Poster: POSA361

# Weight Change on Diabetes Medications: Is There an Association with Adherence and Discontinuation?

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## BACKGROUND

- Weight change associated with type 2 diabetes (T2D) therapy could affect how individuals take their medication at different points of their treatment journey
- Qualitative and quantitative studies have reported that potential weight gain associated with specific diabetes treatments is a barrier at initiation[1–4]
- To our knowledge, a literature review of studies reporting the association between weight change and adherence or discontinuation (i.e. after initiation) has not been undertaken (Figure 1)
  - Collating findings from such studies would provide a useful resource of the evidence

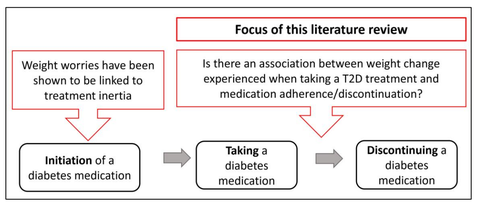
## OBJECTIVE

- To conduct a literature review exploring the association between weight change experienced by people with T2D (PwD) on T2D treatment and medication adherence and/or discontinuation

## METHODS

- Literature search of MEDLINE and EMBASE, and recent congress abstracts conducted to identify English language studies (Jan 2005 to Sep 2020) reporting objective data on weight change and adherence and/or discontinuation in PwD treated with diabetes medications
- Strategy designed to retrieve records that explicitly referred to either non-specific adherence or to specific named adherence/discontinuation measures or questionnaires, and to identify records where weight change was objectively reported
- Search had no geographical limits

**Figure 1. Focus of the literature review**




## SEARCH RESULTS

- Review of 9188 abstracts resulted in identification of 34 potentially eligible records; nine studies remained following full-text review
- Several T2D medications were evaluated across studies (Tables 1–3). Most studies were from the USA (n=7); one was from Israel and one from the UK. Study population sizes varied across the studies (N=120 to N=33,849)
- Of the nine studies, six reported on the association between weight change and adherence,[5–10] two on the association between weight change and discontinuation,[11,12] and one reported data on weight and both adherence and discontinuation[13]

## STUDY RESULTS

**Table 1. Studies reporting association between weight and discontinuation**

| Author | Treatment | Weight loss associated with lower discontinuation? | Results |
|---|---|---|---|
| Meltzer Cohen[11] | Liraglutide | ✓ | Mean body weight reduction greater in continuers than discontinuers (–3.57 kg vs –1.25 kg; p<0.001) |
| Bell[12] | NIAD | ✓ | Lower rates of discontinuation in weight-loss versus weight neutral group (50% vs 57%; p<0.001) |
| Durden[13] | GLP-1 RA | ✓ | Discontinuation rates lower in those with >3% body weight loss at 3–6 months versus those with no early effect (61.9% vs 67.5%; p<0.001) |

GLP-1 RA, glucagon-like peptide-1 receptor agonist; NIAD, non-insulin antidiabetes drug
✓ indicates a significant result

**Table 2. Studies reporting association between absolute weight change (kg) and adherence**

| Author | Treatment | Weight loss associated with better adherence? | Weight gain associated with better adherence? |
|---|---|---|---|
| Patel[5] | Liraglutide + BI | ✓[a] | |
| | BBI | | ✓[a] |
| Carls[6] | GLP-1 RA | ✓** | |
| | DPP-4i | - | - |
| | SU | | ✓** |
| Gordon[7] | OAD monotherapy | ✓† | |
| | OAD dual therapy | | ✓[a] |
| | OAD triple therapy | | ✓[a] |
| McAdam-Marx[8] | Pooled[b] | ✓* | |

