

# Gluten and functional gastrointestinal disorders: is it worth the challenge?

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# Gastrointestinal Functional Disorders

- A functional gastrointestinal disorder is characterised by symptoms not attributable to anatomic or biochemical defects
- Classification: Rome III identifies 18 types of functional disorders
- IBS and dyspepsia are the most common but overlap is frequent
- Up to 40% GI patients could have a functional disorder (higher prevalence of adult females)

# Gastrointestinal Functional Disorders

## Diagnosis

- Clinical suspicion → Epidemiology and Symptoms
- Absence of biomarkers: no alterations at histology, serology, endoscopy or radiology
- Diagnosis of exclusion

# Gastrointestinal Functional Disorders

## Pathogenesis

- Motility Dysfunction
- Visceral Hypersensitivity
- Low Grade Inflammation
- Central Perception
- Psychological component

# Gastrointestinal Functional Disorders Therapy

Listen and appreciate

Understand aggravating factors and modify

Up to 50% Placebo effect

Laxatives

Anti-spasmodics

Tricyclic anti-depressants (low dose); SSRIs

Behavioral and psychological therapies

# Gastrointestinal Functional Disorders

## Food

Gastroenterology. 1980 Nov;79(5 Pt 1):801-6.

### **Gluten-sensitive diarrhea without evidence of celiac disease.**

Cooper BT, Holmes GK, Ferguson R, Thompson RA, Allan RN, Cooke WT.

#### **Abstract**

Eight adult female patients suffering from abdominal pain and chronic diarrhea which was often incapacitating and frequently nocturnal, had dramatic relief on a gluten-free diet and return of symptoms after gluten challenge. Previous nonspecific measures and a milk-free diet were ineffective. Multiple jejunal biopsies showed minor, but significant changes in cellularity which returned to normal on the gluten-free diet. Apart from a slight increase in jejunal cellularity, no immunological abnormalities were found after gluten challenge. Steatorrhea or other biochemical defects, common in celiac disease, were not found. It was concluded that these patients had a gluten-sensitive diarrhea, but had no evidence of celiac disease.

PMID: 7419003 [PubMed - indexed for MEDLINE]

# Non Celiac Gluten Sensitivity 2012

- Syndrome characterised by gastrointestinal and systemic symptoms improving after gluten withdrawal
- Gluten is supposed to be the trigger but other factors could be involved (ATI, FODMAP) and conflicting data are present in literature
- Absence of biomarkers and of an established diagnostic flowchart

A Venn diagram illustrating the relationship between Functional GI patients and Non CD GFD Responders. A large green oval represents 'Functional GI patients'. Inside it is a smaller blue oval representing 'Non CD GFD Responders'. A line connects the blue oval to a box labeled 'Placebo Effect?'. Another line connects the 'Placebo Effect?' box to a box labeled 'GFD Responders ≠ NCGS'.

**Functional GI patients**

Non CD GFD  
Responders

Placebo Effect?

