



## BIBLIOGRAPHY

1. Abdul-Ghani M, Defronzo RA. Is It Time to Change the Type 2 Diabetes Treatment Paradigm? Yes! GLP-1 RAs Should Replace Metformin in the Type 2 Diabetes Algorithm. *Diabetes Care*. 2017; 40(8):1121-7. doi:10.2337/dc16-2368
2. Ahrén B, Atkin SL, Charpentier G, et al. Semaglutide induces weight loss in subjects with type 2 diabetes regardless of baseline BMI or gastrointestinal adverse events in the SUSTAIN 1 to 5 trials. *Diabetes Obesity and Metabolism*. 2018;20(9):2210-2219. doi:10.1111/dom.13353
3. Antuna-Puente B, Feve B, Fellahi S, Bastard JP. Adipokines: The missing link between insulin resistance and obesity. *Diabetes & Metabolism*. 2008;34(1):2-11. doi:10.1016/j.diabet.2007.09.004
4. Antza C, Kostopoulos G, Mostafa S, Nirantharakumar K, Tahrani A. The links between sleep duration, obesity and type 2 diabetes mellitus. *Journal of Endocrinology*. 2022;252(2):125-141. doi:10.1530/joe-21-0155
5. Ard J, Fitch A, Fruh S, Herman L. Weight Loss and Maintenance Related to the Mechanism of Action of Glucagon-Like Peptide 1 Receptor Agonists. *Advances in Therapy*. 2021;38(6):2821-2839. doi:10.1007/s12325-021-01710-0
6. Ashwell M, Gunn P, Gibson S. Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: systematic review and meta-analysis. *Obesity Reviews*. 2012;13(3):275-286. doi:10.1111/j.1467-789X.2011.00952.x
7. Bailey CJ, Flatt PR, Conlon JM. An update on peptide-based therapies for type 2 diabetes and obesity. *Peptides*. 2023 Mar;161:170939. doi: 10.1016/j.peptides.2023.170939.
8. Bays HE, González-Campoy JM, Henry RR, et al. Is adiposopathy (sick fat) an endocrine disease? *International Journal of Clinical Practice*. 2008;62(10):1474-1483. doi:10.1111/j.1742-1241.2008.01848.x
9. Bello-Chavolla OY, Antonio-Villa NE, Vargas-Vázquez A, et al. Metabolic Score for Visceral Fat (METS-VF), a novel estimator of intra-abdominal fat content and cardio-metabolic health. *Clinical Nutrition*. 2020;39(5):1613-1621. doi:10.1016/j.clnu.2019.07.012
10. Berg AH, Scherer PE. Adipose Tissue, Inflammation, and Cardiovascular Disease. *Circulation Research*. 2005;96(9):939-949. doi:10.1161/01.res.0000163635.62927.34
11. Bonnet JP, Cardel MI, Cellini J, Hu FB, Guasch-Ferré M. Breakfast Skipping, Body Composition, and Cardiometabolic Risk: A Systematic Review and Meta-Analysis of Randomized Trials. *Obesity*. 2020;28(6):1098-1109. doi:10.1002/oby.22791
12. Browning LM, Hsieh SD, Ashwell M. A systematic review of waist-to-height ratio as a screening tool for the prediction of cardiovascular disease and diabetes: 0.5 could be a suitable global



## Addressing the Roots

Re-thinking the approach to type 2 diabetes management  
and the role of dual GIP/GLP-1 receptor agonism

---

boundary value. *Nutrition Research Reviews*. 2010;23(2):247-269.  
doi:10.1017/s0954422410000144

