



# Gestione terapeutica della stipsi cronica

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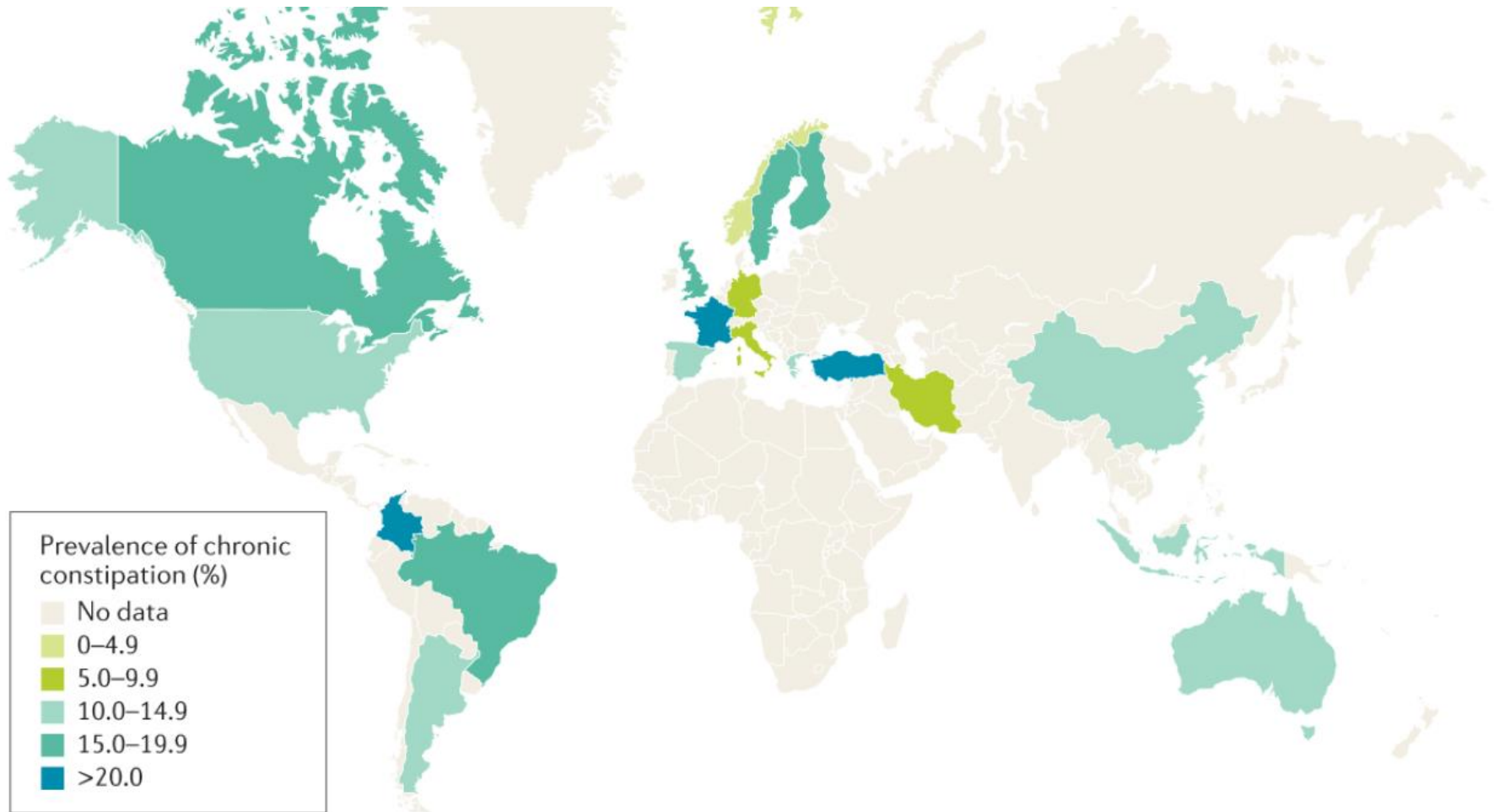
Società Italiana di Neuro-Gastro-Enterologia e Motilità

