Stanford | MEDICINE

Post DDW Update: The best of the best in GI

From Washington DC …

to… San Francisco CA

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July 14th 2018

Consultant to:

- Pentax/C2
- Endostim
- Restech
- G-Tech

Washington DC: An architectural delight

Obama era

Trump era

July 14th: Bastille Day

Then (1789) and… now

Theme:

Revolution, change, difference, excitement, anticipation, new challenges, potential, growth

Change of title: Revolution(s) in GI-DDW 2018

rev·o·lu·tion·ar·y

/ˌrevəˈlo͞oSHəˌnerē/

adjective

1. involving or causing a complete or dramatic change.
   "a revolutionary new drug"
   synonyms: thoroughgoing, thorough, complete, total, absolute, utter, comprehensive, sweeping, far-reaching, extensive, profound More

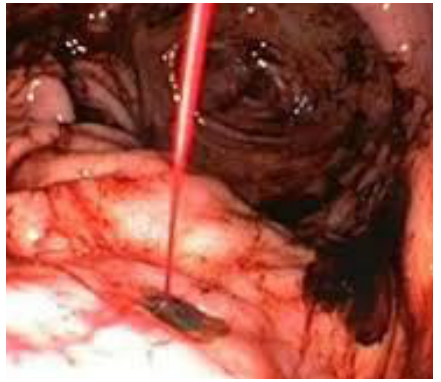
2. engaged in or promoting political revolution.
   "the revolutionary army"
   synonyms: rebellious, rebel, insurgent, rioting, mutinous, renegade, insurrectionary, insurrectionist, seditious, subversive, extremist
   "revolutionary troops"

Resumption of anticoagulants after hospitalization for GI bleeding: A meta-analysis

Pang AS et al. DDW 2018

Here, take these, I'd like to see what they do to you…

Resumption of anticoagulants after hospitalization for GI bleeding: A systematic review & meta-analysis



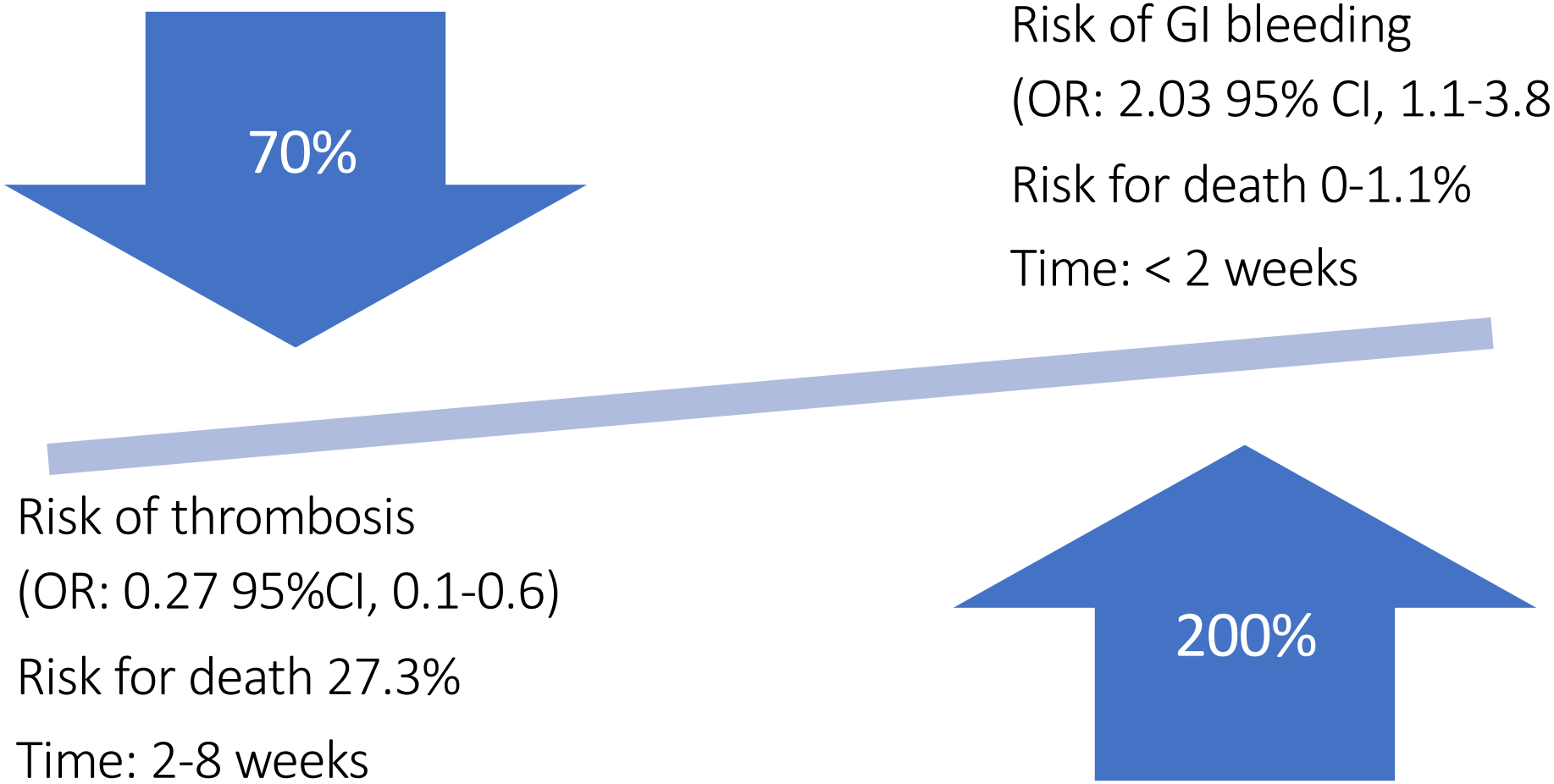
- Systematic review and meta-analysis of studies to determine the risk of recurrent GI bleeding, thromboembolism and mortality after resuming anticoagulation following GI bleeding.

- RCTs and cohort studies in patients with Afib, VTE, or valvular heart disease with data on anticoagulation management and outcomes of recurrent GIB, thromboembolism and mortality following GIB.

- Direct comparison of clinical outcomes in patients in whom anticoagulation was resumed or interrupted after GIB.

Results

Resumption of anticoagulation reduces all-cause mortality (OR 0.503, 95% CI 0.41-0.61).



Message

While resumption of anticoagulation following GI bleeding was associated with a significant increase in recurrent GI bleeding,

it was also associated with a significant decrease in thromboembolic events and all-cause mortality.

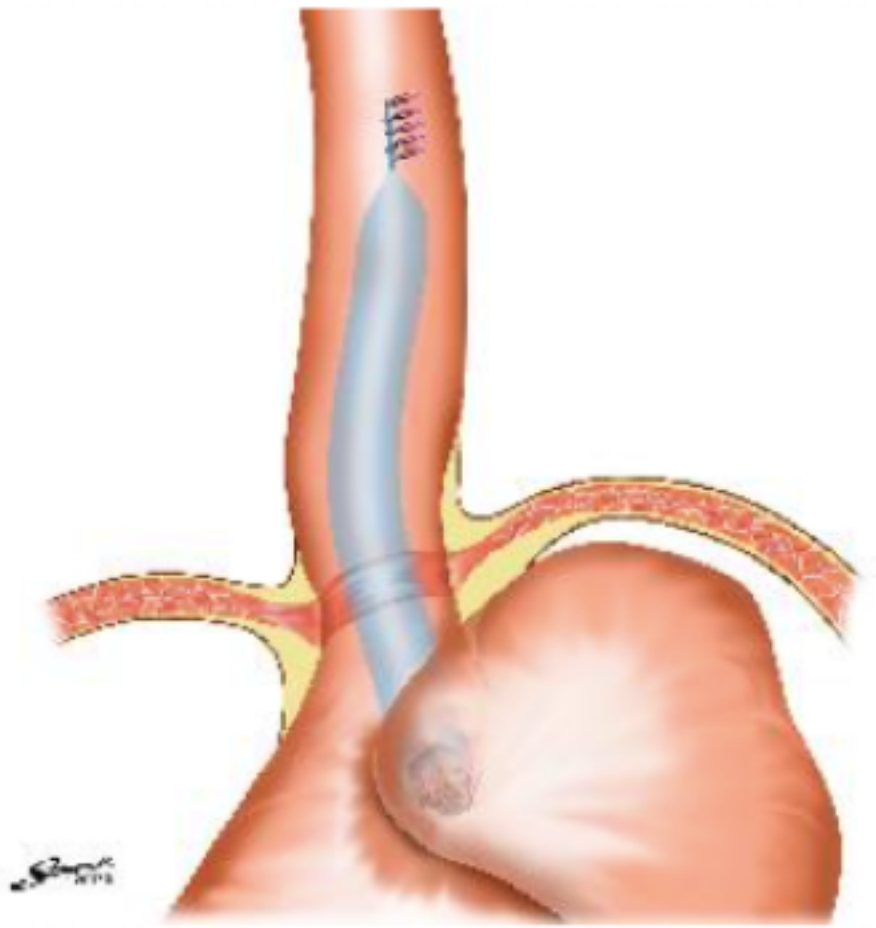
The choice is yours….

POEM+F: Per-oral endoscopic myotomy followed by endoscopic fundoplication

Inoue H et al. DDW 2018

- Endoloop is closed tightly under submucosal endoscopic visual control.

