Use of GLP-1RAs & Other Medication Effects in Older Adults

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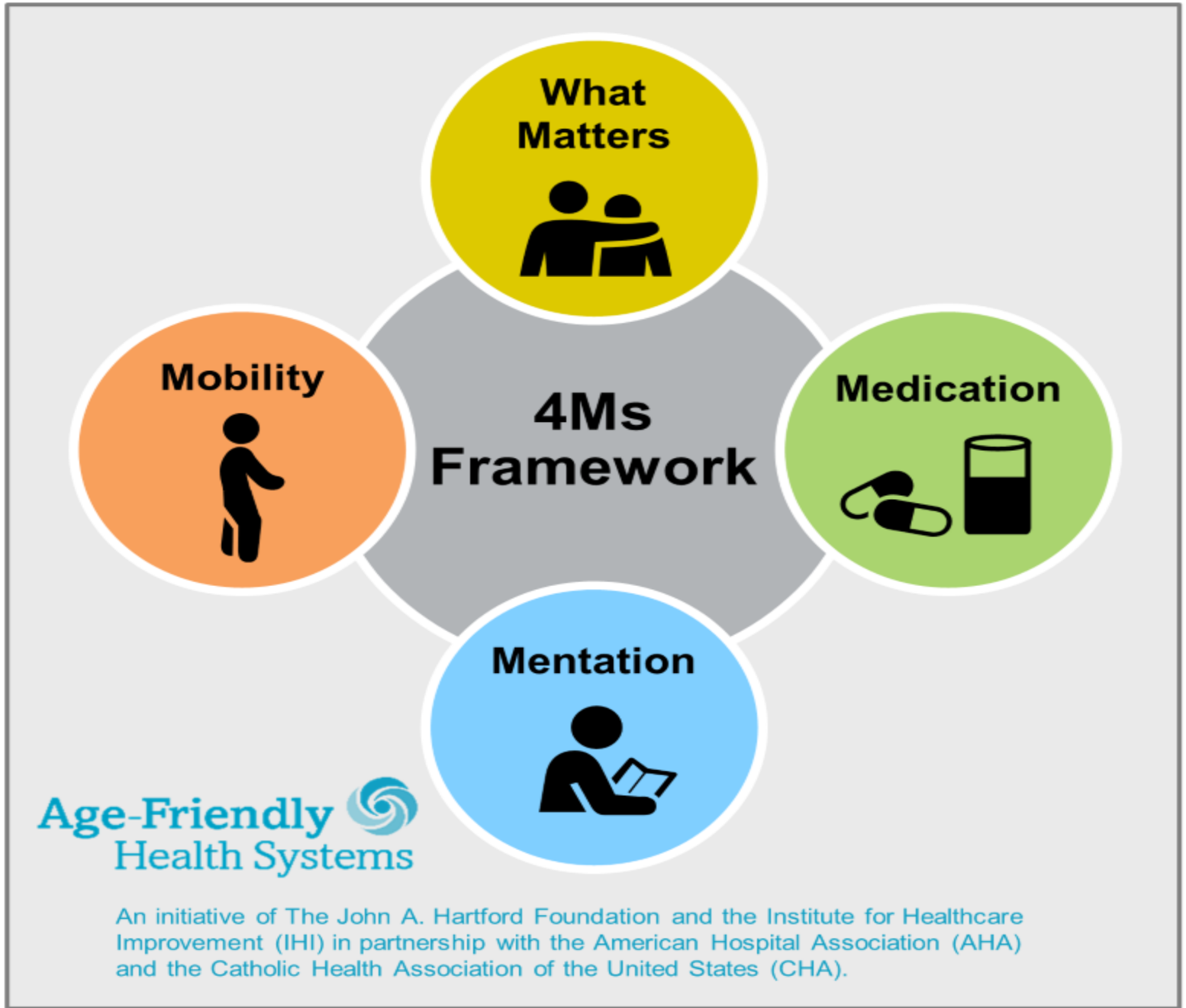
Objectives

- Briefly describe current options and expected outcomes for managing Type-2 Diabetes Mellitus in older individuals living in long-term care settings
- Suggest reasons for potential increased use of GLP-1 medications in older individuals (both diabetic and non-diabetic)
- Characterize specific risks associated with overuse of GLP-1 medications in individuals living in long-term care settings
- Identify methods for identifying and monitoring negative outcomes of GLP-1 medications in long-term care settings

The 4Ms (5Ms) of Care for Older Individuals



What Matters

Know and align care with each older adult's specific health outcome goals and care preferences including, but not limited to, end-of-life care, and across settings of care.

Medication

If medication is necessary, use Age-Friendly medication that does not interfere with What Matters to the older adult, Mobility, or Mentation across settings of care.

Mentation

Prevent, identify, treat, and manage dementia, depression, and delirium across settings of care.

Mobility

Ensure that older adults move safely every day in order to maintain function and do What Matters.

Multicomplexity

The whole older adult, living with multiple chronic conditions, advanced illness, and/or with complicated biopsychosocial needs.

Optimizing Diabetes Care for Elderly Individuals Living in Long-term Care Facilities

- Individualize treatment – balancing excessive vs. insufficient treatment
  - Excessive Treatment = increased risk of hypoglycemia
  - Insufficient Treatment = progression of complications & excess mortality
- Optimize outcomes through routine glucose monitoring and monthly medical follow-up, maintaining quality of life without over-medicalization of interventions
- Check capillary glucose values for unusual behaviors and adjust insulin doses using established criteria
- Implement training to detect hypoglycemia and adjusting therapies independently.

