	Placebo			
Pimentel *et al.*	41.9 (18/43)	15.9 (7/44)	26	3.8	3.81
Lembo *et al.*	46.1 (88/191)	39.6 (78/197)	6.5	15.4	1.33
Target 1	39.5 (122/309)	28.7 (90/314)	10.8	9.3	1.62
Target 2	41.0 (129/315)	31.9 (102/320)	9.1	11	1.48
Pooled OR	41.6 (357/858)	31.7 (277/875)	9.9	10.1	1.55

NNT, number needed to treat; OR, odds ratio.

Menees SB, et al. Am J Gastroenterol 2012; 107:28–35;

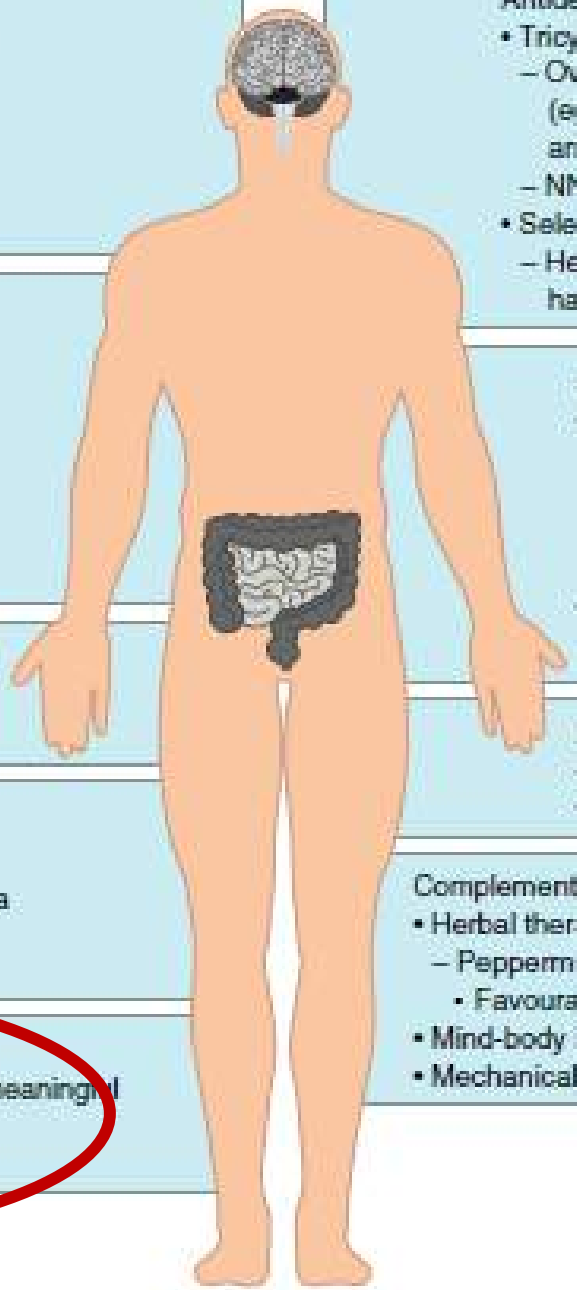
Mu-opioid receptor agonists
- Loperamide
  - Overdosing associated with cardiotoxicity and pancreatitis
- Diphenoxylate/atropine
  - Overdosing associated with severe respiratory depression

Mixed mu-opioid receptor agonist/delta-opioid antagonist
- Eluxadoline
  - Risk of pancreatitis (patients lacking gall-bladder)
  - Risk of sphincter of Oddi dysfunction and colonic ischaemia
  - NNH = 25 (75 mg), 23 (100 mg)

Dietary modification
- Low FODMAP diet
  - Potential for dietary insufficiency

Bile acid sequestrants
- Common AEs with
  - Colesevelam: headache, flatulence, nausea
  - Cholestyramine: constipation, nausea, bloating, flatulence, abdominal pain

Rifaximin
- Favourable safety profile and lacks clinically meaningful antibiotic resistance
- NNH = 8971



Antidepressants (NNH = 8.5)
- Tricyclic antidepressants
  - Overdosing associated with cardiac AEs (eg, electrocardiogram abnormalities, arrhythmias, hypotension)
  - NNH = 9 and 18
- Selective serotonin reuptake inhibitors
  - Headache, poor sleep, anxiety, and nausea have been reported

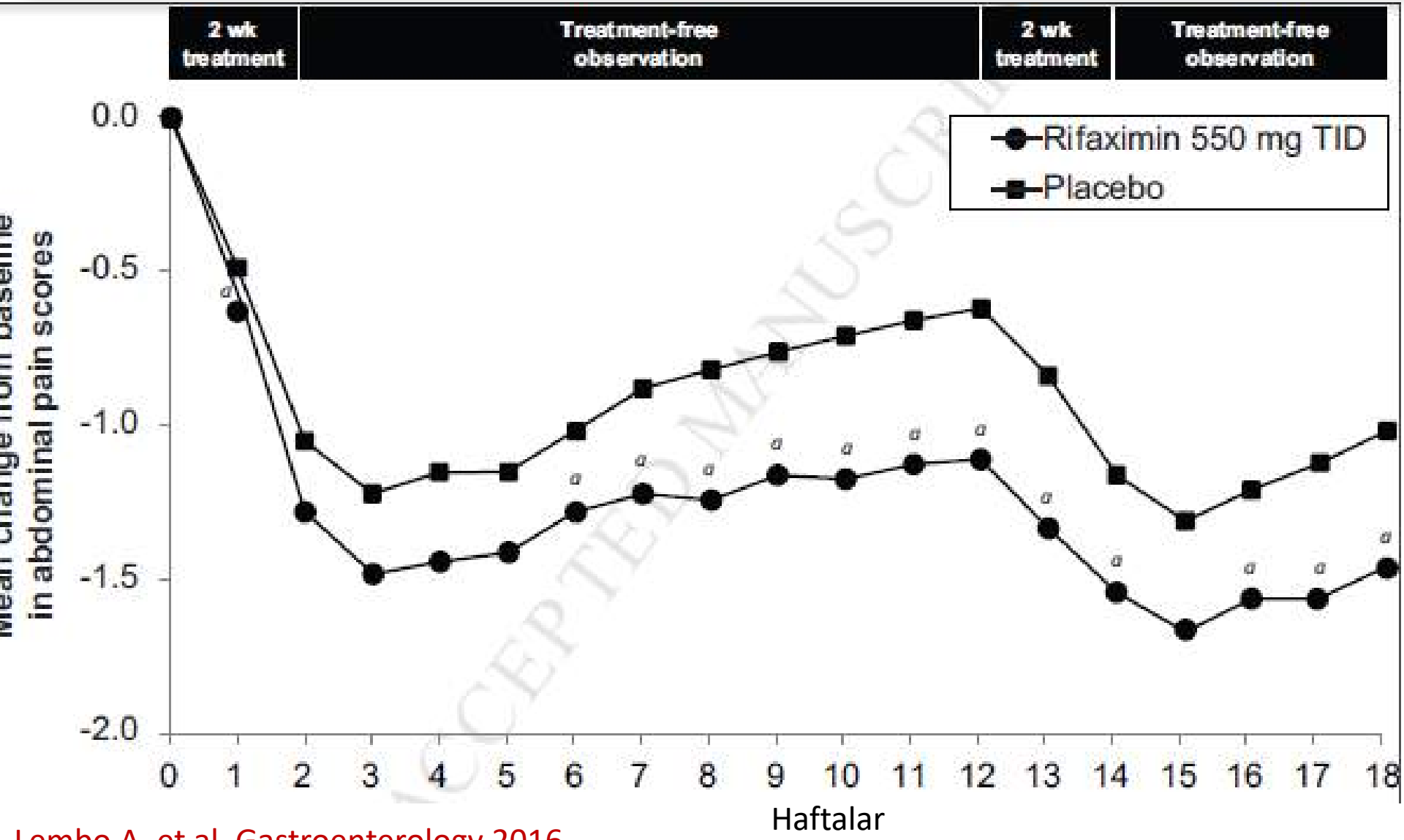
5-HT_3 receptor antagonists
- Alosetron (women only)
  - Marketed under a REMS program
    - Risk of ischaemic colitis and serious complications of constipation
  - NNH = 10 and 19
- Ondansetron
  - Most common AE: constipation