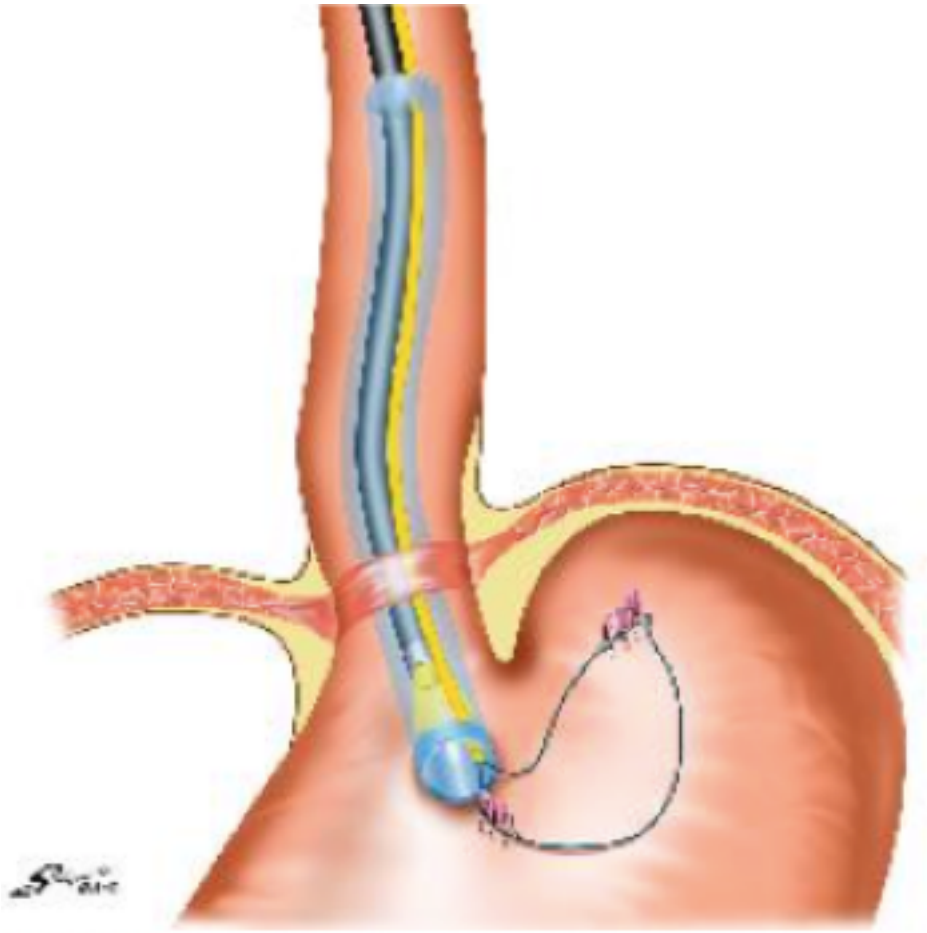
- Grasped anterior wall of gastric cardia is pulled up toward EGJ, creating partial fundoplication at the cardia



POEM+F: Per-oral endoscopic myotomy followed by endoscopic fundoplication

Inoue H et al. DDW 2018

- Right after POEM, submucosal endoscope is advanced into peritoneal cavity.
- Pneumoperitoneum is achieved with CO2 insufflation through endoscope.
- Anterior wall of gastric fundus is grasped and anchored by 4 endoclips together with endoloop.
- Endoloop is fixed again to distal end of myotomy site by 3 more endoclips.



Results

- POEM+F was successfully carried out in all 12 cases.
- POEM+F created visually recognizable fundoplication at gastric cardia.
- Extended operating time was 36 minutes on average.
- Clinical course after POEM+F was uneventful.
- Hospital stay and dosage of pain controller was totally equal to conventional POEM procedure.
- 24hr pH impedance study of two months after POEM+F was carried out in 4 cases and no reflux was identified.

Message

- This combined technique of “tunnel endoscopy” and NOTES promises to reduce the likelihood of GERD post POEM.

- Potential endoscopic treatment for GERD in the absence of achalasia or hiatal hernia

Idiopathic bleeding ulcers

Lau LH et al. DDW 2018

"What do you mean, I have an ulcer? I give ulcers, I don't get them!"

The clinical issue

Lau LH et al. DDW 2018

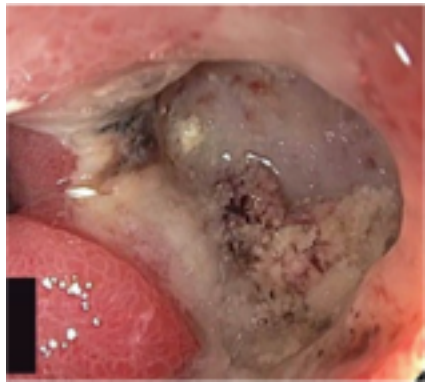
How to **prevent recurrent ulcer bleeding** in patients who:

1) Are *Helicobacter pylori*-negative
2) Have no drug history of ASA, NSAIDs and/or antiplatelet agents.

These patients with **idiopathic bleeding ulcers are at** considerable risk of recurrent ulcer complications, even years after the index bleeding.

Authors hypothesized that a PPI (lansoprazole) is superior to an H2RA (famotidine) for prevention of recurrent ulcer bleeding.

Patients & Methods



- Double-blind, randomized trial in Hong Kong
- Patients with a history of idiopathic bleeding ulcers
- After ulcer healing, patients were randomly assigned (1:1) to either lansoprazole 30mg or famotidine 40mg daily once per day for 24 months.
- Primary endpoint: Recurrent UGI bleeding (hematemesis, rectal bleeding and/or melena, or a drop in hemoglobin ≥2 g/dL, with ulcer and/or erosions confirmed endoscopically) within 24 months.
- Secondary endpoint was any recurrent gastrointestinal bleeding (upper, mid and/or lower)
- ITT analysis
- They report the blinded interim analysis of findings at 12 month data.

Lau LH et al. DDW 2018

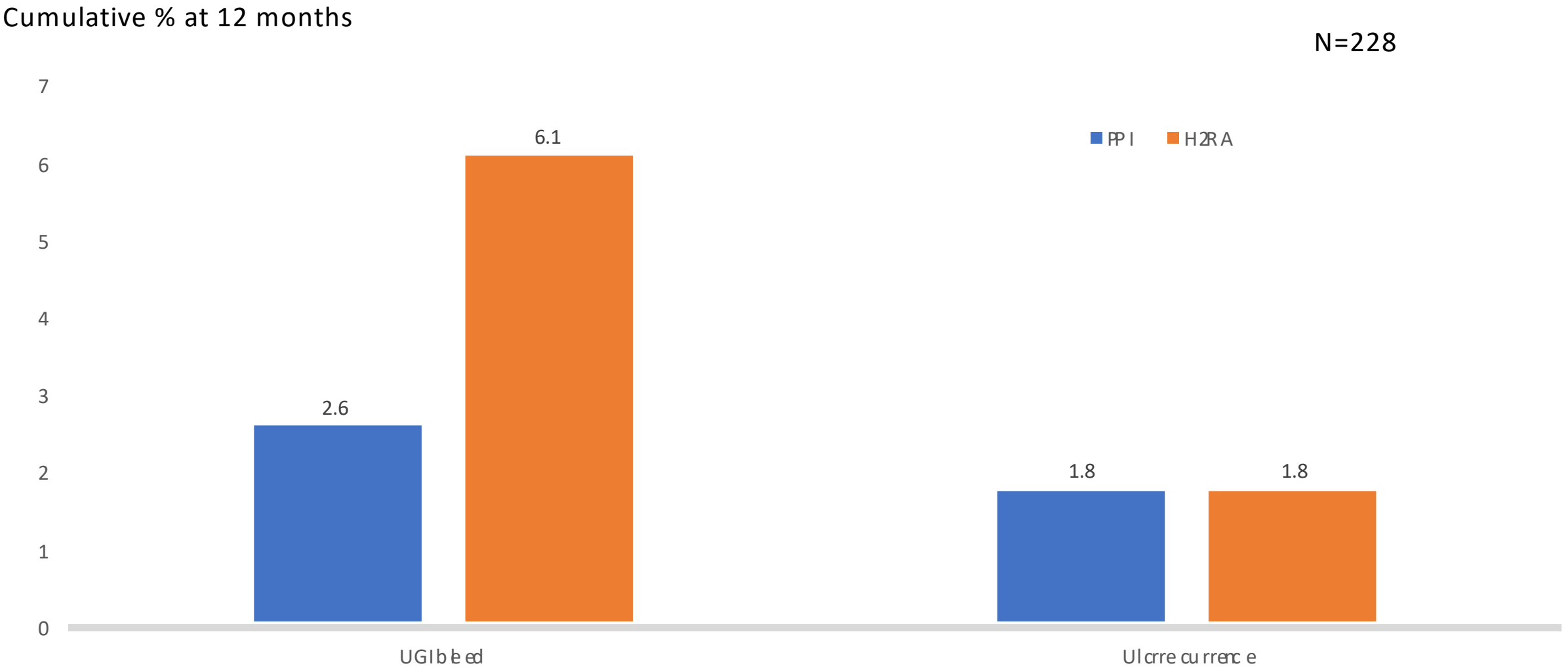
Prevention of recurrent idiopathic gastroduodenal ulcer bleeding: 1 year results of an RCT (NRT Study)

Lau LH et al. DDW 2018

	Arm A N=114	Arm B N=114
Male gender (n, %)	63 (55.3%)	78 (68.4%)
Age (years)	69.6	67.6
Hemoglobin (g/dL)	12.2	12.6
Hematocrit (L/L)	0.357	0.368
White cell count (x109/L)	7.8	7.8
Platelet (x109/L)	220.0	219.6
Prothrombin time (second)	11.43	11.41
International normalised ratio	1.07	1.06
Urea (mmol/L)	7.83	7.54
Creatinine (µmol/l)	109	98
Index ulcer location (%)		
Gastric ulcer	35.96	37.72
Duodenal ulcer	50.00	50.00
Gastroduodenal ulcer	14.04	12.28

	Arm A N=114	Arm B N=114	P-value
Reached endpoints			
Early withdrawal	17 (14.9%)	10 (8.8%)	0.15
Ongoing	11 (9.7%)	6 (5.3%)	
Events			
Clinical gastrointestinal bleeding	3 (2.6%)	7 (6.1%)	0.20
Recurrent ulcer	2 (1.8%)	2 (1.8%)	1.00
Hemoglobin drop > 2g/dl	1 (0.9%)	5 (4.4%)	0.21
Severe epigastric pain	1 (0.9%)	0 (0.0%)	1.00
Deaths	3 (2.6%)	7 (6.1%)	0.20

Results


Cumulative % at 12 months
N=228
7
6
5
4
3
2
1
0
PPI
H2RA
6.1
2.6
1.8
1.8
UGI bleed
Ulcer recurrence

Message

Idiopathic bleeding ulcers are an important clinical issue with substantial re-bleeding risk (up to **6.1%**)

PPI and H2RA are equivalent strategies (interim data; numerically PPI is better)

