

Fall Reporting with GLP-1 Receptor Agonists in Older Adults: A FDA Adverse Event Reporting System (FAERS) Disproportionality Analysis

Tugce Emiroglu Gedik

tugceemiroglu@yahoo.com.tr

Istanbul University-Cerrahpasa Cerrahpasa Faculty of Medicine: Istanbul Universitesi-Cerrahpasa Cerrahpasa Tip Fakultesi <https://orcid.org/0000-0002-5550-6477>

Kubra Cingar Alpay

Istanbul University-Cerrahpasa Cerrahpasa Faculty of Medicine: Istanbul Universitesi-Cerrahpasa Cerrahpasa Tip Fakultesi <https://orcid.org/0000-0001-7017-6966>

Suna Avci Kilivan

Istanbul University Cerrahpasa Faculty of Medicine: Istanbul Universitesi-Cerrahpasa Cerrahpasa Tip Fakultesi <https://orcid.org/0000-0003-4322-5157>

Alper Doventas

Istanbul University Cerrahpasa Faculty of Medicine: Istanbul Universitesi-Cerrahpasa Cerrahpasa Tip Fakultesi <https://orcid.org/0000-0001-5509-2625>

Ulev Deniz Erdinciler

Istanbul University Cerrahpasa Faculty of Medicine: Istanbul Universitesi-Cerrahpasa Cerrahpasa Tip Fakultesi <https://orcid.org/0000-0003-1208-4750>

Research Article

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Abstract

Purpose

This study characterize age-related differences in falls, syncope, and orthostatic hypotension reporting among users of GLP-1 receptor agonists (GLP-1 RAs), and to test whether falls are disproportionately reported in older adults independent of hemodynamic mechanisms.

Methods

We performed a disproportionality analysis of FAERS individual case safety reports for semaglutide, tirzepatide, liraglutide, and dulaglutide. Reporting odds ratios (RORs) compared patients aged 65–84 years with patients aged < 65 years for Fall and a secondary hemodynamic cluster (Syncope, Presyncope, Orthostatic Hypotension, Dizziness, Postural Hypotension). Multivariable adjustment, Fisher's exact/Bonferroni correction, Bayesian credibility intervals, and a supplementary ≥ 85 -year analysis were performed.

Results

Among 186,942 eligible reports, Fall was strongly overrepresented in older patients (ROR 2.75, 95% CI 2.47–3.06), unlike Syncope (ROR 0.96, 95% CI 0.83–1.12) or Orthostatic Hypotension (ROR 1.36, non-significant). This pattern was persisted after multivariable adjustment (adjusted OR 2.34, 95% CI 2.09–2.61). Fall ROR increased with age: 2.30 (65–74y), 3.91 (75–84y), 7.13 (≥ 85 y).

Conclusion

Falls, but not syncope or orthostatic hypotension, show a strong, age-related reporting signal in GLP-1 RA users. These hypothesis-generating findings warrant confirmation with patient studies incorporating frailty and polypharmacy adjustment.

Key Summary Points

Aim: To determine whether falls, syncope, and orthostatic hypotension are disproportionately reported in older (≥ 65 years) versus younger users of GLP-1 receptor agonists in a large pharmacovigilance database.

Findings: Fall reports were markedly and more frequent in older GLP-1 RA users (adjusted OR 2.34), rising from ROR 2.30 (65–74y) to 7.13 (≥ 85 y), while syncope and orthostatic hypotension showed no comparable age-related signal.

Message: Falls may be the dominant age-related safety signal for GLP-1 receptor agonists and warrant dedicated clinical attention and confirmatory studies in older adults.

1. INTRODUCTION

Glucagon-like peptide-1 (GLP-1) is an endogenous incretin hormone secreted by intestinal L-cells [1]. By delaying gastric emptying, and reducing appetite and food intake, GLP-1 receptor agonists (GLP-1 RAs) provide effective management of type 2 diabetes mellitus (T2DM) and obesity [2]. GLP-1 RAs have become a cornerstone of T2DM and obesity management, and their use in older adults is increasing as indications expand beyond glycemic control to weight management and cardiovascular risk reduction [3–6].