Probiotics
- Safety profiles differ by probiotic strain
- NNH = 35

Complementary and alternative therapies
- Herbal therapies
  - Peppermint oil
    - Favourable safety profile
- Mind-body interventions
- Mechanical interventions

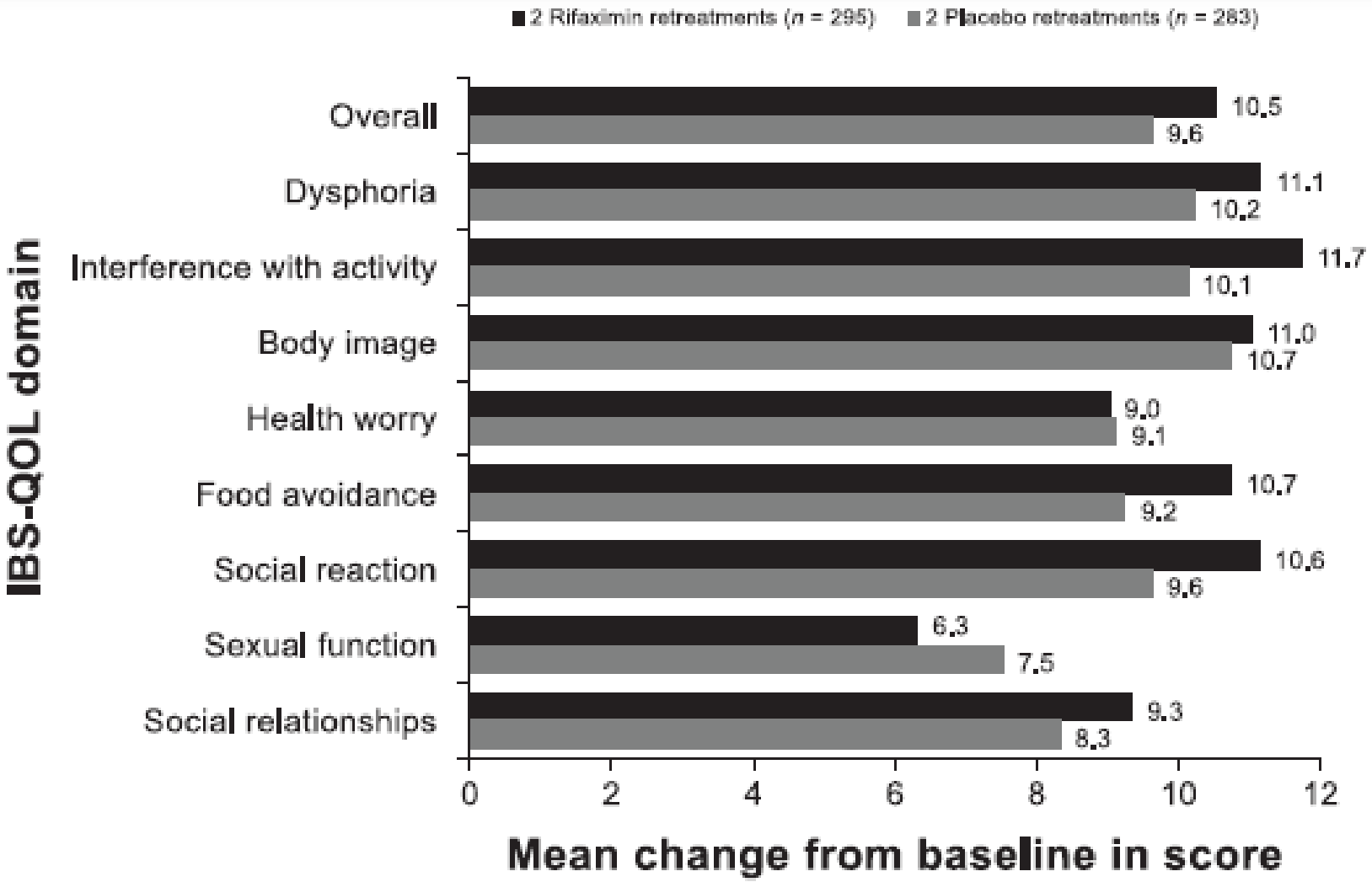
Lacy BE Aliment Pharmacol Ther. 2018;1–14.

RİFAXİMİN TEKRARLAYAN KULLANIMLARDA DA ETKİN



Lembo A, et al. Gastroenterology 2016

RİFAXİMİN TEKRARLAYAN KULLANIMLARDA YAŞAM KALİTESİNDE İYİLEŞME SAĞLAMIŞ



Cash B, et al. Ther Adv Gastroenterol 2017, Vol. 10(9) 689– 699

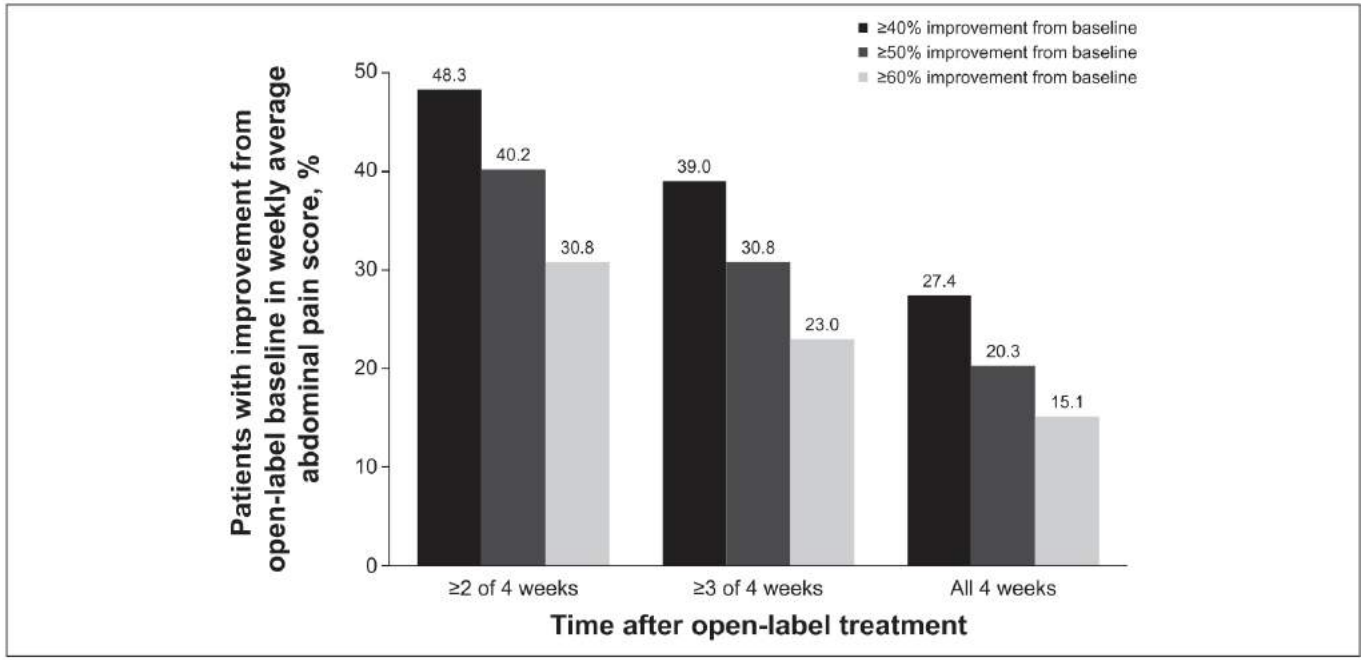


Figure 3. Mean improvement from baseline in average weekly abdominal pain score by responder threshold (open-label treatment phase).

