GLP-1s Lead to Greater Weight Loss and A1C Improvement Than Metformin in Patients with PCOS

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Key Findings

- Among patients with polycystic ovary syndrome (PCOS), the median one-year weight change was an 11.5% loss for those treated with a GLP-1, compared to a 1.9% loss among those treated with metformin.
- Among patients with PCOS, 55.7% of those prescribed a GLP-1 lost at least 10% of their body weight, compared to just 13.7% of those prescribed metformin.
- Among patients with PCOS who were prescribed a GLP-1, 83.5% experienced an HbA1c reduction, compared to only 55.9% of those prescribed metformin.

Polycystic ovary syndrome (PCOS) affects 10 to 13% of reproductive-age women and is closely linked to obesity, insulin resistance, and increased risk of type 2 diabetes.[1] Metformin has historically been the first-line therapy for metabolic management in PCOS.[1] Recently, GLP-1s have emerged as alternatives due to their effects on weight reduction and glycemic control.[2] With rising off-label use of GLP-1s in PCOS, comparative evidence with metformin is needed to inform clinical practice and health policy.

We studied 36,674 women aged 18 to 50 with a diagnosis of PCOS who filled a new prescription for either a GLP-1 or metformin between January 2021 and November 2024. Patients were required to have at least one baseline measurement of weight or HbA1c within a year before drug initiation and one follow-up measurement between 9 and 15 months after initiation.

At one year, patients with PCOS on GLP-1s experienced significantly greater weight loss than those on metformin. The median weight change among GLP-1 users was an 11.5% reduction, compared to a 1.9% reduction for metformin users. Many GLP-1 patients (55.7%) lost over 10% of their body weight, while only 13.7% of metformin patients reached that threshold.