Falls represent one of the most significant adverse outcomes in older adults and frequently lead to fractures, hospitalization, functional decline, and loss of independence. Major fall risk factors include a history of falls, balance and vision impairment, muscle weakness, certain medications, gait problems, cognitive decline, and diabetes [7, 8]. It is known that GLP-1 receptor agonists and SGLT2 inhibitors reduce body weight, affecting both fat and muscle mass, and therefore may contribute to muscle weakness [9]. Given that GLP-1 receptor agonists can cause rapid weight and muscle mass loss, decreased oral nutrient intake, and fluid loss, it is likely that the use of these drugs increases the tendency to fall in older adults. It is not sufficiently characterized whether falls in this population are triggered predominantly by classical hemodynamic/vasovagal mechanisms (syncope, orthostatic hypotension) or by non-hemodynamic mechanisms such as sarcopenia, polypharmacy, visual and gait impairment. This question has gained further clinical relevance following the recent publication of a large retrospective cohort study that found that initiation of GLP-1 RA therapy in adults aged 65 and older with T2DM was associated with an 11% higher risk of fragility fracture compared to dipeptidyl peptidase-4 (DPP-4) and sodium-glucose cotransporter-2 (SGLT2) inhibitors; this increased risk was particularly significant against DPP-4 inhibitors and concentrated in the 65–75 age group [10]. This finding contradicts previous smaller studies that suggested GLP-1 RA therapy may have neutral or even bone-sparing effects [11], highlighting the necessity for additional real-world evidence, particularly in older populations. As falls are the primary cause of fragility fractures in older adults, they may serve as an indicator for fall risk.

Although numerous studies have examined the safety profile of GLP-1 receptor agonists, it remains uncertain whether fall-related adverse events are reported more frequently among older adults compared to younger users of the same drug class. Historically, the real-world safety profile of GLP-1 RAs in elderly populations has not been thoroughly characterized, as baseline randomized controlled trials have inadequately represented patients over 65 years of age and those with significant frailty. Given that age significantly influences fall risk, it is essential to determine whether age affects the reporting of such events. patterns of fall-related adverse events. This understanding could yield clinically pertinent safety insights beyond the general safety profile of GLP-1 receptor agonists. The FDA Adverse Event Reporting System (FAERS) compiles spontaneous reports of adverse events linked to drugs and

therapeutic biological products [12], serving as a comprehensive resource for post-marketing surveillance. Consequently, instead of assessing whether GLP-1 receptor agonists generally elevate the risk of falls, our objective was to ascertain whether fall-related adverse events were disproportionately reported among older users of GLP-1 receptor agonists compared to their younger counterparts within the same drug class. Utilizing the FAERS database, we specifically investigated age-related differences in reports of falls, fainting, and orthostatic hypotension.

2. METHODS

2.1 Data Source and Case De-duplication

We analyzed FAERS reports from 2010 Q1 to 2026 Q2 at 06.07.2026. Individual case safety reports (ICSRs) were extracted from FAERS for semaglutide, tirzepatide, liraglutide, and dulaglutide, with the corresponding drug listed as a suspect product. These drugs are among the most widely prescribed GLP-1 RAs, while tirzepatide — a dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 receptor agonist — has seen rapidly expanding use; these four agents therefore account for the majority of contemporary real-world exposure and were selected for the present analysis. Cases reported under more than one of the four agents ($n = 2,712$), indicating combination or sequential use, were excluded from all analyses to reduce polypharmacy-related confounding. Duplicate entries were resolved through a two-step deduplication protocol: 1) retaining the most recent FDA receipt date (FDA_DT) for identical CASEID entries; 2) selecting the higher PRIMARYID when CASEID and FDA_DT matched [13]. No duplicate records were found within any single drug-specific dataset. GLP-1 RAs were identified in the DRUG files using generic or brand names, including liraglutide (VICTOZA, SAXENDA), dulaglutide (TRULICITY), semaglutide (OZEMPIC, WEGOVY), and tirzepatide (MOUNJARO, ZEPBOUND).

