A Novel Classification Scheme for Gastroparesis Based on Predominant Symptoms

Steve Harrell, MD

CREST Master's Thesis

April 27, 2006

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"Or McDonald's employee of the month"

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May 13, 2006

Notice Date!!!

The Committee Members

Intro

- Gastroparesis is a disorder characterized by delayed gastric emptying.
- Symptoms of gastroparesis (GP) are diverse.

Hornbuckle K, Barnett JL. The diagnosis and work-up of the patient with gastroparesis. J Clin Gastroenterol 2000;30:117-124.

Intro

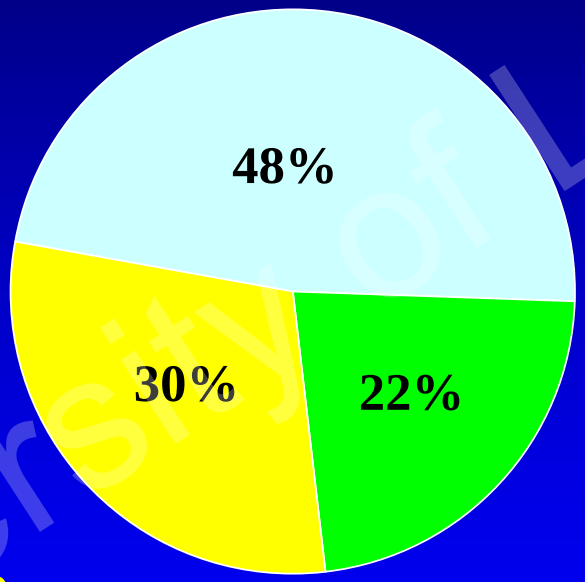
- Other functional GI disorders have proposed classification schemes.
- For instance, irritable bowel syndrome can be divided into diarrhea predominant, constipation predominant or alternating subgroups.
- We believe there are three main subtypes of gastroparesis based on a large retrospective analysis of symptom presentations at our institution (DDW 2005 Abstract: Bizer et al).

Intro

Vomiting-Predominant GP

- Vomiting
- Dehydration
- Hospitalizations
- Weight loss

N=339 patients presenting to University of Louisville



Regurgitation-Predominant GP

- Heartburn
- Effortless regurgitation

Dyspepsia-Predominant GP

- Epigastric pain
- Bloating
- Abdominal distension

Bizer et al. Gastroenterol 2005; 128 (suppl 2): abstract.

Intro

- Functional GI disorders have lower HRQOL than many organic GI diseases.
- Symptom severity correlates with HRQOL

Simren M, Svedlund J, Posserud I, Bjornsson ES, Abrahamsson H. Health-related quality of life in patients attending a gastroenterology outpatient clinic: functional disorders versus organic diseases. Clin Gastroenterol Hepatol 2006;4:187-195.

Example HRQOL Scores

Disease	PCS	MCS	
Male (25-34)	54	51	N=472
Depression	46	37	N=1000
Cancer	41	47	N=244
Diabetes	42	47	N=596
Heart Dz	39	48	N=768
Kidney Dz	38	45	N=87
Liver Dz	42	44	N=59
Ulcers	43	45	N=652

Ware J, Kosinski M, Turner-Bowker D, Gandek B. How to Score Version 2 of the SF-12 Health Survey. QualityMetric Incorporated, 2002.

Intro

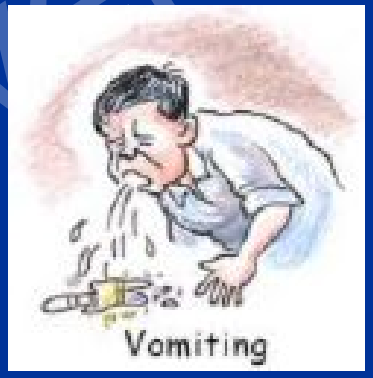
- Current classification of gastroparesis is based on etiology, which does not guide therapy.
- Furthermore, the severity of delayed gastric emptying does not correlate with symptom presentation.
- Other pathophysiologies must be responsible for the diversity of symptom presentation

Hypothesis

- A predominant-symptom classification for gastroparesis is useful for the following reasons:
  - Can direct treatment
  - Can be use as a framework for future research on pathophysiology, prognostic indicators, and treatment for gastroparesis