Despite either therapy, cumulative risk of ulcer recurrence is **1.8%**

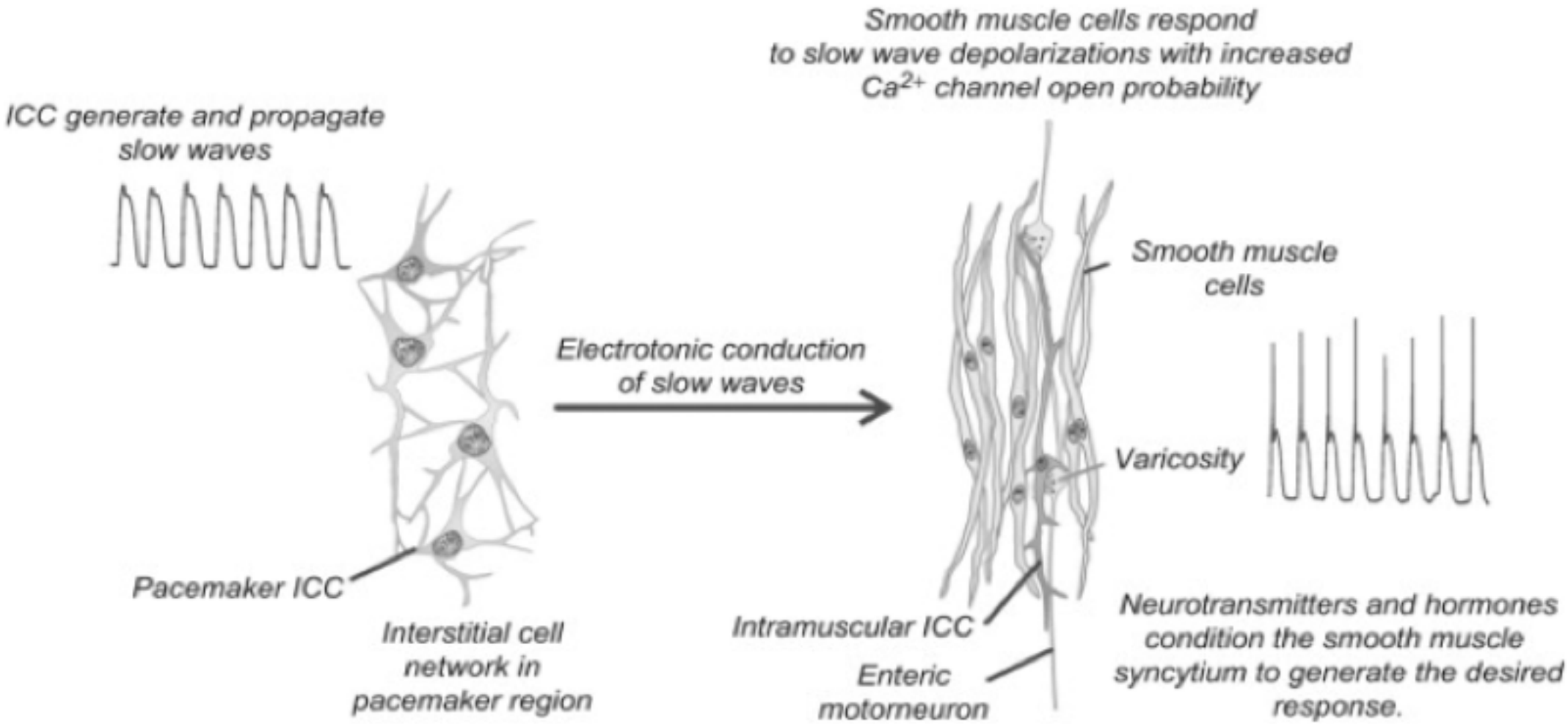
The fun and promise of innovation

People taking selfies in 1920 and in 2017

Imagine…

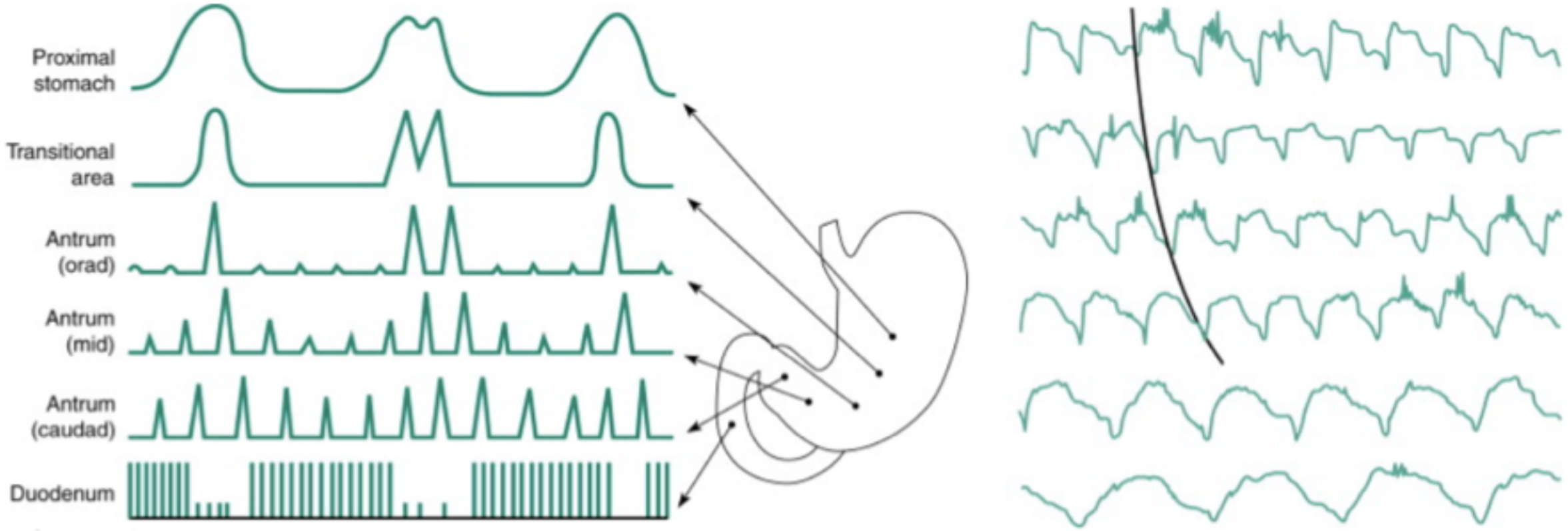
- Making the diagnosis of IBS by taking a “cardiogram of the abdomen”
- Relating abnormal gut motility patterns with specific symptoms
- Differentiating intestinal obstruction from inflammation or dysmotility
- Diagnosing IBD (CD and UC)
- Non-invasively monitoring progression of diseases of the gut
- Understanding the impact of diet or drugs on gut function
- Deciding how to expedite gut recovery after surgery

Functions of ICC and smooth muscle cells in GI muscles



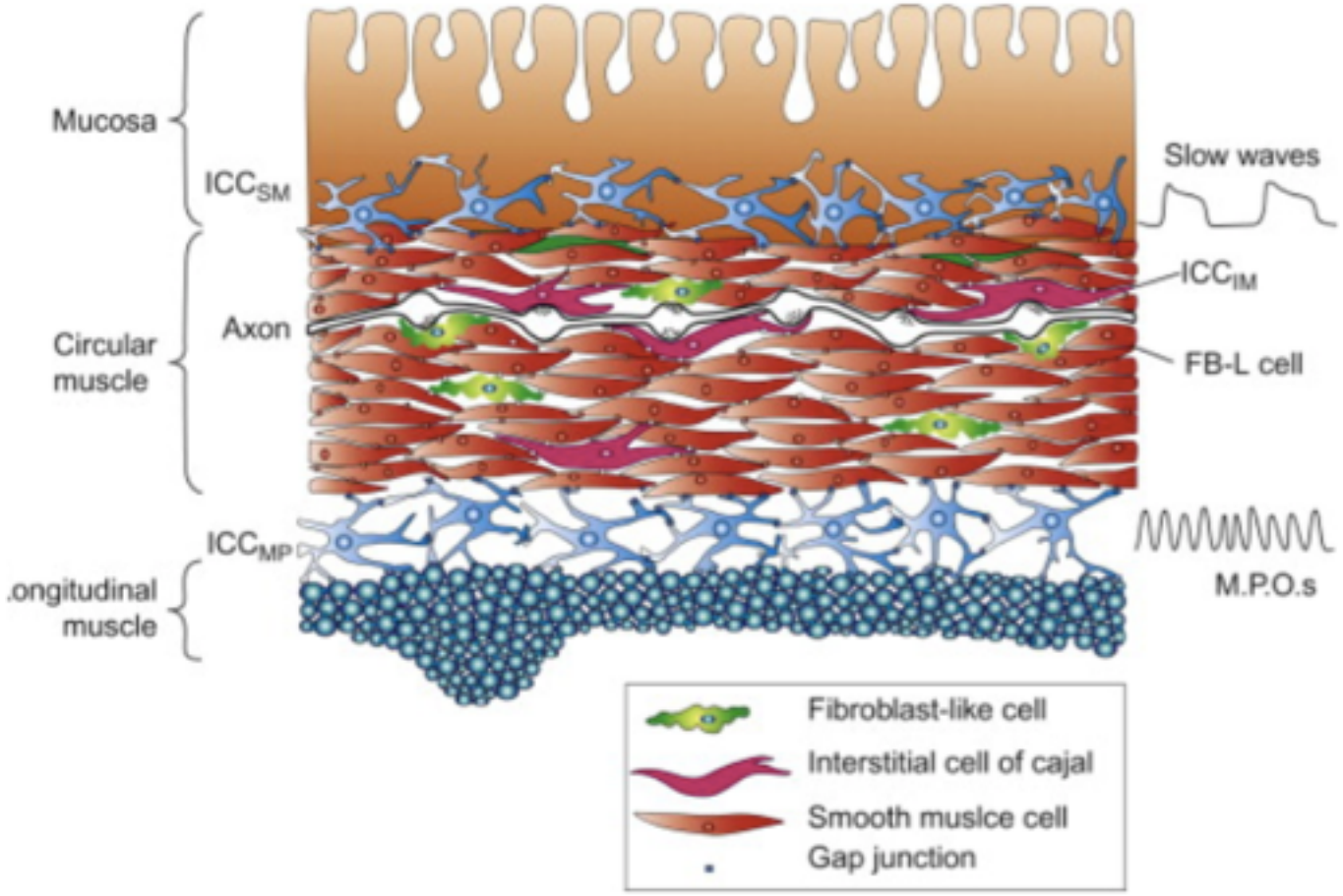
https://doi.org/10.1016/B978-0-12-382026-6.00022-1

