

## Supplementary Material

### **The effects of sodium-glucose cotransporter 2 inhibitors on body composition in type 2 diabetes mellitus: A narrative review**

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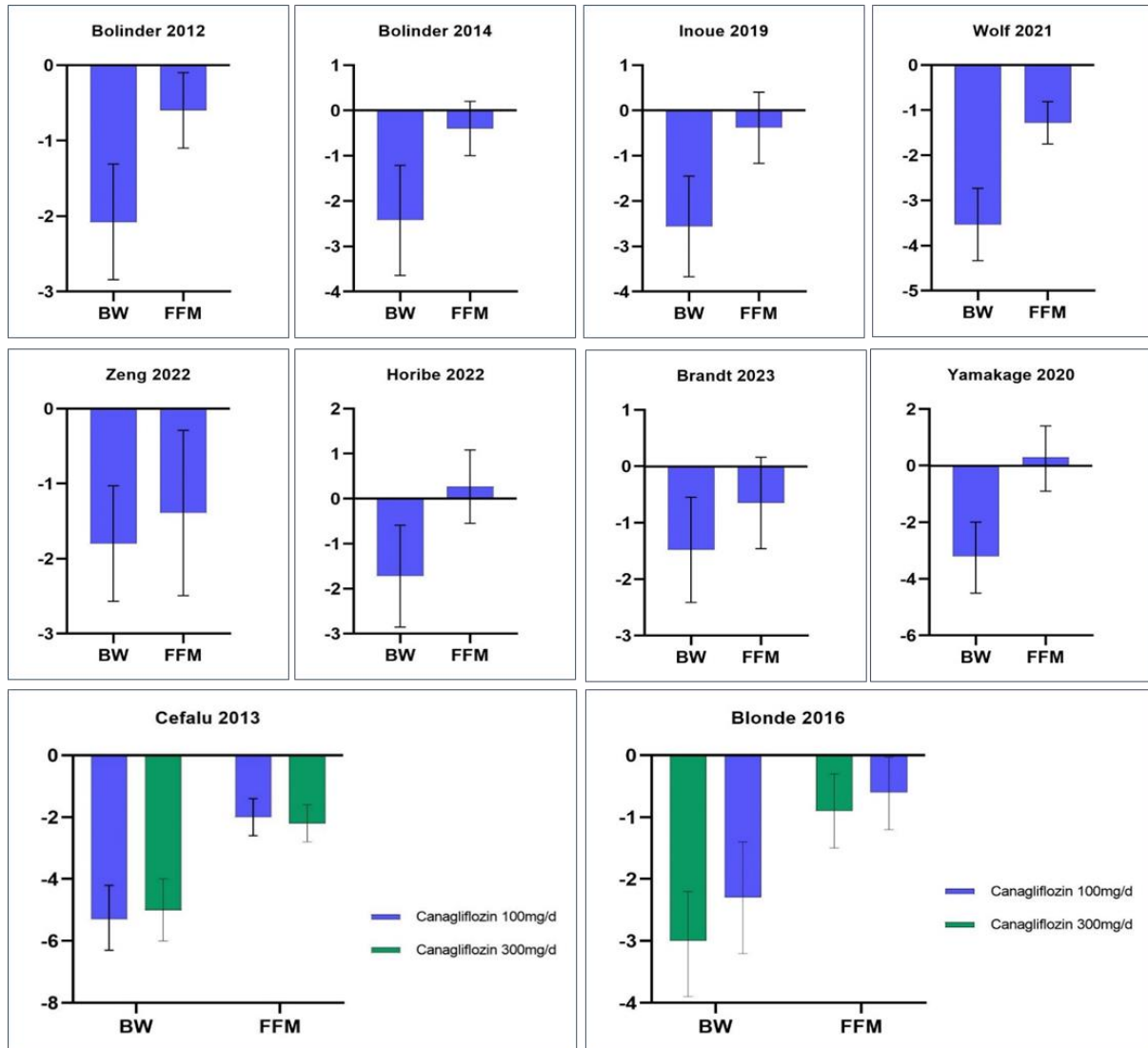
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**Figure S1.** Sodium glucose cotransporter 2 inhibitor versus comparators: Between-Group Mean Difference of Changes in Total Body Weight (BW) and Fat-Free Mass (FFM)



