Best Practice Day

Case study

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Case presentation

- 42-year-old lady presented with a 5 day history of:
  - Abdominal pain
  - Anorexia
  - Nausea
  - Family concerned by odd behaviour

Thomas O, Coulson JM. Br J Clin Pharmacol. 2026 Jan;92(1):312-316.

GLP-1 agonist associated presentations to unscheduled care: an opportunistic pilot study

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Introduction

- Over 1.5 million UK citizens estimated receiving weight-loss medications as of March 2025 [5] .
- 56% increase in UK spending on private prescriptions from October 2024 to October 2025, was largely attributable to weight loss medications [5].

Glucagon-like peptide-1 (GLP-1) receptor agonists

Type 2 Diabetes (2nd line) only	Type 2 DM or weight management*
Dulaglutide	Liraglutide
Exenatide	Semaglutide
Lixisenatide	Tirzepatide**

*In obese (body mass index > 30 $kg.m^{-2}$) or over-weight (body mass index > 27 $kg.m^{-2}$) patients with weight-related co-morbidities [1]

**Dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 receptor agonist

Side-effects
Gastrointestinal (CNS emetic centre-mediated)
Non-arteritic ischaemic optic neuropathy? [2]
Pancreatitis? [3]
42 deaths associated with GLP-1 agonists [4]
18 deaths associated with GIP/GLP-1 agonists [4]

[1] British National Formulary. Accessed on 12 September 2025 at https://bnf.nice.org.uk/
[2] Int Med Case Rep J. 2025;18:991-995.
[3] Pancreatology. 2025;25(5):609-613.
[4] British Medical Journal. 2025;388:r390.
[5] The Pharmacist. 12 May 2025. Accessed on 12 September 2025 at https://www.thepharmacist.co.uk

Aims

- The impact of GLP-1 or GIP/GLP-1 agonist exposure in a significant proportion of the population is associated with safety risks in patients undergoing endoscopy [1] or general anesthesia [2].

- The impact on GLP-1 or GIP/GLP-1 agonists on unscheduled care are not well described.

- We conducted a prospective, single center, observational study using opportunistic screening by clinicians as a first step to understanding the effect of GLP-1 or GIP/GLP-1 agonists on Emergency Department presentations and to guide future studies.

[1] Surg Endosc. 2025;39(8):5135-5151.
[2] Anaesth Intensive Care. 2025;53(5):300-306.

