
2023 SCSG
GI SYMPOSIUM

Upper GI/Motility Abstracts (Focus on Gastric Function)

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Disclosures

Consulting Fees:

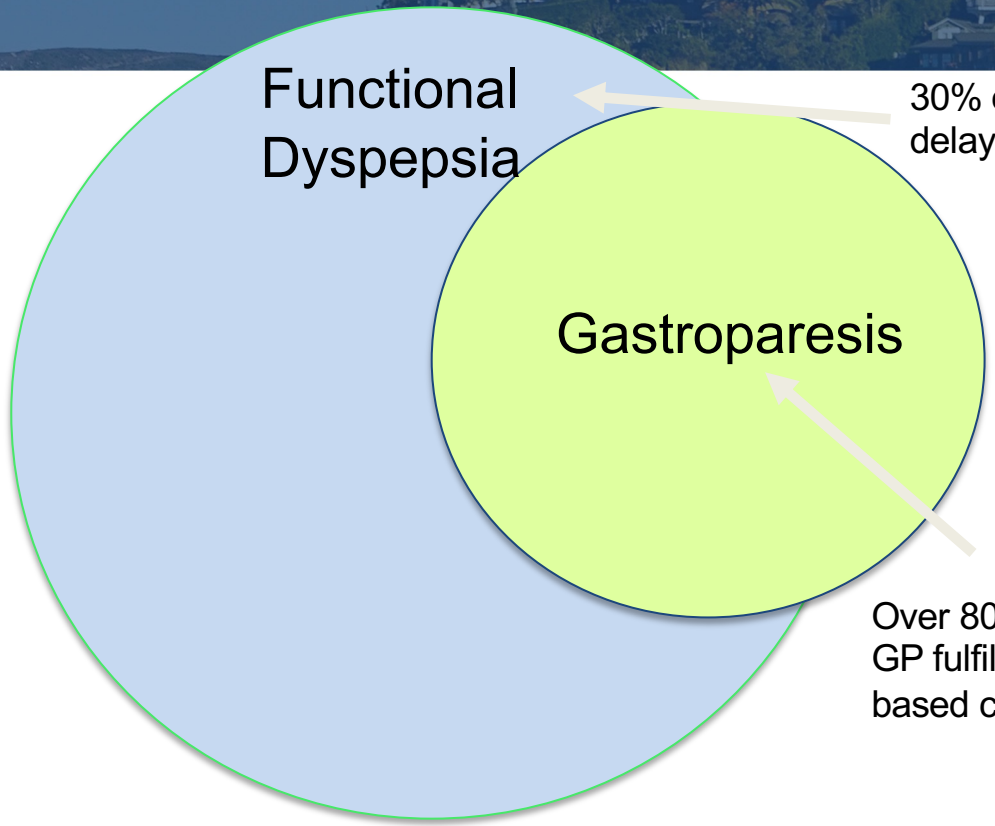
- Evoke Pharma
- Pfizer
- ReStalsis
- Phathom Pharmaceuticals
- Ardelyx
- Mahana Therapeutics

Speakers' Bureau:

- Regeneron

Gastroparesis and Functional Dyspepsia: Significant Overlap

- Symptoms
- Treatment response
- Pathophysiology



30% of FD patients have delayed gastric emptying

Over 80% of patients with GP fulfill the symptom-based criteria for FD

Stanghellini V et al. Gastroenterology 1996;110:1036–42.
Sarnelli G et al. Am J Gastroenterol 2003;98:783–8.
Maes BD et al. Dig Dis Sci 1997;42:1158–62.