13. Caleyachetty R, Barber TM, Mohammed NI, et al. Ethnicity-specific BMI cutoffs for obesity based on type 2 diabetes risk in England: a population-based cohort study. *Lancet Diabetes & Endocrinology*. 2021;9(7):419-426. doi:10.1016/s2213-8587(21)00088-7
14. Clinicaltrials.gov. NCT04537923.
15. Clinicaltrials.gov. NCT04255433.
16. Colberg SR, Zarrabi L, Bennington L, et al. Postprandial Walking is Better for Lowering the Glycemic Effect of Dinner than Pre-Dinner Exercise in Type 2 Diabetic Individuals. *Journal of the American Medical Directors Association*. 2009;10(6):394-397. doi:10.1016/j.jamda.2009.03.015
17. Coskun T, Sloop KW, Loghin C, et al. LY3298176, a novel dual GIP and GLP-1 receptor agonist for the treatment of type 2 diabetes mellitus: From discovery to clinical proof of concept. *Molecular Metabolism*. 2018;18:3-14. doi:10.1016/j.molmet.2018.09.009
18. Dahl D, Onishi Y, Norwood P, et al. Effect of Subcutaneous Tirzepatide vs Placebo Added to Titrated Insulin Glargine on Glycemic Control in Patients With Type 2 Diabetes. *JAMA*. 2022;327(6):534-545. doi:10.1001/jama.2022.0078
19. Davies MJ, Aroda VR, Collins BS, et al. Management of hyperglycaemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetologia*. 2022;65(12):1925-1966. doi: 10.1007/s00125-022-05787-2.
20. DeFronzo RA. From the Triumvirate to the Ominous Octet: A New Paradigm for the Treatment of Type 2 Diabetes Mellitus. *Diabetes*. 2009;58(4):773-795. doi:10.2337/db09-9028
21. Del Prato S, Kahn SE, Pavo I, et al. Tirzepatide versus insulin glargine in type 2 diabetes and increased cardiovascular risk (SURPASS-4): a randomised, open-label, parallel-group, multicentre, phase 3 trial. *Lancet*. 2021;398(10313):1811-1824. doi:10.1016/S0140-6736(21)02188-7
22. Dempsey PC, Larsen RN, Sethi P, et al. Benefits for Type 2 Diabetes of Interrupting Prolonged Sitting With Brief Bouts of Light Walking or Simple Resistance Activities. *Diabetes Care*. 2016;39(6):964-972. doi:10.2337/dc15-2336
23. Dempsey PC, Owen N, Yates TE, Kingwell BA, Dunstan DW. Sitting Less and Moving More: Improved Glycaemic Control for Type 2 Diabetes Prevention and Management. *Current Diabetes Reports*. 2016;16(11):114. doi:10.1007/s11892-016-0797-4
24. Després J-P, Lemieux I, Bergeron J, et al. Abdominal Obesity and the Metabolic Syndrome: Contribution to Global Cardiometabolic Risk. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2008;28(6):1039-1049. doi:10.1161/atvbaha.107.159228



## Addressing the Roots

Re-thinking the approach to type 2 diabetes management  
and the role of dual GIP/GLP-1 receptor agonism

---

25. Diabetes Canada 2020 Quick Reference Guide. Online at <http://guidelines.diabetes.ca/docs/CPG-quick-reference-guide-web-EN.pdf> Accessed June 2022
26. Donga E, Van Dijk M, Van Dijk JG, et al. A Single Night of Partial Sleep Deprivation Induces Insulin Resistance in Multiple Metabolic Pathways in Healthy Subjects. *The Journal of Clinical Endocrinology & Metabolism*. 2010;95(6):2963-2968. doi:10.1210/jc.2009-2430
27. Douketis JD. Canadian guidelines for body weight classification in adults: application in clinical practice to screen for overweight and obesity and to assess disease risk. *Canadian Medical Association Journal*. 2005;172(8):995-998. doi:10.1503/cmaj.045170
28. Drucker DJ. The biology of incretin hormones. *Cell Metabolism*. 2006;3(3):153-165. doi:10.1016/j.cmet.2006.01.004
29. Duvivier BMFM, Schaper NC, Hesselink MKC, et al. Breaking sitting with light activities vs structured exercise: a randomised crossover study demonstrating benefits for glycaemic control and insulin sensitivity in type 2 diabetes. *Diabetologia*. 2017;60(3):490-498. doi:10.1007/s00125-016-4161-7
30. Esposito K, Chiodini P, Bellastella G, Maiorino MI, Giugliano D. Proportion of patients at HbA1c target <7% with eight classes of antidiabetic drugs in type 2 diabetes: systematic review of 218 randomized controlled trials with 78 945 patients. *Diabetes, Obesity and Metabolism*. 2012;14(3):228-233. doi: 10.1111/j.1463-1326.2011.01512.x
31. Farshchi HR, Taylor MA, Macdonald IA. Beneficial metabolic effects of regular meal frequency on dietary thermogenesis, insulin sensitivity, and fasting lipid profiles in healthy obese women. *The American Journal of Clinical Nutrition*. 2005;81(1):16-24. doi:10.1093/ajcn/81.1.16
32. Francois ME, Baldi JC, Manning PJ, et al. 'Exercise snacks' before meals: a novel strategy to improve glycaemic control in individuals with insulin resistance. *Diabetologia*. 2014;57(7):1437-1445. doi:10.1007/s00125-014-3244-6
33. Frías JP, Davies MJ, Rosenstock J, et al. Tirzepatide versus Semaglutide Once Weekly in Patients with Type 2 Diabetes. *New England Journal of Medicine*. 2021;385(6):503-515. doi:10.1056/nejmoa2107519
34. Gasbjerg LS, Bari EJ, Stensen S, et al. Dose-dependent efficacy of the glucose-dependent insulinotropic polypeptide (GIP) receptor antagonist GIP(3-30)NH<sub>2</sub> on GIP actions in humans. *Diabetes, Obesity and Metabolism*. 2021;23(1):68-74. doi: 10.1111/dom.14186
35. Gastaldelli A, Cusi K, Fernández Landó L, Bray R, Brouwers B, Rodríguez Á. Effect of tirzepatide versus insulin degludec on liver fat content and abdominal adipose tissue in people with type 2 diabetes (SURPASS-3 MRI): a substudy of the randomised, open-label, parallel-group, phase 3 SURPASS-3 trial. *Lancet Diabetes & Endocrinology*. 2022;10(6):393-406. doi:10.1016/S2213-8587(22)00070-5



