

# Current Management of Celiac Disease and Identifying an Appropriate Patient Population(s) for Pharmacologic Therapies in Adult Patients

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# DISCLOSURES

## Relevant Financial Relationship(s)

**Alba Therapeutics: Grant support**

**Alvine Inc: Advisory board, grant support**

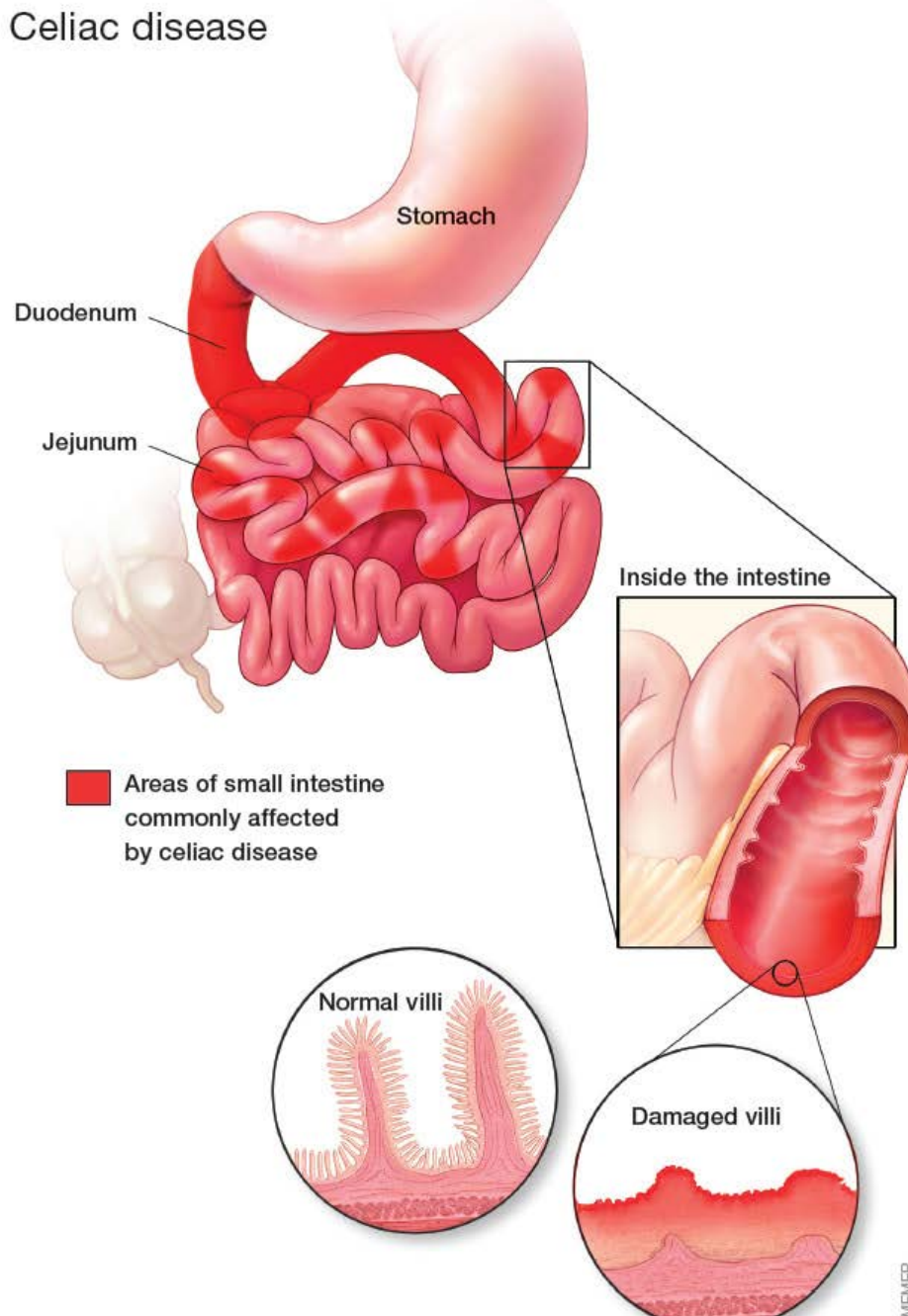
**Consultant: Ferring, Bayer, Immunosant,  
Flamentera, Shire, Enterra health,  
Sonomaceuticals, Genentech, AMAG, Glenmark,  
GSK, Johnson and Johnson,**



# Learning Objectives

- Recognize the gluten free diet (GFD) as the current treatment of celiac disease and its drawbacks and limitations
- Which patients are most likely to benefit from additional therapy options
- Introduce the role for serology and histology to determine the activity of treated celiac disease (CeD)