Symptom overlap in GP and FD

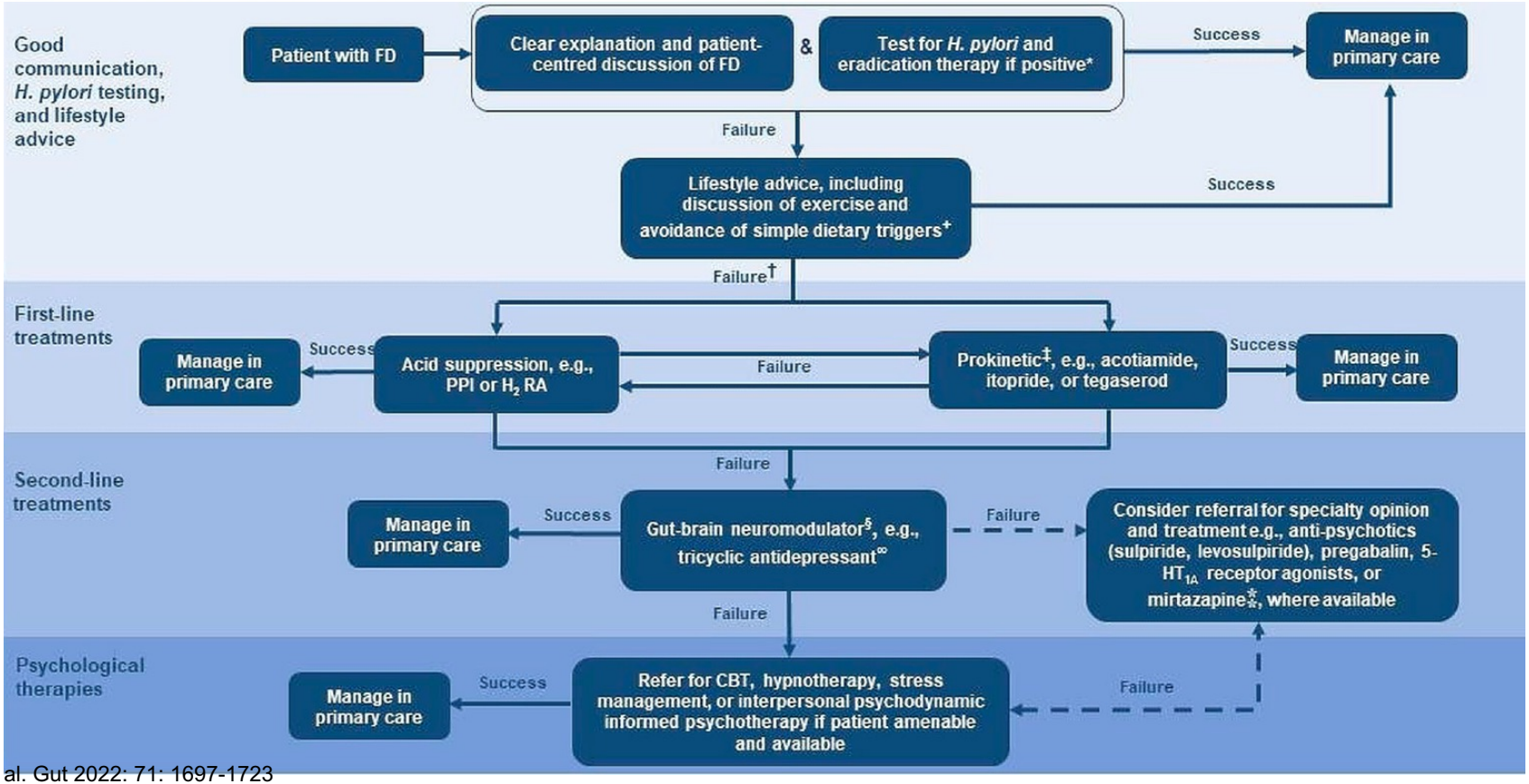
- Six of the nine questions on the GCSI record common symptoms of FD

Table 1. Symptom prevalence (%) in functional dyspepsia and gastroparesis

Symptom	Functional dyspepsia	Gastroparesis
Epigastric pain/discomfort	89–90	89–90
Epigastric fullness	75–90	—
Early satiety	50–82	60–86
Symptoms worsened by eating	79	72
Postprandial fullness	75–88	—
Bloating	68–96	51–75
Belching	45–85	—
Nausea	67–90	92–96
Vomiting	20–33	68–84
Weight loss	58	—

Lacy, B.E., The American Journal of Gastroenterology, 107(11), 2012.