2.2 Age Stratification

Patient age was harmonized to a continuous years variable from heterogeneous FAERS units and dichotomized into a geriatric group (65–84 years) and a reference group (< 65 years). Reports with missing or unspecified age ($n = 12,549$) were excluded from the age-stratified analysis (Additional Supplement figure S1). Patients aged ≥ 85 years (the “oldest-old”) were additionally excluded from the geriatric stratum to limit residual clinical heterogeneity. This subgroup differs substantially from the 65–84-year stratum in comorbidity burden, frailty, and baseline fall/fracture risk, which could otherwise obscure or exaggerate the age effect of interest. Patients aged ≥ 85 years ($n = 1750$) were subsequently re-introduced in a separate sensitivity analysis, where they were analyzed as a third age stratum and compared both against the < 65 -year reference group and against the 65–84 years stratum. The FAERS Public Dashboard returns case-level records, retaining the most recent version of each case; the two age-group extracts contained no shared Case IDs, confirming that no report was counted in both strata. All eligible reports were included regardless of sex, reporter type. Demographic and contextual variables extracted for descriptive analysis included age group, sex, reporter type, and fatal outcome status. Fatal outcomes, such as hospitalization, life-threatening conditions, and death, have been reported multiple

times in the same patient. To assess whether the Fall signal reflects a stable age effect versus a calendar-time artifact (e.g., media-driven “stimulated reporting” during the 2023–2025 surge in GLP-1 RA public attention, or the Weber effect), we computed the yearly Fall ROR by initial FDA receipt year (Additional Figure S2).

2.3 Outcome Definition

The primary outcome was the MedDRA v27.0 Preferred Term (PT) Fall, classified using MedDRA version. A secondary cluster comprised Syncope, Presyncope, Orthostatic Hypotension, Dizziness Postural, and Hypotension. A composite outcome was defined as the presence of at least one PT from either the primary or secondary set. As a sensitivity analysis, we additionally examined the composite outcome after incorporating the broader, less specific term Dizziness (which was not included in the primary composite given its low specificity for orthostatic mechanisms) [14].

2.4 Statistical Analysis

For each outcome, we constructed a 2×2 contingency table comparing reports in the ≥ 65–84 years group with reports in the < 65-years group, within the pooled four-drug dataset and, in sensitivity analyses, after excluding individual drugs. We calculated the reporting odds ratio (ROR) with 95% confidence intervals (Woolf’s method), the proportional reporting ratio (PRR), a chi-square statistic, and an approximate information component ($IC = \log_2[(a + 0.5)/(E + 0.5)]$). We subsequently calculated a formal Bayesian equivalent of this Information Component (IC) directly from the same 2×2 tables, employing the Dirichlet-multinomial Bayesian Confidence Propagation Neural Network (BCPNN) approach as described by Bate et al. (1998) and Nörén et al. (2006) [15, 16]. A weakly informative Dirichlet prior was applied to the four joint cell probabilities, centered on the assumption of independence between age group and outcome, with a total prior mass of $\gamma = 1$ pseudo-observation. The posterior distribution of the IC was derived through Monte Carlo simulation, involving 500,000 iterations, from the resulting Dirichlet posterior. The 2.5th percentile (IC_{25}) was utilized as the lower credibility bound, in accordance with the conventional WHO-UMC signal criterion ($IC_{25} > 0$ indicating a signal). Because eight outcomes were pre-specified for age-related comparison (Fall, Hypotension, Orthostatic Hypotension, Dizziness Postural, Presyncope, Syncope, the secondary cluster composite, and the overall composite), we applied a Bonferroni-adjusted significance threshold of $\alpha = 0.05/8 = 0.00625$ to reduce the risk of false-positive signals from multiple testing. In addition, because several individual Preferred Terms had small absolute case counts (e.g., Orthostatic Hypotension, Dizziness), for which Woolf’s asymptotic confidence interval can be unstable, we recomputed each 2×2 comparison using Fisher’s exact test as a robustness check. Both the Bonferroni-adjusted threshold and the exact-test p-values are reported alongside the primary Woolf/chi-square results.

2.5 Reporting Standard

This manuscript was prepared with reference to the READUS-PV guideline for reporting disproportionality analyses in pharmacovigilance, a consensus-based checklist covering 32 recommendations across 14 items for the main text and 12 recommendations across 4 items for the

abstract [17]. A completed self-assessment checklist is provided as a supplementary file; unresolved items are flagged there for author completion prior to submission.

2.6 Ethical considerations

This study used publicly available, de-identified data and did not involve patient contact or access to identifiable personal health information. Institutional review board approval and informed consent were therefore not required for this secondary analysis of an anonymized public database.