Hypothesis

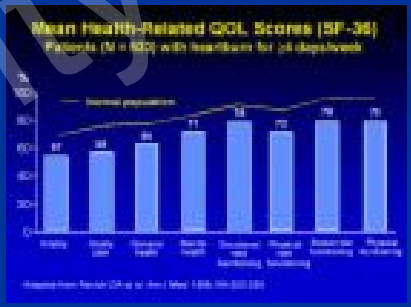
- For this gastroparesis classification scheme to be relevant, it should satisfy the following:
  - Good agreement between patient and physician's perception of the predominant symptoms
  - It should correlate with other measures of symptoms and quality of life



Aim

- To prospectively validate a new predominant-symptom classification for gastroparesis using symptom severity and quality-of-life measures.
- Secondary Aim: To not flunk the CREST program

Materials and Methods



Subject Enrollment

- Consecutive subjects with symptoms of gastroparesis for >2 months and evidence of delayed gastric emptying were prospectively enrolled from a tertiary referral motility clinic.
- Exclusion criteria included pregnancy, prisoners, individuals < 18 years old, and non-ambulatory persons.

Study Protocol

- Questionnaire Asking for Chief Complaint
- Assessment of Symptom Severity
  - **P**atient **A**ssessment of **G**astro**I**ntestinal Disorders-**Sym**ptom Severity Index (PAGI-SYM)
- Assessment of Quality of Life
  - SF-12v2™ HR-QOL

Primary Chief Complaint

- **Vomiting-Predominant GP**: vomiting with retching and nausea are the most bothersome symptoms.
- **Dyspepsia-Predominant GP**: unpleasant or troublesome sensation (discomfort or pain) centered in the upper abdomen is the most bothersome symptom; this sensation may be characterized by or associated with upper abdominal fullness, fullness after small meals, bloating, or nausea.
- **Regurgitation-Predominant GP**: effortless regurgitation of acid or undigested food or heartburn is the most bothersome symptom.
  - ** Adapted from Rome II criteria
  - Talley NJ, Stanghellini V, Heading RC, Koch KL, Malagelada JR, Tytgat GN. Functional gastroduodenal disorders. Gut 1999;45 Suppl 2:II37-II42

PAGI-SYM

- 20-item symptom severity instrument that measures common GI symptoms. 6 subscales include: heartburn/regurgitation, fullness/early satiety, nausea/vomiting, bloating, upper abdominal pain, and lower abdominal pain.
- Results suggest that the PAGI-SYM has good reliability and evidence supporting construct validity and responsiveness in subjects with GERD, dyspepsia, or gastroparesis

Revicki DA, Rentz AM, Tack J, Stanghellini V, Talley NJ, Kahrilas P, De La LC, Trudeau E, Dubois D. Responsiveness and interpretation of a symptom severity index specific to upper gastrointestinal disorders. Clin Gastroenterol Hepatol 2004;2:769-777.

SF-12v2™ HR-QOL

- The SF-12v2™ is a brief but reliable and valid generic measure of health-related quality of life.
- The SF-12 subscale domains included physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE) and mental health (MH).
- Mental and physical component summaries (MCS & PCS) were calculated. SF-12 scores were converted to norm-based scoring (NBS) using a Z-score transformation (mean=50, sd=10).

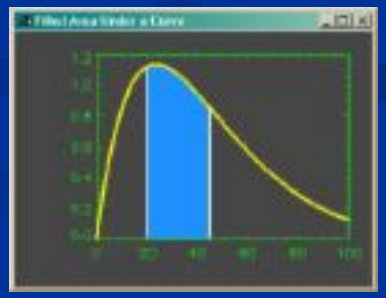
Ware J, Kosinski M, Turner-Bowker D, Gandek B. How to Score Version 2 of the SF-12 Health Survey. QualityMetric Incorporated, 2002.

Sample Size Calculation

- Assumption was that vomiting-predominant GP would have most impaired HRQOL
- A difference of ½ of a standard deviation between subgroups was considered meaningful.
- Norm-based SF-12 standard deviation of 10 would correspond to a difference between means of 5.
- α level of 5% and a power of 80%, a sample size of 93 patients would be required for this study.