2022 BSG Guideline on the management of functional dyspepsia



Black CJ et al. Gut 2022: 71: 1697-1723

ACG Guidelines for Managing Gastroparesis

	Recommendation	Quality of evidence	Strength of recommendation
1	Dietary management of GP should include a small particle diet to increase likelihood of symptom relief and enhanced GE.	Low	Conditional
2	In patients with idiopathic and DG, pharmacologic treatment should be considered to improve GE and GP symptoms, considering benefits and risks of treatment.	Low	Conditional
3	In patients with GP, we suggest treatment with metoclopramide over no treatment for management of refractory symptoms.	Low	Conditional
4	In patients with GP where domperidone is approved, we suggest use of domperidone for symptom management.	Low	Conditional
5	In patients with GP, we suggest use of 5-HT_4 agonists over no treatment to improve GE.	Low	Conditional
6	In patients with GP, use of antiemetic agents is suggested for improved symptom control; however, these medications do not improve GE.	Low	Conditional
7	Central neuromodulators are not recommended for management of GP.	Moderate	Strong
8	Current data do NOT support the use of ghrelin agonists for managing GP.	Moderate	Strong

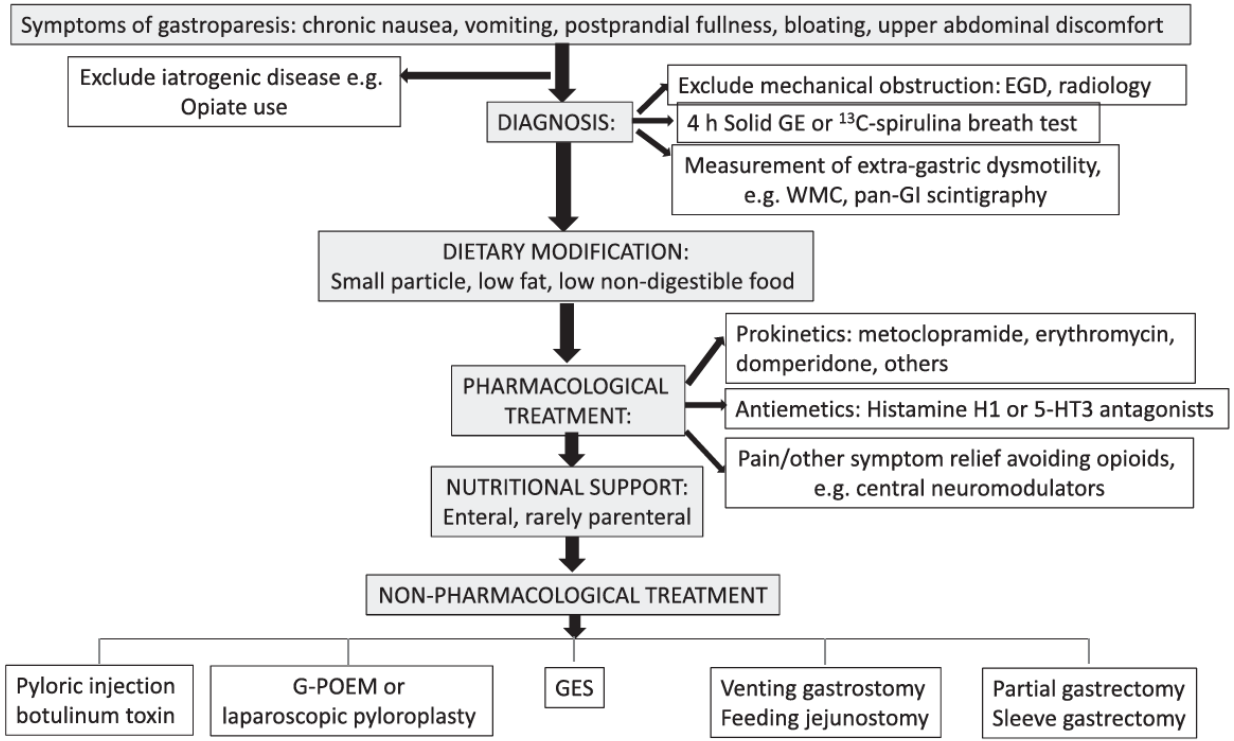
Camilleri M et al. *Am J Gastroenterol.* 2022;117:1197-1220.