3. RESULTS

3.1 Study Population

A total of 186,942 reports for semaglutide, tirzepatide, dulaglutide, and liraglutide were available for the age-stratified analysis. Of these, 62,435 (33.4%) involved patients aged 65–84 years and 124,507 (66.6%) involved patients aged younger than 65 years. The median age was 71 years in the older group and 52 years in the younger group. Within the older group, 45,072 reports (72.2%) were in patients aged 65–74 years and 17,363 (27.8%) in patients aged 75–84 years. Baseline demographic and report-level characteristics differed significantly between the two age groups across sex, reporter type, reported indication, and seriousness (all $p \leq 0.001$), as detailed in Table 1.

Table 1
Baseline Characteristics of GLP-1 RA Cases by Age Group

Characteristic	≥ 65y (65–84) (n = 62,435)	< 65y (n = 124,507)	Total (n = 186,942)	p*
Age				
Median age, years	71	52	—	
65–74 years	45,072 (72.2%)	0 (0.0%)	45,072 (24.1%)	N/A
75–84 years	17,363 (27.8%)	0 (0.0%)	17,363 (9.3%)	N/A
Sex				< 0.001
Female	37,252 (59.7%)	83,991 (67.5%)	121,243 (64.9%)	< 0.001
Male	21,673 (34.7%)	32,749 (26.3%)	54,422 (29.1%)	< 0.001
Not specified	3,510 (5.6%)	7,767 (6.2%)	11,277 (6.0%)	< 0.001
Reporter type				0.001
Healthcare professional	11,673 (18.7%)	24,052 (19.3%)	35,725 (19.1%)	0.001
Consumer / non-HCP	50,636 (81.1%)	100,148 (80.4%)	150,784 (80.7%)	0.001
Not specified	126 (0.2%)	307 (0.2%)	433 (0.2%)	0.058
Reported indication				< 0.001
Type 2 diabetes	28,330 (45.4%)	38,224 (30.7%)	66,554 (35.6%)	< 0.001
Weight / obesity	11,693 (18.7%)	33,498 (26.9%)	45,191 (24.2%)	< 0.001
Unknown indication	20,302 (32.5%)	48,223 (38.7%)	68,525 (36.7%)	< 0.001
Other	1,614 (2.6%)	3,417 (2.7%)	5,031 (2.7%)	0.154
Not reported	496 (0.8%)	1,145 (0.9%)	1,641 (0.9%)	0.006
Seriousness / outcome				< 0.001
Death	1,145 (1.8%)	1,268 (1.0%)	2,413 (1.3%)	< 0.001
Life-threatening	996 (1.6%)	2,199 (1.8%)	3,195 (1.7%)	0.007

Characteristic	≥ 65y (65–84) (n = 62,435)	< 65y (n = 124,507)	Total (n = 186,942)	p*
Age				
Hospitalization	7,706 (12.3%)	14,272 (11.5%)	21,978 (11.8%)	< 0.001
Disability	428 (0.7%)	1,319 (1.1%)	1,747 (0.9%)	< 0.001
Other serious outcomes	8,581 (13.7%)	18,409 (14.8%)	26,990 (14.4%)	< 0.001
Non-serious	43,511 (69.7%)	86,786 (69.7%)	130,297 (69.7%)	0.935
Not specified	68 (0.1%)	254 (0.2%)	322 (0.2%)	< 0.001

*Chi-square test across age groups.

3.2 Primary Disproportionality Analysis

Fall was significantly overrepresented among older patients (799 vs. 585 reports; ROR 2.75, 95% CI 2.47–3.06), the largest signal among all examined terms (Table 2, Fig. 1). Hypotension showed a moderate signal (ROR 1.59, 95% CI 1.38–1.82). In contrast, the classic hemodynamic correlates of orthostatic falls did not show a significant age-related increase. The secondary hemodynamic cluster as a whole was modestly but significantly overrepresented (ROR 1.28, 95% CI 1.16–1.40), driven predominantly by Hypotension, and the overall composite (Fall plus secondary cluster) showed ROR 1.75 (95% CI 1.63–1.87). Every outcome that was significant under the primary Woolf/chi-square approach remained significant after Fisher's exact testing, Bonferroni correction, and a formal Bayesian credibility-interval analysis ($IC_{25} > 0$); every non-significant outcome remained non-significant under all three additional methods (Table 2).

