RWD244

Body weight-associated differences in adverse drug reaction profiles of aromatase inhibitors: A real-world pharmacovigilance study using FAERS Database

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Objectives

- Aromatase inhibitors (AIs), including anastrozole, letrozole, and exemestane, are cornerstone therapies for hormone receptor-positive breast cancer in postmenopausal as well as premenopausal women.
- Given evidence that metabolic factors can alter the risk profiles of therapies, this study investigates the impact of body weight on AI-related adverse drug reactions (ADRs) using real-world pharmacovigilance data.

Methods

- Suspected ADR reports from Q1 2004 to Q4 2023 were extracted from the FDA Adverse Event Reporting System (FAERS) database.
- After deduplication, 3,111,066 case reports with body-weight data were retained (Figure 1).
- Cases were categorized into overweight (n=1,891,356) and non-overweight (n=1,219,710) groups, based on a prespecified CDC*-based weight cutoff.
- Among reports in which aromatase inhibitors were the primary suspected drug, 4,070 were overweight and 2,387 were non-overweight; the remaining reports comprised 1,887,286 overweight and 1,217,323 non-overweight cases.
- Disproportionality analyses were conducted separately for each group using reporting odds ratios (RORs) with 95% confidence intervals (CIs), based on MedDRA preferred terms (PTs). PTs were further classified according to the system organ class (SOC) to provide broader categorical comparisons. We defined a positive signal as ≥3 cases with a 95% CI for the ROR whose lower bound was >1.
- For ADRs with statistically significant signals only in the overweight group, logistic regression was performed to assess the interaction between body weight and AI exposure, estimating the relative ROR. Statistical significance for relative ROR was defined as a lower bound of the 95% CI > 1.

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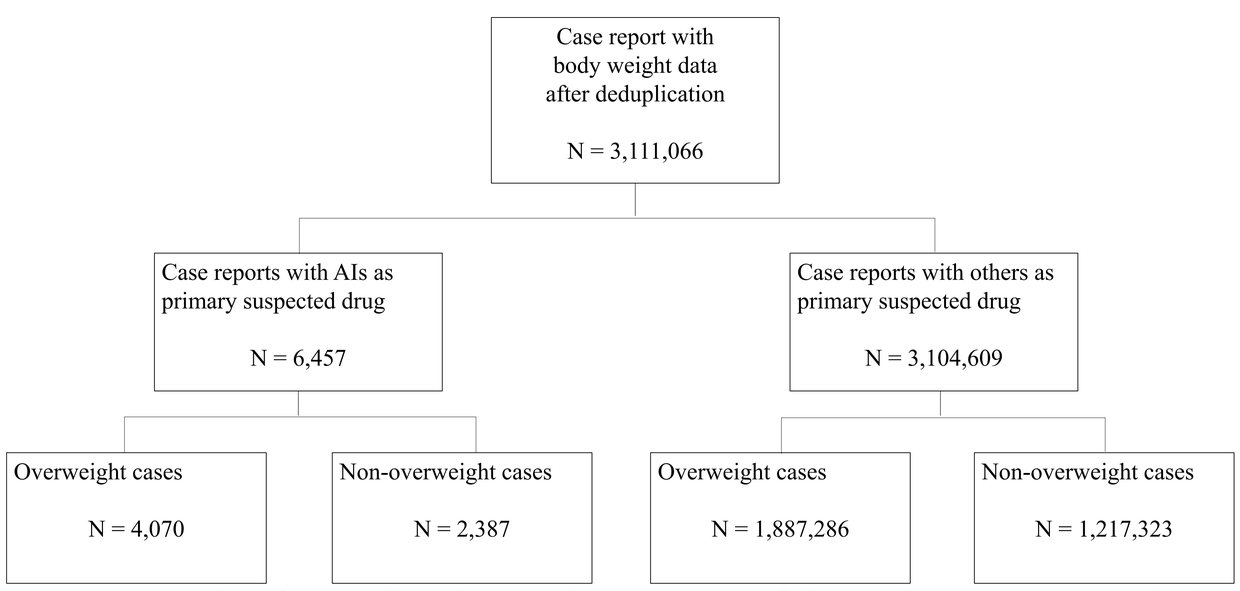