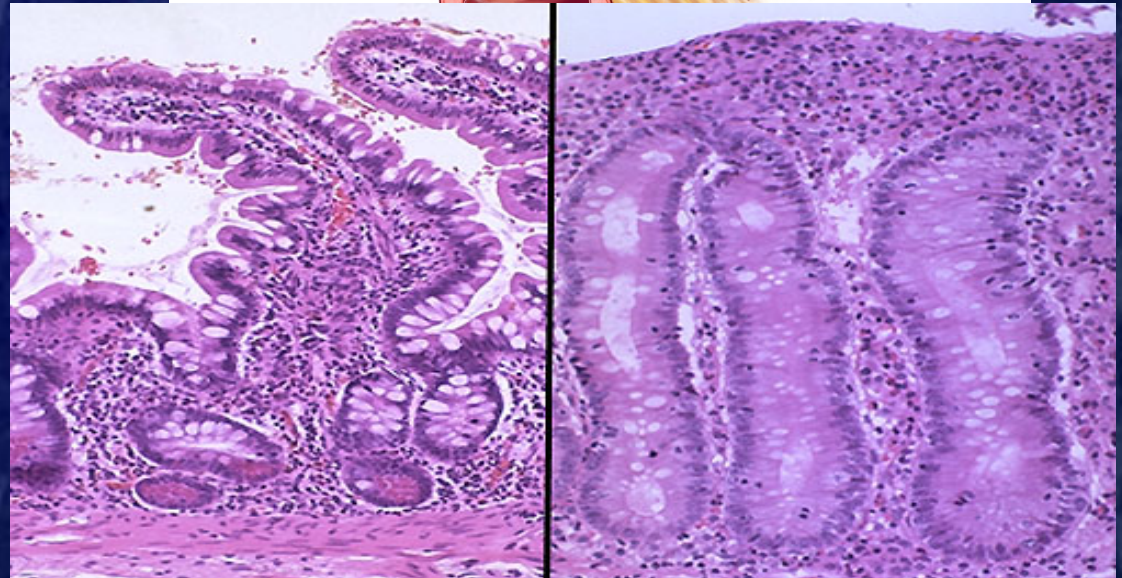
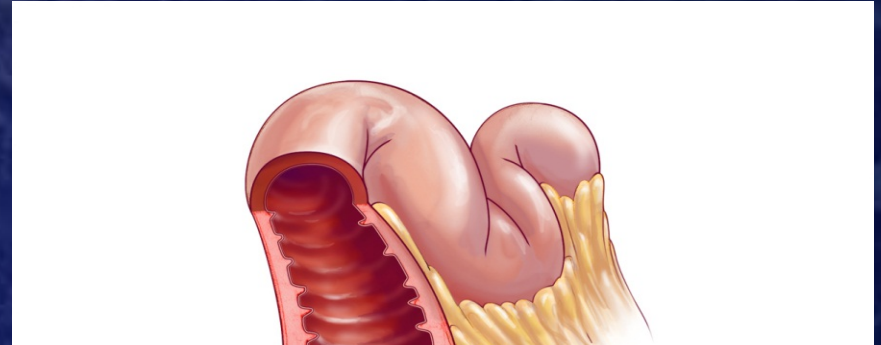
# Celiac disease





# What is Celiac Disease?

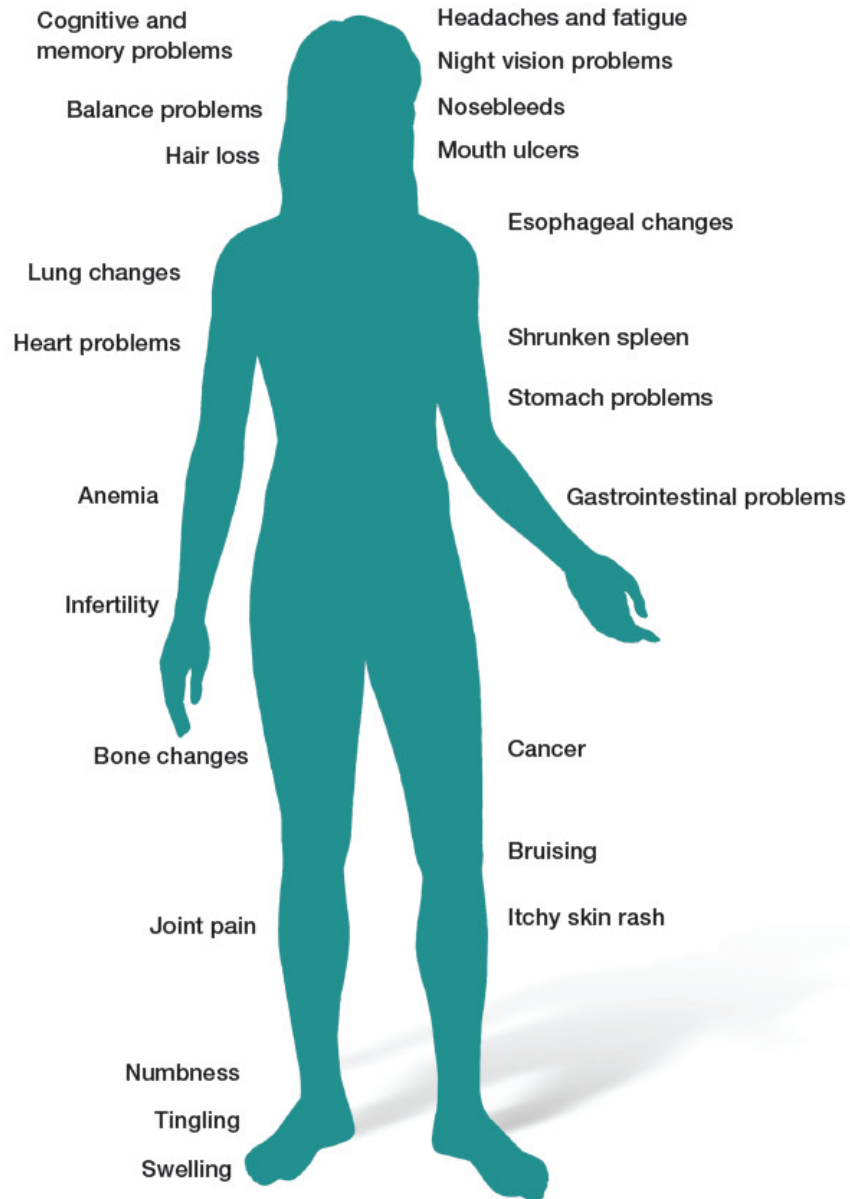
- It is a inflammatory state of the small intestine that occurs in genetically predisposed individuals and resolves with exclusion of dietary gluten.