Table 1. Demographic and baseline disease characteristics (open-label treatment phase)

Parameter	Overall population (N = 2,579)[a]	Abdominal pain responders[b] (n = 1,384)[c]	Abdominal pain nonresponders (n = 1,054)[c]
Age, yr, mean (SD)	46.4 (13.7)	47.0 (13.8)	45.7 (13.5)
Female, n (%)	1,760 (68.2)	952 (68.8)	709 (67.3)
Race, n (%)			
White	2,155 (83.6)	1,177 (85.0)	857 (81.3)
Black	289 (11.2)	129 (9.3)	146 (13.9)
Other	135 (5.2)	78 (5.6)	51 (4.8)
Average daily bowel movements, mean (SD)	3.9 (2.2)	3.7 (2.0)	4.0 (2.4)
Duration since the first onset of IBS symptoms, yr, mean (SD)	10.9 (10.8)	11.4 (11.1)	10.1 (10.2)
Average daily score, mean (SD)			
Abdominal pain	5.5 (1.7)	5.5 (1.6)	5.6 (1.7)
Stool consistency	5.6 (0.8)	5.6 (0.8)	5.6 (0.9)
Bloating	4.1 (0.9)	4.1 (0.9)	4.1 (1.0)
IBS symptoms	4.2 (0.9)	4.1 (0.9)	4.2 (0.9)

IBS, irritable bowel syndrome.
[a]Data from Lembo A, Pimentel M, Rao SS, et al. Repeat treatment with rifaximin is safe and effective in patients with diarrhea-predominant irritable bowel syndrome. *Gastroenterology* 2016;151(6):1113–21 (21).
[b]Abdominal pain responders defined as patients with a ≥30% improvement from baseline in the mean weekly abdominal pain score during ≥2 weeks of the first 4 weeks post-treatment.
[c]One hundred forty-one patients were excluded because of insufficient data to determine response (i.e., observed case methodology).

Lembo et al. Clinical and Translational Gastroenterology 2020;11:e00144.

Emilmeyen antibiyotikler (Rifaximin)

- Hafif orta şiddetli vakalarda gaz ve şişkinlikte yararlı
- 1200mg/gün x 10 gün

Antibiyotik direnci, C.difficile??

Simren M, et al. Gut 2013;62:159–176. 0

Dig Dis Sci (2017) 62:2455–2463
DOI 10.1007/s10620-017-4598-7

ORIGINAL ARTICLE

Repeat Rifaximin for Irritable Bowel Syndrome: No Clinically Significant Changes in Stool Microbial Antibiotic Sensitivity

M. Pimentel[1] · B. D. Cash[2] · A. Lembo[3] · R. A. Wolf[4] · R. J. Israel[4] · P. Schoenfeld[5]

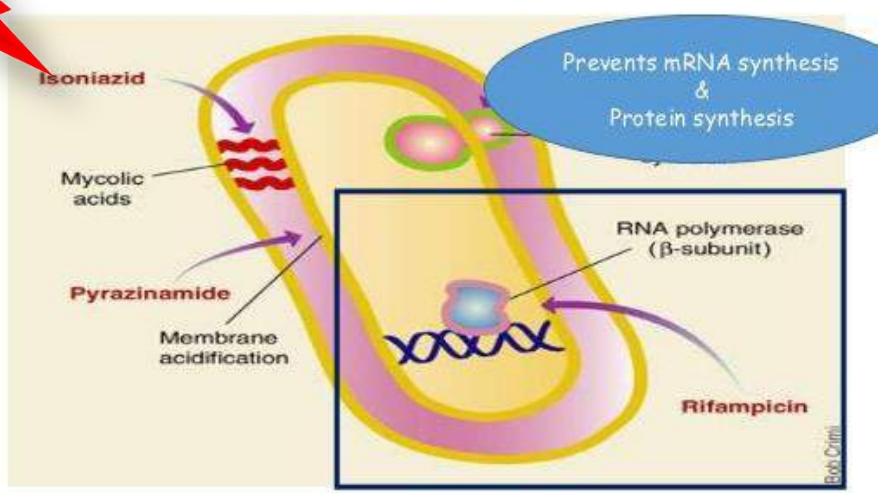
Tekrarlayan rifaximin antibiyotik duyarlılığını değiştirmiyor

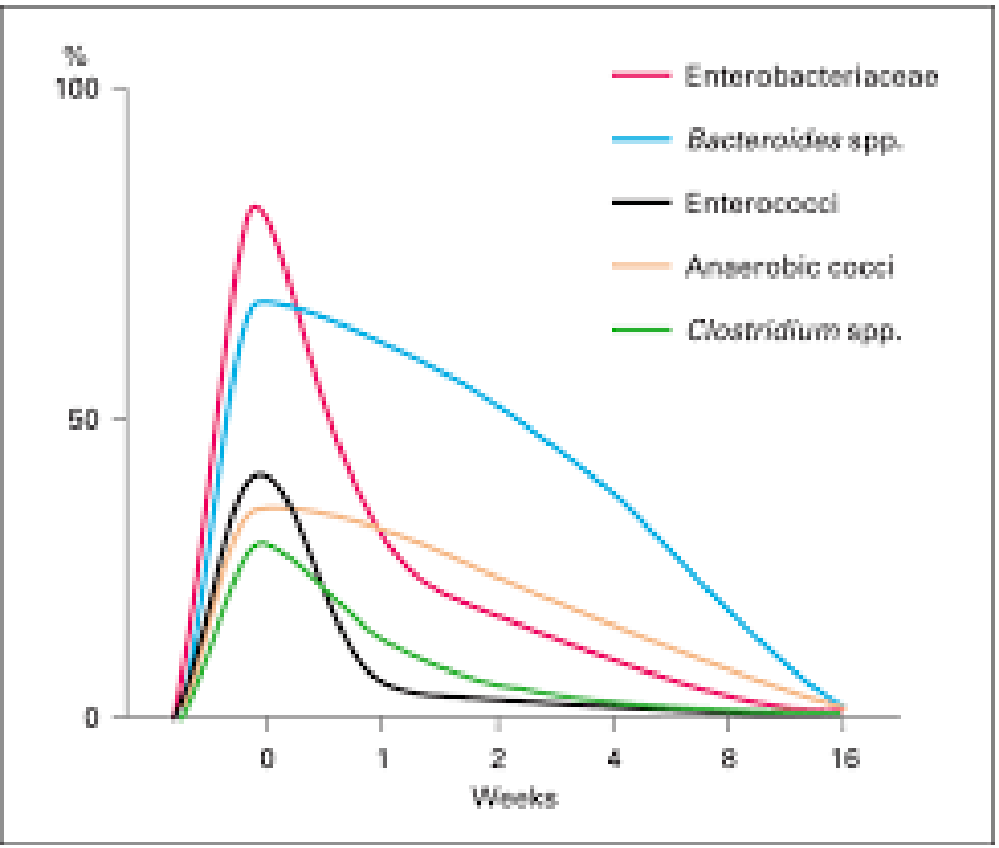
Conclusions In this study, short-term repeat treatment with rifaximin has no apparent long-term effect on stool microbial susceptibility to rifaximin, rifampin, and nonrifamycin antibiotics.
ClinicalTrials.gov Identifier NCT01543178.