One-Year Percent Change in Body Weight by Treatment

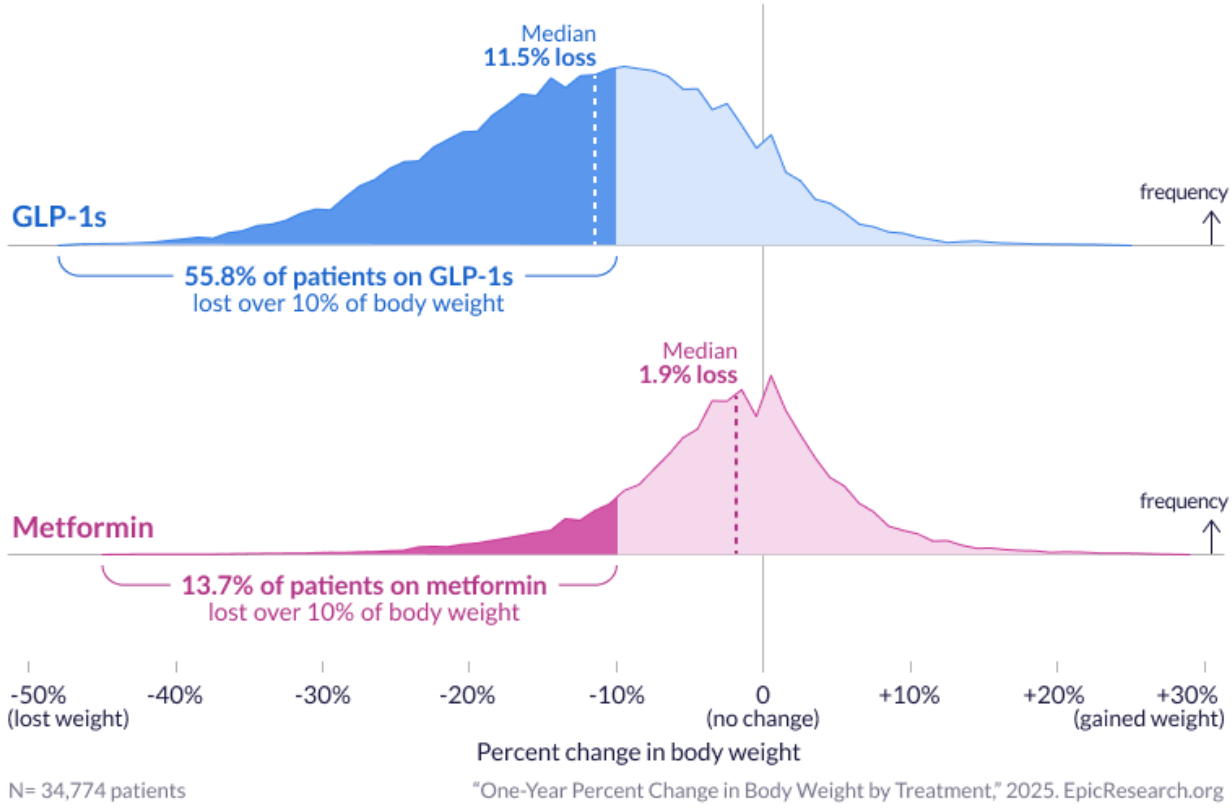

Figure 1. The distribution of one-year weight change among patients with PCOS by treatment type.

For glycemic outcomes, the distribution of absolute HbA1c changes showed greater reductions for GLP-1 users compared to metformin users, as seen in Figure 2. A lower HbA1c is a marker of better blood glucose regulation, with a value below 5.7% representing normal glucose levels, a value between 5.7% and 6.4% representing prediabetes, and a value over 6.4% representing diabetes.[3] Patients on GLP-1s had a median HbA1c reduction of 0.5 points, while those on metformin had a median HbA1c reduction of 0.1 points. 83.5% of patients who received GLP-1s had a reduction of their HbA1c, while only 55.9% of those who received metformin did.

HbA1c Change by Treatment

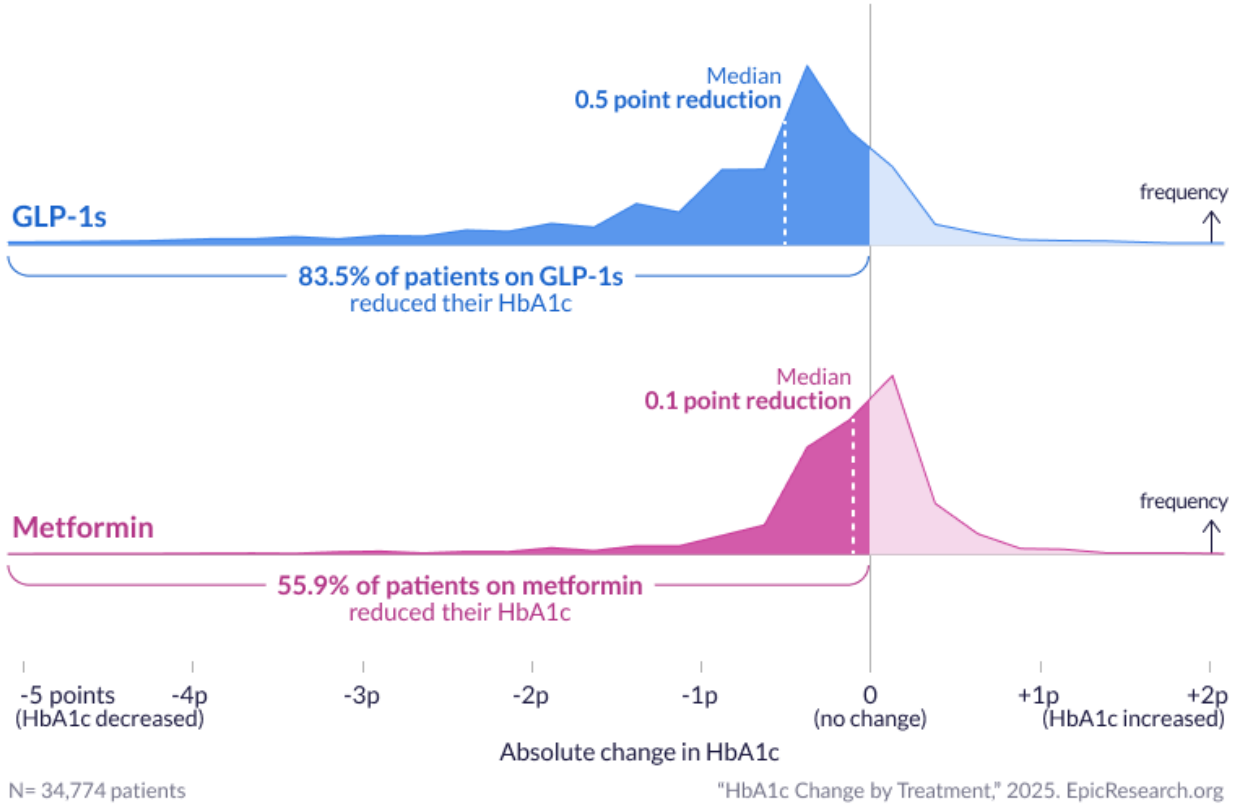

Figure 2. The distribution of HbA1c change among patients with PCOS by treatment type.