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Palazzo dei Congressi

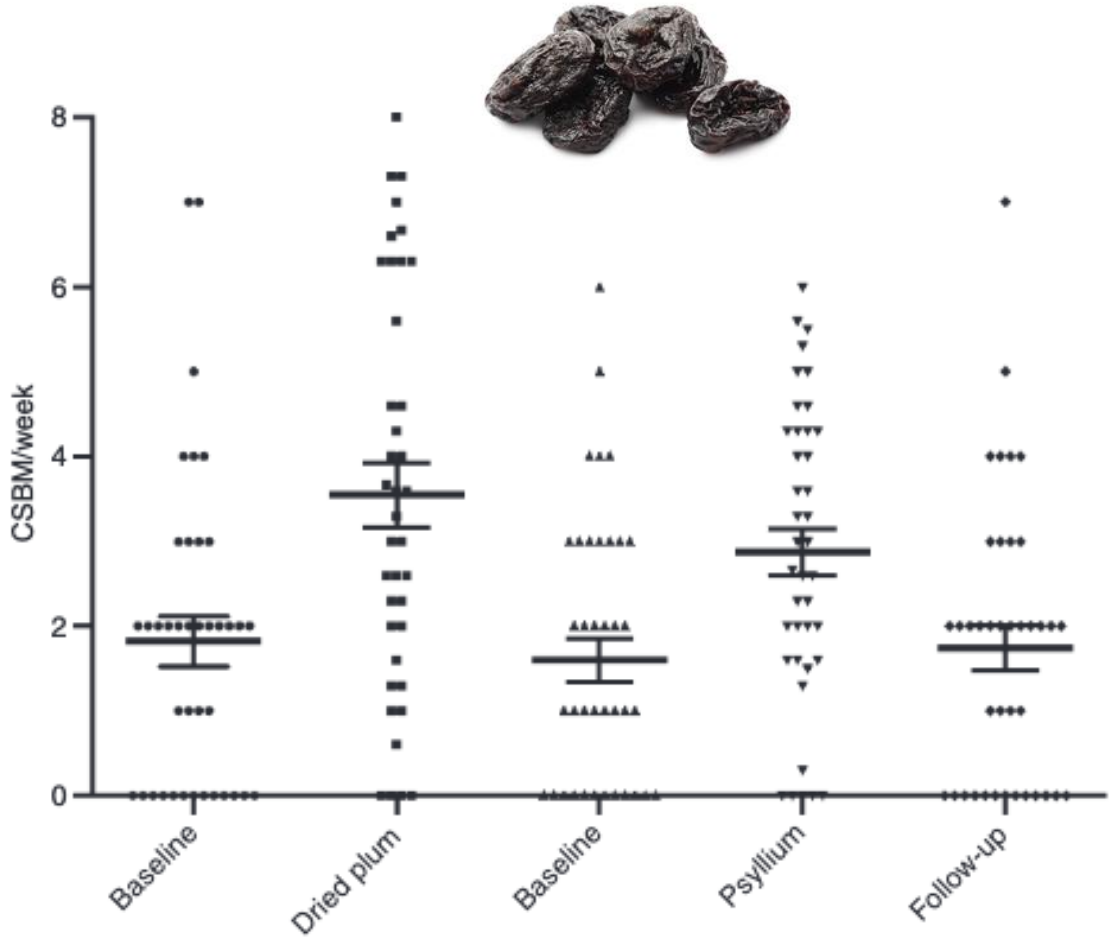
CONGRESSO  
NAZIONALE  