TARGET 3 hastaları

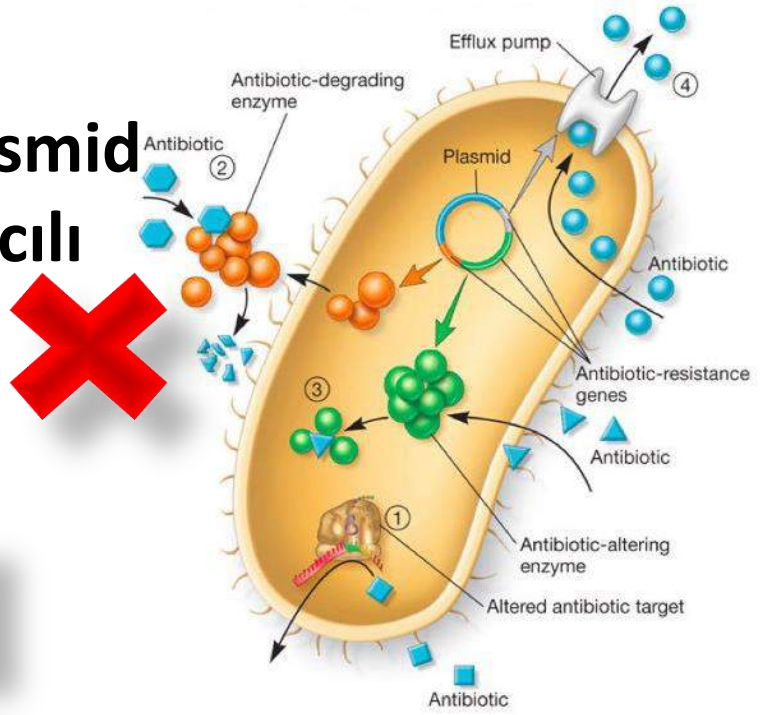
Direnç

Kromozomal mekanizma





Plasmid aracılı



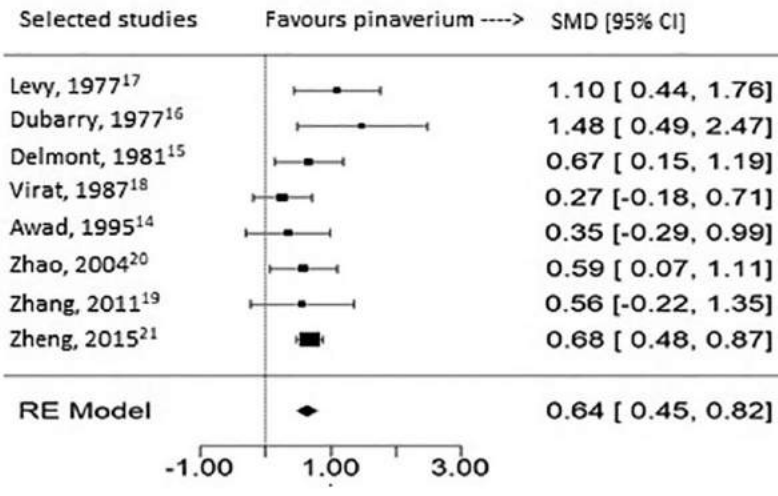
İlaç kesilince düzelir

Antispazmodikler

- 22 çalışma, 12 antispasmodik, 1778 hasta
- NNT: 5
- Semptom iyileşmesi **%61 vs % 44** placebo

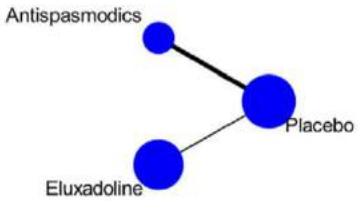
Study (Country)	Sample size (pinaverium, placebo)[a]	Mean age (years)	Proportion of female patients	Medication dosage (schedule)	Diagnostic criteria	Treatment duration (days)	MQS	Outcome assessed	Primary outcome
Awad *et al.* (Mexico)[15]	40 (20, 20)	31	1	50 mg (tid)	Rome I	21	8.11	OSR, API, ADI, SFI, SCI, ASI	Significant API ($p < 0.01$)
Delmont (France)[16]	60 (30, 30)	56	0.67	50 mg (tid)	Clinical	28	5.72	OSR, API, ADI, TPN	Significant OSR ($p < 0.01$) and API ($p < 0.05$)
Dubarry and Quinton (France)[17]	20 (10, 10)	40	0.5	50 mg (tid)	Clinical	6	4.86	APR	Significant APR ($p < 0.01$)
Levy *et al.* (France)[18]	44 (22, 22)	50	0.59	50 mg (tid)	Clinical	15	6.63	OSR, API, ADI, TPN	Significant OSR ($p < 0.01$)
Virat *et al.* (France)[19]	78 (39, 39)	44	0.51	50 mg (tid)	Clinical	7	6.98	OSR, API, ADI, SFI	Significant API ($p < 0.05$)
Zhang *et al.* (China)[20]	28 (18, 10)	40	0.5	50 mg (tid)	Rome III	28	6.06	OSR, API, ADI, SFI, ASI	Significant API, ADI and SFI ($p < 0.05$)
Zhao *et al.* (China)[21]	60 (30, 30)	37	0.5	50 mg (tid)	Rome II	28	2.50	OSR, APR, ADI, TPN	Significant OSR ($p < 0.01$)
Zheng *et al.* (China)[22]	427 (218, 209)	37	0.47	50 mg (tid)	Rome III	28	9.24	OSR, APR, ADI, SFI, SCI	Signifiant APR ($p < 0.01$)

[a]Sample size: number of patients in the pinaverium group and placebo group.
ADI, abdominal distension improvement; API, abdominal pain improvement; APR, abdominal pain resolution; ASI, additional symptoms improvement; MQS, overall methodological quality score; OSR, overall symptoms response; SCI, stool consistency improvement; SFI, stool frequency improvement; tid, three times daily; TPN, transit problems normalization.

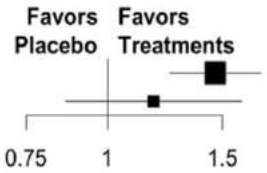


Bor et al. Ther Adv Gastroenterol 2021,

A Abdominal pain

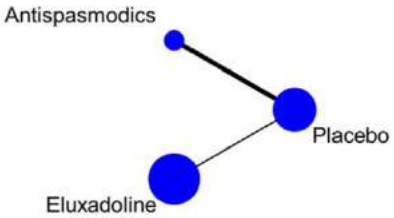


Treatments	Number of patients	RR (95%CI)	P-score
Antispasmodics	1594	1.46 [1.24; 1.72]	0.94
Eluxadoline	2540	1.18 [0.86; 1.60]	0.48

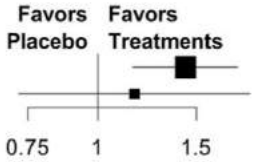


Antispasmodics		
1.24 [0.88; 1.76]	Eluxadoline	
1.46 [1.24; 1.72]	1.18 [0.86; 1.60]	Placebo

B Relief of global IBS symptoms



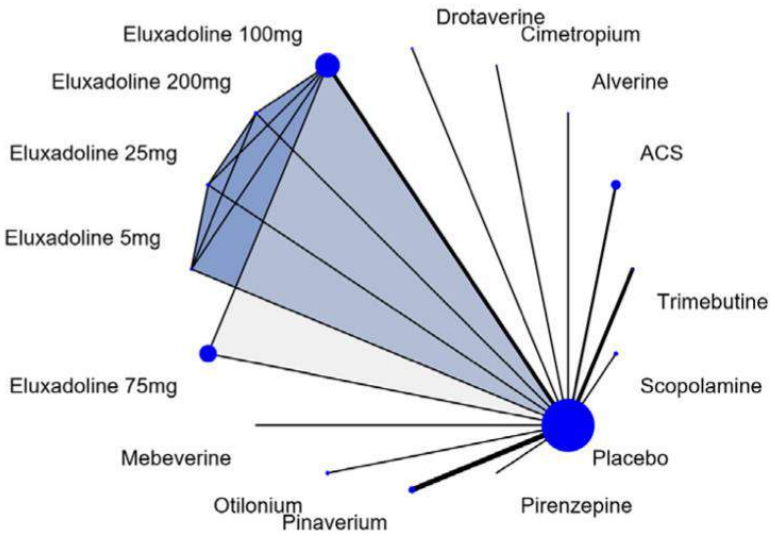
Treatments	Number of patients	RR (95%CI)	P-score
Antispasmodics	929	1.43 [1.15; 1.78]	0.89
Eluxadoline	2381	1.16 [0.72; 1.87]	0.47