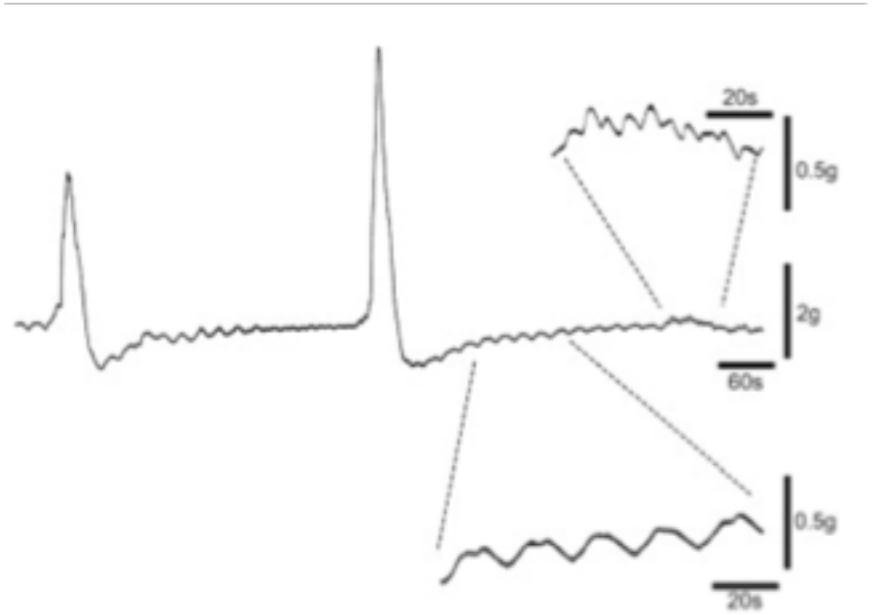
Gastric and small bowel myoelectrical activity



Am J Physiol 1969; 217: 461-471

Neuromuscular apparatus of the human intestine





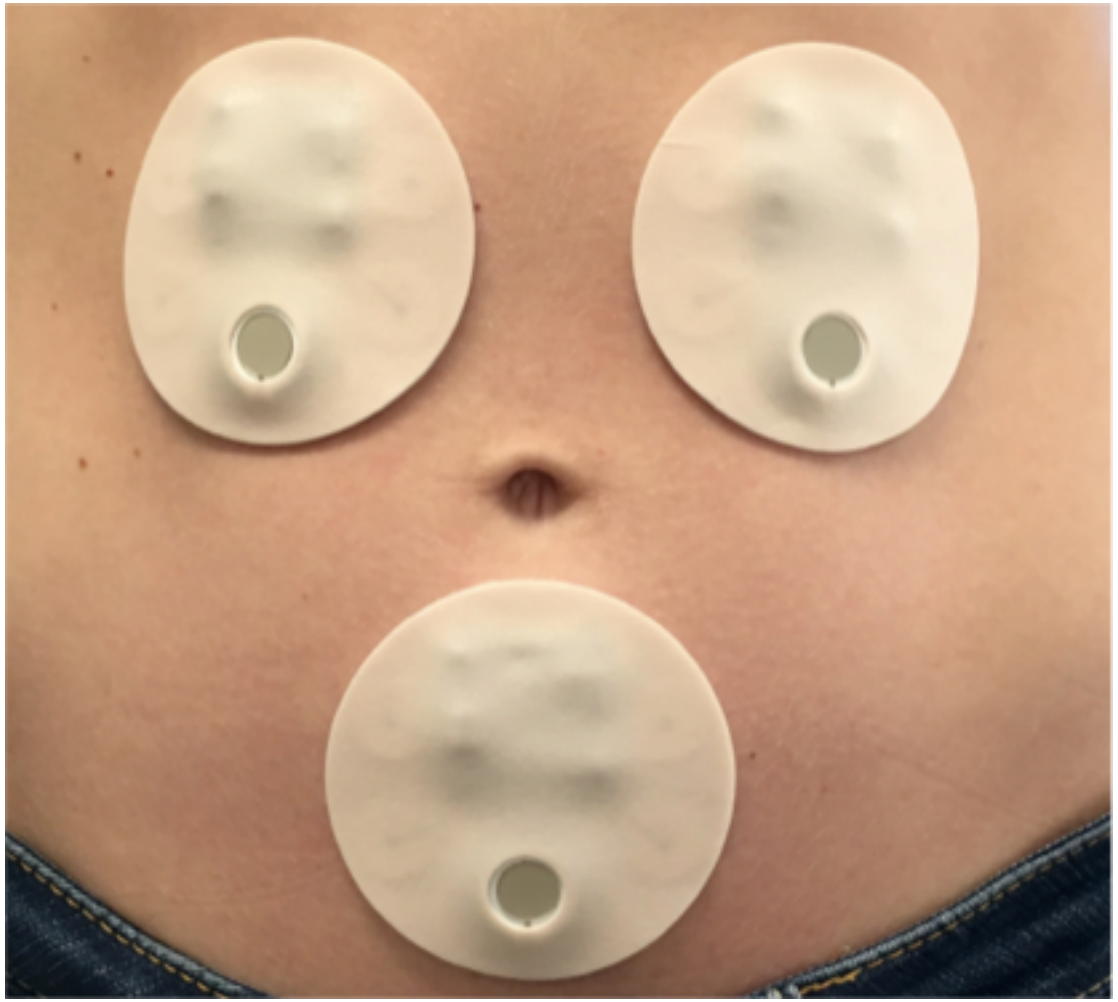
MPOs: membrane oscillation potentials

https://doi.org/10.1016/B978-0-12-382026-6.00022-1

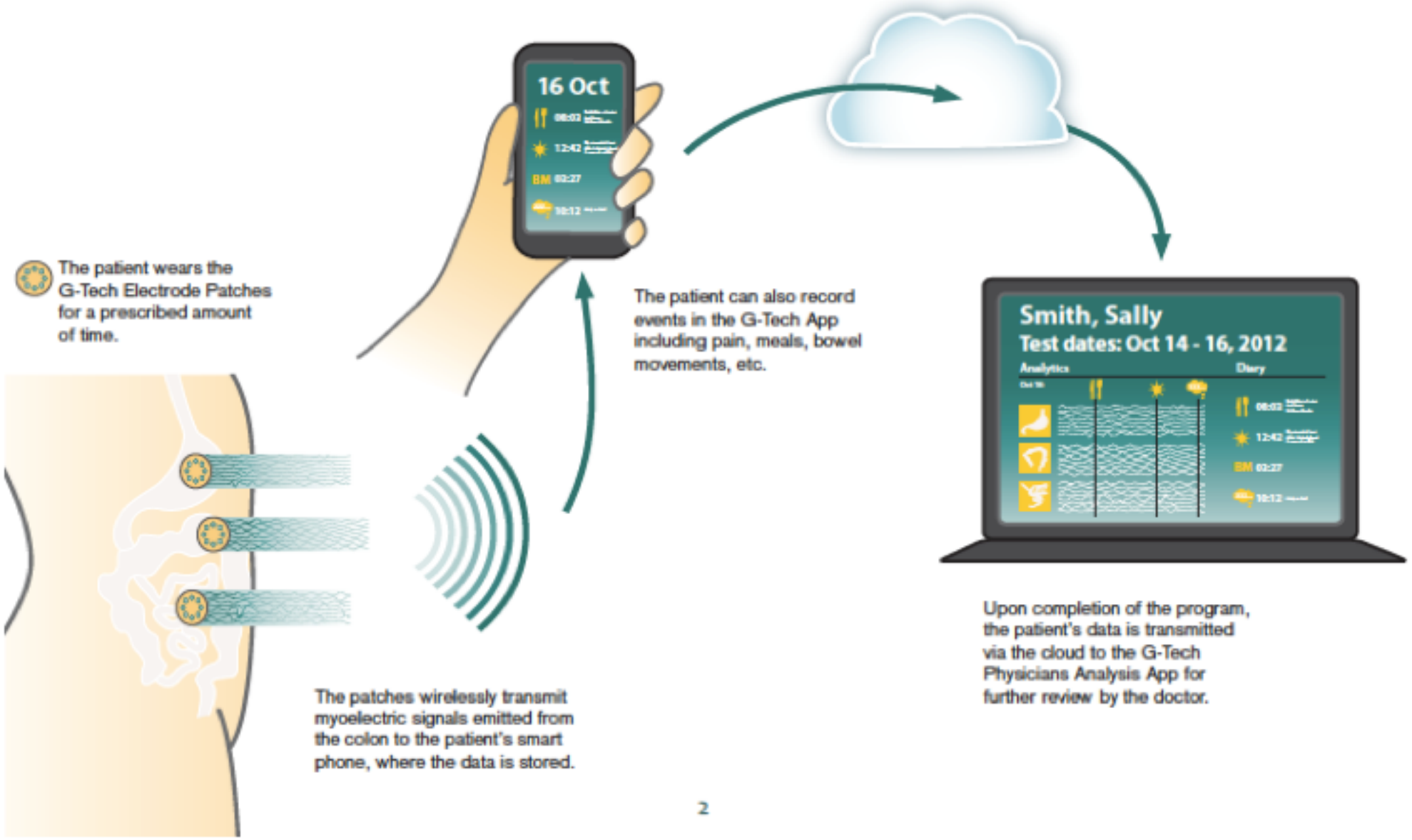
EKG for the Gut

- Measure electrical signals from digestive organs
- Represent motor activity
  - Related to motility, thresholds to abnormal sensation
- Help to understand underlying causes of **FGID**s
- (Hopefully) will help target therapies and management
- Noninvasive, inexpensive alternative to anatomic tests
  - For patients without alarm symptoms
  - When organic disease ruled out