A sensitivity analysis accounting for factors such as demographics, starting BMI classification, residence in a socially vulnerable area, comorbidities, and baseline HbA1c level also found that patients on GLP-1s were more likely to experience weight loss and to reduce their HbA1c levels.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 300 million patient records from 1,800 hospitals and more than 41,000 clinics from all 50 U.S. states, Canada, Lebanon, and Saudi Arabia. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

References

1. Teede HJ, Tay CT, Laven JJE, et al. Recommendations From the 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome. J Clin Endocrinol Metab. 2023;108(10):2447-2469. doi:10.1210/clinem/dgad463
2. Lin S, Deng Y, Huang J, et al. Efficacy and safety of GLP-1 receptor agonists on weight management and metabolic parameters in PCOS women: a meta-analysis of randomized controlled trials. Sci Rep. 2025;15(1):16512. Published 2025 May 13. doi:10.1038/s41598-025-99622-4
3. Ellis RR. Hemoglobin A1c (HbA1c): What to know if you have diabetes or prediabetes or are at risk for these conditions. Harvard Health. June 30, 2025. https://www.health.harvard.edu/diseases-and-conditions/hemoglobin-a1c-hba1c-what-to-know-if-you-have-diabetes-or-prediabetes-or-are-at-risk-for-these-conditions. Accessed November 5, 2025.

Data Definitions

Term	Definition
Study period	1/1/2021 to 10/1/2024 with follow-up possible through 7/1/2025
Study population: inclusion	Patients with: • PCOS (encounter or billing diagnosis with ICD-10-CM code E28.2) before exposure or within two years of drug trial start • Evaluated sex of female or ambiguous • Aged 18 to 50 at drug trial start • No overlap in metformin and GLP-1 use • At least one measurement within one year prior to trial start • At least one measurement 9 to 15 months after trial start • At least 70% of days covered by their **exposure** medication **dispense**

Study population: exclusion	Patients with:
	• Evidence of pregnancy during baseline or outcome measurements
	  • Definitive pregnancy start date: Between 12 months before the first reading through the follow-up reading
	  • Definitive pregnancy end date, delivery, or if it's ambiguous what point in the pregnancy the patient would be at (e.g. an encounter or billing diagnosis with ICD-10-CM O*): Between 12 months before the first reading through 9 months after the follow-up reading
	• Evidence of **amputation** during baseline or outcome measurements for weight outcome

Censoring	First of: • Measurement closest to 12 months. • Last dispense + days supply. Default days supply = 30 for GLP1s and 90 for metformin. Day supply capped at 180 days. • One year without dispense.
Exposures	The first of: Metformin: Dispense of simple generic "Metformin HCl" or ATC code A10BA02 GLP-1: Dispense of a simple generic of "dulaglutide," "exenatide," "exenatide microspheres," "liraglutide," "semaglutide," or "tirzepatide" or a pharmaceutical class of "ANTIHYPERGLYCEMIC - INCRETIN MIMETICS COMBINATION," "ANTIHYPERGLY,INSULIN,LONG ACT-GLP-1 RECEPT.AGONIST," "ANTI-OBESITY GLUCAGON-LIKE PEPTIDE-1 RECEP AGONIST," or "ANTIHYPERGLY,INCRETIN MIMETIC(GLP-1 RECEP.AGONIST)"
Outcomes	Percent change in weight from baseline Change in **HbA1c**
Dispense	Available medication dispense history meeting the following criteria: • Covering the six months prior to baseline measurement, including the baseline measurement • Covering >= nine months of time between drug exposure start and final measurement • With no orders of the exposure medication more than two weeks prior to the drug exposure start date • With no orders of the other exposure medication between baseline reading date and the follow-up reading date