## Addressing the Roots

Re-thinking the approach to type 2 diabetes management  
and the role of dual GIP/GLP-1 receptor agonism

---

36. Gu C, Brereton N, Schweitzer A, et al. Metabolic Effects of Late Dinner in Healthy Volunteers—A Randomized Crossover Clinical Trial. *The Journal of Clinical Endocrinology & Metabolism*. 2020;105(8):2789-2802. doi:10.1210/clinem/dgaa354
37. Guilherme A, Henriques F, Bedard AH, Czech MP. Molecular pathways linking adipose innervation to insulin action in obesity and diabetes mellitus. *Nature Reviews Endocrinology*. 2019;15(4):207-225. doi:10.1038/s41574-019-0165-y
38. Hajer GR, Van Haeften TW, Visseren FLJ. Adipose tissue dysfunction in obesity, diabetes, and vascular diseases. *Eur Heart J*. 2008;29(24):2959-2971. doi:10.1093/eurheartj/ehn387
39. Holst JJ, Gasbjerg LS, Rosenkilde MM. The Role of Incretins on Insulin Function and Glucose Homeostasis. *Endocrinology*. 2021;162(7) :bqab065. doi: 10.1210/endo/bqab065
40. Holst JJ, Rosenkilde MM. GIP as a Therapeutic Target in Diabetes and Obesity: Insight From Incretin Co-agonists. *The Journal of Clinical Endocrinology & Metabolism*. 2020;105(8):e2710-e2716. doi:10.1210/clinem/dgaa327
41. Hutchison AT, Regmi P, Manoogian ENC, et al. Time-Restricted Feeding Improves Glucose Tolerance in Men at Risk for Type 2 Diabetes: A Randomized Crossover Trial. *Obesity*. 2019;27(5):724-732. doi: 10.1002/oby.22449
42. Imran SA, Agarwal G, Bajaj HS, Ross S. Targets for Glycemic Control. *Canadian Journal of Diabetes*. 2018;42:S42-S46. doi:10.1016/j.jcjd.2017.10.030
43. Jamshed H, Beyl R, Della Manna D, Yang E, Ravussin E, Peterson C. Early Time-Restricted Feeding Improves 24-Hour Glucose Levels and Affects Markers of the Circadian Clock, Aging, and Autophagy in Humans. *Nutrients*. 2019;11(6):1234. doi:10.3390/nu11061234
44. Kazlauskaitė R, Avery-Mamer EF, Li H, et al. Race/ethnic comparisons of waist-to-height ratio for cardiometabolic screening: The study of women's health across the nation. *American Journal of Human Biology*. 2017;29(1):e22909. doi:10.1002/ajhb.22909
45. Koren D, Taveras EM. Association of sleep disturbances with obesity, insulin resistance and the metabolic syndrome. *Metabolism - Clinical and Experimental*. 2018;84:67-75. doi:10.1016/j.metabol.2018.04.001
46. Kusminski CM, Bickel PE, Scherer PE. Targeting adipose tissue in the treatment of obesity-associated diabetes. *Nature Reviews Drug Discovery*. 2016;15(9):639-660. doi:10.1038/nrd.2016.75
47. Eli Lilly Canada Inc. MOUNJARO product monograph. Date of Initial Authorization: November 23, 2022.
48. Lingvay I, Sumithran P, Cohen RV, le Roux CW. Obesity management as a primary treatment goal for type 2 diabetes: time to reframe the conversation. *Lancet*. 2022;399(10322):394-405. doi:10.1016/S0140-6736(21)01919-X



## Addressing the Roots

Re-thinking the approach to type 2 diabetes management  
and the role of dual GIP/GLP-1 receptor agonism