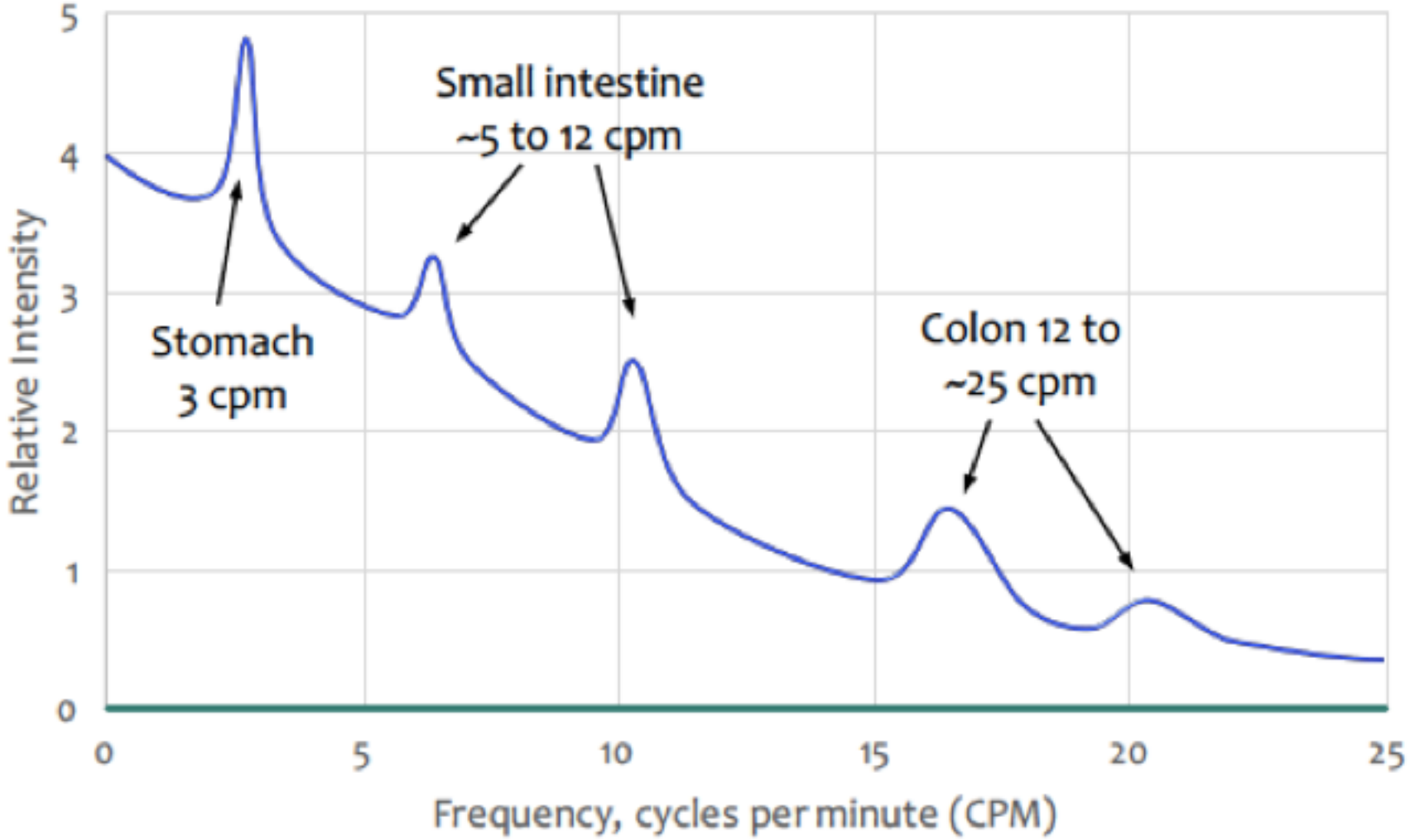
The G-Tech Patch



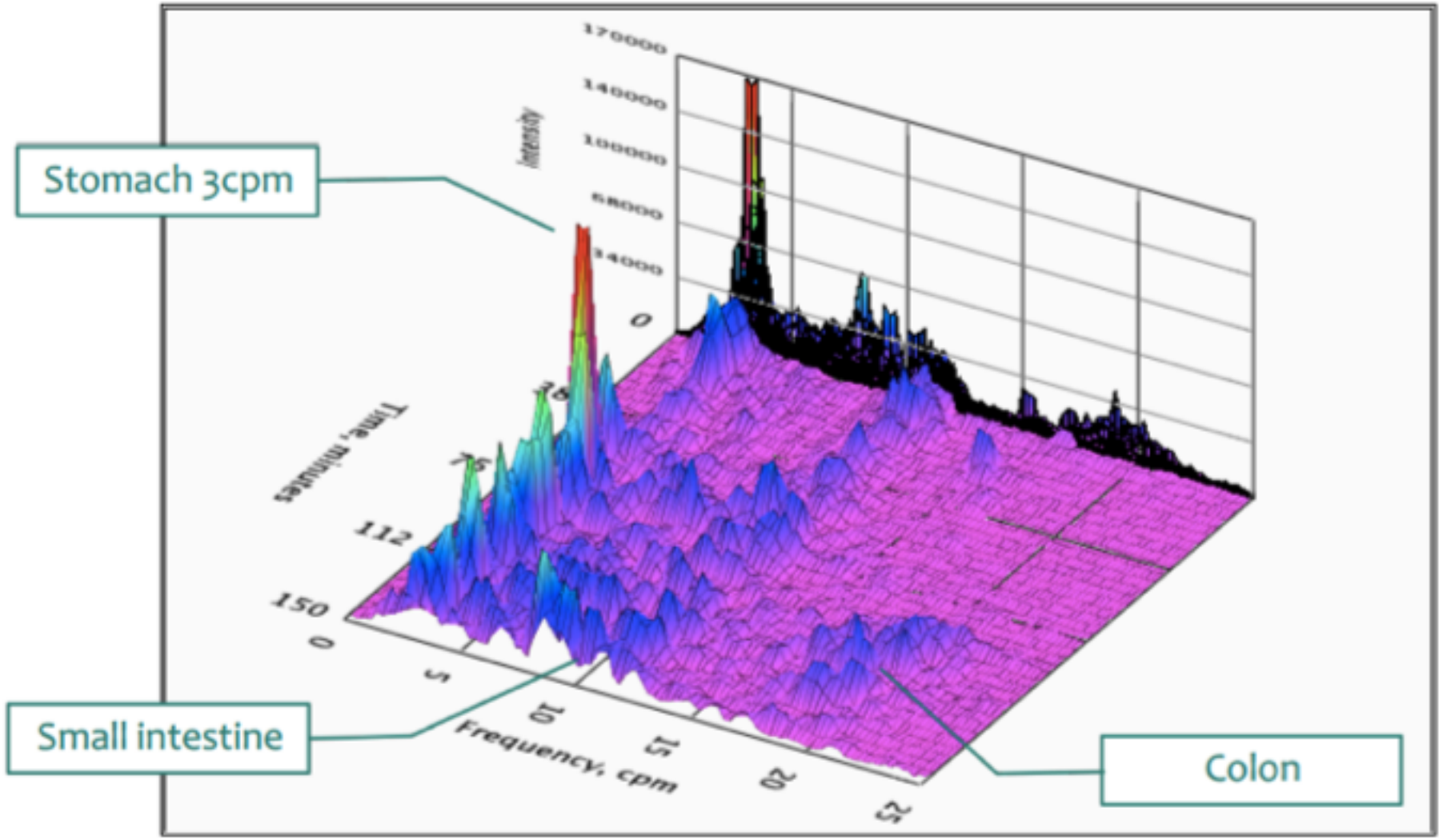
The GutPrint System: Home use



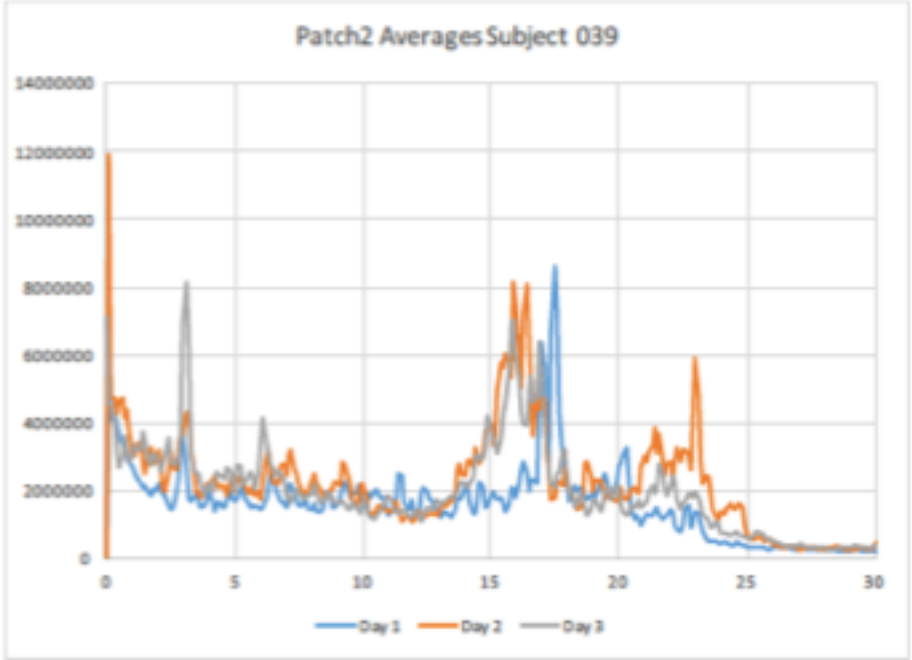
Sample Motor Activity Spectrum

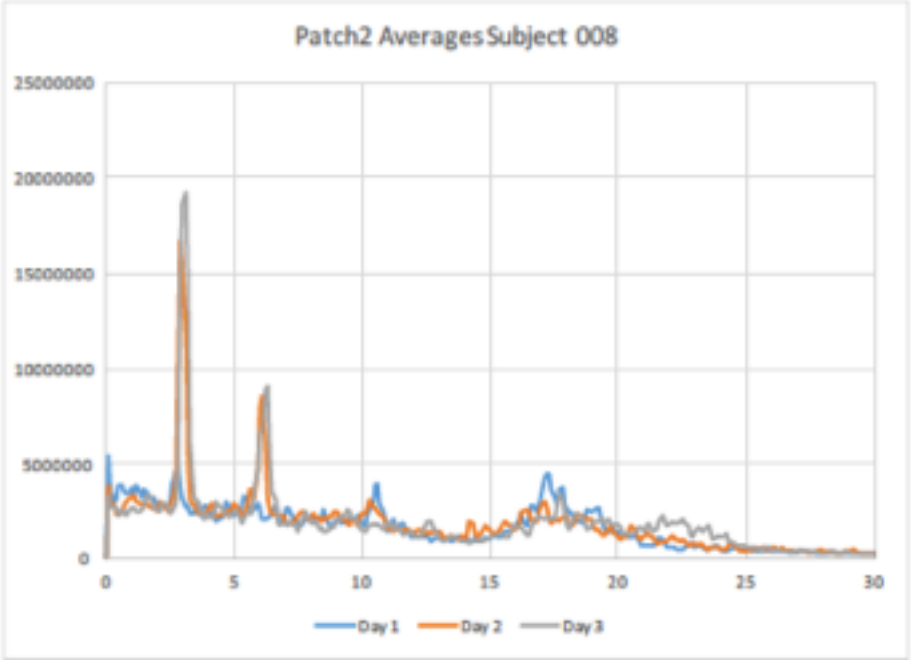


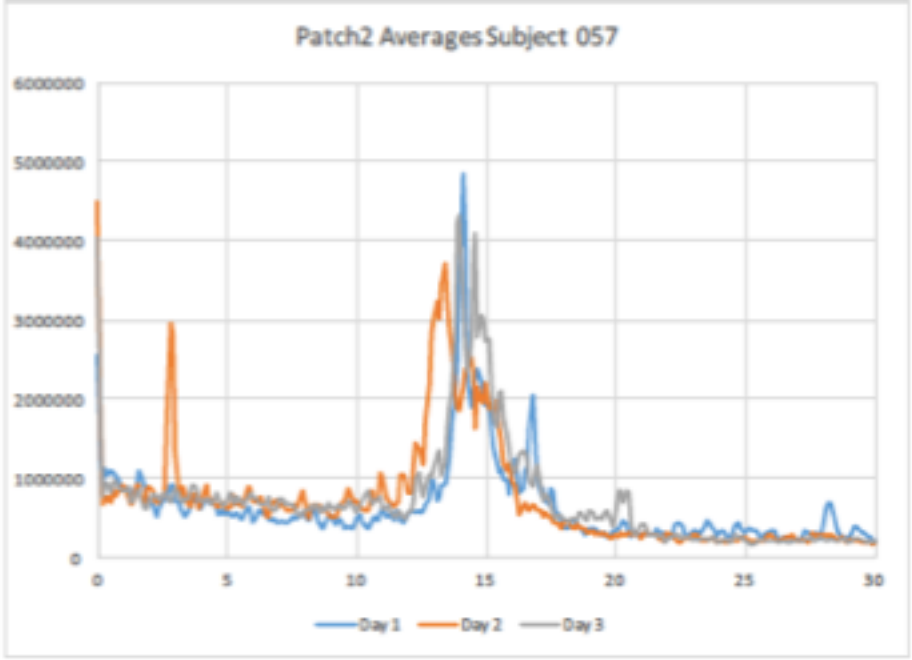
Waterfall Spectra (in 10 min windows) Show Evolution Over Time