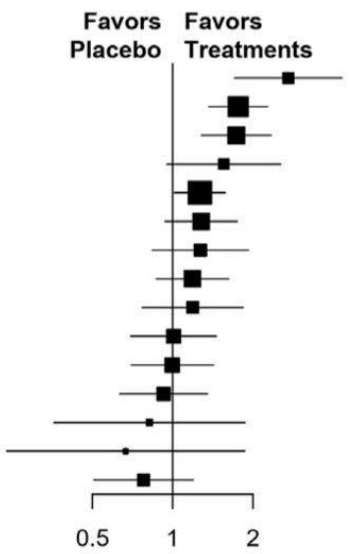
Antispasmodics		
1.23 [0.73; 2.08]	Eluxadoline	
1.43 [1.15; 1.78]	1.16 [0.72; 1.87]	Placebo

Qin D, (2022) Eluxadoline. Front. Pharmacol

A **Abdominal pain**

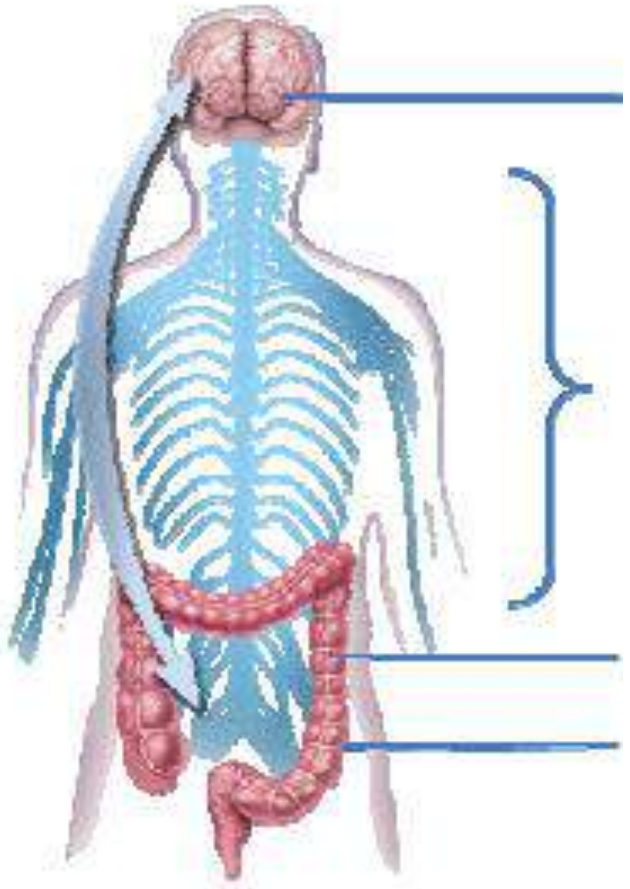


Treatments	Number of patients	RR (95%CI)	P-score
Drotaverine	87	2.71 [1.70; 4.32]	0.99
Pinaverium	297	1.76 [1.37; 2.27]	0.86
ACS	427	1.73 [1.28; 2.34]	0.84
Cimetropium	48	1.56 [0.95; 2.54]	0.74
Eluxadoline 100mg	1141	1.26 [1.02; 1.57]	0.60
Trimebutine	70	1.28 [0.94; 1.75]	0.59
Otilonium	160	1.27 [0.84; 1.93]	0.58
Eluxadoline 75mg	808	1.19 [0.87; 1.62]	0.51
Alverine	53	1.19 [0.77; 1.84]	0.51
Eluxadoline 25mg	167	1.01 [0.70; 1.46]	0.34
Scopolamine	182	1.00 [0.70; 1.42]	0.33
Eluxadoline 200mg	160	0.93 [0.63; 1.35]	0.26
Mebeverine	40	0.82 [0.36; 1.87]	0.24
Pirenzepine	12	0.67 [0.24; 1.86]	0.17
Eluxadoline 5mg	105	0.78 [0.51; 1.19]	0.13



Qin D, (2022) Eluxadoline. Front. Pharmacol

Antidepresanlar



Antidepresan etkisi

Viseral analjezi

Motilite değişimi

Düz kas relaksasyonu

	TCA	SSRI	SNRI
Potential benefit	➢ Pain reduction ➢ Depression	➢ Depression ➢ Panic ➢ Anxiety ➢ (Pain reduction)	➢ Pain reduction ➢ Depression
Side effects	➢ Sedation ➢ Constipation ➢ Hypotension ➢ Xerostoma ➢ Arrhythmias ➢ Weight gain ➢ Sexual dysfunction	➢ Agitation ➢ Diarrhea ➢ Insomnia ➢ Night sweats ➢ Headache ➢ Weight loss ➢ Sexual dysfunction	➢ Nausea ➢ Agitation ➢ Dizziness ➢ Sleep disturbance ➢ Fatigue ➢ Liver dysfunction

TCA, Tricyclic antidepressants; SSRI, Selective serotonin reuptake inhibitors; SNRI, Serotonin-norepinephrine reuptake inhibitors

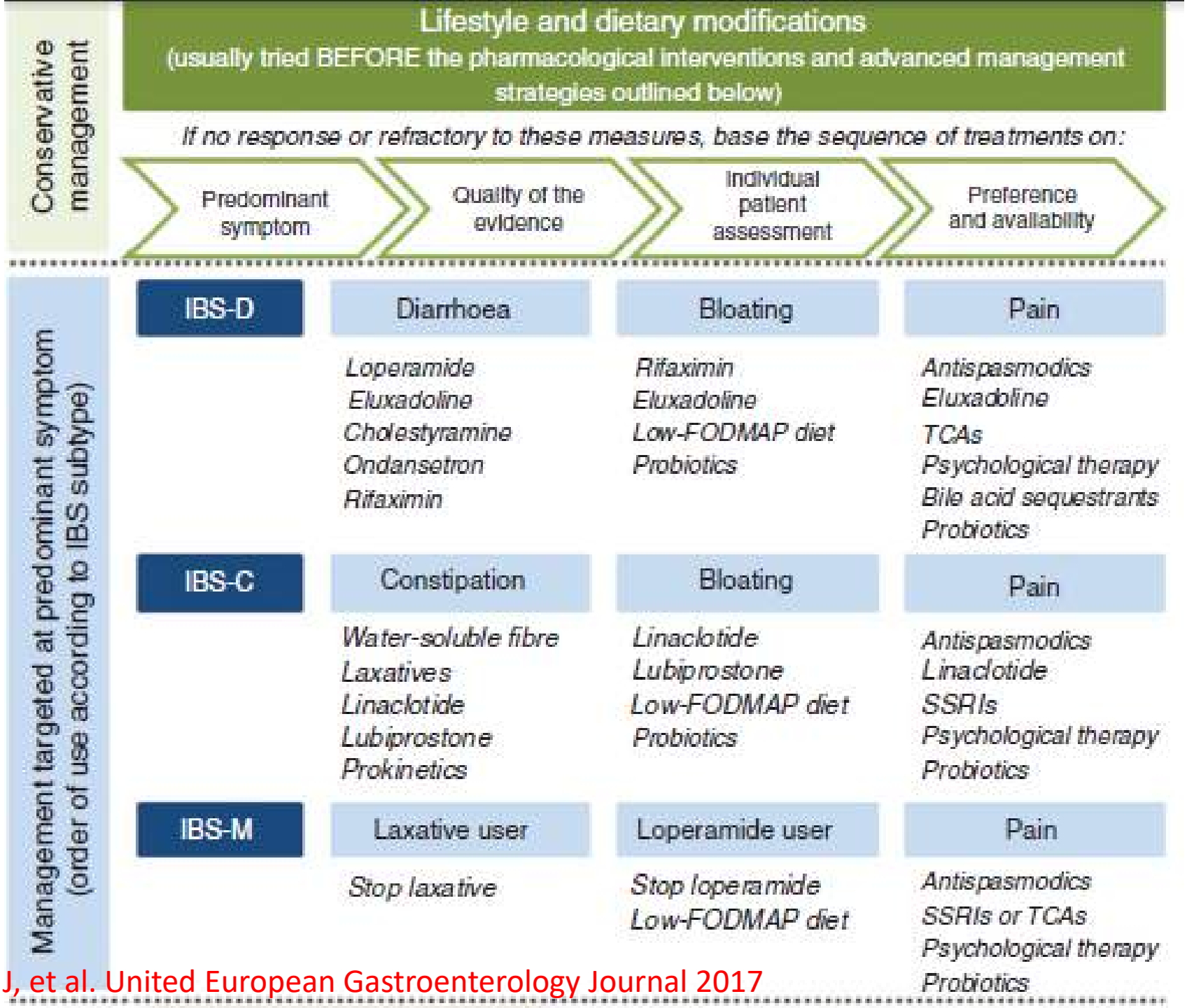
Törnblom & Drossman Neurogastroenterol Motil 2015