**SINGEM**



# Global prevalence of chronic constipation

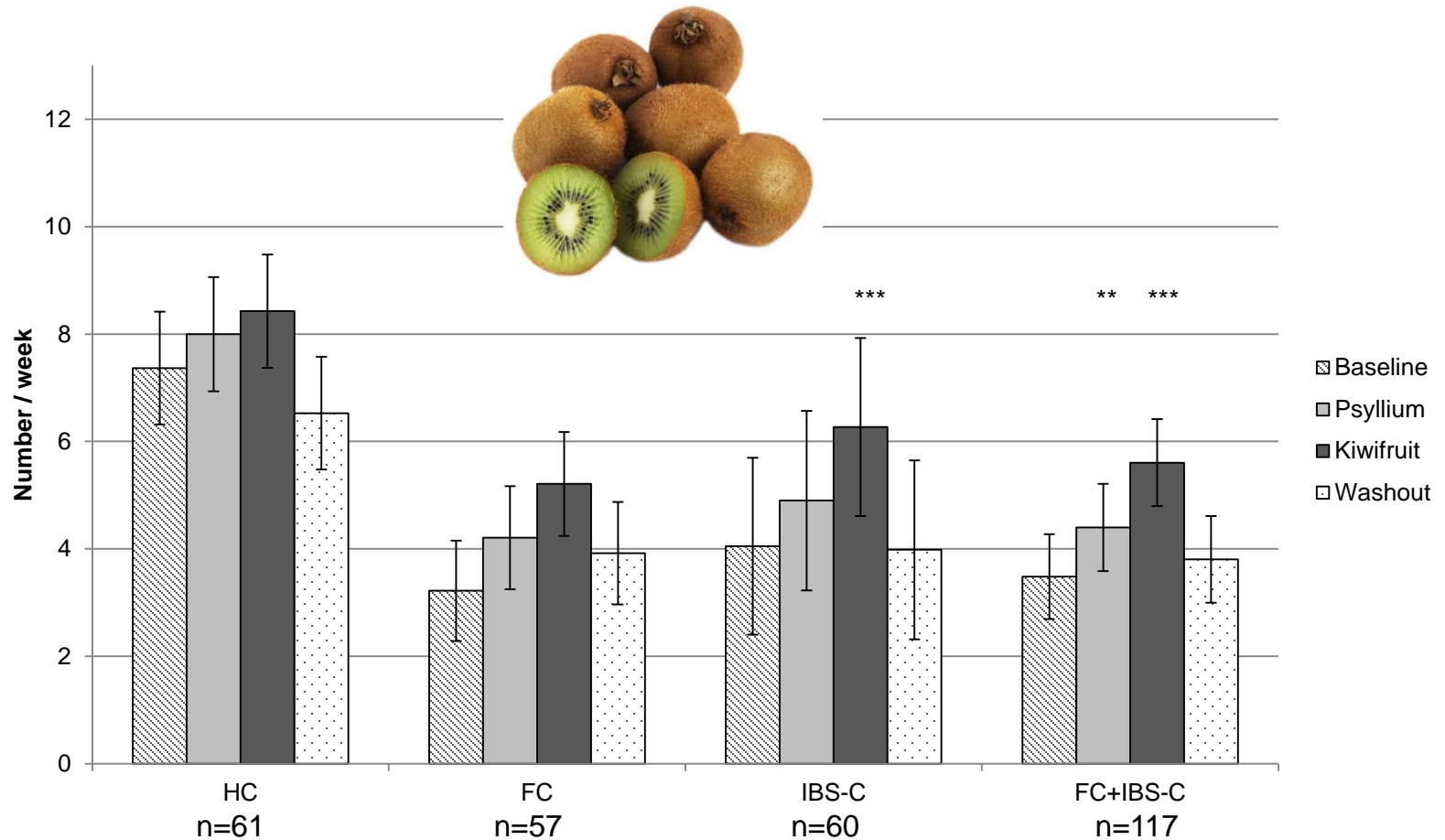


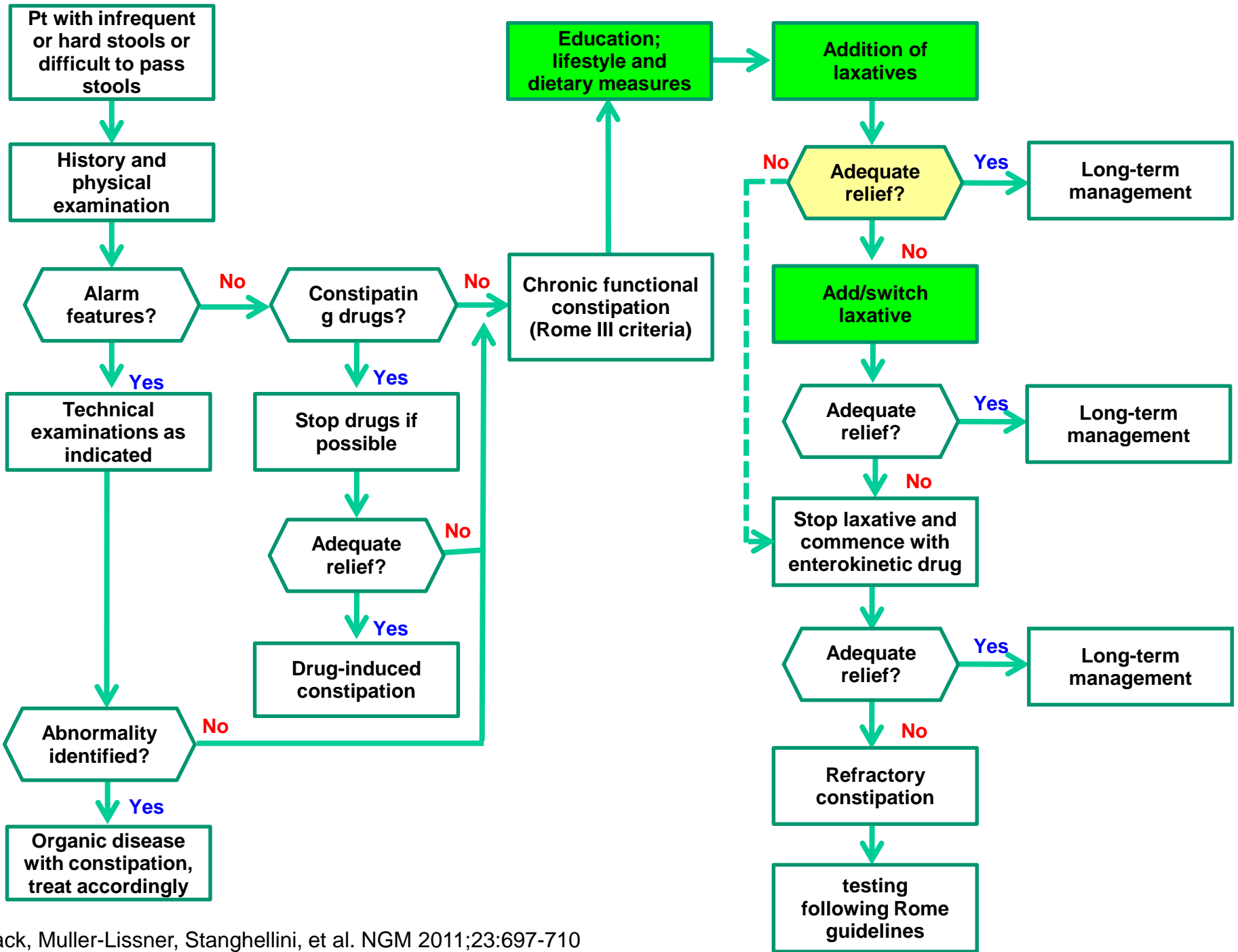
# Dried plums vs. psyllium for constipation