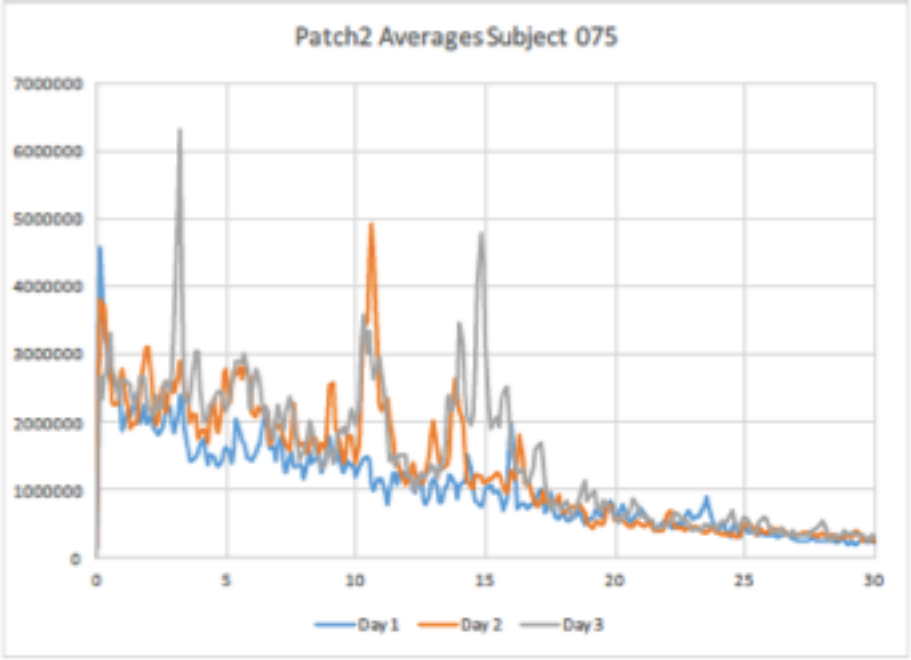


24-hr Reproducibility





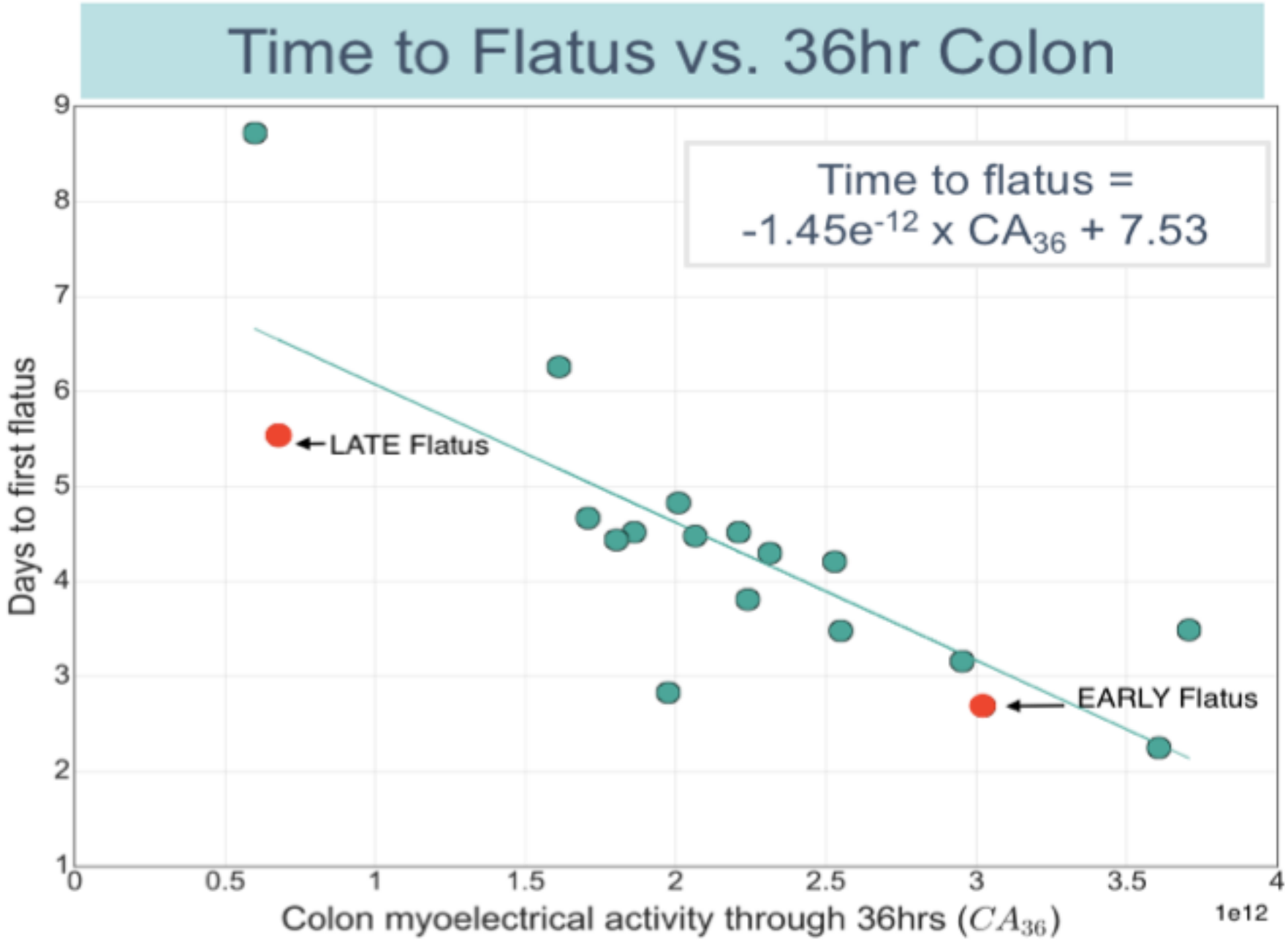




3 day recordings

Axelrod S et al. DDW 2018

POI



Navalgund et al DDW 2018

Correlation between myoelectrical activity and colonic pressures

Axelrod et al DDW 2018

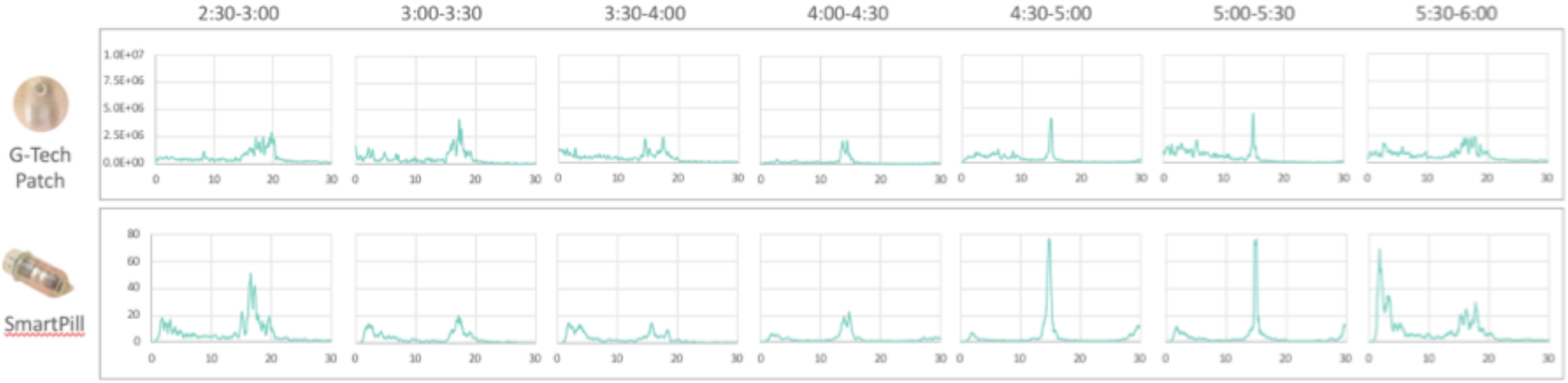


Figure 1. Sequential spectra from G-Tech myoelectric data)top) and SmartPill pressure data (bottom) when SmartPill was in the colon. Each spectrum represents 30 minutes of data. Horizontal scale is frequency in cycles/min (cpm). Vertical scales represent intensity of rhythmic activity, in relative units

Message

Technological advances have made prolonged myoelectrical recordings feasible under physiologic or pathologic conditions (postoperative and motility disorders)

Cloud-based data collection and analysis may allow immediate input and therapy

Validation is needed in both health and disease to define “gut signatures”