Table 2
Disproportionality and Robustness Analyses by Preferred Term/Cluster (< 65y vs 65-84y)

Preferred Term/Cluster	65-84y (n)	< 65y(n)	ROR (95% CI)	Fisher p	Bayesian IC ₂₅	Signal ¹
Fall	799	585	2.75 (2.47–3.06)	< 0.001	0.723	Yes
Hypotension	349	440	1.59 (1.38–1.82)	< 0.001	0.288	Yes
Orthostatic Hypotension	41	60	1.36 (0.92–2.03)	0.139	–0.095	No
Dizziness Postural	40	67	1.19 (0.80–1.76)	0.412	–0.229	No
Presyncope	112	197	1.13 (0.90–1.43)	0.305	–0.108	No
Syncope	245	508	0.96 (0.83–1.12)	0.642	–0.192	No
Secondary cluster	754	1,182	1.28 (1.16–1.40)	< 0.001	0.140	Yes
Overall composite	1,466	1,692	1.75 (1.63–1.87)	< 0.001	0.420	Yes

ROR = reporting odds ratio; IC = information component. ¹Signal = positive under Fisher's exact $p < 0.00625$ (Bonferroni) AND Bayesian $IC_{25} > 0$, concordant with the primary Woolf/chi-square result.

3.3 Composite Outcomes and Drug-Specific Estimates

The pre-specified secondary hemodynamic cluster (Syncope, Presyncope, Orthostatic Hypotension, Dizziness, Postural Hypotension) showed a modest but statistically significant age-related signal (ROR 1.28, 95% CI 1.16–1.40; $p < 0.001$). The overall composite outcome, combining Fall with the secondary cluster, was significantly overrepresented in older patients (ROR 1.75, 95% CI 1.63–1.87; $p < 0.001$), of the Fall signal to the composite estimate.

When the composite outcome was examined separately for each agent, all four GLP-1 receptor agonists showed a statistically significant age-related disproportionality (all $p < 0.001$). Dulaglutide showed the strongest signal (ROR 1.80, 95% CI 1.48–2.18; 247 reports in the ≥ 65 -year group vs. 181 in the < 65 -year group), followed by semaglutide (ROR 1.59, 95% CI 1.42–1.78; 663 vs. 632) and tirzepatide (ROR 1.58, 95% CI 1.38–1.80; 367 vs. 608), while liraglutide showed the weakest, though still significant, signal (ROR 1.38, 95% CI 1.15–1.67; 189 vs. 271).

3.4 Multivariable-Adjusted Analysis

Because reported indication, sex, and reporter type differed by age group, we fitted multivariable logistic regression models adjusting for these covariates plus drug (Table 3). After adjustment, the age effect attenuated modestly but remained large and highly significant for both Fall (ROR 2.75 → adjusted OR 2.34) and the overall composite (ROR 1.75 → adjusted OR 1.64).

Table 3
Multivariable-Adjusted Association of Age (≥ 65 vs < 65y) with Fall and Overall Composite

Outcome	Unadjusted ROR (95% CI)	Adjusted OR (95% CI) ¹	p
Fall	2.75 (2.47–3.06)	2.34 (2.09–2.61)	< 0.001
Overall composite	1.75 (1.63–1.87)	1.64 (1.52–1.76)	< 0.001

¹Adjusted for sex, reporter type, reported-indication category, and drug (logistic regression; reference: age < 65y, female, healthcare-professional reporter, type 2 diabetes indication, semaglutide).

3.5 Additional Sensitivity Analysis

Restricting the analysis separately to healthcare-professional reports and to consumer reports, the Fall and composite signals were of similar magnitude in both strata. Analysis by years show that point estimates for years with adequate case volume (2017 onward) were consistently above 1, mostly in the 2–4 range, with one low year (2020, ROR 0.82, 95% CI 0.54–1.26, n = wide but low event counts) and generally widening precision as report volume grew sharply from 2024 onward. The proportion of reports contributed by patients ≥ 65 years fluctuated between 26% and 45% across years without a directional trend explaining the Fall signal; the lowest proportions of older-patient reports occurred in 2022–2023. Full results are presented in the Additional material (Tables S1, Fig. S2).