Statistical Analysis

- Cohen's kappa (k) was used for correlation between physician and subject classification of gastroparesis.
- ROC curves were constructed to optimize sensitivity and specificity for each of the 6 PAGI-SYM subscales in order to differentiate gastroparetic subjects into symptom-predominant subgroups.
- The concordance statistic (c-statistic) denotes the area under the curve (AUC) and is a global measure of diagnostic utility and was used to compare these subgroups.



Statistical Analysis

- SF-12 scores were converted to norm-based scoring (NBS) using a Z-score transformation (mean=50, sd=10) and compared to the 1998 general U.S. population means using T-tests.
- Total PAGI-SYM scores were compared to SF-12 domains by Pearson correlations.
- Analysis of Variance (ANOVA) with post-hoc analysis was used to detect demographic and HRQOL differences between GP subgroups.

Results

Demographics

Predominant Symptom	Vomiting GP	Dyspepsia GP	Regurgitation GP
Number of Subjects	29	49	22
BMI (SD)	28.0 (6.2) *	27.7 (5.8) *	33.5 (8.4)
Age (SD)	42.9 (9.8)	50.8 (13.5) **	52.6 (11.5) **

87% Females

* $p < .01$ when compared to regurgitation group

** $p < .05$ when compared to vomiting group

Concordance

Between Subject and Physician by Perception of Predominant Symptom

Investigator's perceived CC * Patient Chief Compaint Crosstabulation

Count

		Patient Chief Compaint			Total
		vomiting	dyspepsia	regurg	
Investigator's perceived CC	vomiting	23	5	1	29
	dyspepsia	4	42	3	49
	regurg	1	8	13	22
Total		28	55	17	100

78% concordance between physician and subject's classification of GP

Kappa =0.64 showing good agreement

Symptom Scores

Symptom Scores by GP Subgroup

Investigator's Perception of Predominant Symptom

PAGI-SYM subscales (Mean ± SD)	Vomiting-predominant GP (n=29)	Dyspepsia-Predominant GP (n=49)	Regurgitation-Predominant GP (n=22)
Nausea/vomiting	*3.4 ± 1.4	1.6 ± 1.2	2.0 ± 1.6
Post-prandial fullness/early satiety	**3.7 ± 1.2	3.0 ± 1.3	3.0 ± 1.3
Bloating	3.4 ± 1.3	3.0 ± 1.4	2.9 ± 1.5
Upper abdominal pain	2.8 ± 1.3	2.8 ± 1.1	2.6 ± 1.4
Lower abdominal pain	2.1 ± 1.2	1.9 ± 1.5	1.9 ± 1.5
HB/regurgitation	2.5 ± 1.1	1.6 ± 1.3	†2.9 ± 1.2
Total score	†2.9 ± 1.0	2.2 ± 0.9	2.7 ± 1.1