Symptom correlations and response to diet or drugs can be made

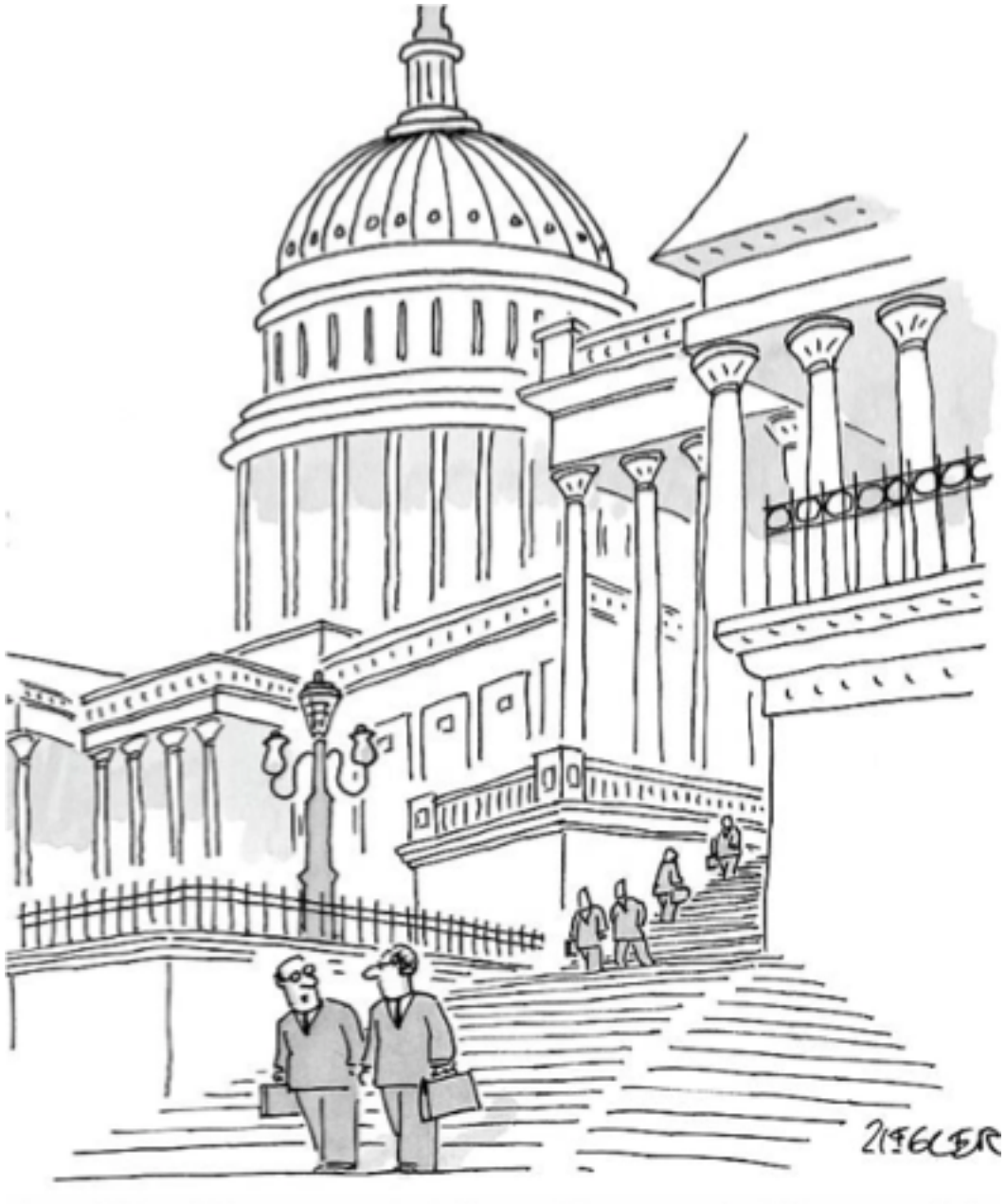
The holy grail in Gastroenterology: Validate IBS

"You have irritable-spouse syndrome"

Some more Washington DC sightseeing

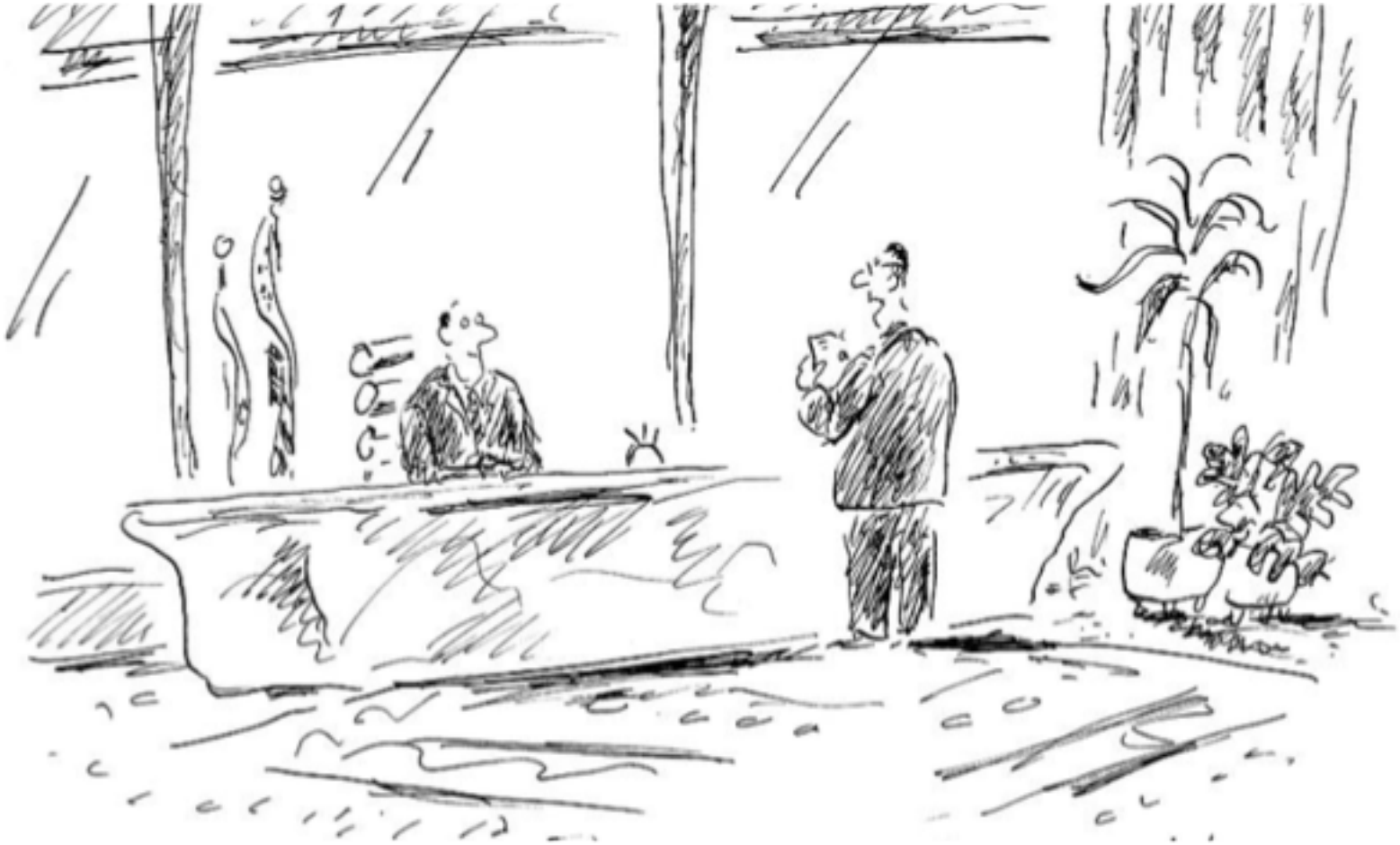
Mr. Mueller's office

Mr. Giuliani's office



“Of course it would be a different story entirely if you could extract crude oil from stem cells.”

PPI use and (potential) long-term effects: Can we avoid them?

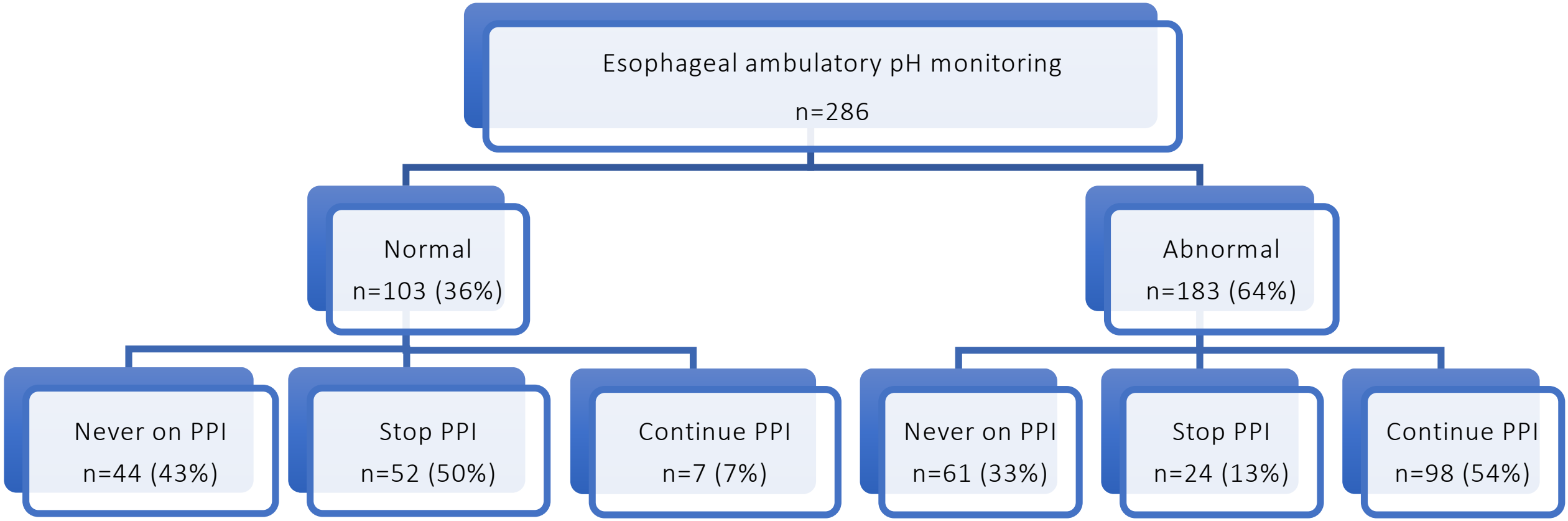


"You can't please all the people all the time, so you might as well please the pharmaceutical lobby"