Figure 1. Case identification flow diagram for aromatase inhibitor adverse events stratified by body weight category

Results

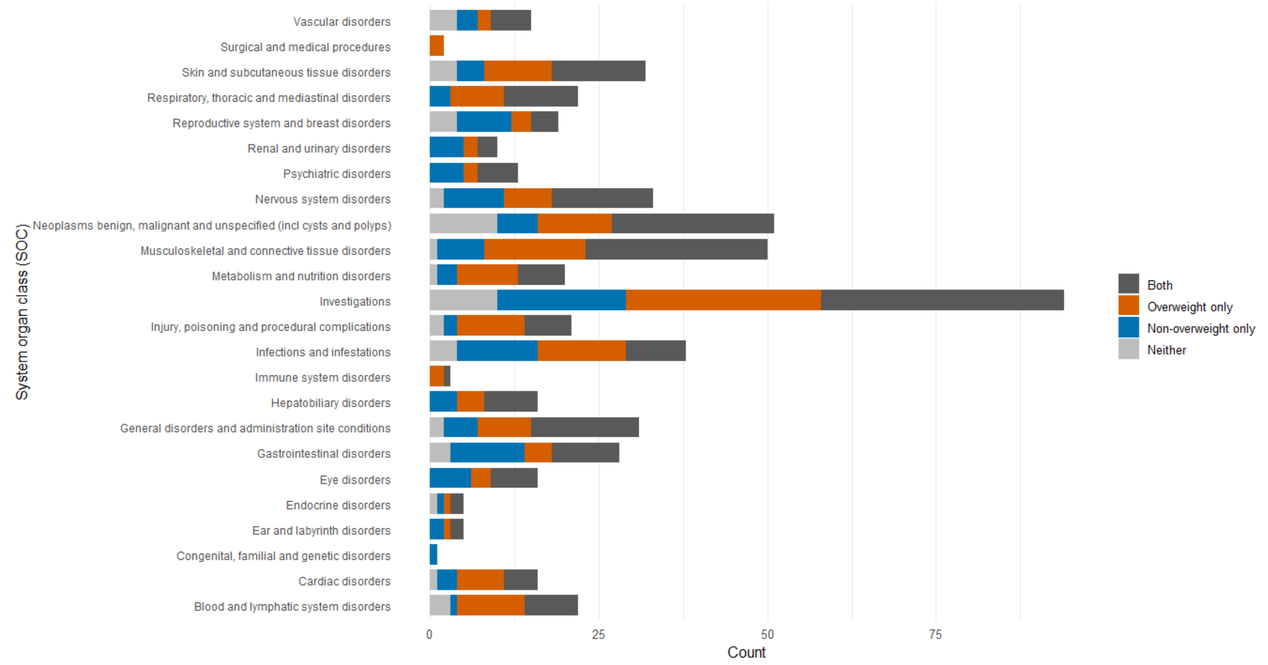
- Table 1 summarizes the baseline characteristics of AI-related adverse event (AE) cases.
- The distribution of demographic and clinical characteristics, including age, sex, and comorbidities, was generally comparable between groups.

Table 1. Baseline Characteristics of Adverse Event Reports for Aromatase Inhibitors, stratified by Body Weight Category

Characteristics	All cases	Overweight group	Non-overweight group
	AIs (n=6,457)	AIs (n=4,070)	AIs (n=2,387)
Age, year, median[Q1, Q3]	66 [58, 74]	66 [58, 73]	67 [58, 75]
Sex, number (%)			
Female	6,395 (99%)	4027 (98.9%)	2368 (99.2%)
Male	62 (1%)	43 (1.1%)	19 (0.8%)
Bodyweight, kg, [Q1, Q3]	69.6 [60, 81]	78 [70, 88.24]	57 [52, 61]
Bodyweight, number (%)			
Overweight	4,070 (63%)	-	-
Non-overweight	2,387 (37%)	-	-
AIs			
Anastrozole	1615 (25%)	1,034 (25.4%)	581 (24.3%)
Exemestane	1476 (22.9%)	977 (24%)	499 (20.9%)
Letrozole	3366 (52.1%)	2,059 (50.6%)	1307 (54.8%)

