

# XPERT PERSPECTIVES

*...from DDW*

## *Reporting on* **FGIDs**

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## ***Epidemiology of Fecal Incontinence in US Adults from 2005 to 2010: Prevalence, Trends, and Risk Factors***

*Ditah IC et al. Abstract Sa2028*

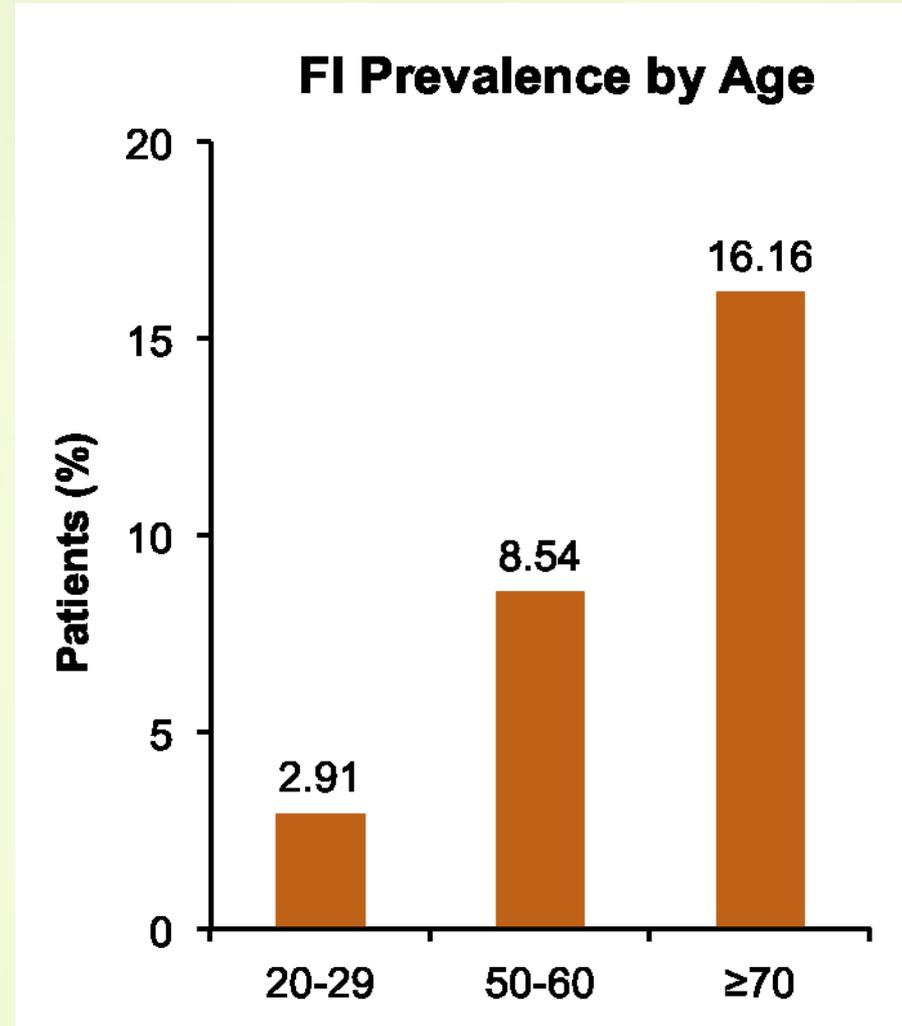
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# Design

- Objective
  - Estimate prevalence of fecal incontinence (FI), analyze trends, and identify risk factors
- Subjects
  - NHANES dataset (N=14,759)
- Methods
  - Validated Fecal Incontinence Severity Index added to NHANES since 2005/2006 survey
  - Data for this study was collected between 2005 and 2010
  - Participants included men and women aged  $\geq 20$  years
  - FI defined as accidental leakage of solid, liquid, or mucus at least once in preceding month

# Results

- Overall prevalence of FI: 8.39%
  - Prevalence similar to that seen in 2005/2006 (8.48%)
- Prevalence of FI by leakage type:
  - Liquid: 6.16%
  - Solid: 1.81%
  - Mucus: 3.0%
- FI occurred at least weekly in 1.13% of study participants
- FI prevalence significantly higher in women (9.45%) vs men (7.27%) ( $P=.002$ )
- FI prevalence increased with age
- Independent risk factors: age, diabetes, female gender, poor health status, urinary incontinence, non-Hispanic whites, >21 stools/week, loose/watery stools



# Conclusions

- FI is a prevalent problem among non-institutionalized US adults, and the incidence remained steady from 2005 to 2010.
- While age remains a strong risk factor, diabetes and chronic diarrhea are potential modifiable risk factors

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## ***Utility of Anorectal Manometry and Anal Ultrasound in Evaluation of Fecal Incontinence***

*Kim SE et al. Abstract Sa2046*

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# Design

- Objective
  - Clarify the utility of anorectal manometry (ARM) and anal endosonography (AES) for diagnosis of FI
- Methods
  - Retrospective chart review of adults referred from October 2007 to November 2012 for FI (N=288)
  - Results for ARM and AES reviewed to determine types of abnormalities seen
  - Patients categorized into 4 groups depending on manometry finding

# Results

- Greatest overall rate of sphincter defect seen in patients with low resting pressure and normal squeeze
- On dividing patients with FI into those with and without sphincter defects, mean resting pressure was not lower in patients with or without defects on AES
- Maximum squeeze pressure was lower in subjects with sphincter defects ( $P=.03$ )
- Anal muscular defects seen infrequently and at a lower rate in males than females ( $P<.05$ )
- Of patients having ARM, 44.6% had normal sphincter resting pressure and squeeze pressure by manometry
- Of those with normal manometry, 24.9% had AES; 25.6% of these patients had notable sphincter defects

## Grouping by Manometry Results

Group	Resting Pressure	Squeeze Pressure	Subjects with AES [n(%)]	AES Subjects with sphincter defects [n(%)]
1 (n=86)	Low	Low	34 (39.5)	10 (29.4)
2 (n=61)	Low	Normal	18 (29.5)	9 (50.0)
3 (n=68)	Normal	Low	19 (27.9)	7 (36.8)
4 (n=173)	Normal	Normal	43 (24.9)	11 (25.6)

# Conclusions

- In one of the largest studies to date, squeeze pressure but not resting pressure is predictive of sphincter defects on AES
- More women are referred for incontinence workup with a higher rate of anal sphincter defect compared to men
- Normal anorectal manometry does not rule out sphincter defects on AES

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***Does Learning of Illness Behavior  
in Childhood Influence the  
Development of IBS?***

*Theron B et al. Abstract Sa1328*

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# Design

- Objective
  - Examine the association of learned illness behavior with IBS in a twin cohort
- Methods
  - 6552 unselected twins asked to complete a validated questionnaire including the social learning of illness scale (4128 replies)
  - Logistic regression used to identify risk factors for each group

# Results

## Factors Associated With Development of IBS (Univariate Analysis)

Variable	ROME III Extended Criteria IBS	ROME III Limited Criteria IBS	Medical Diagnosis IBS
<b>Social Learning of Illness Behavior Scale</b>	0.89 (0.66-1.21, p=0.47)	1.00 (0.99-1.01, p=0.5)	1.15 (1.13-1.17, p<0.01)
<b>Psychomatic Score</b>	1.19 (1.17-1.21, p<0.001)	1.21 (1.19-1.24, p<0.001)	1.15 (1.13-1.17, p<0.001)
<b>Anxiety</b>	1.75 (1.47-2.09, p<0.001)	1.54 (1.19-1.98, p=0.001)	1.84 (1.40-2.42, p<0.001)
<b>Female Gender</b>	2.16 (1.54-3.03, p<0.001)	2.94 (1.48-5.85, p=0.002)	2.19 (1.18-4.05, p<0.001)
<b>Age</b>	0.99 (0.98-0.99, p=0.001)	1.03 (1.03-1.04, p<0.001)	1.11 (1.10-1.12, p<0.001)
<b>Parent IBS</b>	2.48 (2.00-3.08, p=0.001)	1.81 (1.35-2.43, p<0.001)	2.72 (2.15-3.44, p<0.001)