ACG Guidelines for Managing Gastroparesis (cont)

	Recommendation	Quality of evidence	Strength of recommendation
9	Current data do NOT support the use of haloperidol for treatment of GP.	Low	Conditional
10	GES may be considered for controlling GP symptoms as a humanitarian use device.	Low	Conditional
11	Acupuncture alone or acupuncture combined with prokinetic drugs may be beneficial for symptom control in patients with DG. Acupuncture cannot be recommended as beneficial for other etiologies of gastroparesis.	Very low	Conditional
12	Herbal therapies such as Rikkunshito or STW5 (Iberogast) should NOT be recommended for treatment of GP.	Low	Conditional
13	In patients with GP, EndoFLIP evaluation may have a role in characterizing pyloric function and predicting treatment outcomes after peroral pyloromyotomy.	Very low	Conditional
14	Intrapyloric injection of botulinum toxin is not recommended for patients with GP based on randomized, controlled trials.	Moderate	Strong
15	In patients with GP with symptoms refractory to medical therapy, we suggest pyloromyotomy over no treatment for symptom control.	Low	Conditional

Camilleri M et al. *Am J Gastroenterol.* 2022;117:1197-1220.

Latest ACG Treatment Algorithm for Gastroparesis



Camilleri M et al. *Am J Gastroenterol.* 2022;117:1197-1220.

2022 AGA Clinical Practice Update on Gastroparesis

Diagnose Gastroparesis

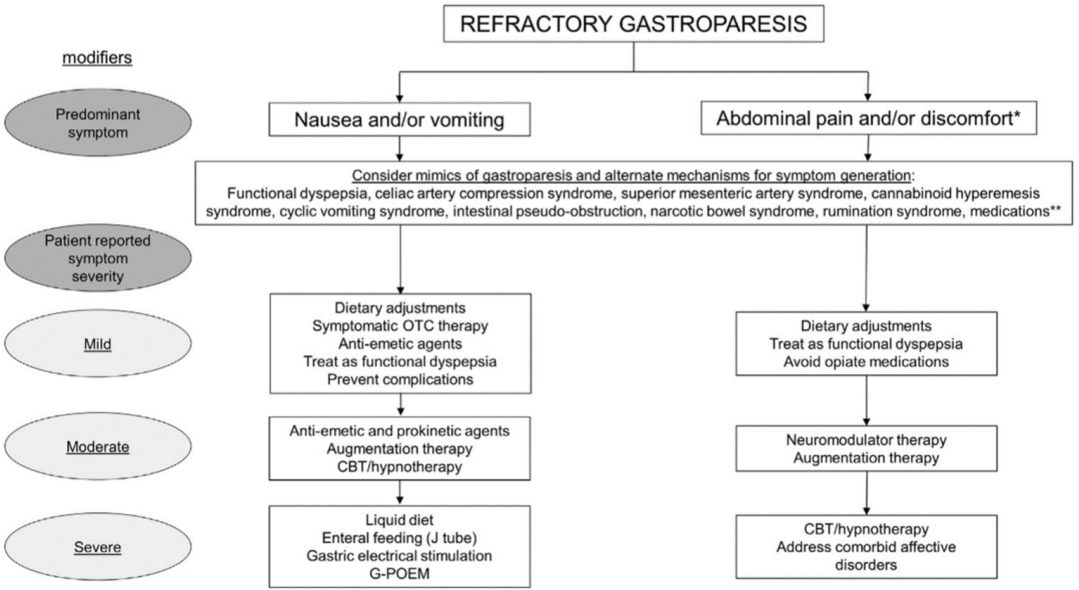
- Avoid overdiagnosis
- Consider overlap with functional dyspepsia