3.6 Sensitivity Analysis Including the Oldest-Old

We provided four supplementary FAERS datas specifically targeting patients aged ≥ 85 years for the same four drugs (n = 1,750 additional cases after the same cross-drug and implausible-age exclusions; median age 87 years, 52.2% female, 70.0% consumer-reported). The Fall ROR (each stratum vs. the < 65 reference) rose from 2.30 (95% CI 2.04–2.59) in the 65–74 group, to 3.91 (95% CI 3.41–4.49) in the 75–84 group, to 7.13 (95% CI 5.41–9.40) in the ≥ 85 group. The same pattern was present for the overall composite outcome (1.58 → 2.18 → 3.43). Comparing ≥ 85 directly against the 65–84 stratum (rather than against < 65), Fall remained significantly more frequent in the oldest-old (ROR 2.60, 95% CI 1.98–3.41; p < 0.001). In contrast, and consistent with the Fall–Syncope dissociation, syncope showed no elevated signal in the ≥ 85 group relative to < 65 (ROR 0.56, 95% CI 0.21–1.50; n = 4 events) and the secondary hemodynamic cluster as a whole remained non-significant (ROR 1.39, 95% CI 0.92–2.11; p = 0.135). Results are in the Additional material (Table S2) and Fig. 2.

4. DISCUSSION

In this large FAERS-based disproportionality analysis, falls were markedly and consistently overrepresented among older GLP-1 RA users, with a magnitude considerably larger than that of any hemodynamic correlate in our secondary cluster, and this pattern was unchanged after exact-method and multiplicity-corrected re-analysis. The association remained significant after adjusting for multiple variables, including sex, reporter type, reported indication, and drug. The observed imbalance in indications between age groups—characterized by a higher prevalence of type 2 diabetes and a lower prevalence of weight/obesity indications among older individuals—does not account for the detected signal. Additionally, a supplementary analysis incorporating patients aged ≥ 85 years corroborates this finding, revealing a disproportionate increase in the over-85 age group. Although the marked increase in reporting signals across age groups is a significant data point, in spontaneous reporting data, this gradient may also reflect age-related differences in reporting behavior or unmeasured confounding factors, and thus cannot be construed as evidence of causality. The differentiation between falls and syncope emerges as the most clinically significant finding of this analysis. If falls among older users of GLP-1 RAs were predominantly due to traditional orthostatic or vasovagal mechanisms, an age-related increase in reports of syncope and orthostatic hypotension would be expected. Syncope did not demonstrate any significant trend and, in fact, appeared to decrease in individuals aged 85 and older. Although orthostatic hypotension showed a similar directional trend, it did not reach statistical significance, even with the large dataset. One hypothesis suggests that this pattern may indicate the involvement of non-hemodynamic factors, such as GLP-1 RA-associated sarcopenia, reduced muscle strength, gait and balance impairments, or the cumulative effects of polypharmacy in older patients. This hypothesis is supported by studies documenting muscle wasting in patients treated with GLP-1 receptor agonists.[18, 19].

Suzuki Y et al. conducted a study on the association of SGLT2 inhibitors and GLP-1RAs with fall risk. The findings indicated that the use of SGLT2 inhibitors significantly elevated the risk of falls, while GLP-1RAs had a minimal impact. The risk was further increased when both medications were used in combination [20]. This interpretation is presented with caution, in conjunction with a recently published population-based retrospective cohort study. This study revealed that initiating GLP-1 RAs in patients aged 65 years or older with type 2 diabetes was linked to an 11% higher risk of fragility fractures compared to the combined use of DPP-4 and SGLT2 inhibitors. The increase was statistically significant when compared specifically to DPP-4 inhibitors, with no significant difference observed in comparison to SGLT2 inhibitors. Notably, the excess risk was predominantly observed in patients aged 65–75 years, rather than those aged 75 years or older [10]. Since the majority of fragile fractures in the older adults are fall-related, the finding of age-dependent differential fall signals in our pharmacovigilance study is a reasonable conclusion based on real-world data. While the two analyses used different designs, data sources, and populations, and the self-reported disproportionate signal alone cannot prove a mechanistic link between falls and fracture risk, it can be said to be consistent with this hypothesis.

A systematic review analyzing the risk of falls in older adults with diabetes mellitus found that diabetic patients were associated with a higher risk of falls compared to non-diabetic patients. Conditions such as hypoglycemia, diabetic neuropathy and retinopathy, polypharmacy, sarcopenia, and frailty are factors that increase this risk[21]. In our study, in geriatric patients using GLP-1 analogs, the indication for use being diabetes mellitus may be one of the factors that increases the risk of falls. In our study, the risk of falls was increased with tirzepatide, semaglutide, dulaglutide, and liraglutide, but we did not have a comparator drug to compare. Conversely, a large retrospective study found that the risk of falls was lower in elderly patients using tirzepatide and semaglutide compared to those using DPP4 [22]. However, there are also studies showing an increased risk [10]. For these reasons, large prospective studies involving different drug groups are needed.