HbA1c	A lab with LOINC code 17856-6, 17855-8, 4548-4, 4549-2, 55454-3, or 41995-2 and a value between 3.2 and 20.
Race and ethnicity	Patients were classified based on self-reported race and ethnicity that were mapped to standards as Hispanic, Multiracial, White only, Black only, or Other
Amputation	An encounter or billing diagnosis with ICD-10-CM code Z89.2*, Z89.6*, S78.011A, S98.011A, S78.012A, S98.012A, S78.019A, S98.019A, S78.021A, S98.021A, S78.022A, S98.022A, S78.029A, S98.029A, S78.111A, S98.111A, S78.112A, S98.112A, S78.119A, S98.119A, S78.121A, S98.121A, S78.122A, S98.122A, S78.129A, S98.129A, S78.911A, S98.131A, S78.912A, S98.132A, S78.919A, S98.139A, S78.921A, S98.141A, S78.922A, S98.142A, S78.929A, S98.149A, S88.011A, S98.211A, S88.012A, S98.212A, S88.019A, S98.219A, S88.021A, S98.221A, S88.022A, S98.222A, S88.029A, S98.229A, S88.111A, S98.311A, S88.112A, S98.312A, S88.119A, S98.319A, S88.121A, S98.321A, S88.122A, S98.322A, S88.129A, S98.329A, S88.911A, S98.911A, S88.912A, S98.912A, S88.919A, S98.919A, S88.921A, S98.921A, S88.922A, S98.922A, S88.929A, or S98.929A or a procedure with ICD-10-PCS code 0Y6[23478CDFGHJ]* or 0X6[012389BCDF]*
Limitations	Because medication dispense information relies upon third-party queries operating in the U.S. and this was required for the study, patients are U.S. based.

Table 1: One-Year Percent Change in Body Weight by Treatment

% Weight Change Lower Bound (Inclusive)	% Weight Change Upper Bound (Exclusive)	GLP	Metformin
-48	-40	63	13
-40	-35	167	15
-35	-30	464	52
-30	-29	122	17
-29	-28	166	16
-28	-27	206	21
-27	-26	226	23
-26	-25	264	29
-25	-24	288	33
-24	-23	291	60
-23	-22	338	65
-22	-21	365	61
-21	-20	391	81
-20	-19	393	91
-19	-18	447	111
-18	-17	482	130
-17	-16	522	152

-16	-15	515	174
-15	-14	576	192
-14	-13	543	284
-13	-12	584	272
-12	-11	587	348
-11	-10	607	400
-10	-9	616	505
-9	-8	608	552
-8	-7	601	669
-7	-6	582	787
-6	-5	538	922
-5	-4	539	993
-4	-3	467	1,216
-3	-2	488	1,213
-2	-1	413	1,304
-1	0	335	1,093
0	1	381	1,415
1	2	252	1,142
2	3	222	948
3	4	159	768
4	5	145	611
5	6	113	542
6	7	73	406
7	8	64	338
8	9	46	225
9	10	42	191
10	11	28	164
11	12	19	107
12	13	10	110
13	14	13	73
14	15	15	50
15	17	18	90
17	20	15	78
20	29	15	90

Table 2: HbA1c Change by Treatment

A1c Change Lower Bound (Inclusive)	A1c Change Upper Bound (Exclusive)	GLP	Metformin
-12	-5	82	49
-5	-4.5	33	22

-4.5	-4	44	22
-4	-3.75	34	14
-3.75	-3.5	35	15
-3.5	-3.25	49	12
-3.25	-3	34	25
-3	-2.75	56	31
-2.75	-2.5	51	15
-2.5	-2.25	91	28
-2.25	-2	82	26
-2	-1.75	134	59
-1.75	-1.5	110	35
-1.5	-1.25	261	74
-1.25	-1	205	73
-1	-0.75	478	157
-0.75	-0.5	480	243
-0.5	-0.25	1,143	877
-0.25	0	725	1,101
0	0.25	496	1,459
0.25	0.5	128	420
0.5	0.75	73	172
0.75	1	29	52
1	1.25	23	46
1.25	1.5	20	16
1.5	2	17	32
2	2.5	16	17
2.5	3.5	-	20
3.5	5	13	20
5	9	-	15