**Table S1.** Quality of Included Studies Based on National Institute of Health (NIH) Assessment Tool

| Study                    | Were the study described as randomized, a randomized trial, a randomized clinical trial, or an RCT? | Were the method of randomization adequate (i.e., use of randomly generated assignment)? | Were the treatment allocation concealed (so that assignments could not be predicted)? | Were study participants and providers blinded to treatment group assignment? | Were the people assessing the outcomes blinded to the participants' group assignments? | The groups similar at baseline on important characteristics that could affect outcomes? | The overall drop-out rate from the study at endpoint 20% or lower of the number allocated to treatment? | The differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower? | Was there high adherence to the intervention protocols for each treatment group? | Were other interventions avoided or similar in the groups (e.g., similar background treatments)? | Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants? | Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power? | Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)? | Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an intention-to-treat analysis? | Rating |
|--------------------------|---|---|---|--|--|---|---|--|--|--|---|--|--|---|--------|
| Bolinder et al. 2012 (1) | Yes   | Yes   | Yes   | Yes  | Yes  | Yes   | Yes   | Yes  | Yes  | Yes  | Yes   | Yes  | Yes  | Yes   | Good   |
| Bolinder et al. 2014 (2) | Yes   | Yes   | Yes   | Yes  | Yes  | Yes   | Yes   | Yes  | NR   | Yes  | Yes   | Yes  | Yes  | Yes   | Good   |
| Blonde et al. (3)        | Yes   | Yes   | Yes   | Yes  | No   | Yes   | Yes   | Yes  | NR   | No   | Yes   | No   | No   | No  | Good   |
| Fadini et al. (4)        | Yes   | Yes   | Yes   | No   | Yes  | Yes   | Yes   | Yes  | Yes  | No   | Yes   | Yes  | No   | Yes   | Fair   |
| Inoue et al. (5)         | Yes   | Yes   | Yes   | No   | Yes  | Yes   | Yes   | Yes  | NR   | No   | Yes   | Yes  | Yes  | Yes   | Good   |
| Chehregosha et al. (6)   | Yes   | Yes   | Yes   | Yes  | Yes  | Yes   | No  | Yes  | Yes  | NR   | Yes   | Yes  | Yes  | Yes   | Good   |
| Lauritsen et al. (7)     | Yes   | NR  | NR  | Yes  | NR   | NR  | Yes   | NA   | Yes  | Yes  | Yes   | No   | Yes  | NA  | Poor   |

|                       |     |     |     |     |     |     |     |     |     |     |     |     |     |     |      |
|-----------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| Horibe et al. (8)     | Yes | Yes | Yes | NR  | Yes | Yes | Yes | Yes | NR  | No  | Yes | Yes | Yes | Yes | Good |
| Brandt et al. (9)     | Yes | Yes | Yes | Yes | NR  | Yes | NR  | NR  | NR  | Yes | Yes | Yes | Yes | Yes | Fair |
| Nakaguchi et al. (10) | Yes | Yes | Yes | No  | Yes | Yes | Yes | Yes | NR  | Yes | Yes | Yes | Yes | Yes | Good |
| McCrimmon et al. (11) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | NR  | Yes | Yes | Yes | Yes | Yes | Good |
| Kitazawa et al. (12)  | Yes | Yes | Yes | No  | NR  | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Good |
| Wolf et al. (13)      | Yes | Yes | NR  | No  | NR  | Yes | Yes | Yes | NR  | Yes | Yes | Yes | Yes | Yes | Fair |
| Tsurutani et al. (14) | Yes | Yes | NR  | No  | No  | Yes | Yes | Yes | NR  | No  | Yes | Yes | Yes | Yes | Good |
| Zeng et al. (15)      | Yes | Yes | Yes | No  | No  | Yes | Yes | Yes | NR  | No  | Yes | NR  | No  | Yes | Fair |
| Kato et al. (16)      | Yes | NR  | NR  | No  | No  | No  | Yes | Yes | NR  | No  | Yes | No  | Yes | NR  | Fair |
| Shimizu et al. (17)   | Yes | Yes | NR  | No  | Yes | Yes | Yes | Yes | NR  | No  | Yes | Yes | Yes | NR  | Fair |
| Yamakage et al. (18)  | Yes | Yes | Yes | No  | Yes | Yes | Yes | Yes | NR  | No  | Yes | Yes | Yes | Yes | Good |
| Han et al. (19)       | Yes | Yes | Yes | No  | NR  | Yes | Yes | Yes | NR  | No  | Yes | Yes | Yes | NR  | Good |