Normal gut

Celiac disease

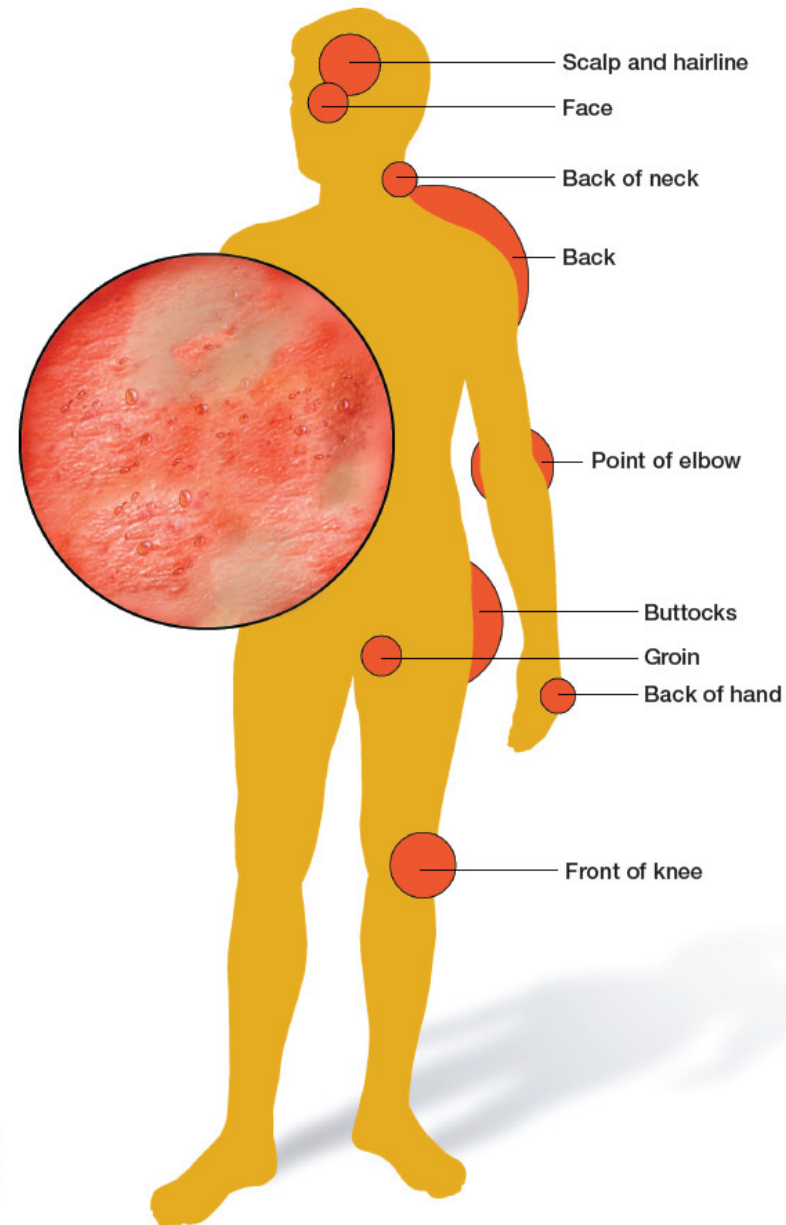
## Signs and symptoms of celiac disease



*In: Mayo Clinic: Going Gluten Free*



## Dermatitis herpetiformis



© MFMER

*In: Mayo Clinic: Going Gluten Free*

# Treatment



- Only treatment for CeD is a GFD
  - Strict, lifelong diet
  - Avoid
    - Wheat
    - Rye
    - Barley



# Other Items to Consider



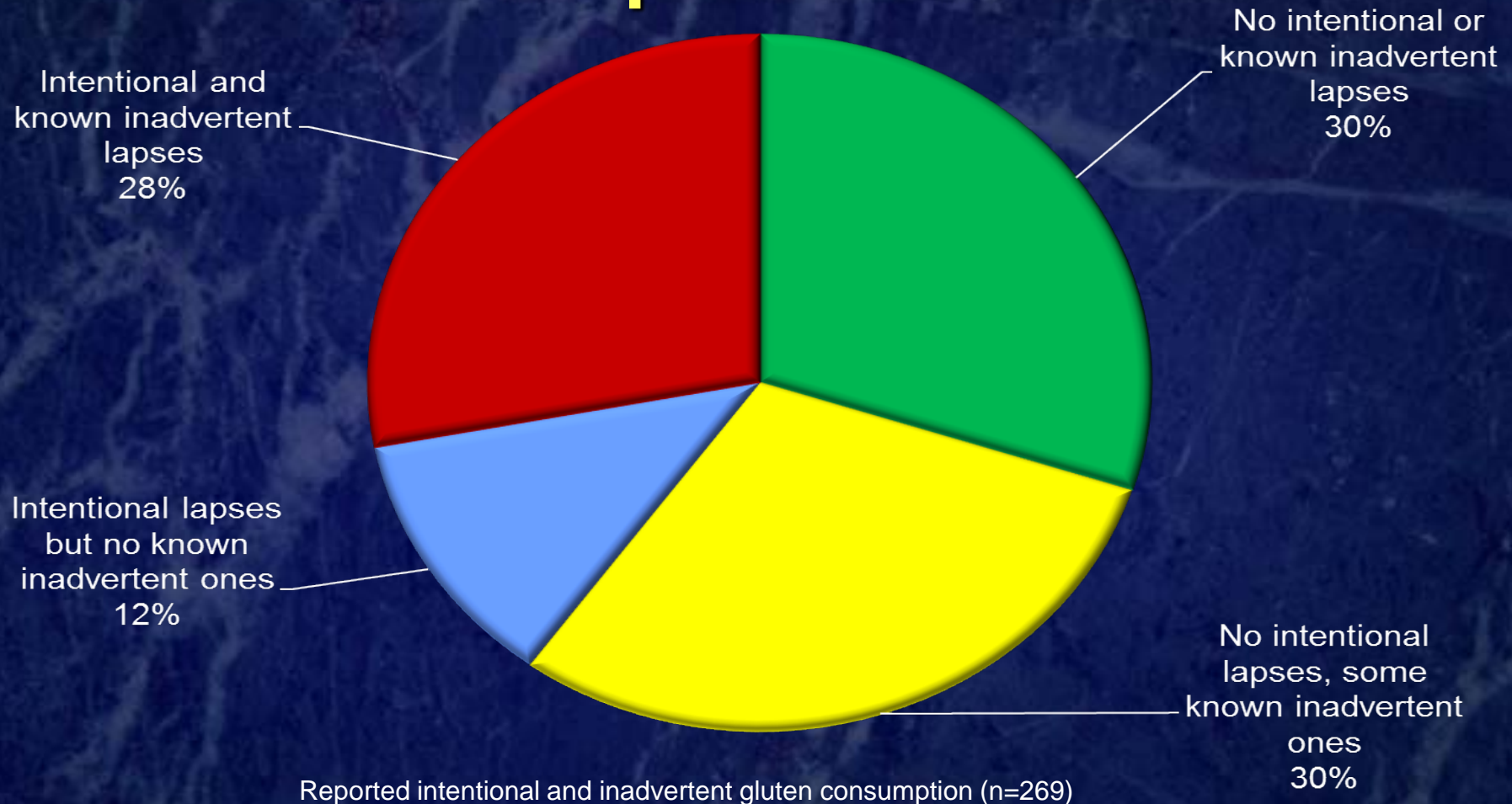
- Lipstick/gloss/balms
- Mouthwash/toothpaste
- Play dough
- Stamp and envelope glues
- Vitamin, herbal, and mineral preparations
- Prescription or OTC medications