---

49. Lipscombe L, Butalia S, Dasgupta K, et al. Pharmacologic Glycemic Management of Type 2 Diabetes in Adults: 2020 Update. *Canadian Journal of Diabetes*. 2020;44(7):575-591. doi:10.1016/j.jcjd.2020.08.001
50. Liu D, Huang Y, Huang C, et al. Calorie Restriction with or without Time-Restricted Eating in Weight Loss. *New England Journal of Medicine*. 2022;386(16):1495-1504. doi:10.1056/nejmoa2114833
51. Ludvik B, Giorgino F, Jódar E, et al. Once-weekly tirzepatide versus once-daily insulin degludec as add-on to metformin with or without SGLT2 inhibitors in patients with type 2 diabetes (SURPASS-3): a randomised, open-label, parallel-group, phase 3 trial. *Lancet*. 2021;398(10300):583-598. doi:10.1016/S0140-6736(21)01443-4
52. Mesarwi O, Polak J, Jun J, Polotsky VY. Sleep Disorders and the Development of Insulin Resistance and Obesity. *Endocrinology and Metabolism Clinics of North America*. 2013;42(3):617-634. doi:10.1016/j.ecl.2013.05.001
53. Miller SA, St. Onge EL. Sitagliptin: A Dipeptidyl Peptidase IV Inhibitor for the Treatment of Type 2 Diabetes. *Annals of Pharmacotherapy*. 2006;40(7-8):1336-1343. doi:10.1345/aph.1g665
54. Oikonomou EK, Antoniadis C. The role of adipose tissue in cardiovascular health and disease. *Nature Reviews Cardiology*. 2019;16(2):83-99. doi:10.1038/s41569-018-0097-6
55. Oosterman JE, Wopereis S, Kalsbeek A. The Circadian Clock, Shift Work, and Tissue-Specific Insulin Resistance. *Endocrinology*. 2020;161(12)doi:10.1210/endo/bqaa180
56. Patterson RE, Sears DD. Metabolic Effects of Intermittent Fasting. *Annual Review of Nutrition*. 2017;37(1):371-393. doi:10.1146/annurev-nutr-071816-064634
57. Peeke PM, Greenway FL, Billes SK, Zhang D, Fujioka K. Effect of time restricted eating on body weight and fasting glucose in participants with obesity: results of a randomized, controlled, virtual clinical trial. *Nutrition & Diabetes*. 2021;11(1):6; doi:10.1038/s41387-021-00149-0
58. Poggiogalle E, Jamshed H, Peterson CM. Circadian regulation of glucose, lipid, and energy metabolism in humans. *Metabolism*. 2018;84:11-27. doi:10.1016/j.metabol.2017.11.017
59. Rosenstock J, Wysham C, Frías JP, et al. Efficacy and safety of a novel dual GIP and GLP-1 receptor agonist tirzepatide in patients with type 2 diabetes (SURPASS-1): a double-blind, randomised, phase 3 trial. *Lancet*. 2021;398(10295):143-155. doi:10.1016/S0140-6736(21)01324-6
60. Samms RJ, Coghlan MP, Sloop KW. How May GIP Enhance the Therapeutic Efficacy of GLP-1? *Trends in Endocrinology & Metabolism*. 2020;31(6):410-421. doi:10.1016/j.tem.2020.02.006
61. Sievenpiper JL, Chan CB, Dworatzek PD, Freeze C, Williams SL. Nutrition Therapy. *Canadian Journal of Diabetes*. 2018;42:S64-S79. doi:10.1016/j.jcjd.2017.10.009



## Addressing the Roots

Re-thinking the approach to type 2 diabetes management  
and the role of dual GIP/GLP-1 receptor agonism

---

62. Skow MA, Bergmann NC, Knop FK. Diabetes and obesity treatment based on dual incretin receptor activation: 'twincretins'. *Diabetes, Obesity and Metabolism*. 2016;18(9):847-854. doi:10.1111/dom.12685
63. *The Practical Guide*, NIH, 2000
64. van Eyk HJ, Paiman EHM, Bizino MB, et al. A double-blind, placebo-controlled, randomised trial to assess the effect of liraglutide on ectopic fat accumulation in South Asian type 2 diabetes patients. *Cardiovascular Diabetology*. 2019;18(1): 87. doi:10.1186/s12933-019-0890-5
65. Wharton S, Lau DCW, Vallis M, et al. Obesity in adults: a clinical practice guideline. *CMAJ*. 2020 Aug 4;192(31):E875-E891. doi: 10.1503/cmaj.191707.
66. Winkler EAH, Chastin S, Eakin EG, et al. Cardiometabolic Impact of Changing Sitting, Standing, and Stepping in the Workplace. *Medicine & Science in Sports & Exercise*. 2018;50(3): 516-524. doi: 10.1249/MSS.0000000000001453.
67. Yaghootkar H, Whitcher B, Bell JD, Thomas EL. Ethnic differences in adiposity and diabetes risk – insights from genetic studies. *Journal of Internal Medicine*. 2020;288(3):271-283. doi:10.1111/joim.13082
68. Zhao L, Zhu C, Lu M, et al. The key role of a glucagon-like peptide-1 receptor agonist in body fat redistribution. *Journal of Endocrinology*. 2019;240(2):271-286. doi:10.1530/joe-18-0374