The inclusion of the nonspecific term "Dizziness" highlights a critical methodological consideration for pharmacovigilance research in this domain: broad, low-specificity adverse event terms can obscure a genuine, more specific signal. Therefore, outcome definitions should be selected with care, and sensitivity analyses should be transparently reported, as demonstrated in this study. Clinically, these findings suggest that fall-risk assessment should be considered alongside, rather than as a replacement for, orthostatic vital sign screening in older adults who are initiating or continuing GLP-1 RA therapy. This consideration should include attention to muscle strength, gait, balance, and medication reconciliation for other drugs that may contribute to falls. It is important to note that this is a suggestion for clinical attention based on a hypothesis-generating signal, rather than a practice recommendation supported by causal evidence. The analysis presented here does not establish that GLP-1 RA use causes falls; it only indicates that fall reports are disproportionately more common among older users compared to younger users of the same medications.

Strength and Limitations

This study has several strengths and limitations. It draws on a large, real-world pharmacovigilance dataset of nearly 187,000 reports across four widely used GLP-1 receptor agonists, providing substantial statistical power to detect age-related differences that clinical trials. The analysis is further strengthened by a pre-specified outcome structure distinguishing fall from hemodynamic terms, systematic removal of cross-drug overlapping cases to reduce polypharmacy confounding, and consistency of the age-related signal across all four individual agents and across sensitivity analyses. This analysis shares the general limitations of spontaneous-report pharmacovigilance data: susceptibility to reporting bias and the Weber effect, absence of a total-exposed-population denominator precluding incidence estimation, and an inability to establish causality from disproportionality measures alone. The reference group consisted of younger patients using the same drug class rather than an external, non-GLP-1 comparator, which controls for indication-related confounding but cannot fully separate a GLP-1 RA-specific age effect from a generic tendency toward more frequent or detailed fall reporting in older patients across all medications. We could not adjust for polypharmacy, frailty status, baseline mobility, prior fall history, or concomitant insulin/sulfonylurea use, all of which are plausible confounders. Orthostatic Hypotension

and Dizziness had relatively small absolute case counts, limiting statistical power for these specific terms.

5. CONCLUSIONS

In patients aged 65–84 years using GLP-1 receptor agonists, falls were reported significantly and disproportionately more frequently than syncope or orthostatic hypotension. This signal remained robust across various analyses, including Woolf, Fisher's exact test, Bonferroni correction, multivariate adjustment, stratification by reporter type, and calendar year sensitivity analyses. An additional analysis that included patients aged ≥ 85 years indicated an increasing trend, with the fall signal approximately tripling from the 65–74 age range to the ≥ 85 age range. Although these findings are hypothetical, the persistence of the signal after adjusting for measured confounding factors in this dataset underscores the necessity for further investigation into fall risk associated with GLP-1 RA prescribing in the older adults. More studies are needed that include clinical assessments of fall events using active comparators and corrections for unmeasured confounding factors such as neuropathy, retinopathy, fragility, and polypharmacy.

Declarations

Competing Interests:

The authors have no competing interests to declare that are relevant to the content of this article.

Ethics Approval:

This study used publicly available, de-identified, aggregate spontaneous-report data from FAERS and did not involve direct patient contact or access to identifiable personal health information; institutional review board approval and informed consent were therefore not required.

Consent to Participate:

Not applicable. All data were obtained from publicly available, de-identified spontaneous adverse event reports.

Consent to Publish:

Not applicable.

Use of Artificial Intelligence

During the preparation of this manuscript, the authors utilized artificial intelligence-assisted technologies (Claude Sonet 5) solely for English language editing and visual refinement. Following this process, all content was thoroughly reviewed, verified, and approved by the authors, who accept full responsibility for the integrity of the final work.

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Author Contributions:

Study concept and design: TEG, KCA, SA, AD, UDE, Acquisition of the data: TEG, KCA Statistical analysis: TEG, KCA, Drafting of the manuscript: TEG, KCA, SA, AD, UDE,, Critical revision of the manuscript for important intellectual content: TEG, KCA, SA, AD, UDE.

Data Availability:

FAERS data are publicly available from the U.S. Food and Drug Administration (<https://fis.fda.gov/extensions/FPD-QDE-FAERS/FPD-QDE-FAERS.html>). The cleaned analytic dataset and calculation spreadsheet are available from the corresponding author upon reasonable request.