# Adequacy of Gluten-Free Diet for Celiac Disease

- Response to a GFD is expected and historically a component of the diagnosis of CeD
- But does it work adequately in adults
- Symptom improvement does not reflect symptom resolution
- Healing is not “healed”
- Future risk may be predicated by healed/ non healed status



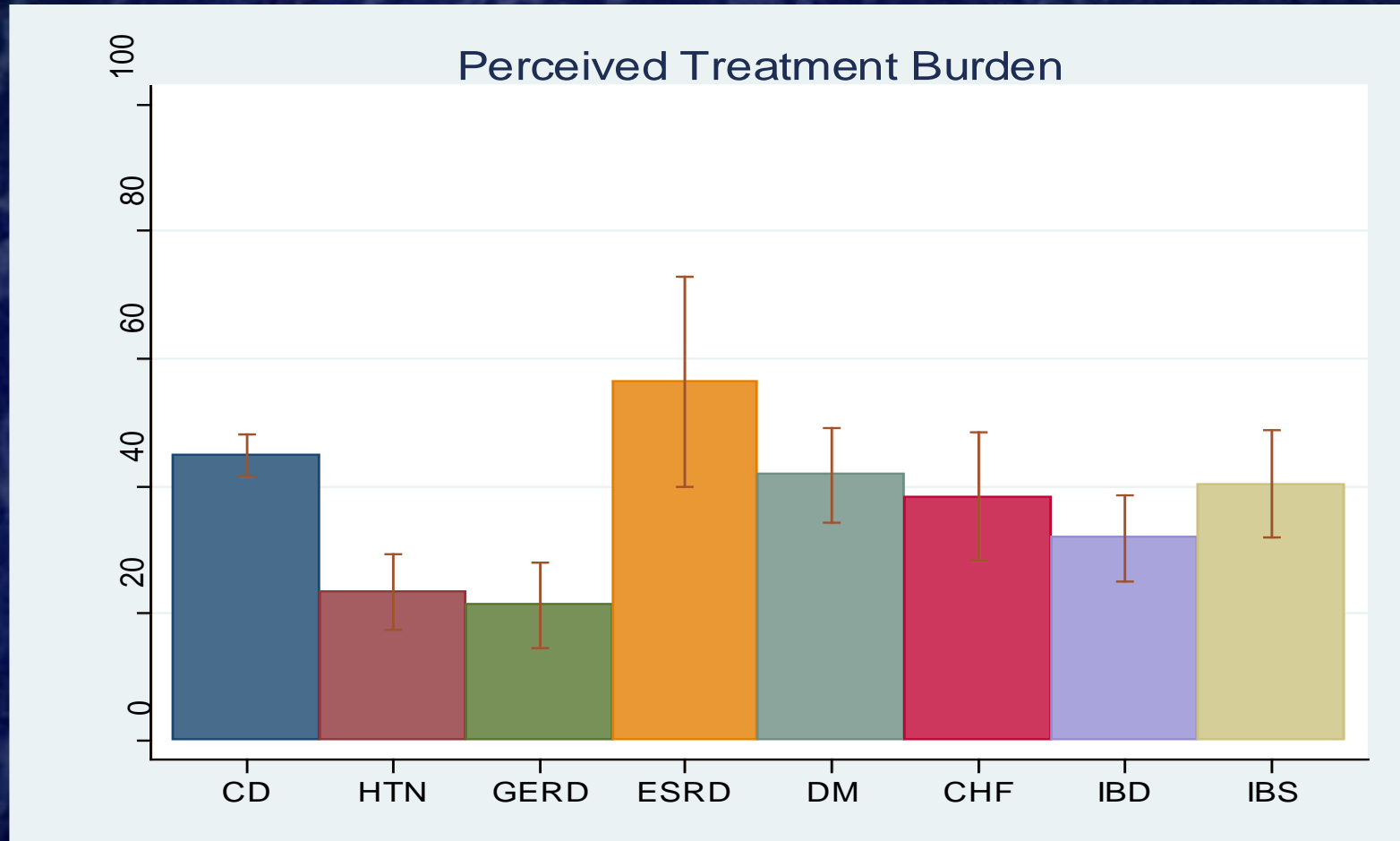
# 70% of Celiac Disease Subjects Report Gluten Exposure on GFD<sup>1</sup>



1. Hall NJ, Rubin GP, Charnock A, Intentional and Inadvertent Non Adherence in Adult Coeliac Disease. A Cross-Sectional Survey Appetite 68:56-62, 2013