*p=0.016, **p<0.01, †p<0.001 vs non-adherent
[a]✓ Based on trends and/or study author conclusions, not statistical significance, whereas ✓ indicates statistically significant result
[b]Self-reported adherence as per 5-item Medication Adherence Report Scale
BI, basal insulin; BBI, basal-bolus insulin; DPP-4i, dipeptidyl peptidase-4 inhibitor; GLP-1 RA, glucagon-like peptide-1 receptor agonist; OAD, oral antidiabetes drug; SU, sulfonylurea

**Table 3. Studies reporting association between categorical weight change and adherence**

| Author | Treatment | Weight loss associated with better adherence? | Weight gain associated with better adherence? |
|---|---|---|---|
| McAdam-Marx[9] | Pooled | ✓[a] | Weight gain was not observed in the study participants and was not reported as a category |
| | Metformin | ✓[a] | |
| | GLP-1 RA | ✓[a] | |
| | SU | ✓[a] | |
| | TZD | ✓[a] | |
| | DPP-4i | ✓[a] | |
| | Insulin | ✓[a] | |
| | other | ✓[a] | |
| Durden[13] | GLP-1 RA | ✓† | |

† Odds ratio (95% confidence interval): 1.18 [1.02,1.36]
[a] ✓ Based on trends and/or author conclusions, not statistical significance, whereas ✓ indicates a statistically significant result
DPP-4i, dipeptidyl peptidase-4 inhibitor; GLP-1 RA, glucagon-like peptide-1 receptor agonist; SU, sulfonylurea; TZD, thiazolidinedione.

## OVERVIEW OF STUDY RESULTS

- Three studies reported on the association between weight and discontinuation (Table 1):
  - All reported weight loss to be associated with higher persistence[11–13]
- Four studies reported on the association between absolute weight change and adherence (Table 2):
  - One pooled data from different medications and demonstrated that weight loss was significantly greater in adherent versus non-adherent PwD (–1.7 kg vs –1.1 kg) when adherence was self-reported according to the MARS-5 (odds ratio [OR] 1.70 [95% confidence interval (CI) 1.11, 2.61]; p=0.016).[8] In three studies, significant or numeric differences in weight change were reported between adherent and non-adherent PwD in the direction of the known weight profile (loss/gain) of the evaluated drug[5–7]
- Two studies reported on the association between categorical weight loss and adherence (Table 3):
  - One study reported that more adherent versus non-adherent PwD lost ≥3% body weight regardless of the drug's known weight profile (pooled treatments, 29.9% vs 24.2%, respectively, lost ≥3% body weight).[9] Another showed that PwD who experienced early weight loss (>3% body weight at 3–6 months) with a GLP-1 RA had a higher likelihood of medication adherence compared with those with no early weight loss (OR [95% CI] 1.18 [1.02,1.36])[13]
- One study reported adherence by categorical weight change; in the whole study population, as weight loss increased (>1%, ≥3%,≥5%), adherence (Morisky Medication Adherence Scale [MMAS]) improved (0.39, 0.37, 0.33; p≤0.05 vs weight gain)
  - Significant improvement in MMAS across weight loss categories (p≤0.05) in PwD on drugs with weight gain profile and trend for improvement in PwD on drugs with weight loss profile

## CONCLUSIONS

- Studies in this review found that weight loss on diabetes treatment was associated with lower rates of discontinuation
- Relationship between weight change and on-treatment adherence is more complex
  - Direction of adherence–weight relationship generally depended on the known weight-loss or weight-gain properties of the evaluated drug although this was not always the case
- Cross-sectional nature of the evidence base does not allow a direct explanation of causation
  - Data from longitudinal studies are needed to determine causality between weight change and adherence and discontinuation with T2D medication and to assess the impact of confounders (e.g. lifestyle interventions, weight management support, patient characteristics and expectations)
- Supporting better medication adherence and persistence is key in improving outcomes in T2D; therefore, further exploration of weight in impacting treatment-taking behavior is warranted

**DISCLOSURES**

- KB, SS, and VT are employees of Eli Lilly and Company; TKM and SR received. funding from Eli Lilly and Company for time spent conducting this research

**References:**

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