GFD Responders  $\neq$  NCGS





# Gluten Blind Challenge

# Gluten Challenge: Questions

**What challenge?** Wheat or gluten

**How much?** mg, grams

**How long?** Day, week, month

**Which vehicle?** Muffins, capsules, bars

**How to measure response?** VAS, scores

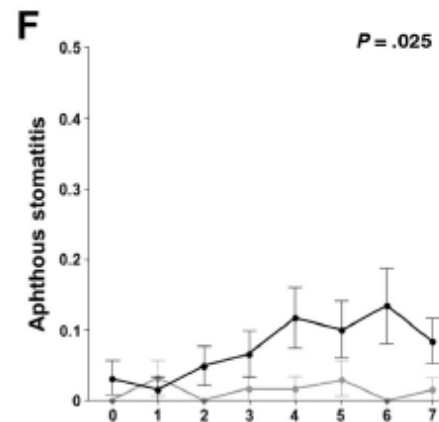
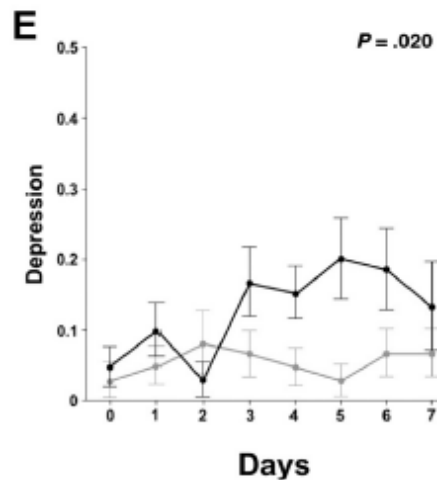
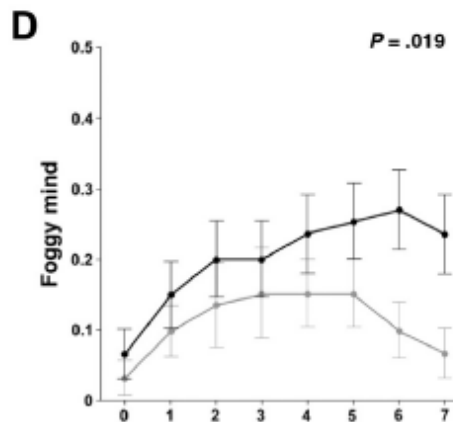
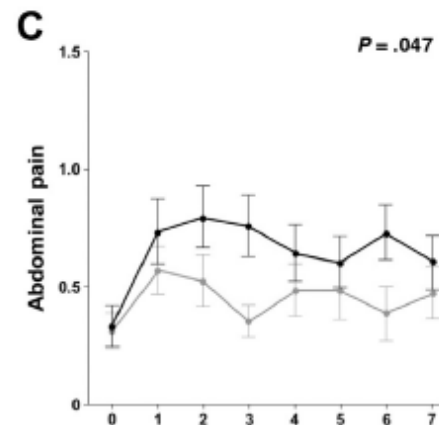
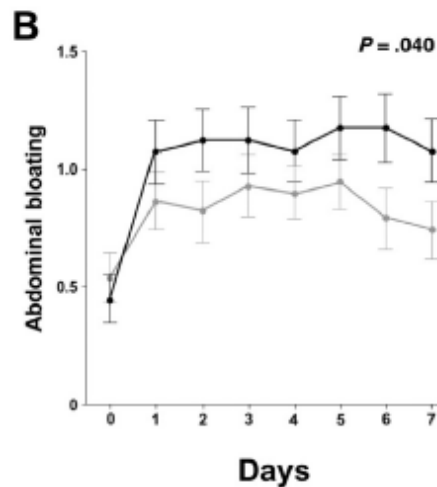
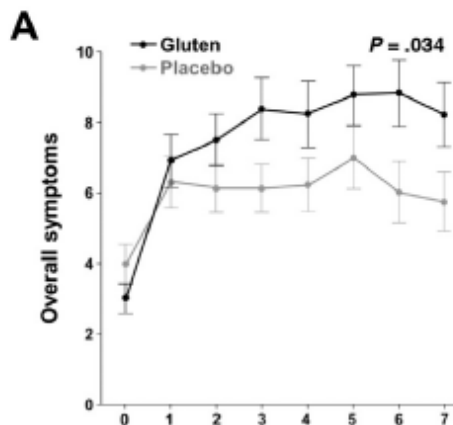
**Expectations?** Complete vs partial response