# Treatment burden is second only to hemodialysis, but patients achieve high disease-specific health

VAS\*

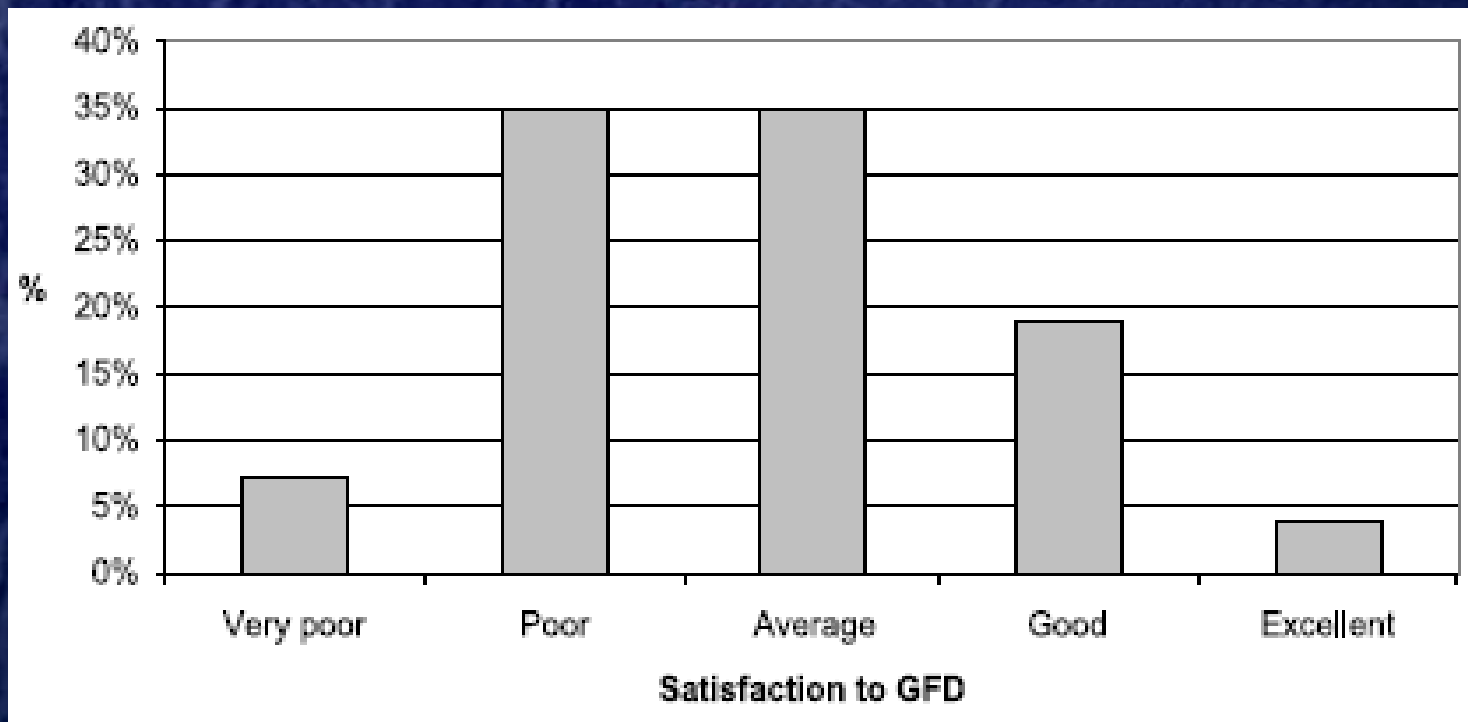


\*VAS: 0=Very Easy  
100=Very Difficult



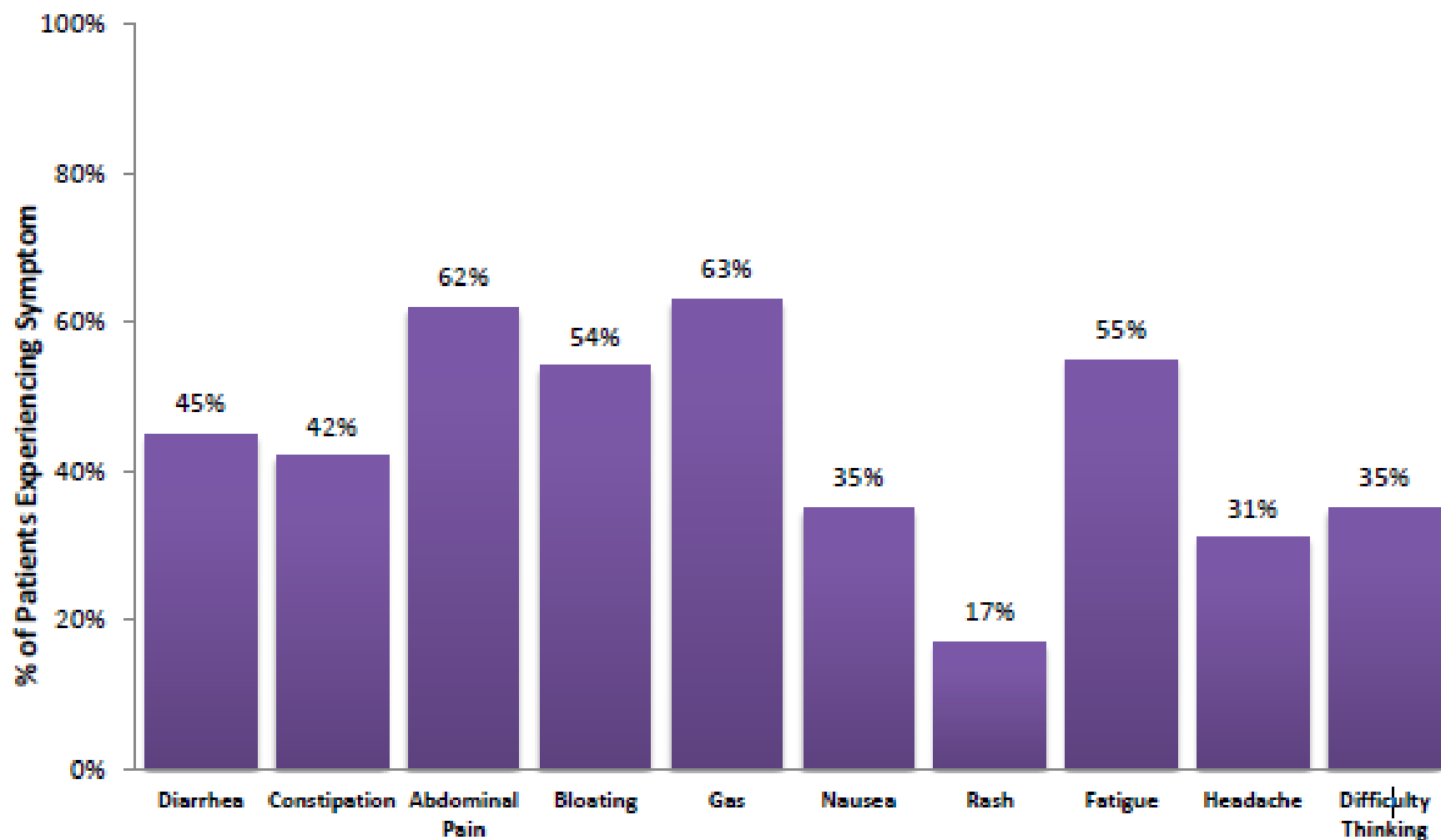
# Patient Satisfaction with the Gluten-Free Diet is Low