Assess Predominant Symptom & Severity

- Choose therapies based on predominant symptom
- Start with dietary modifications
- Augment medical therapies

Consider Surgical Therapies

- Moderate to Severe symptoms refractory to medical therapy



Lacy B et al. Clin Gastroenterol Hepatol 2022;20:491-500

Current FDA approved medications

- Diabetic Gastroparesis
  - Metoclopramide
    - Oral, oral dissolvable tablet, IV, & nasal spray formulations

Medication Pipeline

Product	Class	Route	Company	Development Status
Tradipitant	NK-1 antagonist	Oral	Vanda	**Phase 3 (Failed to meet primary endpoint)** January 2019 partial clinical hold requiring 12-month toxicity trials
Metopimazine	D2/D3 receptor antagonist	Oral	Neurogastrx	**Phase 2 (enrolling as of March 2020)** Studying 3 doses in idiopathic & diabetic gastroparesis. Primary endpoint is nausea
Velusetrag	5-HT_4 receptor agonist	Oral	AlfaSigma/ Theravance	**Phase 2b (n = 232) No Further Studies Noted** Mixed results with three doses, no dose response.
TAK-906	D2/D3 antagonist	Oral	Takeda/ Altos	**Phase 2a (n=242) (Failed to meet primary endpoint)** No futures studies noted
CIN-102	D2/D3 antagonist	Oral	CinRx	**Phase 2a (n=60) Completed; Phase 2b recently started** No results reported
PCS12852	5-HT4 receptor agonist	Oral	Processa	**Phase 2a (n=25) Completed** Not powered to show a statistically significant difference from the placebo

DDW 2023 Abstract: Cannabidiol

- Randomized placebo-controlled trial at Mayo Clinic
- Cannabidiol, selective cannabinoid receptor agonist with limited side effects in the central nervouse system
- -Oral formulation of purified cannabidiol 100 mg/mL approved by the FDA
- -Over 4 weeks, assess Gastroparesis Cardinal Symptom Index scores in an FDA dose-escalation guidance pathway
- -29 patients idiopathic, 6 type1 DM, 6 type 2 DM
- Patients receiving cannabidiol had improvement in all their tolerance symptoms and the ability to tolerate a normal-sized meal

DDW 2023 Abstract: Buspirone

- Buspirone: 5-HT1 receptor agonist reported to improve fundic accommodation
- -4-week, multicenter, randomized trial, 96 patients with symptoms of gastroparesis, 50% were delayed and 39% were diabetic
- While overall symptoms did not change vs placebo, secondary post hoc analysis showed that buspirone 10 mg TID was significantly better in patients with more severe bloating