Biesiekierski et al.  
AMJG 2011

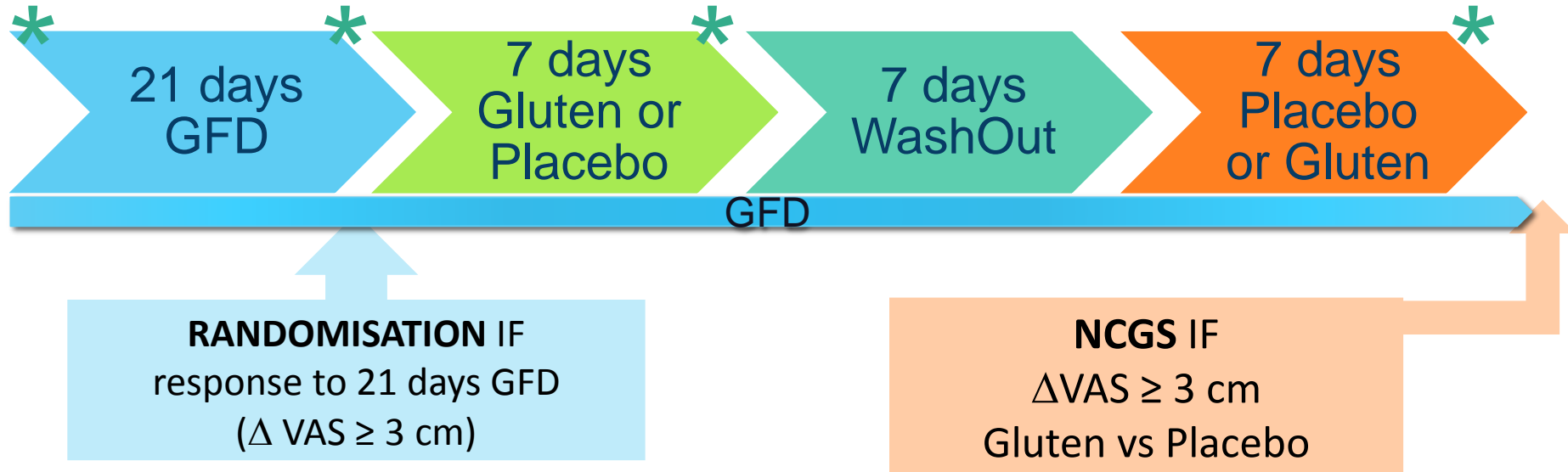
Carroccio et al.  
AMJG 2012

Vazquez-Roque et al.  