- Controversial in the past
- Better scientific data and a more diverse celiac population → general acceptance



# Symptoms in Treated Celiac Disease Patients

## Frequency Distribution of Symptoms Experienced Over 7 Days



Adelman,  
ACG 2012



# Symptom Diversity on GFD

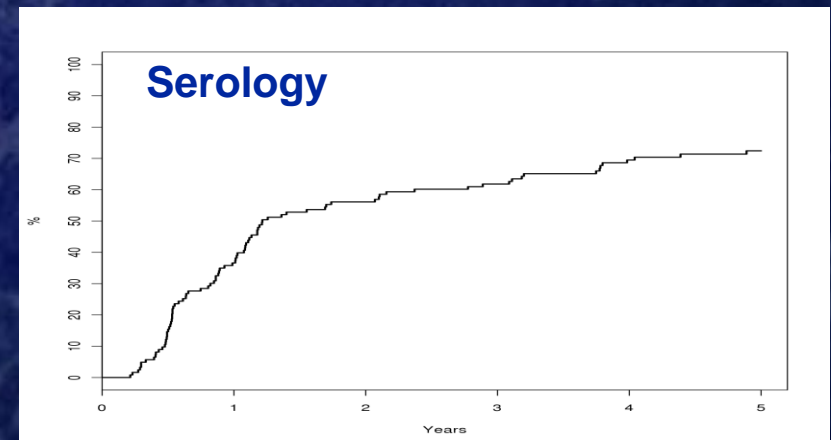
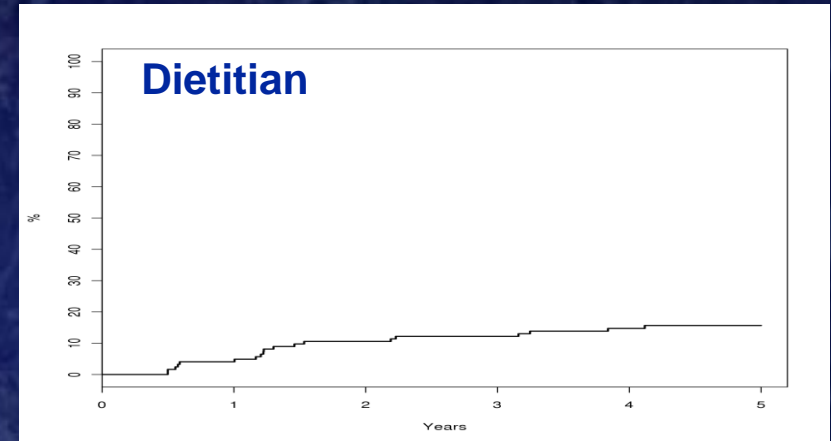
No. of Unique Symptoms	No. of Pts	%
0	12	5.9
1	15	7.4
2	36	17.8
3	20	9.9
4	32	15.8
5	20	9.9
6	18	8.9
7	18	8.9
8	18	8.9
9	12	5.9
10	3	1.5

Number (%) Of Patients Reporting The Presence/Absence Of A Severity Item Score Exceeding 'Moderate' Or 'Severe' Levels Across The Week			
Threshold	Present	Absent	Total
≥ Moderate	153 (76%)	49 (24%)	202
≥ Severe	83 (41%)	119 (59%)	202

- >20% of patients reported moderate-to-complete daily disruption
  - Work and social activities
  - Physical activities
  - Emotional well-being

# Medical Follow-Up Less Than Optimal in Practice

- 123 incident cases diagnosed 1996-2006
- 70% female, median age 42 years
- Initial dietitian: 84%
- Assessment of compliance: 57%
- F-U Dietician: 4%
- F-U Serology: 37%



Herman M, Rubio-Tapia A, et al. Clin Gastroenterol Hepatol 2012; 10: 893



# Dangers of Non-Adherence

- **Increased mortality** (Holmes et al. 1989; Corrao et al.)
- **Osteoporosis** (Cellier)
- **Lymphoma** (Holmes et al.)
- **Other cancers** (Green, 2006)
- **Psychological effects** (Hallert)
- **Failure to heal** (RubioTapia, 2010)

# Persistent Atrophy is Frequent When Celiac Disease Diagnosed as Adults

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- Associated with complications such as osteoporosis, autoimmune diseases, lymphoma<sup>1</sup>
- Persistent atrophy and symptoms despite GFD are major criteria for refractory CeD, a rare condition associated with high mortality<sup>2</sup>
- Even without symptoms: higher risk of osteoporosis, development of refractory sprue, and lymphoma<sup>3</sup>