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Figures

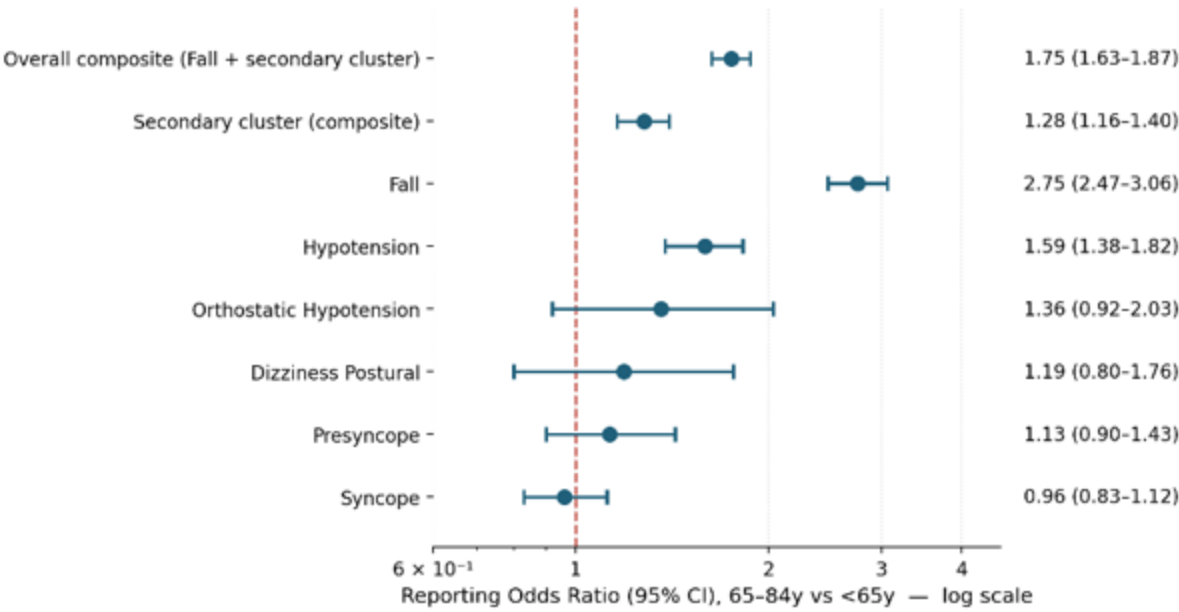


Figure 1

Forest plot of reporting odds ratios (95% CI) for age-related disproportionality (65-84 years vs <65 years) across all pre-specified outcomes.

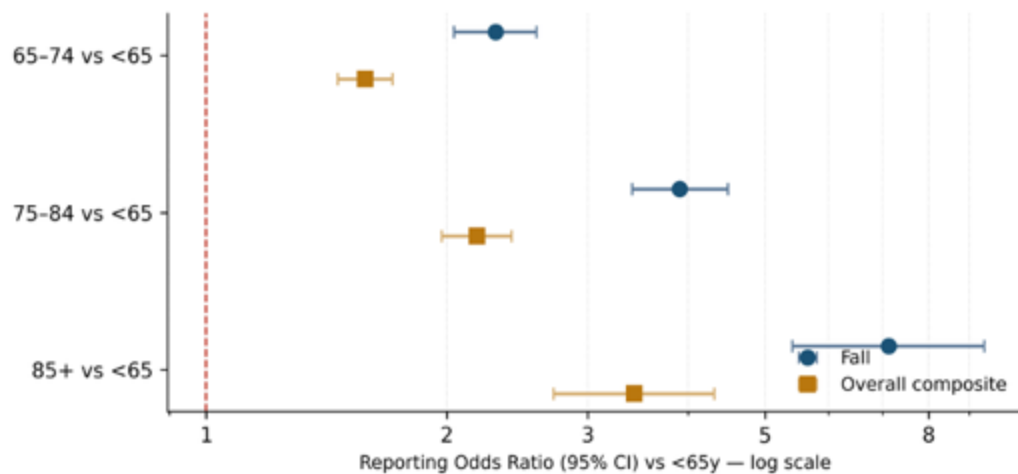


Figure 2

Age-stratified reporting odds ratios for Fall and the Overall composite outcome across 65–74, 75–84, and ≥85-year

Supplementary Files

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