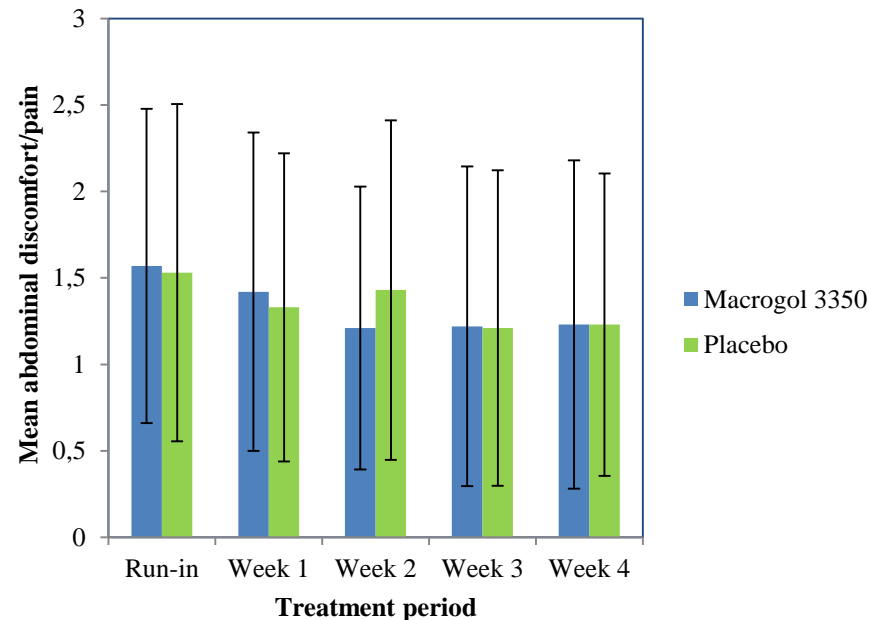
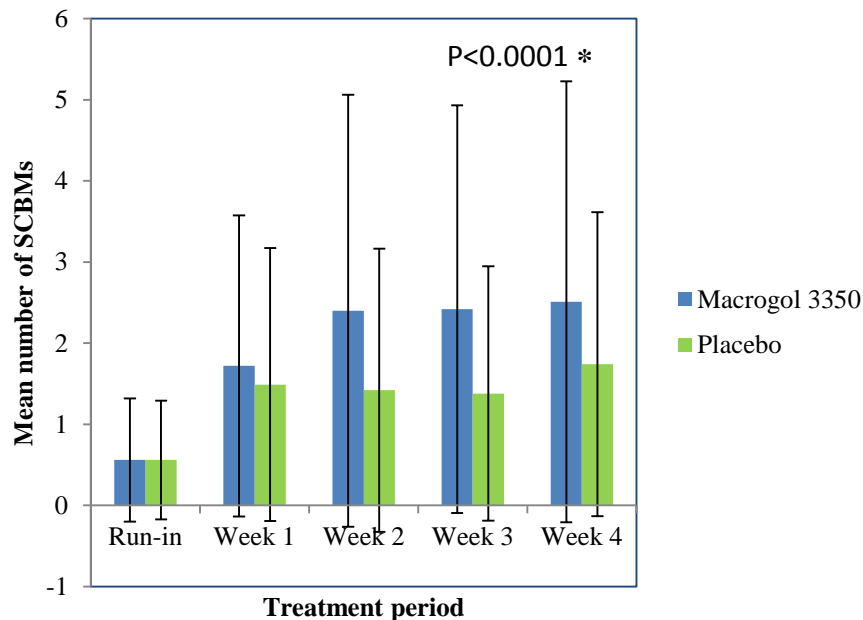
# Effect of kiwifruit in FC and IBS-C