# Results

## Factors Associated With Development of IBS (Multivariate Analysis)

Variable	ODDS Ratio (p value)
Social Learning	1.02 (1.01-1.03, p<0.001)
Anxiety	1.17 (1.12-1.16, p<0.001)
Psychosomatism	1.14 (1.12-1.16, p=0.003)
Female Gender	2.2 (1.3-3.7, p=0.003)
Parent IBS	2.07 (1.6-2.7, p<0.001)
Age	0.99 (0.98-0.99, p=0.009)

# Conclusions

- A higher score for social learning of illness behavior was associated with a medical diagnosis of IBS and this was independent of other risk factors for IBS
- The aspects of learned illness behavior which influenced the development of IBS were reinforcement of the sick role and modeling of illness behavior
- Social learning of illness behavior did not appear to influence IBS as defined by Rome III criteria when a medical diagnosis was not made, suggesting that it drives health care seeking behavior rather than necessarily being an etiologic factor for IBS.

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***Efficacy of Pharmacological Therapies  
for the Treatment of Opioid-Induced  
Constipation: Systematic Review  
and Meta-analysis***

*Brenner DM et al. Abstract Sa1150*

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# Design

- Objective
  - Synthesize evidence on benefit of pharmacologic therapies for the treatment of opioid-induced constipation
- Methods
  - Systematic meta-analysis based on literature search
  - 17 clinical trials included in meta-analysis
    - 14 trials utilized mu-opioid receptor antagonists (N=4101)
    - 2 trials utilized lubiprostone (N=892)
    - 1 trial utilized prucalopride (N=196)

# Results

- Mu-opioid receptor antagonists were superior to placebo for treatment of opioid-induced constipation (RR of failure to respond to therapy = 0.69; 95% CI 0.63-0.75)
- All mu-opioid receptor antagonists were superior to placebo:
  - Methylnaltrexone (six RCTs, 1610 patients, RR = 0.66; 95% CI 0.53-0.83)
  - Naloxone (four trials, 798 patients, RR = 0.64; 95% CI 0.56-0.72),
  - Alvimopan (four RCTs, 1693 patients, RR = 0.71; 95% CI 0.65-0.78)
- Reversal of analgesia did not occur more frequently with active therapy

# Conclusions

- Mu-opioid receptor antagonists are safe and effective for management of OIC
- Additional data are needed to assess lubiprostone and prucalopride for OIC

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## ***Effect of Linaclotide in the Treatment of Irritable Bowel Syndrome and Chronic Constipation: A Meta-Analysis***

*Ahman D et al. Abstract Sa1151*

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# Design

- Objective
  - Estimate efficacy and safety of different daily doses of oral linaclotide in the management of IBS-C and CC
- Methods
  - Systematic meta-analysis based on literature search
  - A meta-analysis was performed using a random effects model to assess the primary outcome ( $\geq 3$  CSBMs/week and an increase of  $\geq 1$  CSBM/ week from baseline) and secondary outcome (frequency of adverse events)
  - Subgroup analysis was performed by dividing the studies into a high-dose group (290-300 mcg daily) and low-dose group (145-150 mcg daily)

# Results

- 6 studies identified (N=3644)
- The mean percentage of patients who reached the primary endpoint for linaclotide and placebo was 22% and 9%, respectively

Outcome	OR (95% CI)	P
<b>CSBM</b>	3.42 (2.06-5.68)	<.01
<b>Adverse events</b>	1.28 (1.11-1.48)	<.01
<b>CSBM (145-150 µg)</b>	3.50 (1.92-6.38)	<.01
<b>CSBM (290-300 µg)</b>	3.84 (2.20-6.69)	<.01
<b>Adverse events (145-150 µg)</b>	1.39 (1.09-1.76)	<.01
<b>Adverse events (290-300 µg)</b>	1.24 (1.07-1.45)	<.01

# Conclusions

- Linaclotide appears to be effective in the treatment of IBS-C and chronic constipation
- Adverse events do not appear to be dose-related

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## ***The Number of Drug Side Effects is Associated with Greater Efficacy in IBS Clinical Trials: The Potential Influence of Unblinding***

*Brenner DM et al. Abstract Sa1158*

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# Design

- Background
  - Placebo and “pre-cebo” effect can influence outcomes
  - Telling patients that a placebo is “powerful” produces a greater response in patients
  - In active compounds, drug activity may lead to adverse events, leading to inadvertent unblinding of subjects during the trial
- Objective
  - Understand the effect of AEs on study outcome in IBS
- Methods
  - Therapies receiving at least a grade IIb from ACG guidelines were included in analysis
  - Peer-reviewed RCTs for each drug were evaluated
  - Efficacy and adverse event data were pooled; number of adverse events in excess of placebo was recorded for each therapy

# Results

- 25 studies were included in analysis (4 tricyclic antidepressants, 7 alosetron, 3 rifaximin, 2 lubiprostone, 3 linaclotide, 6 tegaserod)
  - 5 adverse events were significantly more frequent on TCA than placebo (dry mouth, flushing, constipation, insomnia, and decreased appetite)
  - 2 adverse events were significantly more frequent for alosetron (constipation and abdominal pain/discomfort)
  - 1 adverse event was significantly more frequent for rifaximin
  - 2 adverse events were significantly more frequent for lubiprostone (nausea and diarrhea)
  - 3 adverse events were significantly more frequent for linaclotide (diarrhea, flatulence, and abdominal pain)
  - 1 adverse event was significantly more frequent tegaserod (diarrhea)
- In comparing the number of side effects to the efficacy from meta-analysis, there was a direct correlation using Spearman rank-order correlation ( $R=0.90$ ,  $P<.05$ )

# Conclusions

- This study suggests that in addition to placebo and precebo effects, a third factor that could influence study outcome in IBS is unblinding due to drug side effects
- This systematic review and meta-analysis demonstrates that drugs with more side effects have greater efficacy
- Two possible explanations:
  - Drug is “strong” and drives efficacy
  - Unblinding due to side effects creates a greater placebo effect

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## ***Dextranomer Hyaluronic Acid Sub-Mucosal Injection for the Treatment of Fecal Incontinence: Systematic Review and Meta-Analysis of Clinical Trials***

*Cremonini F et al. Abstract Sa1160*

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# Design

- Objective
  - Assess the efficacy of dextranomer hyaluronic acid sub-mucosal injection for treatment of FI
- Methods
  - Systematic review and meta-analysis of clinical trials assessing dextranomer efficacy in FI

# Results

- Four clinical studies were retrieved, enrolling a total of 306 patients with follow-up 20-36 months
- Pooled rates of FI improvement:
  - 3-6 months: 50.3%
  - 12 months: 56%
  - 20-24 months: 50%
- Mean reduction in FI episodes/month at 6 months was 9.2/month

# Conclusions

- At least half of the patients treated with Dextranomer hyaluronic acid injection appear to show meaningful FI improvement across published studies, with efficacy maintained over time up to at least 24-36 months.
- Caution remains to be exerted when extrapolating results to clinical reality, given the relatively limited number of subjects treated, as opposed to the large general population burden from FI, and since only one out of four studies was randomized and sham-controlled.