<sup>1</sup> Rostom A, et al. Gastroenterology 2006

<sup>2</sup> Rubio-Tapia A, et al. Gut 2009

<sup>3</sup> Kaukinen K, et al. Aliment Pharmacol Ther 2007

# Histologic Healing in Adults is Incomplete

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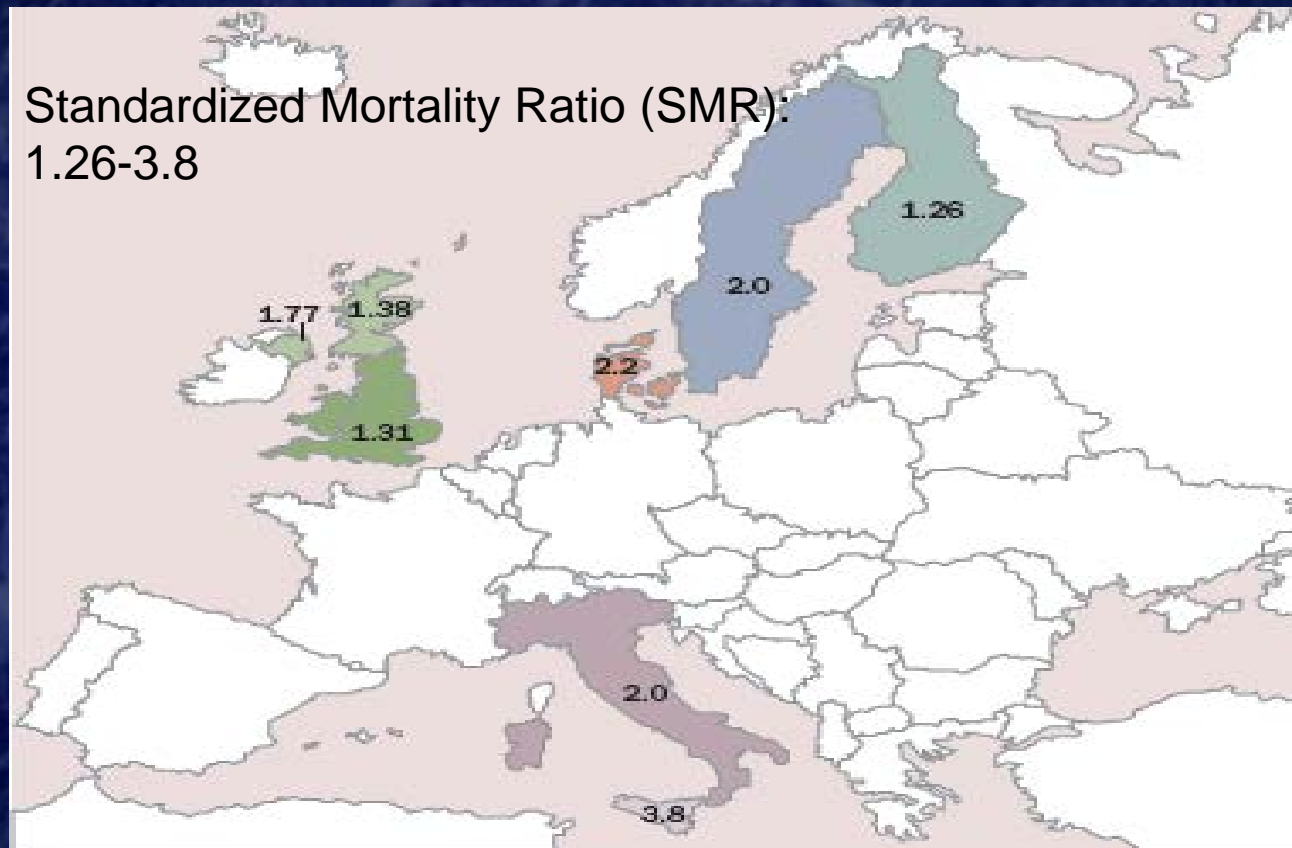
Author	Country	“n”	% healing	Time on GFD
Grefte J <sup>1</sup>	Holland	22	0%	2 years
Bardella M <sup>2</sup>	Italy	114	17.5%	2 years
Rubio-Tapia*	USA	241	34% 66%	2 years 5 years
Ciacci C <sup>3</sup>	Italy	390	44%	7 years
Tursi A <sup>4</sup>	Italy	42	59.5%	2 years
Collin P <sup>5</sup>	Finland	65	96%	8 years

<sup>1</sup>J Clin Pathol 1988; <sup>2</sup>Histopathology 2007; <sup>3</sup>Digestion 2002; <sup>4</sup>Endoscopy 2006;  
<sup>5</sup>Gastrointest Endosc 2004; \* Rubio-Tapia A, et al. Am J Gastro 2010



# Increased Mortality in Symptomatic Celiac Disease

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Biagi F, et al. Nat Rev Gastroenterol Hepatol 2010

# Clinical Scenarios

## Patient Groups

- Newly-diagnosed patients
- Treated patients
  - Symptomatic TTG positive\*
  - Asymptomatic TTG positive\*
  - Symptomatic TTG negative
  - Asymptomatic TTG negative
    - Healed
    - Non-healed