Primary Outcome: CSBM

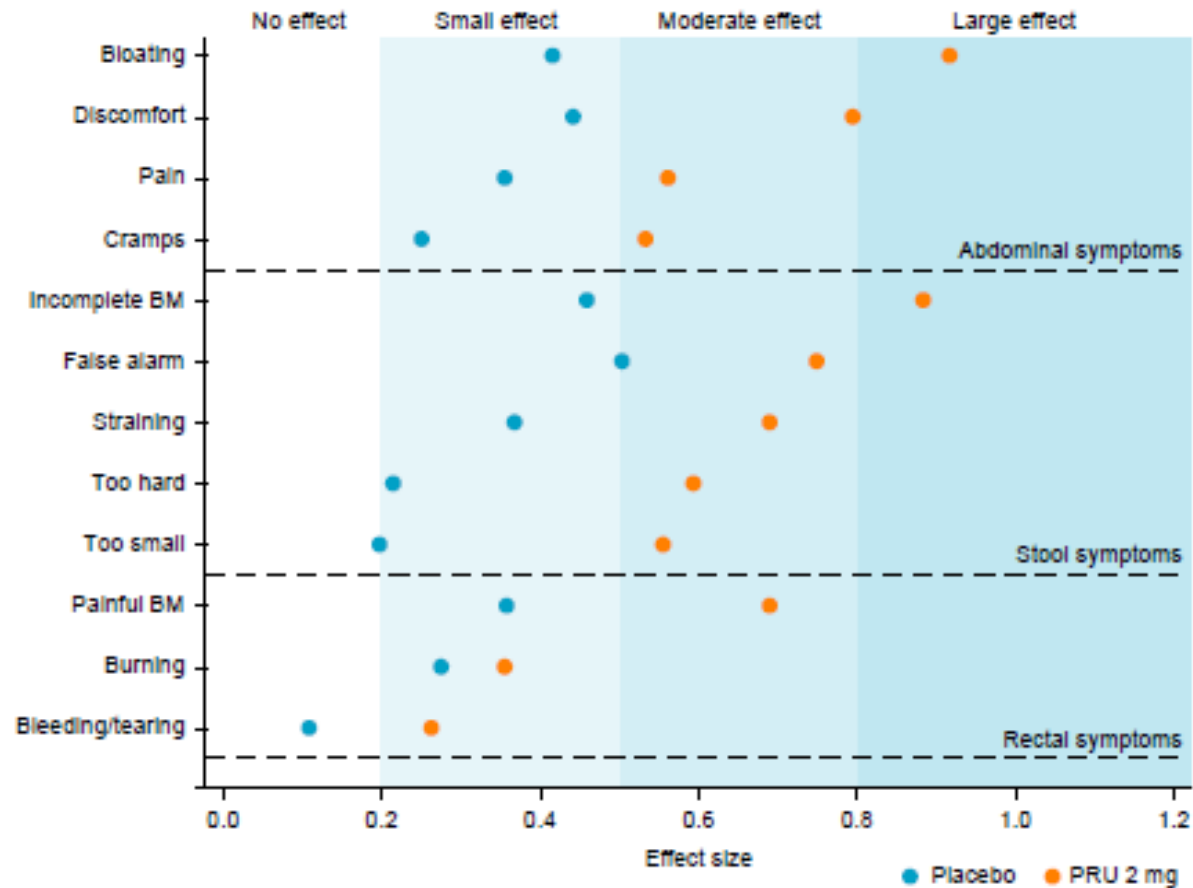




# Effect of macrogol on bowel movements and abdominal symptoms in IBS-C patients



# Effect of prucalopride 2 mg on abdominal, stool and rectal symptoms of patients with chronic constipation



# Linaclootide mechanisms of action

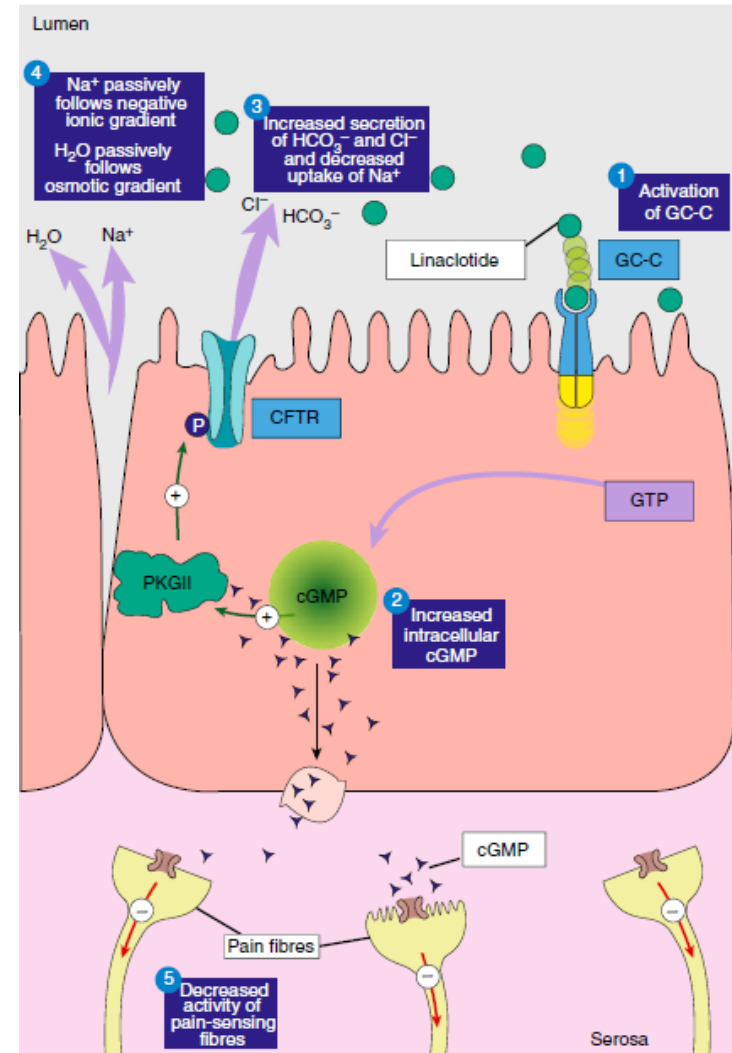
- GC-C: guanylate cyclase c