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***Identification of Immunological Biomarkers  
in Post-Infectious Irritable Bowel Syndrome:  
A Pilot Study***

*Paden KA et al. Abstract Sa2075*

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# Design

- Background
  - ~1/3 of all IBS cases may be triggered by antecedent infectious gastroenteritis (IGE)
  - The mechanisms underlying this association are poorly understood though immune dysregulation has been implicated
- Objective
  - Identify immunologic biomarkers in post-infectious IBS
- Methods
  - Sera taken from 120 military personnel
  - Patients categorized by:
    - Infectious gastroenteritis followed by IBS
    - IBS without antecedent IGE
    - IGE without subsequent IBS within 2 years of exposure
  - Assayed for analytes previously shown to be associated with immune dysregulation

# Results

- There are measurable differences in levels of IL-8, MIP-1 $\beta$ , and IL-5 between subjects with PI-IBS compared with those with IGE but no subsequent IBS
- Unique post-infectious immune disturbances may relate to development of IBS
- These biomarkers may have clinical utility for IBS diagnosis

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## ***Fodmap Diet Modulates Visceral Nociception by Changing Gut Microbiota and Intestinal Inflammation***

*Zhou S-Y et al. Abstract 164*

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# Design

- Background
  - High-FODMAP foods may exacerbate symptoms of IBS
  - Restricted-FODMAP diets may alleviate IBS
- Objective
  - Examine the effect of FODMAP on visceral nociception
- Methods
  - Wistar rats fed low-FODMAP, high-FODMAP, and regular chow for 2 weeks

# Results

- Results
  - High-FODMAP diet caused intestinal inflammation with 2.8- and 2.5-fold increases in mRNA levels for TNF-alpha and IL-6 in ileal mucosa
  - High-FODMAP diet was associated with 3-fold increase in intestinal permeability
  - Behavioral pain studies showed that rats fed high-FODMAP diet were more significantly more sensitive to colorectal distension
  - HFM increased plasma LPS levels from 0.27 to 0.69 EU/ml, ( $P < 0.05$ ).
  - decrease in unclassified clostridiales (18% vs 70%), Peptostreptococaceal (<1% vs 12%) and Lactobacillaceae (<1% vs 12%) accompanied by a significant increase in Erysipelotrichaceae (69% vs 5%) and Lachnospiraceae (5% vs <1%;  $P < 0.05$  for all comparison).

# Conclusions

- Low FODMAP diet is associated with changes in viscerosensory function, gut microbes and intestinal permeability

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## ***Relationship Between Colonic Transit Time and Symptoms of Constipation: Integrated Results From Clinical Trials of Prucalopride***

*Emmanuel A et al. Abstract Su2061*

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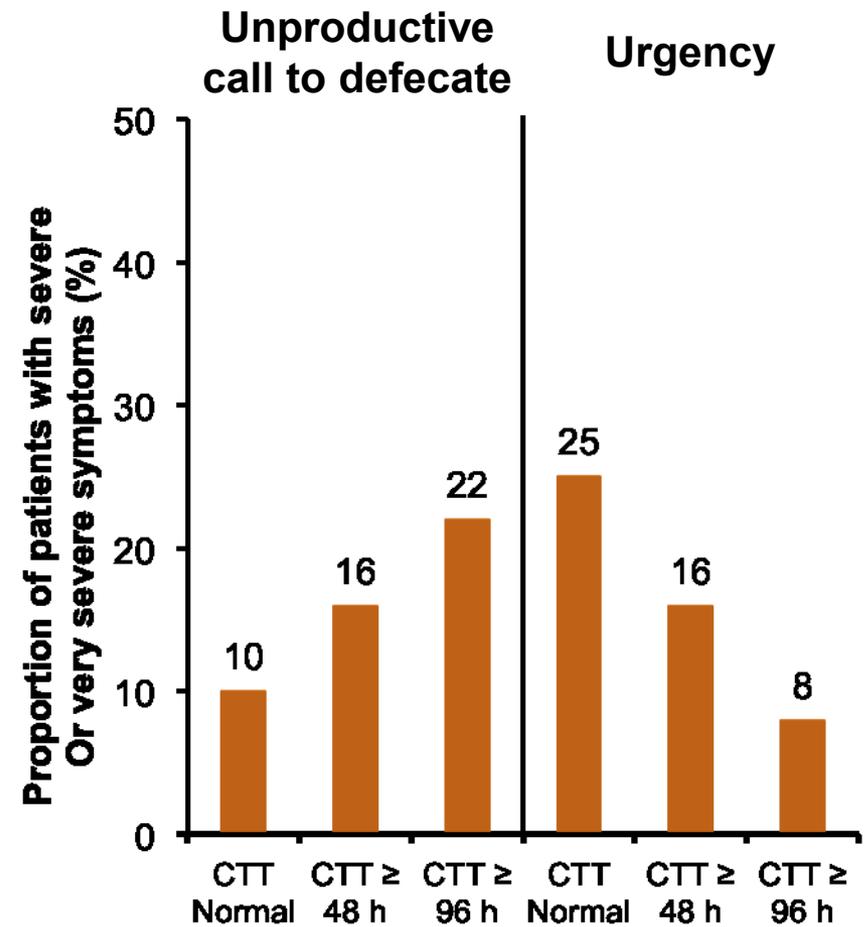
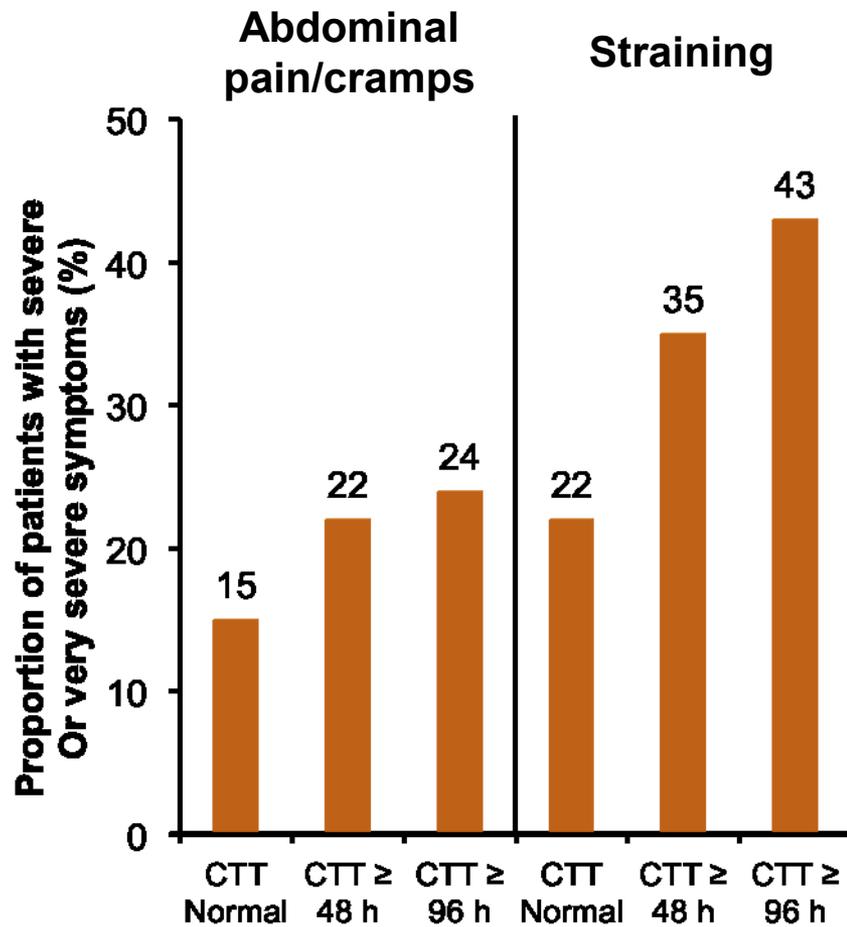
# Design