\*Assumed unhealed likely substantial gluten exposure

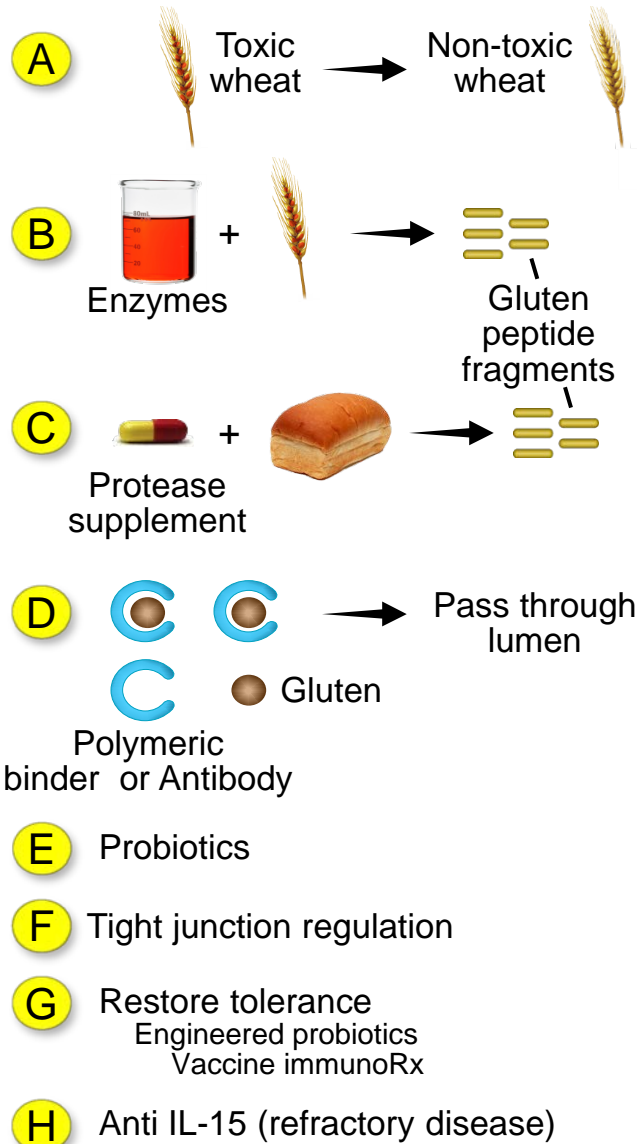


# Pharmacological Therapeutic Need

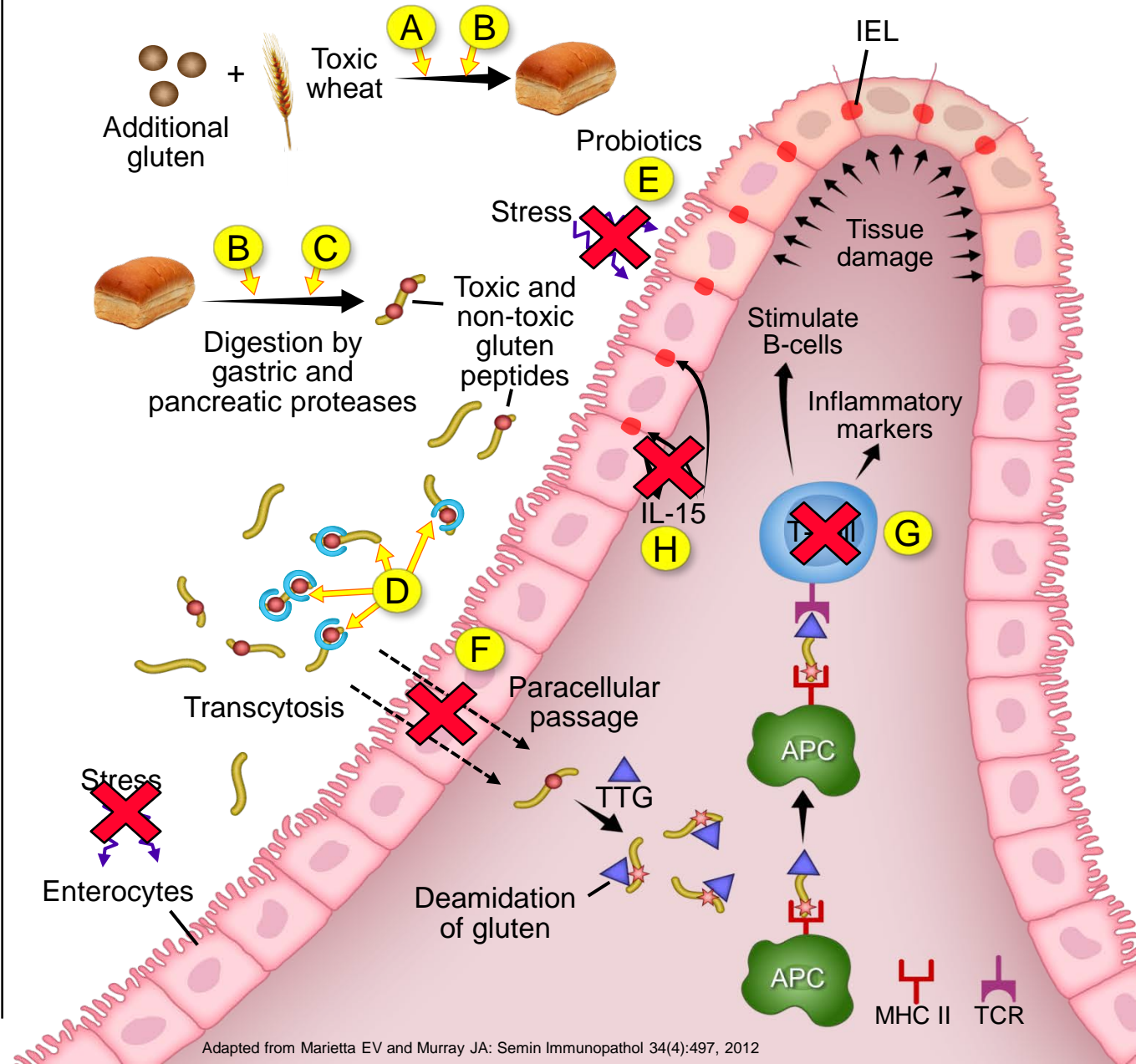
- Relief of ongoing symptoms in treated CeD doing their best on GFD
- To accelerate the response of symptoms and immune markers and healing in patients with untreated CeD
- To reduce risks of long term consequences of ongoing inflammation
- Refractory celiac disease
- ? Allied with a recommendation for a GFD
- Reduce burden in treated patients to permit some degree of gluten exposure



# Therapeutic Targets



# Points of Action in Pathogenesis



**Why should a patient with celiac disease be denied the opportunity to live a normal life or a least a healthy one in a gluten rich environment?**

**Is this inherently any different from a ragweed allergic person from living in the Midwest?**