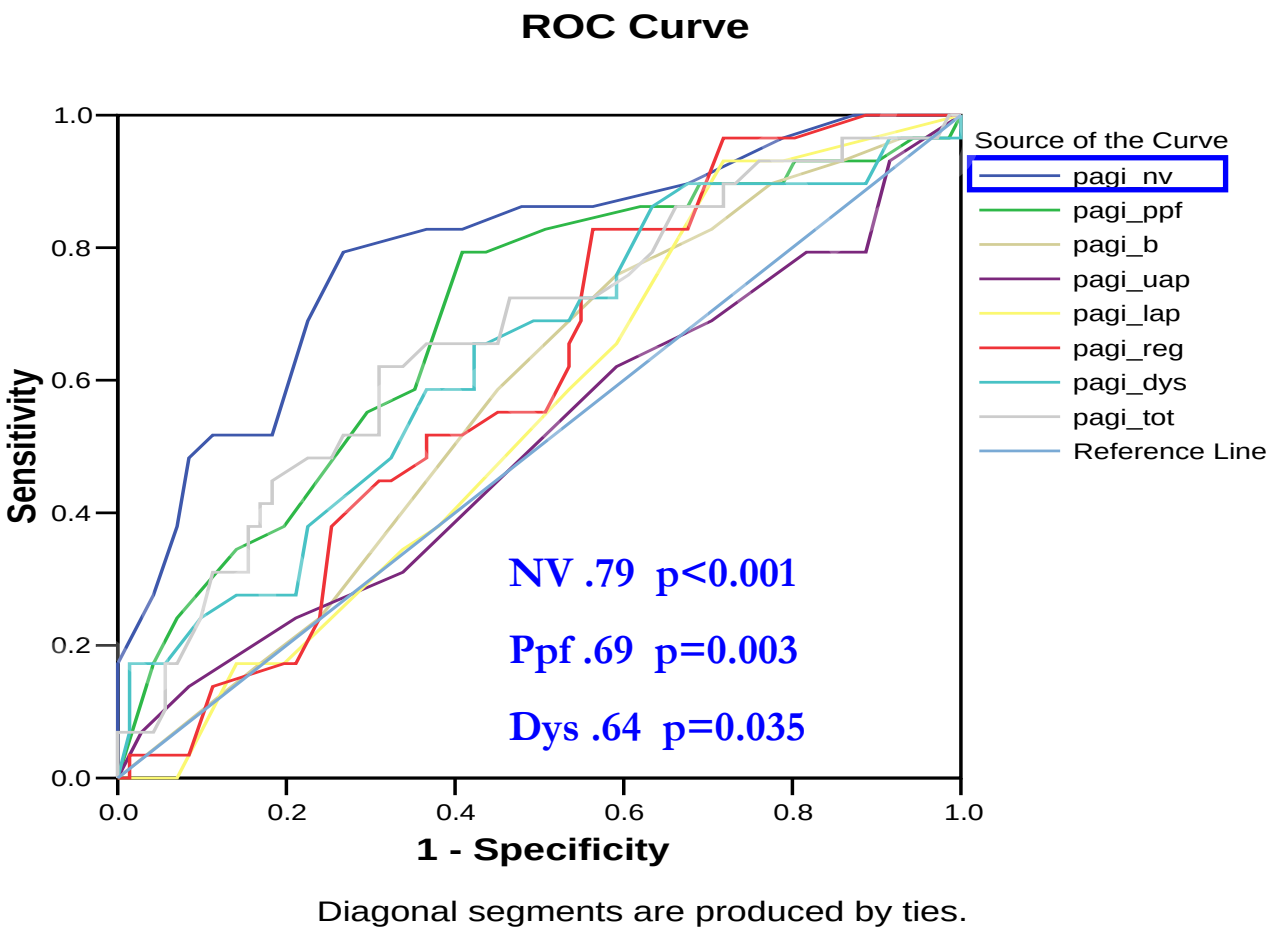
* $p<0.01$ vs dyspepsia and regurgitation-predominant GP
** $p<0.05$ vs dyspepsia-predominant GP
† $p<0.01$ vs dyspepsia-predominant GP