GP: Oral Plenary on Nasal Metoclopramide

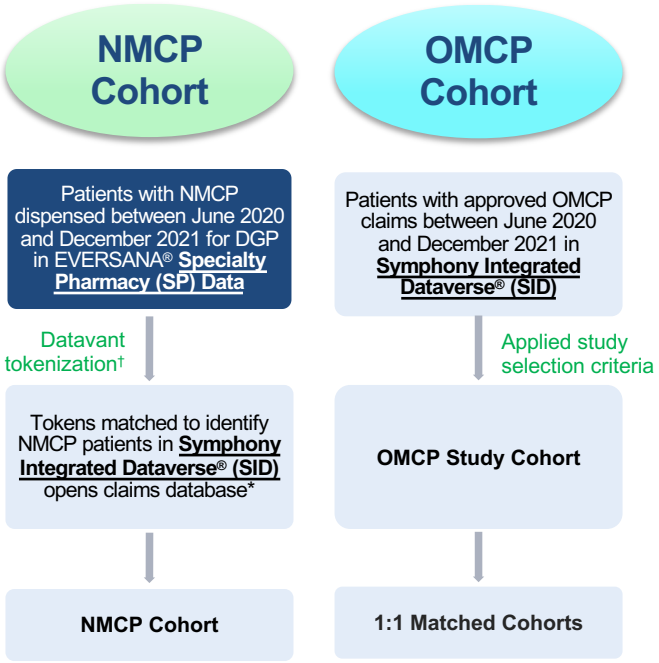
- In June 2020, MCP nasal spray (NMCP) became the first non-oral, outpatient treatment FDA approved for patients with acute and recurrent DGP.[1]
- Moderate to severe NMCP patients in the phase 3 double-blind, placebo-controlled trial experienced a significant reduction in nausea and upper abdominal pain ($P<0.05$) compared to placebo.[2]
- Given the high burden DGP places on patients and payers, we hypothesized that better symptom control in patients treated with NMCP may result in lower healthcare resource utilization (HCRU) compared to patients treated with oral MCP (OMCP).

Research Objective

To compare the frequency of physician office, outpatient facility, ED, and inpatient hospital visits for patients with DGP treated with NMCP versus OMCP.

References: 1. Gajendran M et al. Expert Rev Endocrinol Metab. 2021; 16(2):25-35. 2. McCallum RW et al., Poster presented at: Digestive Disease Week 2017; Washington, DC

Study Design



OMCP Selection Criteria

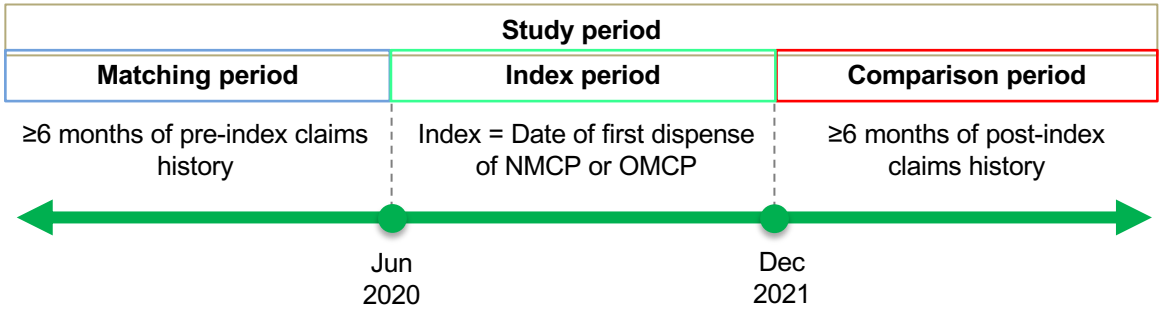
- ≥2 insurance claims with a diagnosis for GP (ICD-10: K31.84) >30 days apart
- >1 insurance claim for diabetes with gastroparesis (E8.43, E9.43, E10.43, E11.43)
- ≥6 months of pre-index claims history (date OMCP/ NMCP claim) and ≥6 months post-index claims history
- ≥18 years of age at index date

† Datavant tokenization is a HIPAA-compliant process to maintain de-identification

* The SID is a US insurance claims database including pharmacy and medical claims data for >300M individuals in the US

Statistical Analysis

- OMCP patients were matched to NMCP patients using propensity score (PS) matching.
- HCRU categories of physician office, hospital outpatient, inpatient hospitalization, and ED visits were captured by examining place of service and CPT codes for evaluation and management on each medical claim.
- Mean number of each type of HCRU (all-cause and DGP-related†, respectively), and number of visits avoided, were compared between NMCP and matched OMCP for the 6-month follow-up period using Mann-Whitney test.
- Incidence rate ratio, likelihood of utilizing service by category was also calculated.