Methods

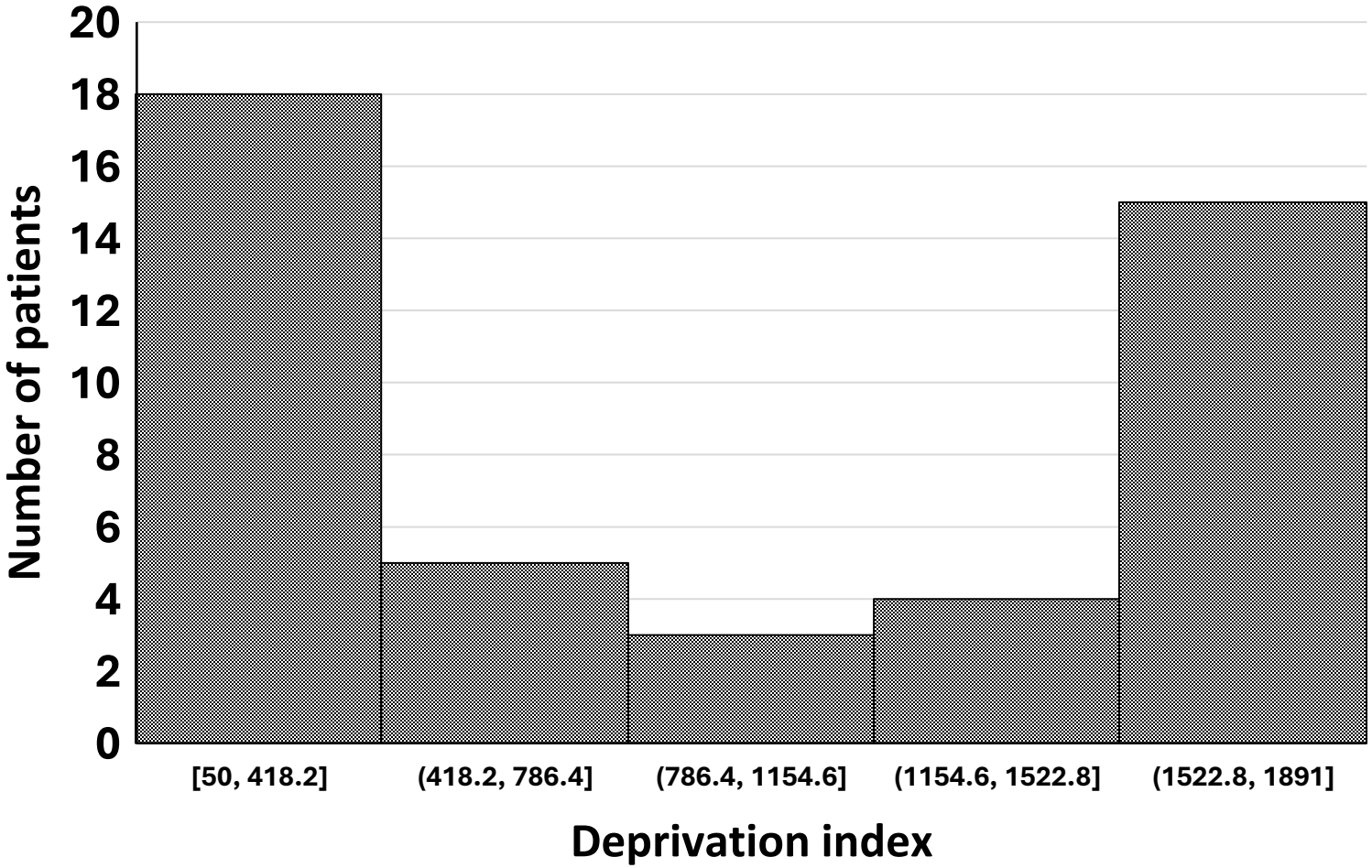
- **Prospective, observational study using opportunistic screening of Emergency Department presentations from April to August 2025 at the University Hospital of Wales, Cardiff, for non-trauma adult patients with self-reported GLP-1 or GIP/GLP-1 agonist exposure.**
- **Data was collected on patient demographics; presenting complaint and clinical symptoms; clinical diagnosis at discharge; type, dosage and recent dose changes of GLP-1 agonist.**
- **Clinicians were also asked if, in their professional judgement, the patient's presentation was a result of GLP-1 or GIP/GLP-1 agonist exposure.**
- **Electronic records were screened for co-existing medical conditions, including obesity, defined as a body mass index >30 kg.m^{-2}. The Welsh Index of Multiple Deprivation Score was determined from the patient's postcode using the Data Cymru website** [1].
- **Chi-squared or Fishers exact test were used to test independence of categories. The Kruskal-Wallis test was used to compare non-parametric data, alpha < 0.05 significant.**
- **Data was collected in accordance with the relevant University Health Board policies, as part of a service evaluation and was approved by the Quality and Safety lead for Emergency Medicine.**

[1] Data Cymru. Accessed on 12 September 2025 at https://www.data.cymru/wimd

Results: demographics

Co-morbidity	n (%)
Depression	26 (46%)
BMI > 30 kg.m^{-2}	14 (25%)
CV disease	10 (18%)
T2DM	4 (7%)

n = 56, 44 female (79%), p <0.0001
Median age 38 (IQR 29-51) years



Median Welsh Index of Multiple Deprivation (WIMD) Score was 785 (IQR 181 – 1657. The number of cases in each WIMD quintile was not evenly distributed across the quintiles, p < 0.00001. Eighteen cases (32%) were in the lowest quintile and 15 (27%) in the highest.