ROME IV

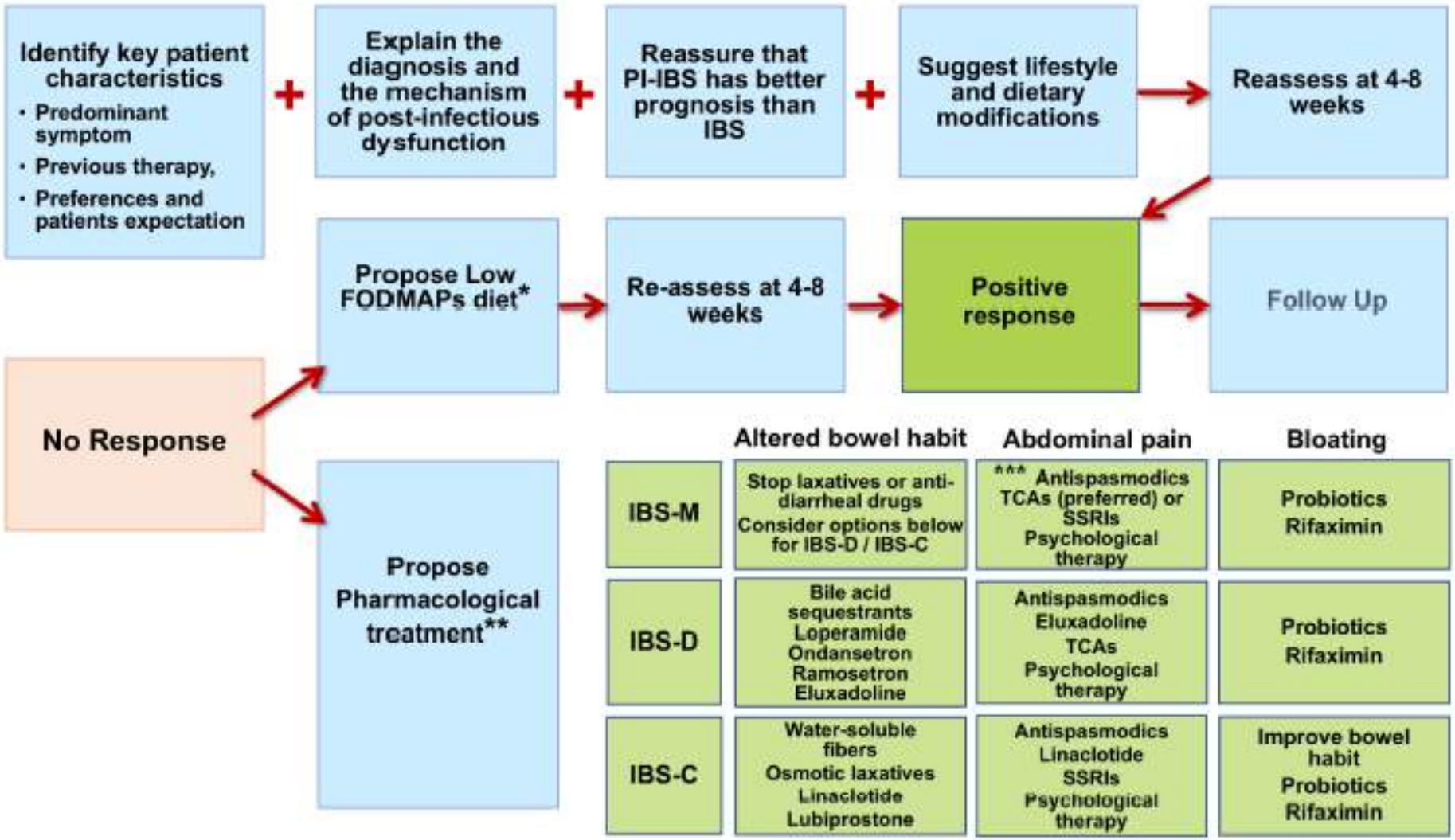
Diarrhea	Opioid agonists	Loperamide; 2–4 mg; when necessary Titrate up to 16 mg/d
	Diet	Low/no gluten; low FODMAP
	Bile salt sequestrants	cholestyramine (9 g bid–tid) colestipol (2 g qd–bid) colesevelam (625 mg qd–bid)
	Probiotics	Multiple products available
	Antibiotics	Rifaximin, 550 mg po tid × 14 d
	5-HT_3 antagonists	Alosetron (0.5–1 mg bid) Ondansetron (4–8 mg tid) Ramosetron 5 μg qd
	Mixed opioid agonists/antagonists	Eluxadoline, 100 mg bid
Constipation	Psyllium	up to 30 g/d in divided doses
	PEG	17–34 g/d
	Chloride channel activators	Lubiprostone, 8 μg bid
	Guanylate Cyclase C agonists	Linaclotide 290 μg qd
Abdominal pain	Smooth muscle antispasmodics	dicycylomine (10–20 mg qd–qid) Otilonium (40–80 mg bid–tid) Mebeverine (135 mg tid)
	Peppermint oil	Enteric-coated capsules, 250–750 mg, bid–tid
	Tricyclic antidepressants	Desipramine (25–100 mg qhs), amitriptyline (10–50 mg qhs)
	SSRIs	paroxetine (10–40 mg qd) sertraline (25–100 mg qd) citalopram (10–40 mg qd)
	Chloride channel activators	Lubiprostone 8 μg bid
	Guanylate cyclase C agonists	Linaclotide 290 μg qd
	5-HT_3 antagonists	Alosetron 0.5–1.0 mg bid