† A DGP-related event was determined by the presence of a diagnosis code for nausea, vomiting, or GP on the billing claim

Cohort Selection

NMCP Cohort Selection Criteria

1,569 Number of DGP patients with a record of a prescription for NMCP from EVERSANA® Specialty Pharmacy*

879 Any patients with matching Datavant Token between EVERSANA® Specialty Pharmacy and SID database

602 Number of patients who filled NMCP prescription†

257† ≥6 months of pre-index claims history (date of first nasal or oral MCP claim) and ≥6 months post-index claims history

OMCP Cohort Selection Criteria

1. **2,919,392** Adult with a record of prescription fill for OMCP from SID
2. **244,532** >1 insurance claim for diabetes (ICD-10: E8.43, E9.43, E10.43, E11.43)
3. **15,627** ≥2 insurance claims with a diagnosis for GP (ICD-10: K31.84) >30 days apart
4. **7,797** ≥6 months of pre-index claims history (date of first nasal or oral MCP claim) and ≥6 months post-index claims history
5. **257** 1:1 Match to NMCP Cohort

*A written prescription does not indicate the patient received NMCP. Patients may not receive NMCP do plan denials or other factors.

† All patients additional met the criteria of having a diagnosis for GP and gastroparesis based on SP records or SID claims.

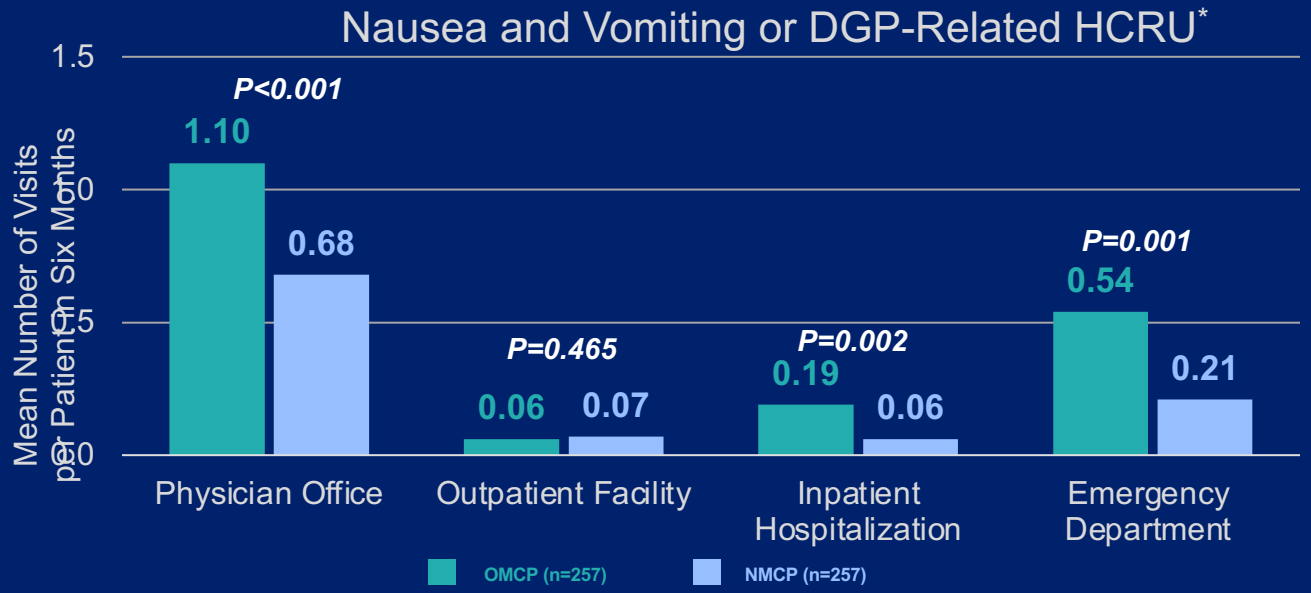
Demographics and Clinical Characteristics Post Match

- Mean (SD) age at index was 53.5 (14.3) for NMCP and 52.7 (13.8) for OMCP.
- 77.0% of patients in both cohorts were female.
- Mean CCI (SD) score was 2.2 in both cohorts.
- 31.1% of both cohorts experienced an ED visit or inpatient hospitalization in the 6-months prior to index.