- Background
  - In patients with CC, treatment with the 5-HT<sub>4</sub> receptor agonist prucalopride is associated with improvements in colonic transit time (CTT) that correlate with bowel movement frequency
- Background
  - Assess relationship between colonic transit time and gastrointestinal symptoms relative to prucalopride use
- Methods
  - Integrated analysis was conducted of three randomized, placebo-controlled, phase 2 dose-finding trials of prucalopride in patients with CC
  - CTT was assessed at start and end of treatment using radio-opaque markers
  - Slow CTT defined as  $\geq 48$  hours; very slow CTT defined as  $\geq 96$  hours
  - Symptoms assessed at every visit for symptom severity
  - 280 patients included in analysis

# Results

- Mean baseline CTT was 66 hours (range: 2-144 hours)
- 70% of patients (n = 196) had slow CTT
- After treatment with prucalopride 2mg and 4mg, CTT was reduced by 12 hours (95% confidence interval [CI]: -18.9, -5.1) and 14 hours (CI: -20.5, -7.4), respectively; CTT increased by 0.5 hours (CI: -4.5, +5.5) with placebo
- Of patients with slow CTT at baseline, 16%, 68% and 65% had normal CTT after treatment with placebo, prucalopride 2mg and prucalopride 4mg, respectively

# Results



# Conclusions

- This study is the first to show a relationship between idiopathic slow CTT and symptom severity in patients with CC
- Slower CTT is associated with a greater need to strain, unproductive calls to defecate and abdominal pain/cramps

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***Impact of Chronic Constipation Severity  
on the Developing Colorectal Cancer  
and Benign Neoplasm***

*Guerin A et al. Abstract Su2017*

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# Design

- Objective
  - To estimate the impact of CC severity on the risk of developing CRC or benign neoplasm
- Methods
  - Patients with CC identified from a large retrospective US claims database
  - Indicators of severity included:
    - $\geq 2$  CC-related office visits
    - A CC-related medical procedure
    - Gastrointestinal specialist visit
    - A prescription fill for a laxative
  - Based on number of indicators, patients were stratified as:
    - Mild (no indicator)
    - Severe (1 indicator)
    - Very severe ( $\geq 2$  indicators)
  - CC patients matched 1:3 to CC-free patients by demographics

# Results

- Compared to CC-free patients, the adjusted incidence of developing CRC was significantly higher in severe and very severe patients
- Risk for CRC increased incrementally with severity of CC

	Adjusted Incidence Rate Ratio CC vs. CC-free patients IRR (95% CI)	P-Value	
<b>CRC</b>			
<b>Mild</b>	0.83 (0.62-1.10)	0.190	
<b>Severe</b>	1.40 (1.18-1.66)	<0.001	*
<b>Very Severe</b>	2.26 (1.94-2.64)	<0.001	*
<b>Colorectal Benign Neoplasm</b>			
<b>Mild</b>	1.40 (1.29-1.52)	<0.001	*
<b>Severe</b>	2.03 (1.93-2.13)	<0.001	*
<b>Very Severe</b>	3.30 (3.16-3.45)	<0.001	*

# Conclusions

- In a large, retrospective, US claims database, the risk of developing CRC and benign neoplasms over time increased with the level of CC severity

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***Postinfectious Irritable Bowel Syndrome and  
Functional Dyspepsia Following an  
Outbreak of Tap Water Contamination***

*Van Wanrooij S et al. Abstract Su2031*

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# Design

- Objective
  - Evaluate risk factors for PI-IBS and PI-FD in a cohort of patients exposed to contaminated drinking water
- Methods
  - Subjects included those exposed to an outbreak of infectious gastroenteritis caused by contamination of drinking water (N=18,398)
  - Survey sent focusing on demographics, Rome III criteria, and bowel habits before, during, and after outbreak, and psychological profile within 0-3 months and 1 year after outbreak
  - 1377 surveys returned

# Results

- 311 cases of infectious gastroenteritis reported
  - 15.6% of those who developed IGE during outbreak had PI-IBS after 1 year vs 6.5% who did not develop IGE during outbreak (OR 2.6; 95% CI 1.4-1.7;  $P=.001$ )
  - 19% of IGE patients developed FD at 1 year vs 12% of those who did not develop IGE (OR 1.8; 95% CI 1.1-3.1;  $P=.030$ )

## Risk Factors for PI-IBS and PI-FD

	PI-IBS	nonIBS	Univariate	PF-FD	nonFD	Univariate
	N=28	N=151	p-value	N=28	N=117	p-value
Female, N (%)	18 (64)	77 (51)	§ NS	22 (79)	55 (49)	§ NS
Age at time of outbreak, years: mean (SD)	41,3 (±12,8)	52,0 (14,9)	*0.001	50 (±13)	50 (±15)	*0.004
<b>Exposure to tap water, N (%):</b>						
Not reported	11	46		7	38	
High Exposure (=drinking tap water)	11 (64,7)	60 (57,1)	NS	8 (38)	32 (41)	NS
<b>Self reported symptoms during outbreak:</b>						
> 7 days	7 (25)	17 (11)	*0.003	5 (22)	7 (17)	§ NS
Bloody diarrhea, N (%)	1 (4)	4 (3)	NS	1 (4)	2 (2)	NS
Fever, N (%)	2 (7)	33 (22)	NS	7 (25)	21 (18)	NS
Severe abdominal cramps, N (%)	12 (43)	34 (23)	*0.027	7 (25)	30 (26)	§ NS
Severe abdominal pain, N (%)	7 (25)	23 (15)	NS	5 (18)	18 (15)	Ns
<b>Self reported medication during outbreak, N (%):</b>						
Antibiotics	4 (14)	18 (12)	NS	4 (14)	15 (13)	NS
<b>Psychological factors:</b>						
Abnormal anxiety (HADS score ≥11), N (%)	7 (25)	12 (8)	*0.011	5 (18)	8 (7)	§ NS
Abnormal depression (HADS score ≥11), N (%)	1 (4)	6 (4)	NS	4 (14)	2 (2)	NS
Somatization score (PHQ-12, mean ±SD)	7,1 (±4,6)	3,9 (±3,2)	*0.001	6,0 (±4,7)	3,3 (±2,8)	*0.006

# Conclusions

- An episode of acute gastroenteritis due to contaminated drinking water is associated with an increased risk to develop IBS or FD
- Somatization, but not anxiety or depression, and younger age were identified as independent risk factors for both PI-IBS and PI-FD

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***Functional Bowel Symptoms in Quiescent  
Inflammatory Bowel Diseases:  
Role of Epithelial Barrier Disruption  
and Low Grade Inflammation***

*Vivines-Nebot M et al. Abstract Su2035*

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# Design

- Objective
  - Determine the role of colonic barrier defects and low-grade inflammation to explain the presence of irritable bowel syndrome (IBS)-like in quiescent inflammatory bowel disease (IBD)
- Methods
  - Caecal biopsies were collected in 51 IBS, 49 quiescent IBD (31 Crohn disease (CD) and 18 ulcerative colitis (UC)), and 27 healthy controls
  - Integrity of epithelial barrier was evaluated by measuring paracellular permeability in biopsies
  - Low-grade inflammation assessed by evaluating mucosal intraepithelial lymphocyte and mast cell counts and mRNA expression of TNF- $\alpha$

# Results

- IBS-like disease found in 35.4% and 38% of CD and UC patients
- Paracellular permeability was significantly increased in both quiescent IBD having IBS-like symptoms and IBS, compared with quiescent IBD without IBS-like symptoms ( $P<.01$  respectively) or controls ( $P<.01$  respectively)
- Significant lower expression of ZO-1 and alpha catenin were found in both IBS and quiescent IBD having IBS-like symptoms
- Intraepithelial lymphocytes and TNF- $\alpha$  were significantly increased in quiescent IBD having IBS-like symptoms, but not in IBS
- Mast cells were significantly elevated in IBS and quiescent IBD

