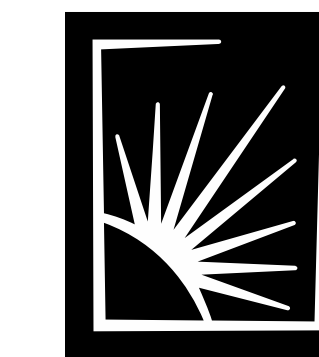




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GLP-1 Receptor Agonists in Fibromyalgia: Opioid sparing signals, Lower Acute-Care Use, and Improved Psychiatric Symptoms



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Background

GLP-1 receptor agonists (GLP-1RAs) reduce appetite, energy intake, and serum glucose levels by activating GLP-1 receptors. They, potentially, act on the CNS and PNS to reduce nerve damage, inflammation, and pain hypersensitivity. Fibromyalgia (FM) presents with neuropathic pain and small fiber neuropathy, resulting in significant opioid use, estimates range from 20-55%. We hypothesize that GLP-1RAs might prove to be opioid sparing, reduce acute care use, and increase the overall mental health quality in FM

Materials and Methods

A retrospective, multi-network cohort study on the TriNetX Research Network. Adults (≥ 18 years) with an FM diagnosis (ICD-10-CM M79.7) and ≥ 12 months of data before and after the index drug initiation (GLP-1RAs) were eligible. The exposure was incident GLP-1RA initiation (semaglutide, liraglutide, exenatide, lixisenatide, dulaglutide, or tirzepatide) identified in EMR; the comparator was patients with FM without GLP-1RA exposure on a random outpatient visit. Propensity scores using demographics, BMI, type 2 DM, baseline pain score, PHQ-9/GAD-7 score, antidepressant/anxiolytic use, ED visits, and comorbidities (depression, anxiety, OSA, osteoarthritis). Primary outcome: Comparing any opioid fills. Secondary outcomes: Comparing neuromodulator/adjunct fills (duloxetine/pregabalin/gabapentin/tizanidine), pain-related ED/hospital utilization, and symptom-burden proxies (PHQ-9 ≥ 10 , GAD-7 ≥ 10 , or pain NRS ≥ 4 where available)

Table 2 Primary opioid outcomes (6–12 months post-index)

Metric	GLP-1 RA	Comparator	Effect
Any opioid fill (risk)	0.335 (7 665/22 887)	0.472 (14 762/31 278)	RR 0.710 (95 % CI 0.694–0.725), RD –0.137, OR 0.563
Time to first opioid	Median 1 299 days, survival probability 41.0 %	Median 1 170 days, survival probability 40.8 %	HR 0.872 (95 % CI 0.848–0.897); log-rank χ^2 93.1, $p < 0.001$
Opioid instances per patient	Mean 4.68 $\pm$ 12.74 (median 1)	8.05 $\pm$ 18.87 (median 2)	$t = -53.56$, $df \approx 262\,794$, $p < 0.001$

Discussion:

In a large national EHR network, GLP-1RA initiation among adults with FM and obesity was associated with clinically meaningful reductions in opioid exposure and other pain-related utilization over 6-12 months. Our findings support prospective evaluation of GLP-1RAs as adjuncts for FM care and opioid-sparing strategies.

Table 3 Secondary outcomes

Outcome	GLP-1 RA	Comparator	Effect
Neuromodulator/adjunct fills	Risk 0.246 (8 848/35 895)	0.343 (19 052/55 554)	RR 0.719 (95 % CI 0.704–0.734), RD –0.096, OR 0.627; HR 0.922 (95 % CI 0.898–0.945); mean instances 5.53 vs 6.57 ($p < 0.001$)
Symptom-burden proxies	Risk 0.002 (218/130 648)	0.002 (267/131 058)	RR 0.819 (95 % CI 0.685–0.979), RD ≈ 0 ; HR 1.186 (95 % CI 0.989–1.421); mean instances 0.010 vs 0.011 ($p = 0.50$)
Pain-related ED/inpatient encounters	Risk 0.425 (5 181/12 193)	0.512 (9 735/18 998)	RR 0.829 (95 % CI 0.809–0.850), RD –0.088, OR 0.703; HR 1.035 (95 % CI 1.001–1.071); mean encounters 8.29 vs 9.95 ($p < 0.001$)

Results

After exclusions, opioid risk was lower with GLP-1RA vs comparator (risk 0.334 [7,574/22,686] vs 0.460 [13,690/29,767]; risk ratio 0.726, 95% CI 0.710-0.742). Opioid hazard was lower (HR 0.893, 95% CI 0.868-0.919; log-rank $p < 0.001$). Opioid instances per patient were also lower (mean 1.34 vs 2.55; $t = -22.35$, $p < 0.001$) (Figure 2).

Neuromodulator/adjunct fills showed lower risk with GLP-1RA (0.246 vs 0.329; RR 0.748, 95% CI 0.732-0.765). A composite of pain-related ED/hospital outcomes favored GLP-1RA (risk 0.424 vs 0.494; RR 0.858, 95% CI 0.837-0.880) (Figure 3). Symptom-burden proxies were infrequent overall but nominally lower with GLP-1RA (RR 0.756, 95% CI 0.634-0.903).

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