**Table S2.** Changes in Visceral and Subcutaneous Adipose Tissue Following Treatment

| Study                  | Assessment method | Parameter   | SGLT2is            |                     | Control            |                    |
|------------------------|-------------------|---|--------------------|---------------------|--------------------|--------------------|
|                        |                   |   | Baseline value     | Change              | Baseline value     | Change             |
| Bolinder et al. (1)    | MRI               | Visceral adipose tissue volume (cm <sup>3</sup> )     | 3242.0             | -297.5              | 2798.2             | -39.2              |
|                        |                   | Subcutaneous adipose tissue volume (cm <sup>3</sup> ) | 4582.2             | -306.4              | 4679.3             | -121.4             |
| Inoue et al. (5)       | MRI               | Navel subcutaneous fat area (cm <sup>2</sup> )        | 334.9 ± 157.7      | -18.9 ± 15.7        | 315 ± 121.3        | 6.7 ± 14.1         |
|                        |                   | Navel visceral fat area (cm <sup>2</sup> )            | 138.8 ± 101.3      | -12.0 ± 12.7        | 122.7 ± 46.4       | 11.3 ± 11.5        |
|                        |                   | Iliopsoas muscle surface area (cm <sup>2</sup> )      | 20.6 ± 6.6         | -1.8 ± 1.3          | 21.2 ± 6.3         | -0.5 ± 1.2         |
| Horibe et al. (8)      | MRI               | Navel subcutaneous fat area (cm <sup>2</sup> )        | 341 (240.0, 417.0) | -35.0 (-68.0, 1.0)  | 311 (220.3, 411.5) | -3.5 (-27.0, 12.0) |
|                        |                   | Navel visceral fat area (cm <sup>2</sup> )            | 135 (10.40, 157.0) | -19.0 (-34.0, -2.0) | 133 (99.3, 170.8)  | -4.5 (-19.3, 12.8) |
| Chehregosha et al. (6) | DXA               | Visceral adipose tissue area (cm <sup>2</sup> )       | 178.9 ± 40.7       | -0.6                | 174.6 ± 52.5       | 11.6               |
| McCrimmon et al. (11)  | DXA               | Visceral fat mass (kg)                                | 1.5 ± 0.8          | -0.1                | 1.5 ± 0.8          | -0.2               |
| Kato et al. (16)       | BIA               | Visceral fat area (cm <sup>2</sup> )                  | 132.5 ± 50.5       | -10.6               | 131.7 ± 52.1       | -19.5              |
|                        |                   | Subcutaneous fat area (cm <sup>2</sup> )              | 253.8 ± 81.6       | -10.4               | 248.2 ± 94.2       | -14.3              |
| Zeng et al. (15)       | BIA               | Visceral fat mass (kg)                                | 2.9 ± 1.3          | -0.22 ± 0.1         | 3.1 ± 1.1          | -0.08 ± 0.1        |
|                        |                   | Subcutaneous fat mass (kg)                            | 17.9 ± 6.4         | -0.8 ± 0.31         | 19.4 ± 4.6         | -0.27 ± 0.35       |
| Shimizu et al. (17)    | BIA               | Visceral adipose tissue area (cm <sup>2</sup> )       | 108.7 ± 42.9       | -7.3                | 125.7 ± 32.2       | -5.7               |
|                        |                   | Subcutaneous adipose tissue area (cm <sup>2</sup> )   | 226.7 ± 90         | -11.2               | 249.5 ± 82.5       | 1.3                |
| Yamakage et al. (18)   | BIA               | Intra-abdominal fat area (cm <sup>2</sup> )           | 101.4 ± 28         | -9.8 (-17.7, -2.0)  | 110.5 ± 39.8       | 3.5 (-3.5, 10.5)   |
|                        |                   | Subcutaneous fat area (cm <sup>2</sup> )              | 254.4 ± 81         | -16.3 (-31.2, -1.4) | 223.8 ± 60.7       | 13.3 (-7.9, 34.5)  |
| Han et al. (19)        | CT scan           | Visceral fat area (cm <sup>2</sup> )                  | 209.1 ± 63.3       | -26.2 ± 3.7         | 223 ± 90.8         | 7 ± 7.7            |
|                        |                   | Subcutaneous fat area (cm <sup>2</sup> )              | 267.5 ± 115.4      | -9.3 ± 7.2          | 230.1 ± 80.6       | -1.4 ± 5.0         |

SGLT2is, sodium glucose cotransporter 2 inhibitors; MRI, magnetic resonance imaging; DXA, dual x-ray absorptiometry; BIA, Bioelectrical Impedance Analysis, CT scan, computed tomography scan

Data are presented as mean ± standard deviation or median (interquartile range) when available.

**Table S3.** Body Composition Changes Following Lifestyle Interventions and Bariatric Surgery in Previous Studies

| Study                | Design            | Intervention   | Absolute changes                    | %FFM change      |
|----------------------|-------------------|--|-------------------------------------|------------------|
| Nuijten et al. (20)  | Meta-analysis     | Bariatric surgery – 1 year                           | LBM: -8.13 kg [95%CI -7.26; -9.01]  | -23.4%           |
|                      |                   |  | FFM: -8.23 kg [95%CI -5.73; -10.74] | -20.8%           |
|                      |                   |  | SMM: -3.18 kg [95%CI -0.71; -5.64]  | -8.2%            |
| Chatson et al. (21)  | Systematic review | Dietary, behavioral and pharmaceutical interventions | TBW: -10 kg to -22.1 kg             | -4.3% to -38.3%  |
|                      |                   | bariatric surgery                                    | TBW: -12.3 kg to -60.4              | -12.7% to -52.7% |
| Turicchi et al. (22) | Randomized trial  | Low-calorie diet – 8 weeks                           | TBW: -11.17 ± 3.52                  | -30.37%          |

LBM, lean body mass; FFM, fat-free mass; SMM, skeletal muscle mass  
%FFM: relative to total weight loss

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