  - LIGANDS: linaclootide, (uro)guanylin (enteroendocrine, goblet cells), E. coli, Yersinia enterotoxin
- GTP: guanosine triphosphate
- cGMP: cyclic guanosine monophosphate
- PKG: cGMP-dependent protein kinase
- CFTR: cystic fibrosis transmembrane conductance regulator



Linaclootide binds to GC-C receptors on enterocytes



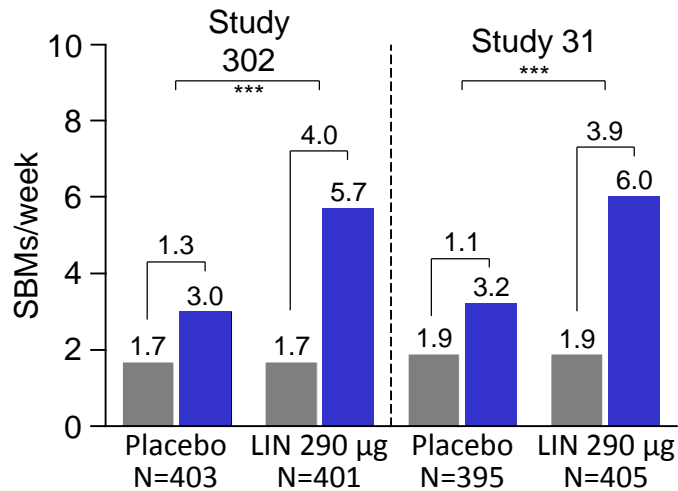
Elevation of cGMP levels increase in anion efflux and fluid secretion