Gastroenterology 2013

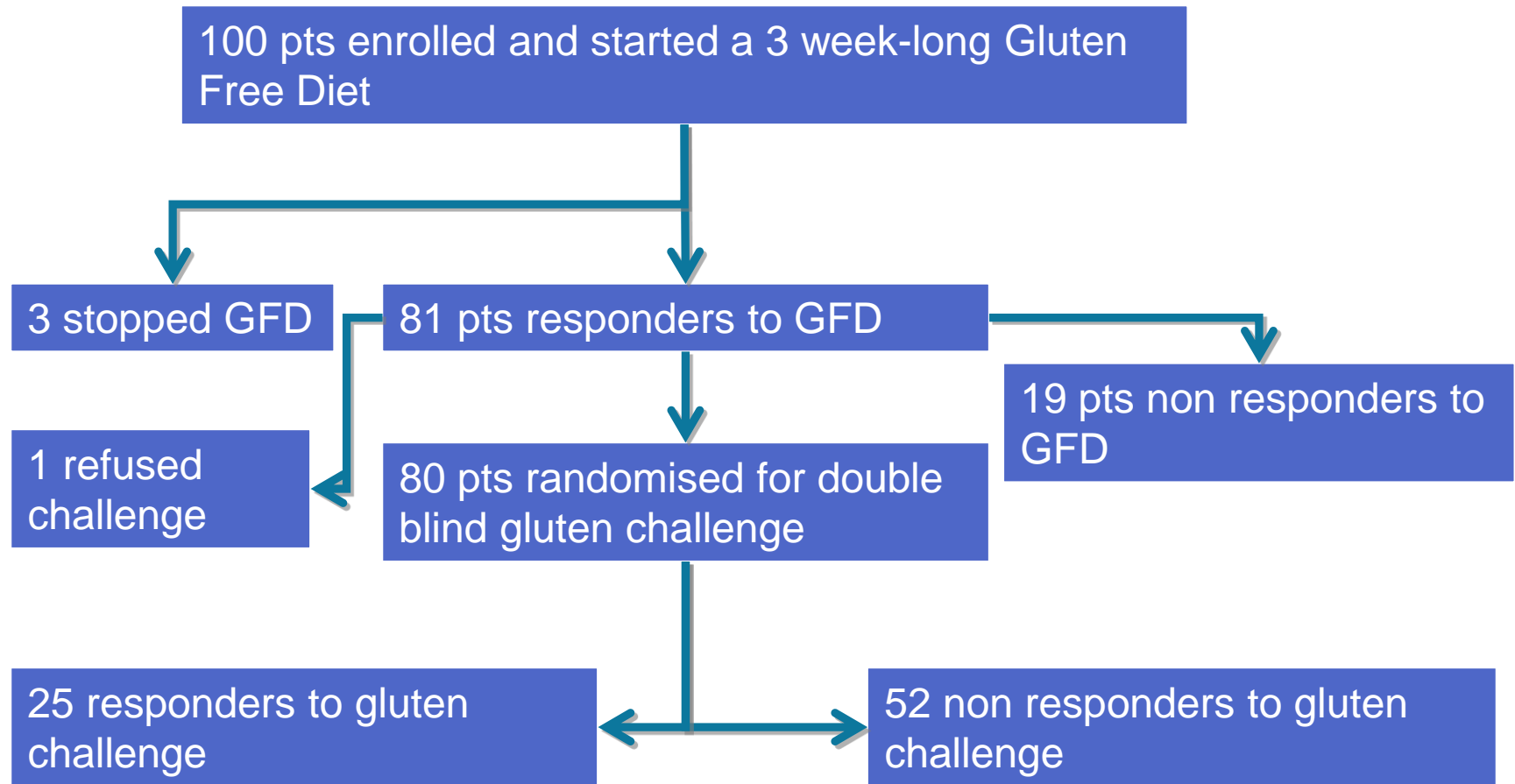
Di Sabatino et al.  
Clin Gastroenterol Hepa  
2015