AIs, Aromatase inhibitors

Figure 2 . Number of Preferred Terms with significant disproportionality signals, stratified by system organ class and significance pattern (overweight only, non-overweight only, both, or neither)



- Figure 2 shows the number of PTs with significant disproportionality signals across system organ classes.
- Investigations accounted for the largest number of signals, predominantly observed in both overweight and non-overweight groups and overweight group only.
- Overweight-only signals were relatively more frequent in cardiac, infections and infestations, musculoskeletal and connective tissue, skin and subcutaneous tissue, and reproductive system and breast disorders; by contrast, non-overweight-only signals were more frequent in gastrointestinal, hepatobiliary, respiratory/thoracic/mediastinal, renal and urinary, nervous system, and metabolism & nutrition disorders.
- The analysis identified 163 PTs with signals in the overweight group; 12 PTs showed significantly stronger signals in the overweight group compared to the non-overweight group (Table 2).
- The highest relative RORs were observed for tenosynovitis stenosans (20.94; 95% CI, 2.67-164.25) and pneumothorax (15.18; 1.97-117), while other PTs showed 2.49-11.94-fold higher RORs in the overweight group versus the non-overweight group.

Table 2. Disproportionality analysis results of AI-related adverse events at the PT level, stratified by body weight and compared between subgroups

	Overweight (N=1,891,356)			Non-overweight (N=1,219,710)			Overweight group vs. non-overweight group	
Preferred Terms	AIs cases	ROR AIs/ all other drugs	95%CI	AIs cases	ROR AIs/ all other drugs	95%CI	Relative ROR	95%CI
Hypothyroidism	24	3.61	(2.41, 5.4)	7	1.45	(0.69, 3.04)	2.49	(1.07, 5.81)
Hypocalcaemia	24	8.07	(5.38, 12.09)	6	2.02	(0.9, 4.51)	3.99	(1.63, 9.81)
Palmar-plantar erythrodysaesthesia syndrome	17	5.46	(3.38, 8.82)	7	2.05	(0.97, 4.3)	2.67	(1.1, 6.46)
Ageusia	21	3.67	(2.39, 5.65)	2	0.58	(0.15, 2.34)	6.28	(1.47, 26.82)
Tenosynovitis stenosans	14	130.28	(71.97, 235.84)	1	6.22	(0.87, 44.72)	20.94	(2.67, 164.25)
Muscle atrophy	11	4.33	(2.39, 7.85)	2	0.82	(0.21, 3.3)	5.25	(1.16, 23.78)
Pneumothorax	12	5.19	(2.93, 9.17)	1	0.34	(0.05, 2.43)	15.18	(1.97, 117)
Hyperuricaemia	8	10.02	(4.97, 20.19)	1	0.84	(0.12, 5.98)	11.92	(1.48, 95.78)
Pelvic fracture	8	7.19	(3.57, 14.46)	1	0.83	(0.12, 5.88)	8.70	(1.08, 69.81)
Toxic skin eruption	8	5.57	(2.77, 11.19)	1	0.69	(0.1, 4.92)	8.05	(1, 64.59)
Granulocyte count decreased	6	49.75	(21.43, 115.54)	2	4.17	(1.04, 16.76)	11.94	(2.35, 60.79)
Lymphangiosis carcinomatosa	4	37.13	(13.4, 102.86)	2	5.90	(1.46, 23.79)	6.29	(1.12, 35.4)

AIs, Aromatase inhibitors; ROR, reporting odds ratio; CI, confidence interval.

Conclusions

- This study highlights differences in AI-related ADR profiles based on patient body weight.
- Further research is needed to refine personalized treatment strategies and enhance risk stratification by patient characteristics.

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Conflict of Interest

- No relevant relationships to disclose.