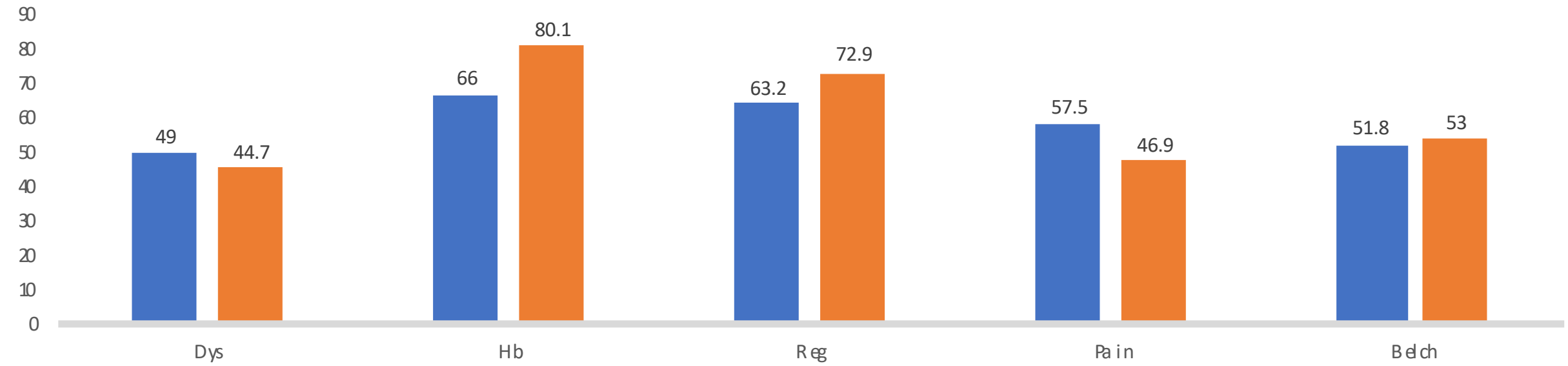
Use of ambulatory esophageal pH monitoring to minimize PPI utilization in patients with GERD symptoms

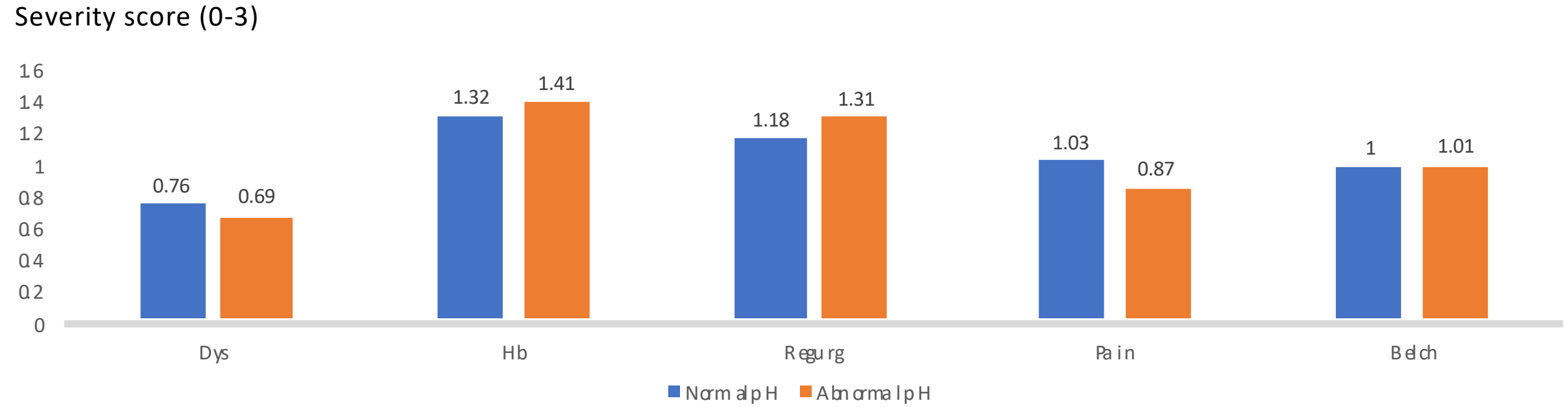
A pilot, retrospective cohort analysis

Triadafilopoulos et al. DDW 2018

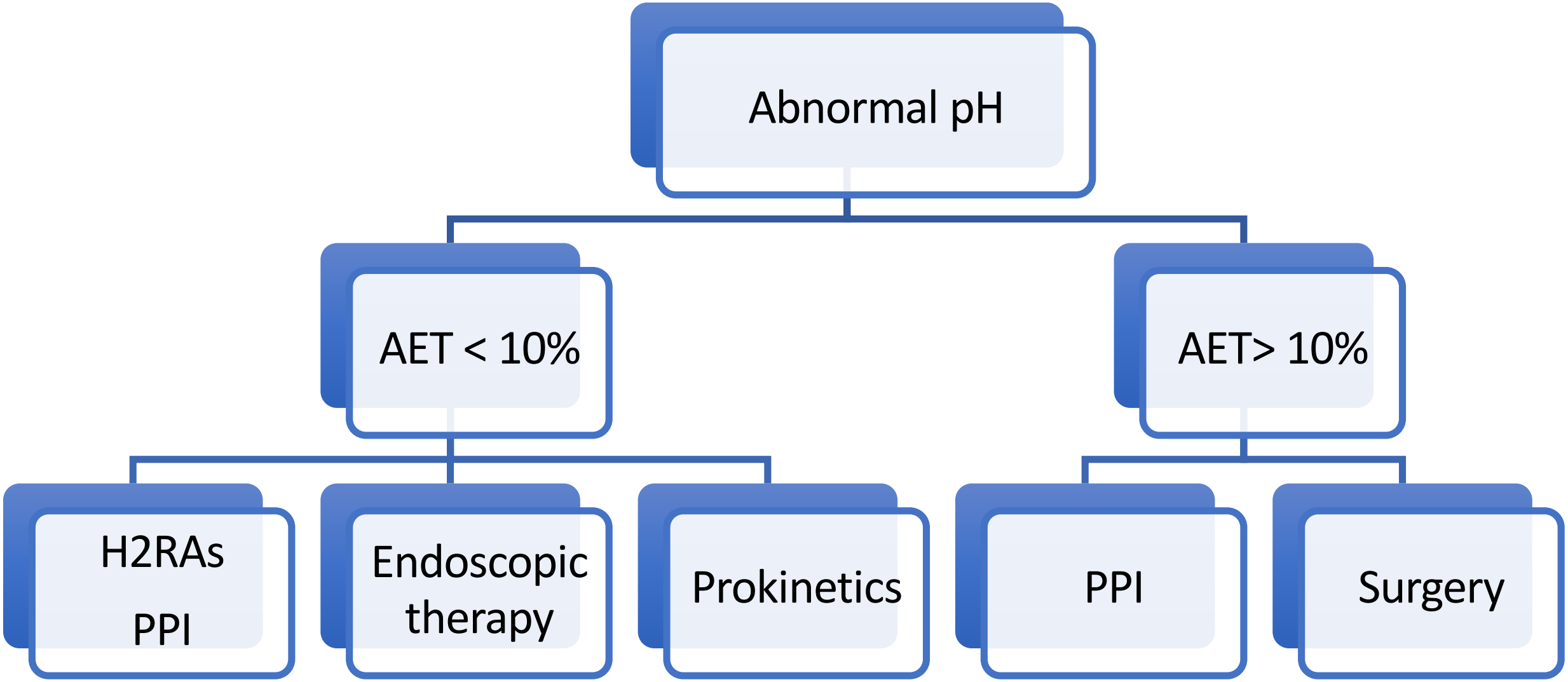


Symptoms


% Prevalence
90
80
70
60
50
40
30
20
10
0
49
44.7
66
80.1
63.2
72.9
57.5
46.9
51.8
53
Dys
Hb
Reg
Pain
Belch


Severity score (0-3)
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0.76
0.69
1.32
1.41
1.18
1.31
1.03
0.87
1
1.01
Dys
Hb
Regurg
Pain
Belch
Normal pH
Abnormal pH

Decisions based on AET



Treatment	Rationale	Number of patients
H2RAs	Partial PPI response or intolerance; % pH time < 10	20
Stretta	Partial PPI response or intolerance	8
POEM	Achalasia	1
LINX	Partial PPI response	1
LARS	Partial PPI response and hiatal hernia	5
RYB	GERD and morbid obesity	1
Prokinetics	Partial PPI response and IEM; % pH time < 10	5
Botulinum toxin	Achalasia, DES, or EGJOO	6

Variable	Normal AET (n= 103)	Abnormal AET (n=183)	P value
Age (mean & range)	52 (15-89)	48 (16-86)	NS
Gender	49M:54F	97M:86F	NS
Mean BMI (+/- SEM)	22.6+/-0.4	26.2+/-0.3	p<0.0001
Endoscopy	Normal: 92; Sliding hiatal hernia: 13; Para-esophageal hernia: 2; Erosive esophagitis: 4; EoE: 5; BE: 2	Normal: 135; Sliding hiatal hernia: 51; Erosive esophagitis: 33; EoE: 3; BE: 12	
Mean LESP (mmHg) (+/- SEM)	24+/-2	21+/-1	NS
Mean % pH <4.0 (+/- SEM)	1.6 +/- 0.1	15.0+/- 0.9	P<0.0001
% symptom correlation (+/-SEM)	18.7 +/- 3	33.5 +/- 3	p=0.001
Never on PPI (%)	44 (43)	61 (33)	NS
Stop PPI (%)	52 (50)	24 (13)	P<0.0001
Continue PPI (%)	7 (7)	98 (54)	P<0.0001
Total PPI avoidance (%)	96 (93)	47 (26)	P<0.0001

Diagnosis	Normal AET (n=103)	Abnormal AET (n=183)
Achalasia	2	5
Barrett's esophagus	2	18
DES/JE	3	7
Non-ulcer dyspepsia	19	0
EGJOO	13	17
EoE	8	7
Gastroparesis	4	5
Hypersensitive esophagus	3	0
IEM/absent peristalsis	19	42
Para-esophageal hernia	2	0
GERD	0	82
Functional heartburn	28	0

% PPI use & Rx response	Normal AET (n=103)	Abnormal AET (n=183)	P value
PPI never used	0.42+/-0.04	0.33+/-0.03	0.12
Complete PPI response	0.16+/-0.03	0.19+/-0.02	0.57
Partial PPI response	0.27+/-0.04	0.44+/-0.03	**0.003**
PPI non-response	0.13+/-0.03	0.02+/-0.01	**0.003**

Message

This retrospective cohort analysis examined the potential of using ambulatory esophageal pH monitoring (in conjunction with endoscopy and manometry) as a tool to minimize PPI utilization in patients with GERD symptoms

Based on pH testing, clinicians **could avoid initiating** or **discontinue** previously introduced PPI therapy in 50% of patients, thereby minimizing the risks or concerns for long-term adverse events.

Stanford MEDICINE | SEMPIRE

Stanford Esophageal Multi-Disciplinary Program in Innovative Research Excellence

“I wrote you a prescription for some pills and a check so you can afford them.”