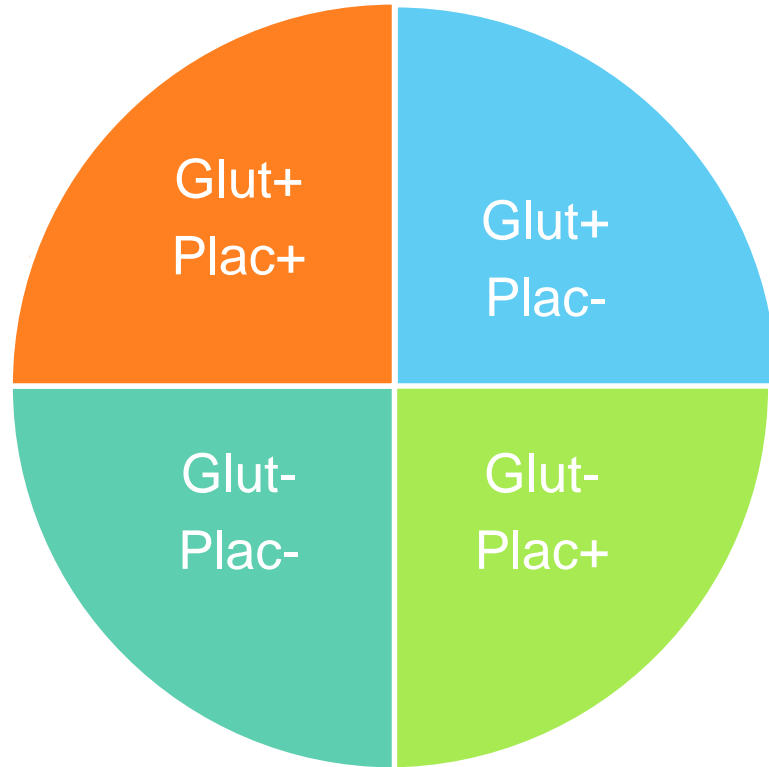
# GluTox Trial



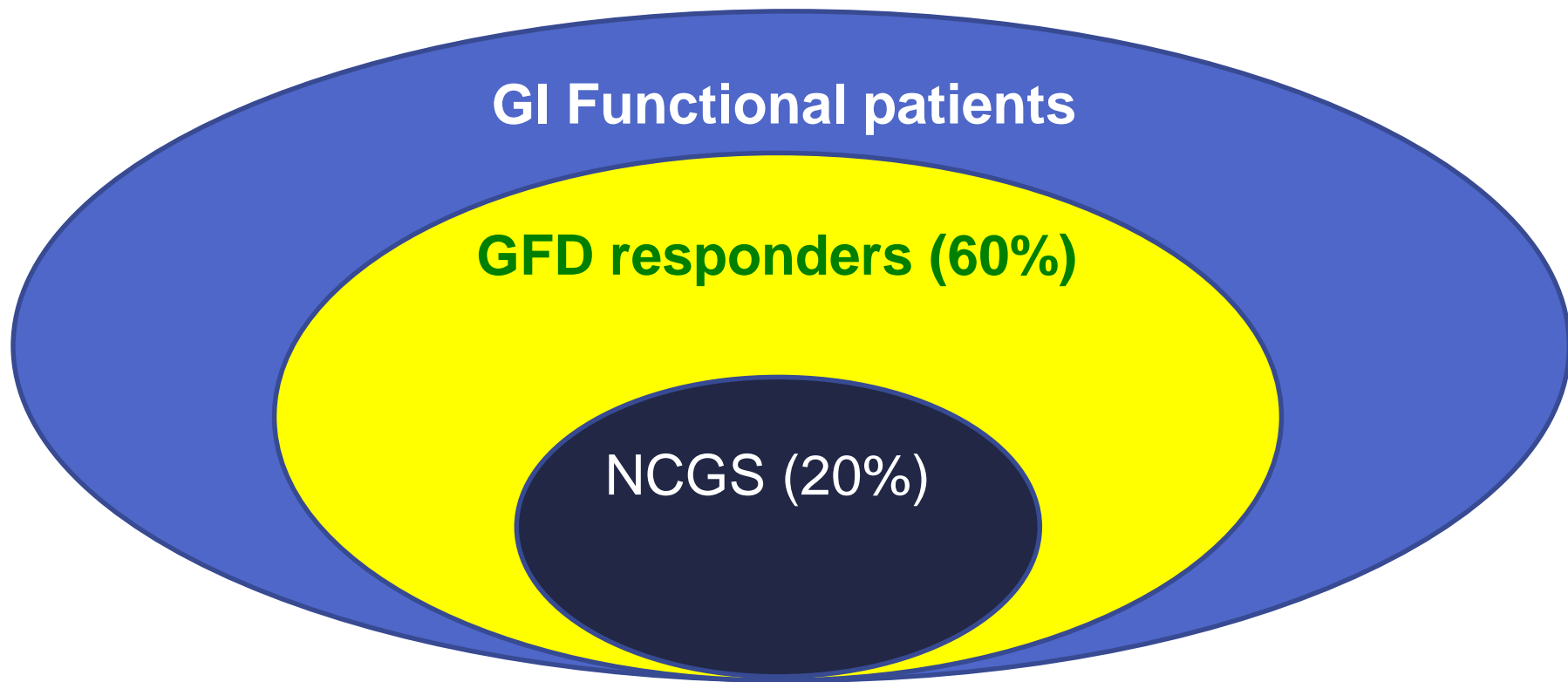
- **\*Evaluation of VAS symptoms**
- **Gluten 800 mg/capsule: 7 capsules per day (5.6 g/day)**



# Possible results



# Scenario after challenge



# Gluten Challenge: Answers

**What challenge?** Wheat or gluten → Gluten

**How much?** mg, grams → 5-10 grams

**How long?** Days, weeks, months → 7 Days

**Which vehicle?** Muffins, capsules, bars → Capsules (high number), bars

**How measure response?** VAS, scores → VAS

**Expectations?** Complete vs partial response → 3 cm cut off



# Conclusions

- DBPC challenge could be useful to discriminate patients with NCGS among the large groups of GFD responders
- There is a need to create a standardised DBPC challenge protocol
- The role of molecules other than gluten is still an open issue