Results: GLP-1/GIP agonists, indications and sources

Drug	n (%)	Weekly sc dose
Tirzapetide	51 (92%)	5 mg (IQR 2.5 – 8.75 mg)
Semaglutide sc	3 (5%)	1 – 1.25 mg
Semaglutide po	1 (1.5%)	0.25 mg (7 mg daily po)
Dulaglutide	1 (1.5%)	3 mg

Indication	n (%)	Sex	Age, median (IQR), years
Weight management	52 (93%)	Female (84%)	38 (29-49)
T2DM	4 (7%)	Female (50%)	69.5 (37-77)

Source

Drug	Private	Primary care	Secondary care	Elicit
Tirzapetide	41 (36 internet)	4	2	4
Semaglutide	2 (both internet)	1		1
Dulaglutide		1		

Results: GLP-1/GIP agonists dose-response

- **Median time between starting GLP-1/GIP agonist and attendance to hospital was 45 days (IQR 20 – 123 days).**
- **The median time to hospital admission did not differ between GLP-1 or GLP-1/GIP agonists, p = 0.1259.**
- **19 (34%) reported a dose increase within two weeks of ED attendance.**
- **35 (62.5%) reported no change in dose within 2 weeks of ED attendance.**
- **Two discontinued drug 1.5 and 4 weeks prior to ED attendance.**

Results: clinical features

Clinical feature	n (%)
Gastrointestinal	44 (49%), 2 acute pancreatitis
Constitutional	19 (43%)
Neurological	8 (14%)
Cardiovascular	6 (11%)
Metabolic	6 (11%)

- **44 cases (79%) (CI95% 66% to 88%) the assessing clinician considered or suspected that the presentation was due to GLP/GiP exposure.**
- **Attribution of a causal relationship was independent of clinical features, p = 0.2476.**

Results: outcome data

Outcome	n (%)
Discharged home from the Emergency Department (ED)	42 (75%)
Discharged home from ED with planned follow-up	5 (9%)
Admitted under General Surgery	9 (16%)
Admitted under General Internal Medicine	5 (9%)

Discussion

- **Opportunistic screening of Emergency Department attendees identified 56 patients exposed to GLP-1 or GLP-1/GIP agonists.**
  - **The vast majority were female.**
  - **Majority reported using tirzapetide prescribed by a private prescriber for weight management.**
  - **In 79% of cases (CI95% 66% to 88%) GLP-1 or GLP-1/GIP agonist exposure caused or might have caused the presenting features.**
  - **There was a “U-shaped” relationship between postcode-derived deprivation score, with the majority of in the lowest or highest quintiles.**

Discussion

- Almost half of patients had a co-existing depression.
- GLP-1 agonist use does not appear to be associated with an increased risk of depression [Prim Care Diabetes. 2024;18(4):422-426].
- The prevalence of depression increases with body mass index and is greater in females compared with males [Int J Obes (Lond). 2009;33(2):257-66].
- However, only 25% of our study had a body mass index > 30 $kg.m^{-2}$ suggesting that the association is not fully explained by a bidirectional relationship.
- GLP-1 agonists are less effective in patients co-prescribed antidepressants [J Pharm Technol. 2022;38(5):283-288].
- The mechanisms for this are unclear but it is possible that incidence of GLP-1 or GLP-1/GIP agonist side-effects is increased in those with depression or receiving antidepressants.

Limitations

- Patient identification was opportunistic at a single point of admission to a single site and relied on patients self-reporting in response to clinician screening.
- Not possible to estimate the prevalence of cases presenting to the Emergency Department with a history of GLP-1 or GLP-1/GIP agonist exposure or to determine odds ratios for identified associations.
- There was also a strong risk of selection bias, however, the independence of clinical features from the attribution of a causal association by clinicians suggests that the risk of confirmatory bias was not high.
- We did not undertake any analytical confirmation of GLP-1 or GLP-1/GIP agonist exposure, however, the clinical features reported generally confirmed to recognized GLP-1 or GLP-1/GIP agonist side-effects.

Conclusions

Clinical message: take a comprehensive drug history

- The majority of patients presenting to a single ED who reported GLP-1 or GLP-1/GIP agonist use were females using tirzapetide for weight management from private prescribers.
- In 79% of cases, the presenting features were due to GLP-1 or GLP-1/GIP agonist use.
- Presentations were greatest in the lowest and highest deprivation quintiles and a significant number had co-existing depression.
- There is a need for formal observational studies to rigorously assess the true impact of GLP-1 or GLP-1/GIP agonist exposure on unscheduled care and explore these tentative associations.

Thanks to:

- **Dr Oliver (Ollie) Thomas**
- **Our patients and colleagues in the Emergency Department, University Hospital of Wales, for participating in this service evaluation**
- **You for listening, many thanks**