Gaz/şişkinlik		**Diyet değişikliği rifaximin, probiyotik**

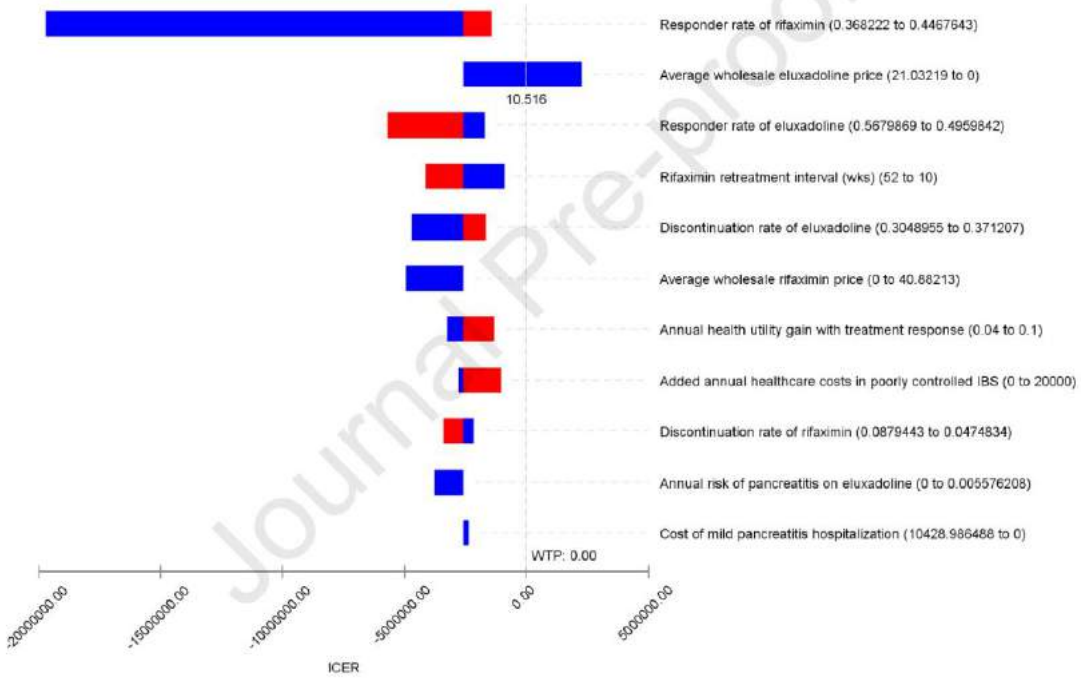
Lacy BE, et al. Gastroenterology 2016;150:1393–1407



Tack J, et al. United European Gastroenterology Journal 2017



Barbara G, et al. Gastroenterology 2018



Eluxadoline vs Rifaksimin
Daha etkili ve daha ucuz

TCA vs Rifaximin etkili ama pahalı

Shah ED, et al. Clinical Gastroenterology and Hepatology (2020),

IBS-ishal

We recommend the use of rifaximin to treat global IBS-D symptoms. Strong recommendation; moderate quality of evidence.

Lacy et al. Am J Gastroenterol 2021;116:17–44.

New or updated recommendations[a]	Strength of recommendation	Certainty in evidence
1. In patients with IBS-D, the AGA suggests using eluxadoline Implementation remark: eluxadoline is contraindicated in patients without a gallbladder or those who drink more than 3 alcoholic beverages per day	Conditional	Moderate
2a. In patients with IBS-D, the AGA suggests using rifaximin	Conditional	Moderate
2b. In patients with IBS-D with initial response to rifaximin who develop recurrent symptoms, the AGA suggests retreatment with rifaximin	Conditional	Moderate
3. In patients with IBS-D, the AGA suggests using alosetron	Conditional	Moderate
4. In patients with IBS-D, the AGA suggests using loperamide	Conditional	Very low
5. In patients with IBS, the AGA suggests using TCAs	Conditional	Low
6. In patients with IBS, the AGA suggests against using SSRIs	Conditional	Low
7. In patients with IBS, the AGA suggests using antispasmodics	Conditional	Low

[a]For all recommendation statements, the comparator was no drug treatment.

Lembo et al. Gastroenterology 2022;163:137–151

IBS-kabız

9. Should Antispasmodics Be Used in Patients With Irritable Bowel Syndrome?

The AGA suggests using antispasmodics in patients with IBS.
(Conditional recommendation, low certainty)

New or updated recommendations[a]	Strength of recommendation	Certainty of evidence
1. In patients with IBS-C, the AGA suggests using tenapanor	Conditional	Moderate
2. In patients with IBS-C, the AGA suggests using plecanatide	Conditional	Moderate
3. In patients with IBS-C, the AGA recommends using linaclotide	Strong	High
4. In patients with IBS-C, the AGA suggests using tegaserod Implementation remark: Tegaserod was reapproved for women under the age of 65 years without a history of cardiovascular ischemic events (such as myocardial infarction, stroke, TIA, or angina)	Conditional	Moderate
5. In patients with IBS-C, the AGA suggests using lubiprostone	Conditional	Moderate
6. In patients with IBS-C, the AGA suggests using PEG laxatives	Conditional	Low
7. In patients with IBS, the AGA suggests using TCAs	Conditional	Low
8. In patients with IBS, the AGA suggests against using SSRIs	Conditional	Low
9. In patients with IBS, the AGA suggests using antispasmodics	Conditional	Low

[a]For all recommendation statements, the comparator was no drug treatment.

Chang et al.Gastroenterology 2022;163:118–136

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DOI: 10.1002/ueg2.12259

REVIEW ARTICLE

ueg journal WILEY

Functional bowel disorders with diarrhoea: Clinical guidelines of the United European Gastroenterology and European Society for Neurogastroenterology and Motility

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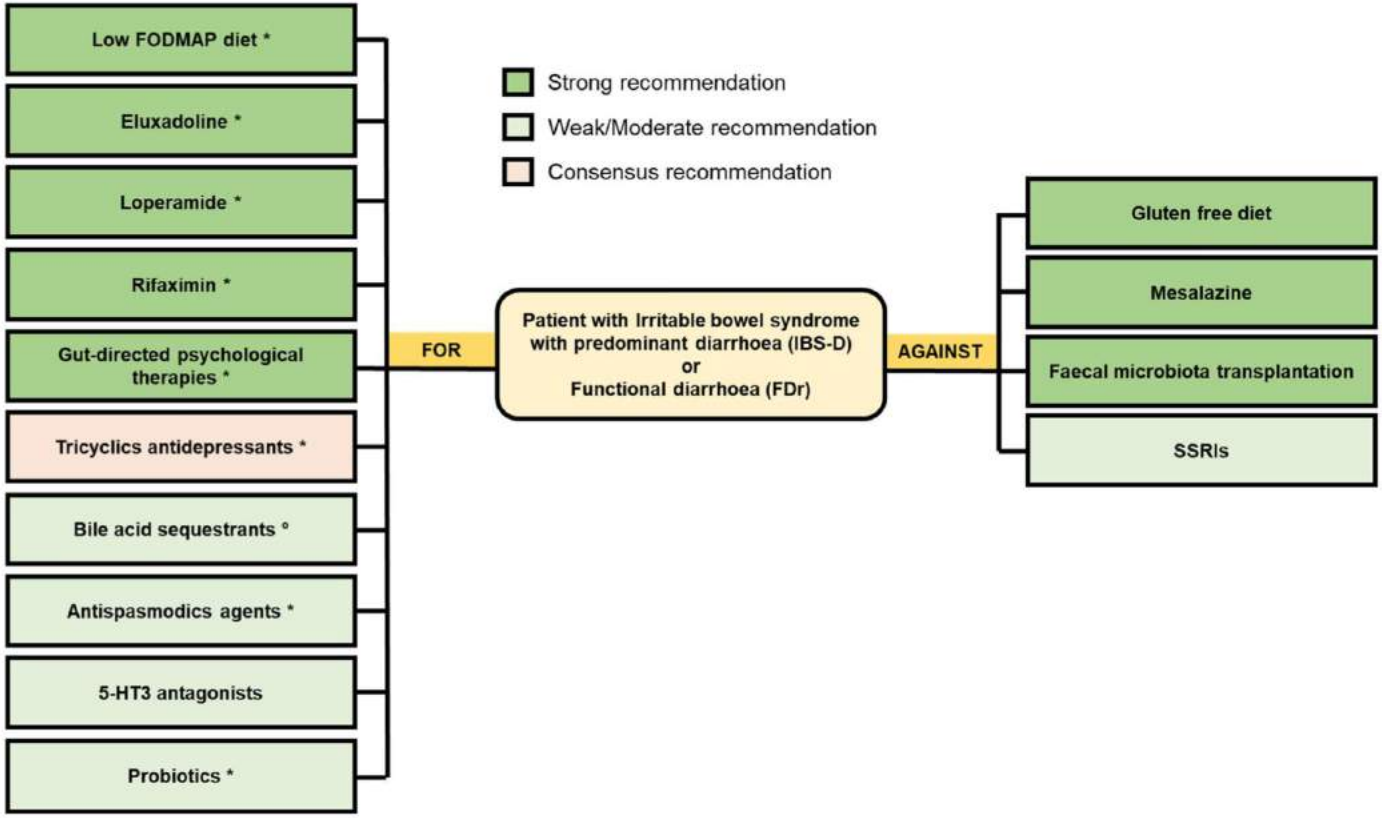