# Conclusions

- In quiescent IBD, IBS-like symptoms relate to the persistence of subclinical inflammation associated with elevated colonic paracellular permeability
- Persistent increased of TNF- $\alpha$  in colonic mucosa may contribute to epithelial barrier defects associated with abdominal pain in quiescent IBD, but not in IBS
- Optimization of anti-inflammatory therapy may be considered in quiescent IBD having IBS-like symptoms

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## ***Lubiprostone Improves Complete Spontaneous Bowel Movement Frequency in Chronic Non-Cancer Pain Patients With Opioid-Induced Constipation***

*Mareya SM et al. Abstract Su2041*

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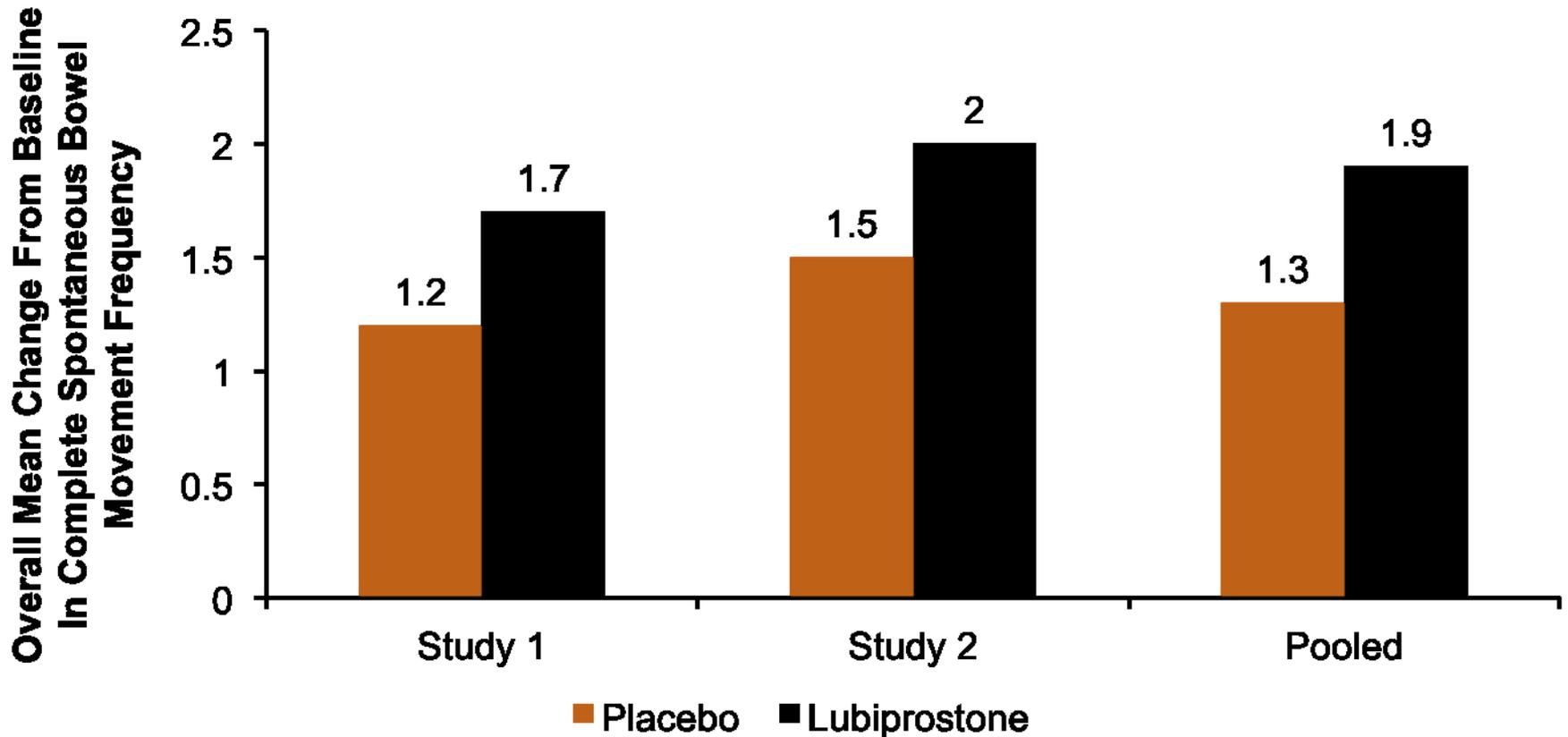
Gastrointestinal  
Health Foundation

# Design

- Objective
  - Examine effect of linaclotide on CSBM frequency in patients with opioid-induced constipation
- Methods
  - Adults  $\geq 18$  years on chronic opioid therapy with OIC, defined as  $< 3$  spontaneous bowel movements (SBMs)/week, were randomized to receive lubiprostone 24 mcg or placebo twice daily in a double-blind fashion for 12 weeks
  - An SBM was defined as a bowel movement for which no use of a rescue medication (eg, laxative or stool softener) had occurred for the previous 24 hours
  - Overall change from baseline in CSBM weekly rate ( $[168 \text{ hours} \times \text{number of CSBMs}] / [\text{hours observed}]$ ) for the 12-week treatment period was examined for the lubiprostone and placebo groups, as well as weekly and monthly changes in CSBM frequency

# Results

## CSBM Frequency



$P=$ .001 for study 1;  $P=$ .101 for study 2;  $P\leq$ .001 for pooled analysis

# Conclusions

- Integrated analysis of pooled data from 2 randomized, double-blind, placebo-controlled studies confirmed the efficacy of lubiprostone in increasing CSBM rates in chronic, non-cancer patients with OIC

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***Spirochaetosis Is Associated With  
Symptoms of Irritable Bowel Syndrome (IBS)  
in a General Population (the Popcol Study)***

*Walker MM et al. Abstract Mo2047*

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# Design, Results, and Conclusions

- Objective
  - Examine relationship between spirochaetosis in colonic biopsies and IBS
- Methods
  - Colonoscopy with biopsies performed in 746 subjects
  - Spirochaetosis was identified by immunohistochemistry
- Results
  - 17 patients diagnosed with intestinal spirochaetosis
  - 37% of cases with spirochaetosis had IBS symptoms (Rome II) (OR 3.59;  $P=.015$ )
- Conclusions
  - Prevalence of spirochaetosis is ~2.2%
  - Spirochaetosis is commonly associated with symptoms of IBS

**XPERT**  
**PERSPECTIVES**  
*...from DDW*



**Reporting on FGIDs**

***ROME III Functional Constipation (FC) and  
Irritable Bowel Syndrome - Constipation  
Predominant (IBS-C) - Truly Distinct  
Disorders or One Disease Spectrum?***

*Koloski NA et al. Abstract Tu2064*

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# Design

- Objective
  - To determine whether FC and IBS-C can be discriminated in terms of demographic, lifestyle, psychological and quality of life variables
- Methods
  - Survey including questions on Rome III functional gastrointestinal symptoms, health care seeking, demographics, lifestyle, anxiety and depression, and mental and physical functioning (returned by 3260 patients)
  - FC and IBS defined by strict Rome III criteria