		NMCP N = 257	OMCP N = 257
Age, years	Mean (SD)	53.5 (14.3)	52.7 (13.8)
Age groups, n (%)	18-35	35 (13.6%)	28 (10.9%)
	36 – 55	106 (41.2%)	115 (44.7%)
	56 – 65	57 (22.2%)	62 (24.1%)
	66 +	59 (23.0%)	52 (20.2%)
Sex, n (%)	Female	198 (77.0%)	198 (77.0%)
	Male	59 (23.0%)	59 (23.0%)
US Region of Primary Residence, n (%)	Midwest	20 (7.8%)	24 (9.3%)
	Northeast	61 (23.7%)	52 (20.2%)
	South	166 (64.6%)	172 (66.9%)
	West	10 (3.9%)	9 (3.5%)
Payer type, n (%)	Commercial	170 (66.1%)	158 (61.5%)
	Medicaid	20 (7.8%)	25 (9.7%)
	Medicare	67 (26.1%)	74 (28.8%)
CCI Score	Mean (SD)	2.2 (2.2)	2.2 (2.4)
CCI Score categories, n (%)	0	55 (21.4%)	57 (22.2%)
	1	67 (26.1%)	67 (26.1%)
	2	49 (19.1%)	53 (20.6%)
	3	36 (14.0%)	33 (12.8%)
	4+	50 (19.5%)	47 (18.3%)
Severity, n (%)	No	177 (68.9%)	177 (68.9%)
	Yes	80 (31.1%)	80 (31.1%)
Prior OMCP Treatment, n (%)	No	99 (38.5%)	N/A
	Yes	158 (61.5%)	N/A

Abbreviation: CCI=Charlson Comorbidity Index

Patients Treated with Nasal Metoclopramide (NMCP) Showed a Significant Reduction in the Number of Healthcare Visits Compared to Oral (OMCP) Patients



NMCP-treated patients had 99 fewer physician office visits, 1 additional outpatient facility visit, 34 fewer inpatient hospitalizations, and 84 fewer ED visits for DGP in the 6-month follow-up period.

Abbreviations: DGP=Diabetic Gastroparesis; MCP=metoclopramide

* Nausea, vomiting, and gastroparesis related HCRU were assessed by examining only insurance claims with ICD-10 diagnosis codes specific to each condition.

Patients Treated with Nasal Metoclopramide (NMCP) Showed a Significant Reduction in the Incidence Rate of Healthcare Visits Compared to Oral (OMCP) Patients

Likelihood of Utilizing Resource in NMCP Cohort Compared to OMCP Cohort†

	Nausea and Vomiting or DGP-related HCRU		All Cause HCRU	
	IRR (95% CI)	*P*-value	IRR (95% CI)	*P*-value
Physician Office	0.64 (0.47, 0.87)	0.005	0.83 (0.67, 1.02)	0.077
Outpatient Facility	0.22 (0.03, 1.16)	0.098	0.41 (0.17, 1.02)	0.053
Inpatient Hospitalization	0.32 (0.14, 0.7)	0.005	0.64 (0.36, 1.13)	0.128
Emergency Department	0.40 (0.2, 0.78)	0.007	0.39 (0.25, 0.61)	<0.001

The likelihood of a patient treated having a DGP-related physician office visit was 36% lower in the NMPC cohort. Similarly, for inpatient hospitalizations and ED visits the likelihood was 68% and 60% lower, respectively, for NMCP-treated patients versus OMCP.

† A generalized linear model (GLM) with Poisson distribution and log-link was used to report incidence rate ratios (IRR) and 95% confidence intervals (CI) for all-cause HRU