Correlations between PAGI-SYM & SF-12

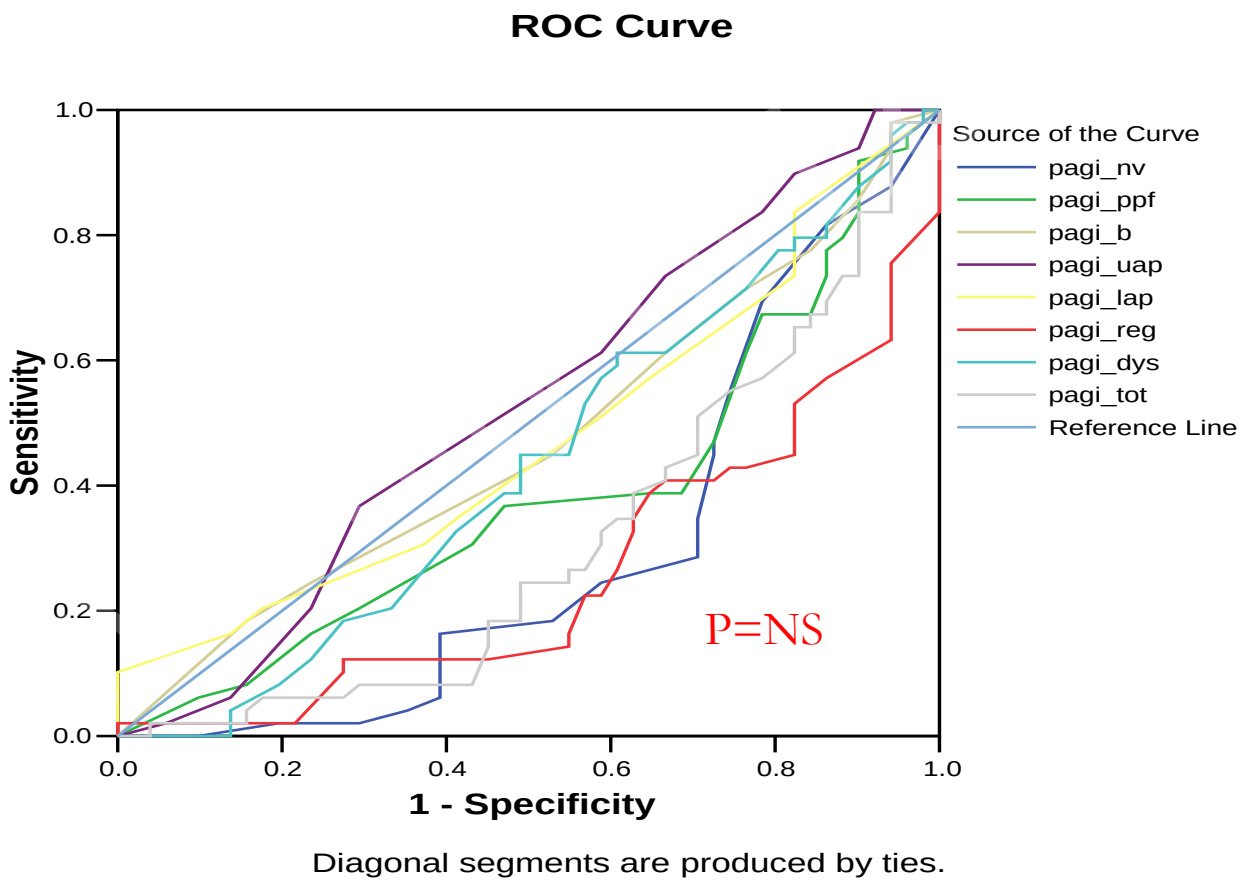
	GH	PF	RP	RE	BP	MH	VT	SF
pagi_nv	-.549(**)	-.374(**)	-.430(**)	-.470(**)	-.411(**)	-.389(**)	-.387(**)	-.364(**)
pagi_ppf	-.445(**)	-.194	-.400(**)	-.383(**)	-.426(**)	-.307(**)	-.351(**)	-.289(**)
pagi_b	-.353(**)	-.229(*)	-.284(**)	-.319(**)	-.445(**)	-.272(**)	-.231(*)	-.260(**)
pagi_uap	-.321(**)	-.153	-.272(**)	-.331(**)	-.619(**)	-.188	-.095	-.243(*)
pagi_lap	-.424(**)	-.350(**)	-.297(**)	-.241(*)	-.414(**)	-.205(*)	-.277(**)	-.232(*)
pagi_reg	-.489(**)	-.329(**)	-.288(**)	-.426(**)	-.381(**)	-.345(**)	-.212(*)	-.194
pagi_dys	-.477(**)	-.233(*)	-.407(**)	-.422(**)	-.581(**)	-.327(**)	-.309(**)	-.329(**)
pagi_tot	-.600(**)	-.377(**)	-.435(**)	-.510(**)	-.565(**)	-.407(**)	-.347(**)	-.339(**)

** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).

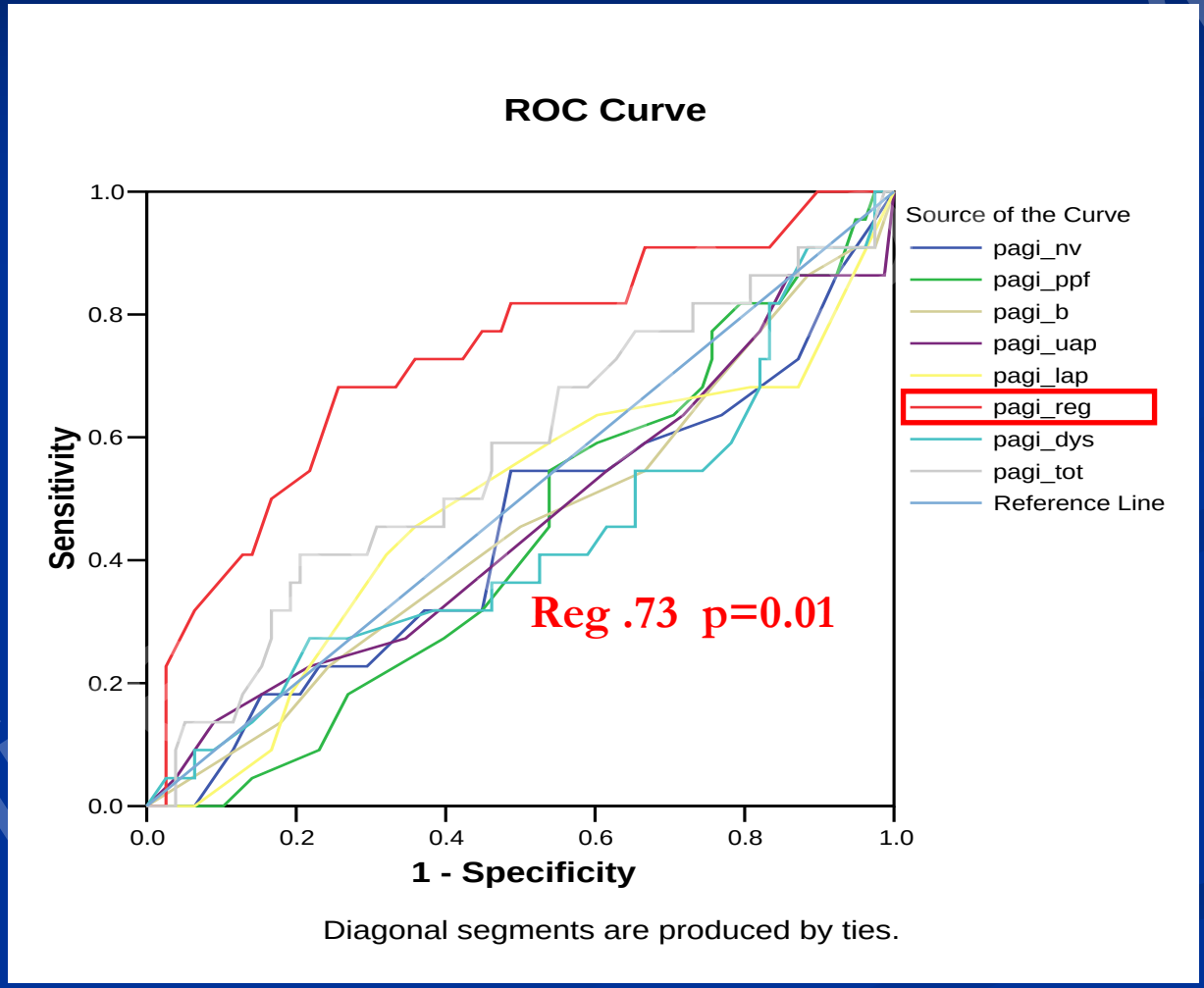
PAGI-SYM Subscales to Differentiate Vomiting-Predominant Gastroparesis



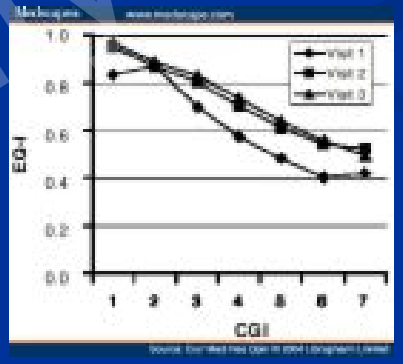
PAGI-SYM Subscales to Differentiate Dyspepsia-Predominant Gastroparesis