# Results

- 206 people met criteria for Rome III FC
- 109 met Rome III criteria for IBS-C

	FC	IBS-C	Controls
Age (M in yrs)	56.3	52.9	55.9
Constipation Onset Age (M in yrs)	33.7 a	27.8	N/A
Gender (% female)	76.2 b	83.3 c	46.5
>High School Education (% never)	58.2	61.5	63.0
Health Care Seeking (% never)	64.6 a	49.5	86.2
Smoking (% never)	56.2	49.5	52.5
Alcohol (% risky level)	7.6b	12.2	16.9
Exercise (% walked/2wks)	58.5 a	70.6	63.5
Anxiety (M)	10.1 b	10.5 c	9.7
Depression (M)	5.7 a,b	6.1c	5.0
Mental Functioning (M)	45.6 a,b	41.5 c	47.3
Physical Functioning (M)	46.5 b	44.4 c	49.9

<sup>a</sup> $P < .05$  FC vs IBS-C, <sup>b</sup> $P < .05$  FC vs. controls, <sup>c</sup> $P < .05$  IBS-C vs controls

# Conclusions

- FC and IBS-C appear to be distinct disorders with FC associated with better outcomes and links with lower exercise levels compared with IBS-C

# **XPERT PERSPECTIVES**

*...from DDW*

*Reporting on **FGIDs***



## ***Antibodies to Cytolethal Distending Toxin B and Auto-Antibodies to Human Vinculin Are Elevated in IBS Subjects***

*Morales PB et al. Abstract Tu2056*

Accredited by

# Design

- Background
  - Recent data support that irritable bowel syndrome (IBS) can develop after gastroenteritis. In an animal model of post-infectious IBS, cytolethal distending toxin B (CdtB) appears to be important in the development of IBS and small intestinal bacterial overgrowth (SIBO).
- Methods
  - Consecutive IBS subjects meeting Rome III criteria were recruited from a GI Motility clinic (n=45).
  - 30 subjects with IBD were recruited from a tertiary care IBD clinic.
  - 20 healthy controls were identified based on a negative symptom questionnaire.

# Results

- In plates coated with CdtB, the mean OD for IBS serum was  $1.89 \pm 0.12$ . This was significantly greater than for subjects with IBD ( $1.35 \pm 0.22$ ) ( $P < 0.05$ ) or healthy controls ( $1.46 \pm 0.20$ ) ( $P < 0.05$ ).
- In plates coated with vinculin, the mean OD for IBS serum was  $0.53 \pm 0.07$ . This was significantly greater than for subjects with IBD ( $0.21 \pm 0.09$ ) ( $P < 0.05$ ).
- There was a trend for a difference from healthy controls ( $0.31 \pm 0.10$ ) ( $P = 0.11$ ).
- There was no difference between IBS-C or IBS-D for either antibody.

# Conclusions

- Both anti-CdtB and autoimmune anti-vinculin antibodies are detectable in IBS subjects and are seen to be elevated in IBS compared to controls and IBD.
- The detection of anti-CdtB and anti-vinculin suggest new clues to the diagnosis and pathophysiology of IBS. This is the first study to link acute gastroenteritis to an autoimmune process in IBS.

# ***The Functional Dyspepsia Treatment Trial (FDTT) Key Results***

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Hasheem El-serag,<sup>7</sup> Paul Moayyedi,<sup>8</sup> Lawrence A. Szarka,<sup>1</sup> Linda M. Herrick,<sup>1</sup> Katherine  
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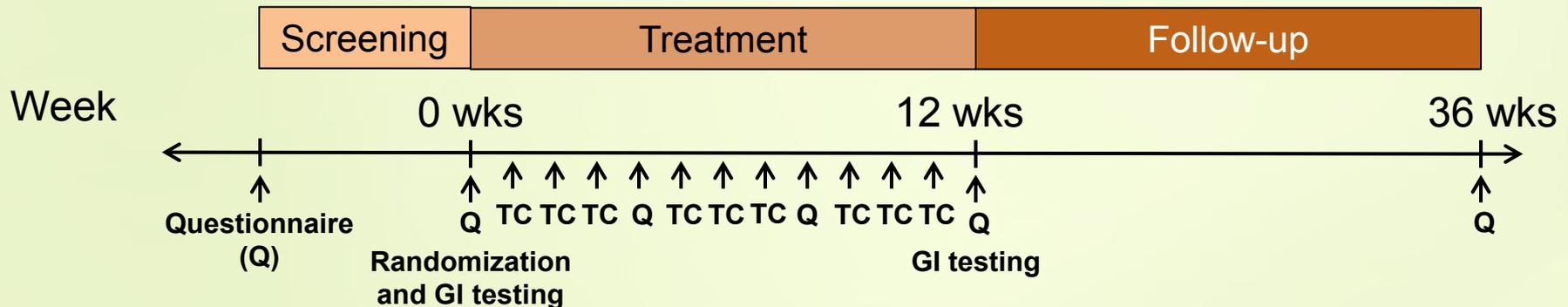
# Background

- Functional dyspepsia (FD) is a common functional GI disorder characterized by epigastric pain or discomfort, or meal related symptoms
- Although alterations in gastric emptying or accommodation has been documented in a subset of patients with FD, the pathophysiology remains unknown
- “Antidepressant” neuromodulating agents are frequently used to treat FD, but any efficacy in FD—particularly in those without depression—remains unclear