* No / limited evidence for FDr
° in patients with proven bile acid diarrhoea or as initial trial in patients with persistent unexplained chronic diarrhoea

Standard gastroenterologist versus multidisciplinary treatment for functional gastrointestinal disorders (MANTRA): an open-label, single-centre, randomised controlled trial

Chamara Basnayake, Michael A Kamm, Annalise Stanley, Amy Wilson-O'Brien, Kathryn Burrell, Isabella Lees-Trinca, Angela Khera, Jim Kantidakis, Olivia Wong, Kate Fox, Nicholas J Talley, Danny Liew, Michael R Salzberg, Alexander J Thompson

	Standard-care group	Multidisciplinary-care group	p value
Primary outcome (modified intention-to-treat analysis)	26/46 (57%)	82/98 (84%)	0·00045
Intention-to-treat analysis	26/56 (46%)	82/112 (73%)	0·001
Per-protocol analysis	18/34 (53%)	58/69 (84%)	0·001
Much better (Likert 5/5) only	13/46 (28%)	50/98 (51%)	0·010
Patient had adequate relief of symptoms in the past 7 days	29/46 (63%)	81/98 (83%)	0·010

Table 3: **Primary outcome and global symptom improvement**

	Standard-care group	Multidisciplinary-care group	p value
IBS*			
Global symptom improvement	17/26 (65%)	50/59 (85%)	0·044
Mean IBS-SSS score at baseline (SD)	233 (99)	246 (94)*	0·30
Mean IBS-SSS score at discharge (SD)	193 (128)	152 (92)*	0·18
50-point reduction in IBS-SSS from baseline	10/26 (38%)	39/59 (66%)	0·017
50% reduction in IBS-SSS from baseline	5/26 (19%)	21/59 (36%)	0·13
Functional dyspepsia			
Global symptom improvement	6/11 (55%)	23/28 (82%)	0·076
Median Nepean Dyspepsia Index at baseline (IQR)	59 (35–89)	47 (31–67)*	0·33
Median Nepean Dyspepsia Index at discharge (IQR)	35 (18–59)	20 (7–33)*	0·11
50% reduction in the Nepean Dyspepsia Index	3/11 (27%)	13/28 (46%)	0·47

All data are n (%) or n/N (%) unless otherwise specified. IBS=irritable bowel syndrome. SSS=Severity Scoring System.
*Within group reduction from baseline to discharge p<0·05.

Table 4: **Symptom outcomes in IBS and functional dyspepsia**

Lancet Gastroenterol Hepatol 2020

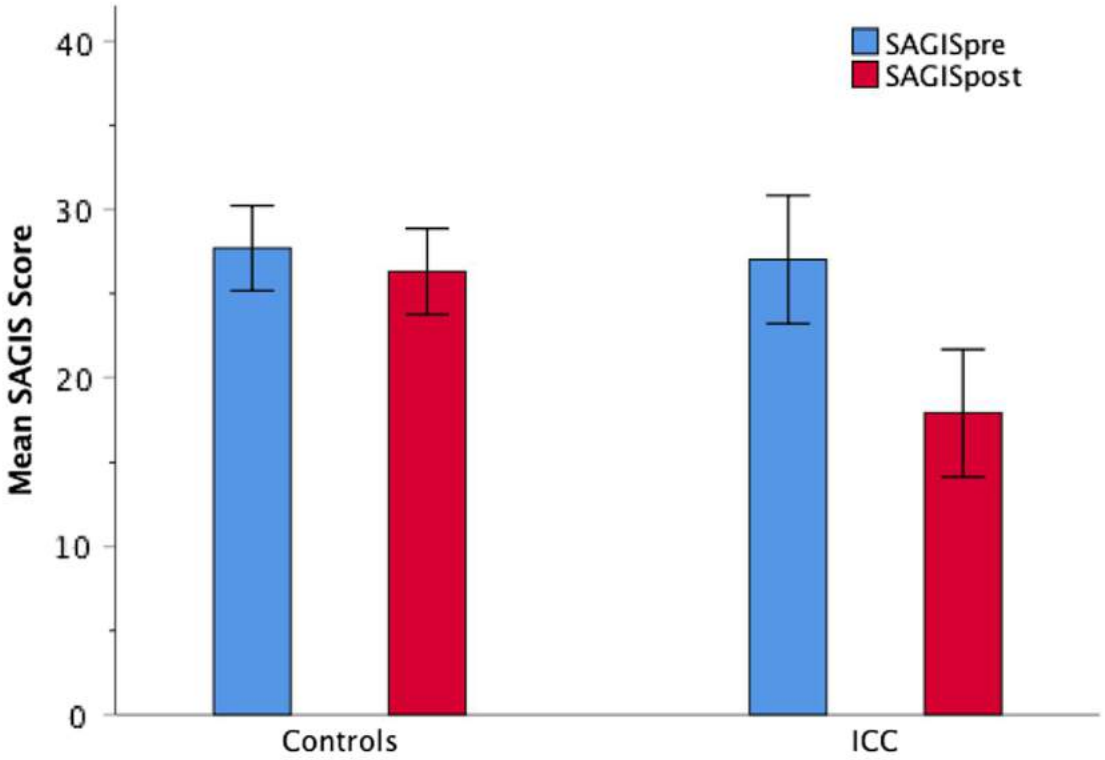
	Standard-care group (n=46)	Multidisciplinary-care group (n=98)	p value
Health-care use in hospital (AU$)			
Median hospital cost per patient (IQR)	$2421 (470–2485)	$2485 (878–2895)	0·0085
Average cost per primary outcome*	$3136	$2549	..
Health-care use outside hospital			
Median number of visits to their GP for any reason	1 (1–3)	1 (0–2)	0·0072
Number of patients who saw their GP for any reason	35 (76%)	52 (53%)	0·008
Median number of visits to their GP for gut symptoms	0 (0–1)	0 (0–0)	0·015
Number of patients who their GP for gut symptoms	16 (35%)	16 (16%)	0·013
Blood tests	13 (28%)	5 (5%)	<0·0001
Gastroscopy	7 (15%)	5 (5%)	0·041
Colonoscopy	5 (11%)	4 (4%)	0·15
Ultrasound	3 (7%)	1 (1%)	0·096
Number of patients absent from work because of gut symptoms during follow-up	17 (37%)	25 (26%)	0·16

Data are n (%) unless otherwise stated. GP=general practitioner. *Calculated as total costs divided by the number of patients with primary outcomes.

Table 6: **Costs and health-care use**

***Lancet Gastroenterol Hepatol* 2020**

Multidisipliner yaklaşım yararlı……



Nicola A. Bray et al. Digestive Diseases and Sciences (2022) 67:5593–5601

KISA MESAJ

- FBH sıklığı benzer oranlarda
- Yönetiminde multidisipliner yaklaşım ön plana çıkmaktadır