PAGI-SYM Subscales to Differentiate Regurgitation-Predominant Gastroparesis



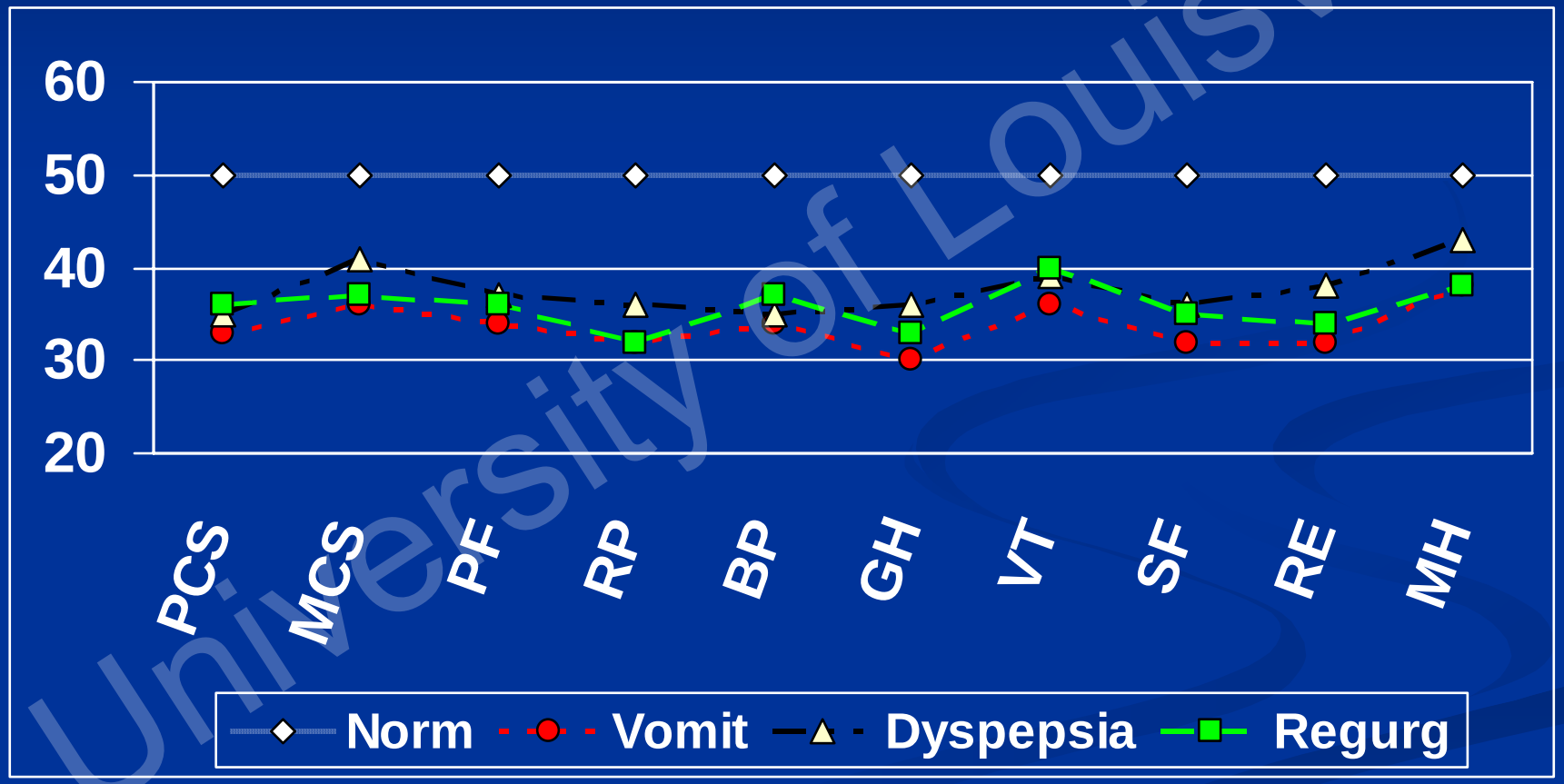
HRQOL



HRQOL Summary Scores

Disease	PCS	MCS	
Our Study	**35**	**39**	N=100
Depression	46	37	N=1000
Cancer	41	47	N=244
Diabetes	42	47	N=596
Heart Dz	39	48	N=768
Kidney Dz	38	45	N=87
Liver Dz	42	44	N=59
Ulcers	43	45	N=652

Quality of Life by SF-12 Domains



P < .05 compared to normal population; p=NS compared to GP subgroups

Conclusions

- The results of this study suggest that predominant-symptom classification is a valid means of categorizing subjects with GP
- There was a substantial agreement between physician and patient using a symptom-predominant classification of GP.

Conclusions

- Vomiting and regurgitation-predominant GP corresponded very well with patient's assessment of symptom severity.
- Generic measurement of HRQOL revealed significant impairment overall, but no differences were found between symptom-predominant subgroups.

Future Directions

- Dyspepsia group is very heterogeneous and warrants further investigation and classification.
- Additional data for cluster analysis to let data generate a hypothesis might be a means of better understanding this group.
- Use a disease-specific HRQOL measure for next study

Special Thanks

- Dr. Wo
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- Drs. Dryden & Studts
- Fellows & Attendings on Service Last Fall
- Jennifer Koopman & Luwa Cai

Questions?