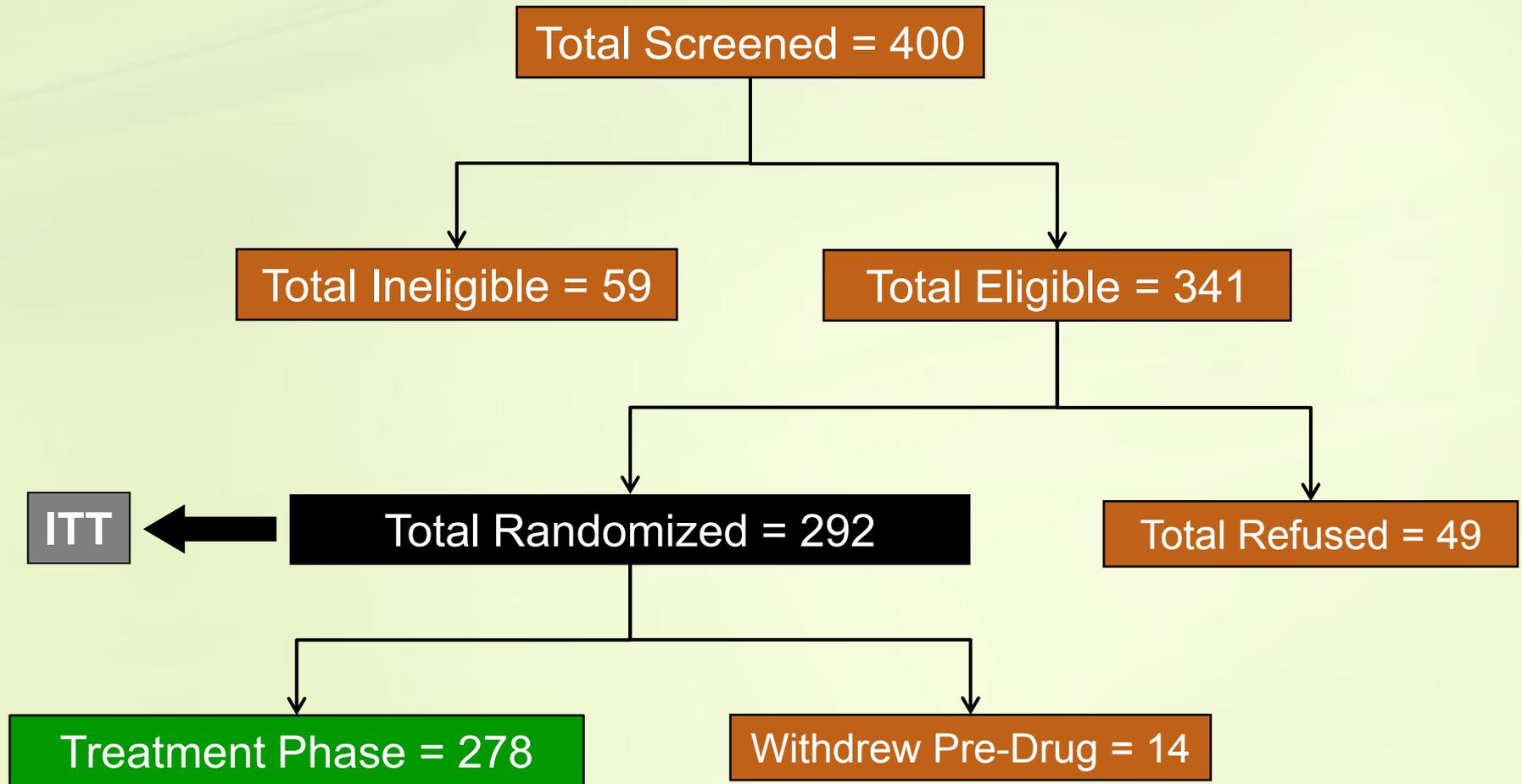


# Methods: Study Design

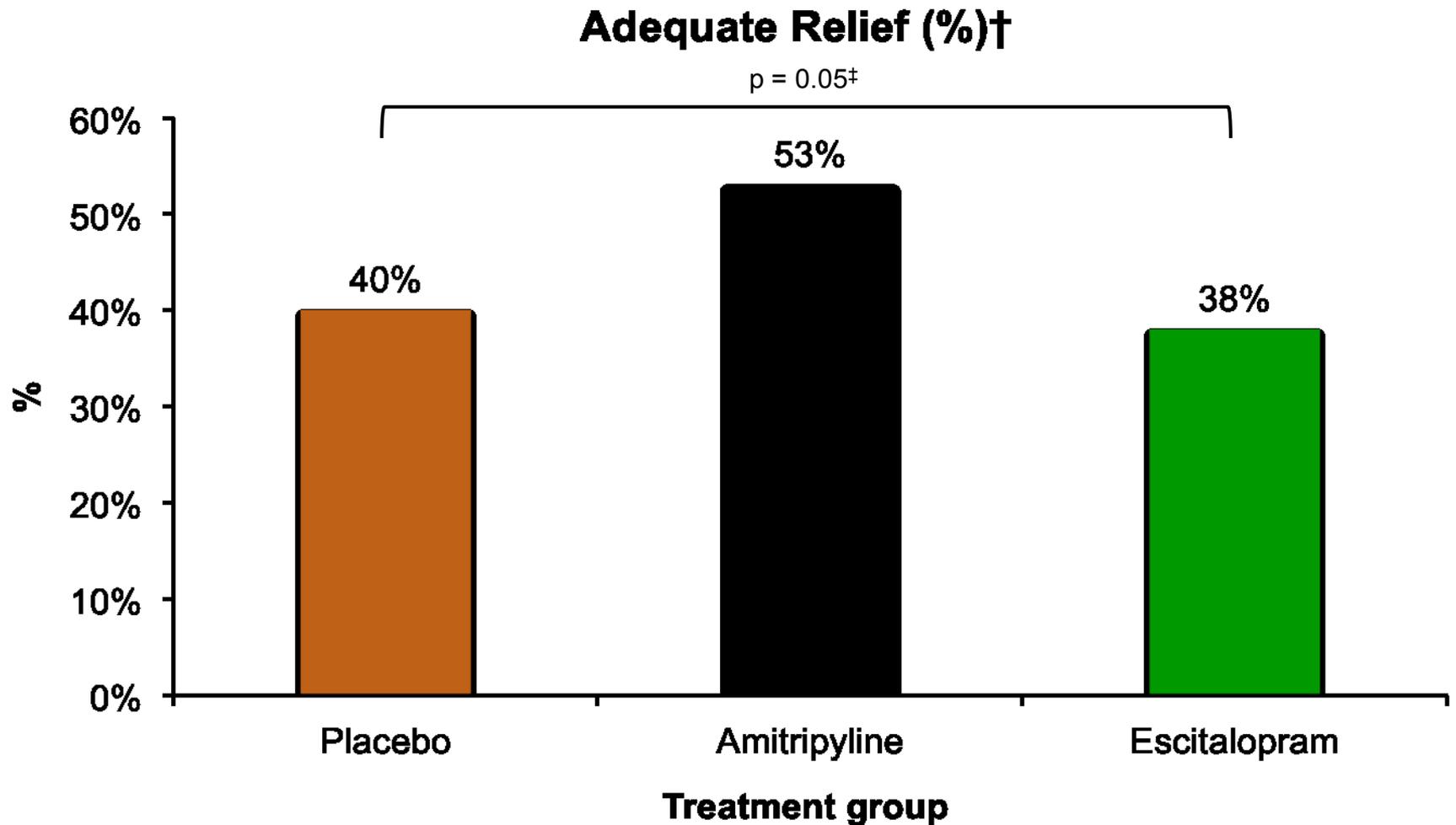
- Design: Prospective, randomized, double-blind, double-dummy parallel group trial:
  - 3 arms
    1. Placebo
    2. Amitriptyline 50 mg
    3. Escitalopram 10 mg