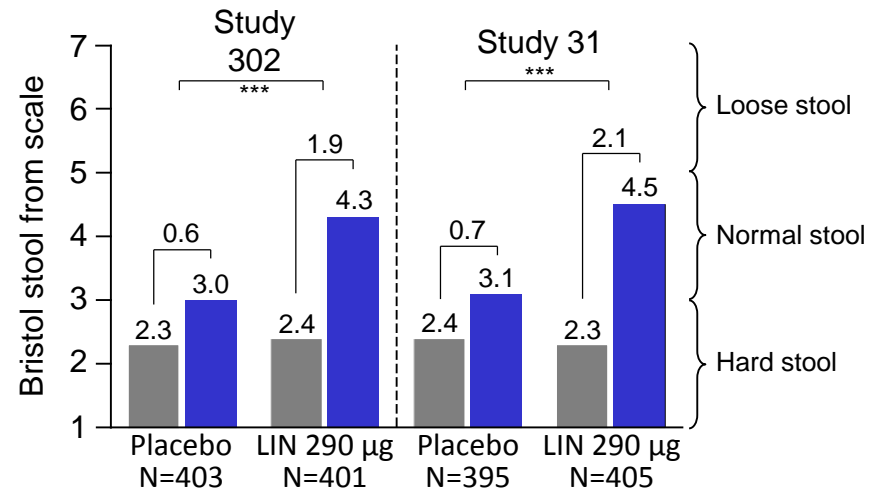


# Effects of linaclotide 290 µg on IBS-C symptoms in Phase III studies

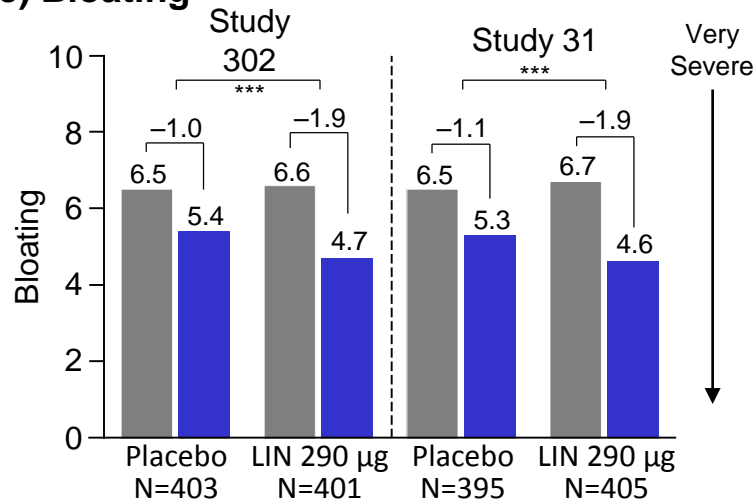
**a) SBM frequency**



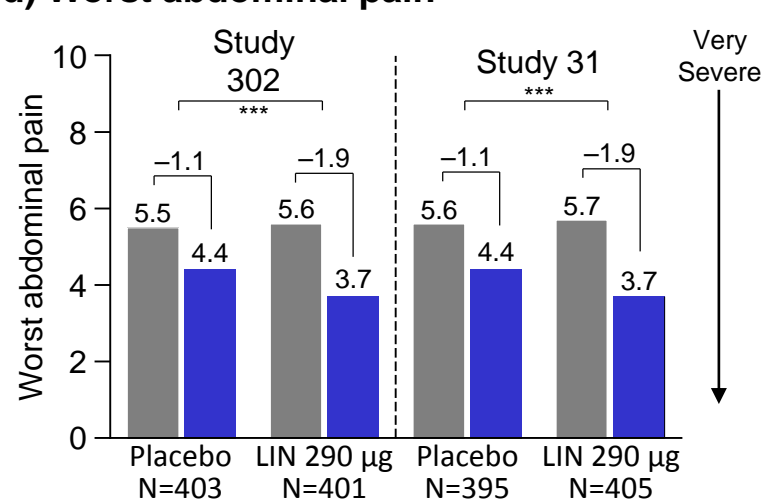
**b) Stool consistency**



**c) Bloating**



**d) Worst abdominal pain**



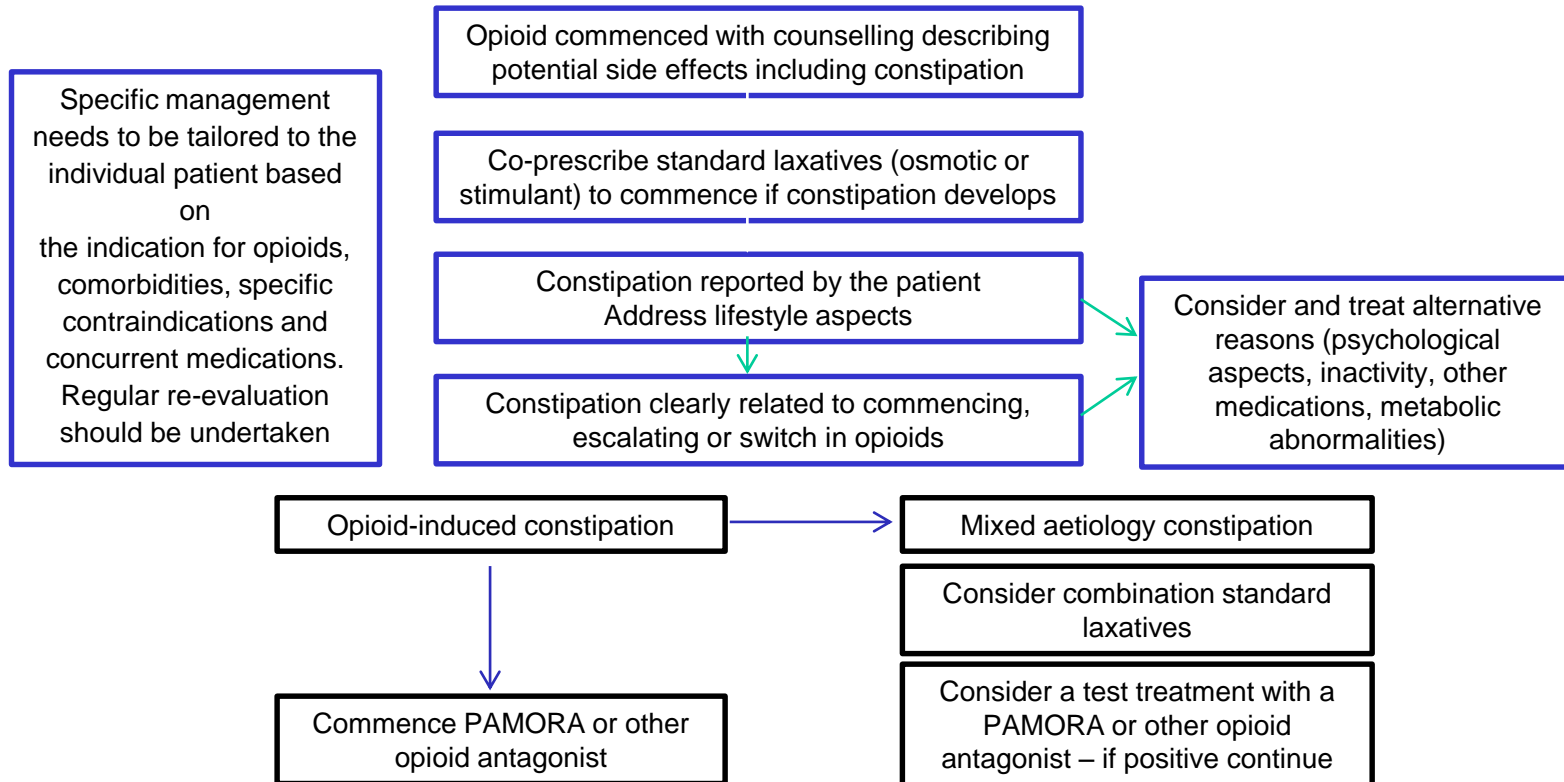
■ Baseline ■ Treatment

\*\* $P < 0.001$  vs placebo; \*\*\* $P < 0.0001$  vs placebo

# Laxatives primarily acting on intestinal mucosal functions

	Mechanism of action	Comment
Linacotide	$\uparrow$ GC-C-R $\rightarrow$ $\uparrow$ cGMP $\rightarrow$ $\uparrow$ CFTR $\rightarrow$ $\uparrow$ H <sub>2</sub> O/HCO <sub>3</sub> /Cl <sup>-</sup>	IBS-C (and CC in US) $\downarrow$ symptoms
Plecanatide	= Linacotide, but pH dependent (= uroguanylin)	FDA approved for CC – role of mucosa pH unclear
Lubiprostone	$\uparrow$ CIC-2 + $\rightarrow$ $\uparrow$ Pg-EP-R on CFTR $\rightarrow$ $\uparrow$ H <sub>2</sub> O/Cl <sup>-</sup>	FDA / EMA approved for CC and IBS-C
Elobixibat	$\downarrow$ ileal BA transporter	IBS-C, $\downarrow$ symptoms (phase 3 results submitted)
Tenapanor	$\downarrow$ Enterocyte Na/H exchanger isoform 3 (NHE3)	IBS-C, $\downarrow$ symptoms (phase 3 ongoing)

# Pragmatic clinical recommendations algorithm



# Efficacy of pharmacological therapies for the treatment of opioid-induced constipation: systematic review and network meta-analysis

Pavit Luthra,<sup>1,2</sup> Nicholas E Burr,<sup>1,2</sup> Darren M Brenner,<sup>3</sup> Alexander C Ford<sup>1,2</sup>