# Methods: Recruitment



# Results: Primary Endpoint (ITT)

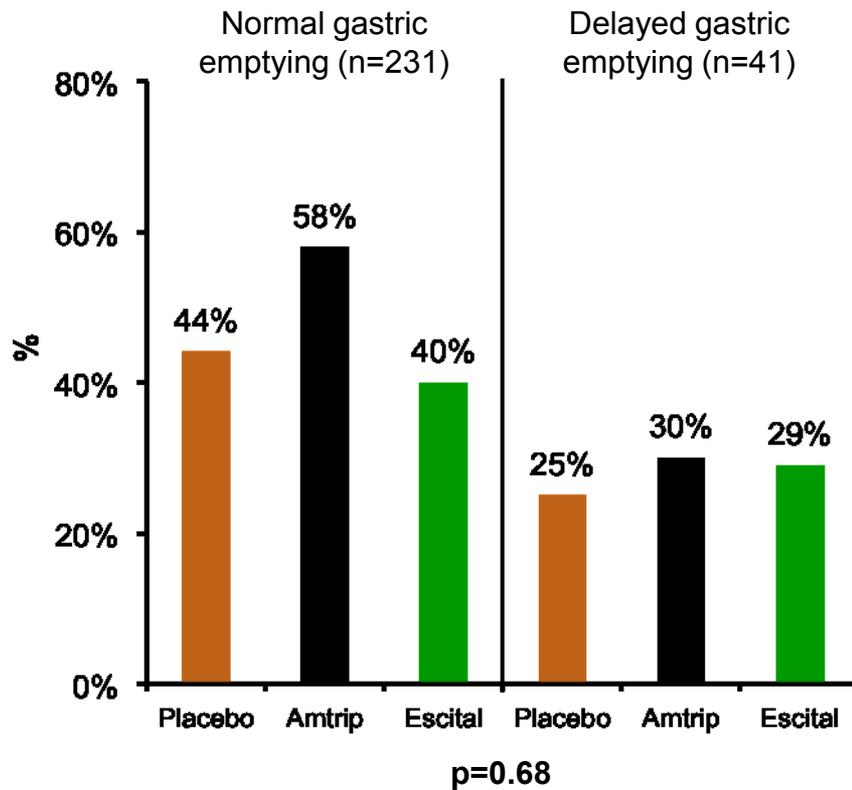


† ≥ 5 weeks of adequate relief

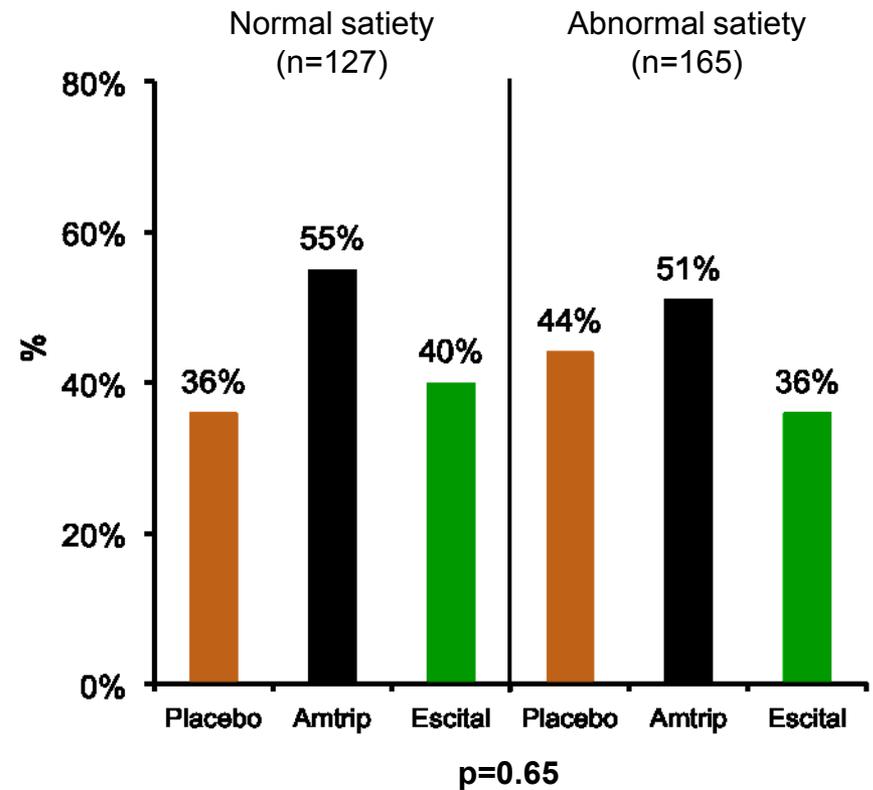
‡Overall treatment effect from logistic regression model incorporating balancing factors

# Results: Baseline GI Physiology

## Adequate Relief



## Adequate Relief



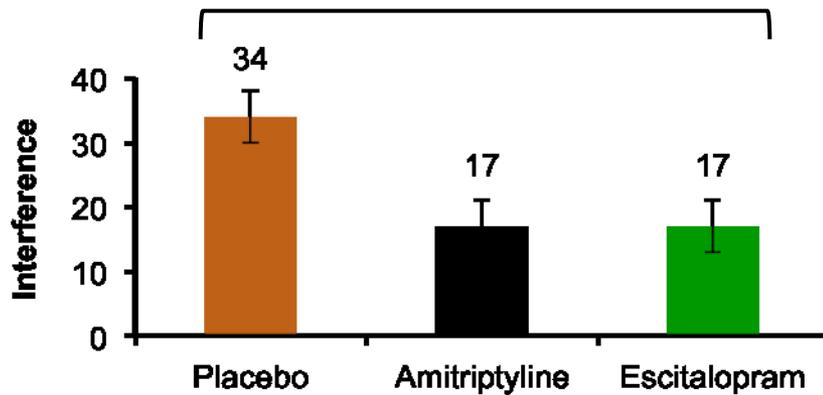
Gastric emptying was associated with adequate relief (pooled over all treatments), p=0.006

# Results: Nepean Dyspepsia Index

(lower score = better)

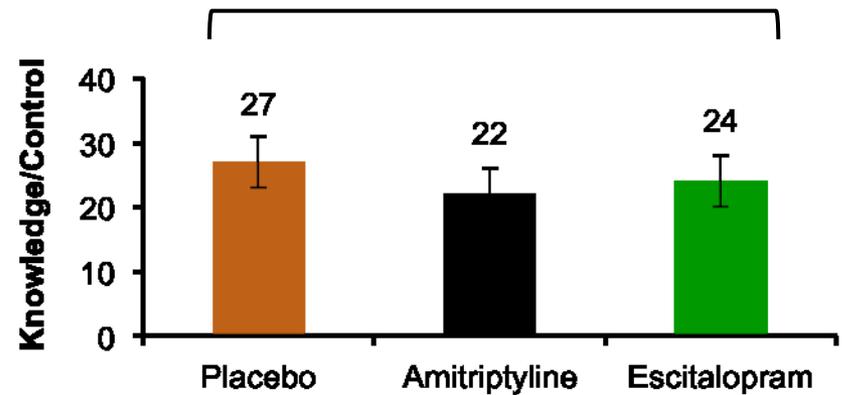
## QOL Interference Score

P = 0.06



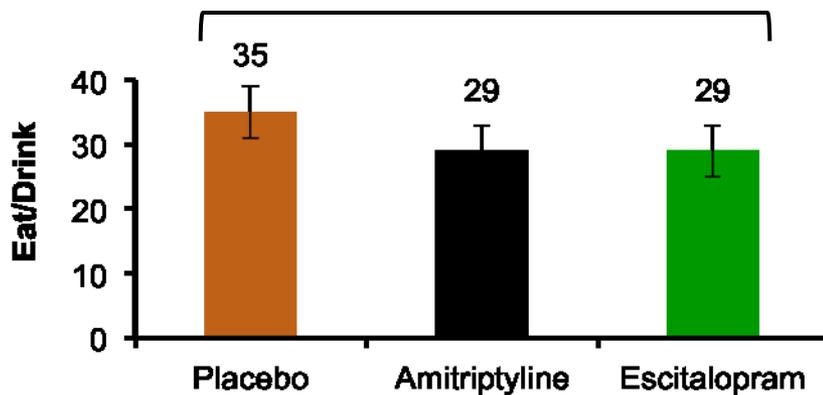
## QOL Knowledge/Control Score

P = 0.13



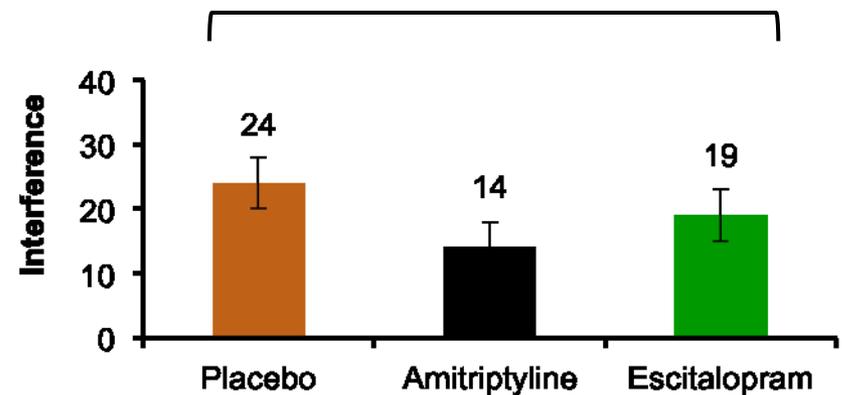
## QOL Eat/Drink Score

P = 0.07



## QOL Sleep Disturbance Score

P = 0.01



# Conclusions: Functional Dyspepsia and Antidepressants

- **Amitriptyline** appears to be an efficacious treatment for functional dyspepsia (FD)
- **Escitalopram** was *not* efficacious for FD
- Treatment effect of amitriptyline was greatest in ulcer-like FD subtype group and in males
- Overall response to treatment (adequate relief) was predicted by gastric emptying but not other patient characteristics (e.g., anxiety, BMI)