Vergely N. DiabetesJournal.ORG/Clinical. 2023 Volume 41(3), 339-350.

Treatment Options for T2DM

- Lifestyle Modifications: diet, exercise, weight management
- Medications:
  - Metformin
  - Sulfonylureas (glipizide, glimepiride, glyburide)
  - Thiazolidinediones (alogliptin, pioglitazone, rosiglitazone)
  - Incretin mimetics:
    - Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RAs) (dulaglutide, exenatide, liraglutide, lixisenatide, semaglutide)
    - Glucose-Dependent Insulinotropic Polypeptide(GIP)/GLP-1RA (tirzepatide)
  - Insulin
  - Other Medications: antihypertensives, lipid-lowering medications, others

Importance of Optimizing Diabetes Care for Individuals with Dementia

- Reduced cognition associated with tight glycemic control in elderly individuals with dementia
- Aggressive glucose-lowering therapies (insulin & sulfonylureas) linked to negative outcomes
- Increased dementia symptoms associated with low body mass index, increased ADL disability and number of fractures.
- Optimizing glycemic control and weight for individuals with diabetes in LTC important to maintaining cognitive and physical function

Hatano Y, Araki A, Matsumoto M. Geriatr Gerontol Int 2019;19:854-860.

Causes of Hospitalization Secondary to Hypoglycemia in Older LTC Residents

- 1 in 100 of 55,734 older Australians (median age 84 years) hospitalized for hypoglycemia and 1 in 200 for hyperglycemia during first year after entry into long-term care facility

Increased hypoglycemia risk:

- Increased level of care (2.5x)
- Renal disease (1.2x)
- Prior hospitalization with hypo- (2.2x) or hyperglycemia (1.6x)
- Insulin use (6x)
- Sulfonylurea use (1.4x)
- ACEI use (1.2x)

Increased hyperglycemia risk:

- English as second language (1.4x)
- Dementia (1.4x)
- Prior hospitalization with hypo- (2.5x) or hyperglycemia (3.9x)
- Insulin use (2x)
- Metformin use (1.4x)

Wondimkun YA, Caughey GE, Inacio MC, et al. Factors Associated with Hospitalization for Hypoglycemia and Hyperglycemia Among Older People in Long-Term Care Facilities. J Am Ger Soc 2025;73:2859-2867.

Managing T2DM in Older Individuals

- Nearly 1 in 3 older individuals may have diabetes mellitus and more than 10 medication classes are available for treatment of T2DM
- Base treatment goals on comorbid conditions, life expectancy, risk of complications, expected benefits of glycemic control
- Avoid treatment-related hypoglycemia (and especially severe hypoglycemia)
  - Especially in older patients and those with chronic renal insufficiency
- Insulin treatment often implemented for individuals with long duration of T2DM
- Combined use of GLP-1 receptor agonists with insulin
  - Reduced insulin requirements
  - Lower risk of hypoglycemia
  - Potential weight loss
  - Reduced cardiovascular risk

Triplitt CL. Managing Diabetes in Patients with Diabetes of Long Duration. Diabetes Educator 2012;38(4S):23-30.

Incretin Peptides 'Primer'

- Since 2023: "Explosion" of interest in incretin peptides for multiple effects
- Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) – key regulators of nutrient metabolism
  - Peptide mixtures and modifications developed to interact with multiple receptor sites
  - Examples: Semaglutide (GLP-1RA) and tirzepatide (GIPR/GLP-1RA co-agonist)
  - GLP-1 receptor antagonists – used to lower blood glucose in T2DM and reduce body weight in obesity
- Expanding focus of study & use in recent years
  - Metabolic (glucose modulation) and weight-lowering effects
  - Reducing risk of cardiovascular disease
  - Reducing risk of renal diseases
  - Other therapeutic relevance

Bailey CJ, Flatt PR, Conlon JM. Multifunctional incretin peptides in therapies for type 2 diabetes, obesity and associated comorbidities. Peptides 2025:187;171380.

Incretin Peptides 'Primer'

- Targeted therapies for T2DM

C.J. Bailey et al.

Table 1
Efficacy of currently available incretin-based peptide agents in phase 3 trials that assessed lowering of A1C and body weight.

Agent *(Brand)*	Trial name *n number* *Duration (wks)*	Route, timing Dose(s)	Efficacy in phase 3 randomised control trial*	
Type 2 diabetes			**Baseline** A1C %; BMI kg/m^2	**Efficacy*** ↓A1c%; ↓BW kg
Exenatide[a] *(Byetta)*	migo−1 *272, 30 wks*	SC, BD 5, 10 ug	A1C 8.2 BMI 34.2	↓ A1c 0.8 ↓ BW 2.8
Exenatide *(Bydureon)*	uration−1 *295, 30 wks*	SC, QW 2 mg	A1C 8.3 BMI 35	↓ A1c 1.9 ↓ BW 3.9
Lixisenatide[b] *(Lyxumia)*	etGoal−1 *484, 24 wks*	SC, OD 20 ug	A1C 8.1 BMI 32.1	↓ A1c 0.4 ↓ BW 1.1
Liraglutide[c] *(Victoza)*	ead−2 *1091, 26 wks*	SC, OD 0.6, 1.2, 1.8 mg	A1C 8.4 BMI 30.9	↓ A1c 1.1 ↓ BW 3.8
Dulaglutide *(Trulicity)*	ward−1 *976, 26 wks*	SC, QW 0.75, 1.5 mg	A1C 8.1 BMI 33	↓ A1c 1.0 ↓ BW 2.5
Semaglutide ** *(Ozempic)*	ustain−1 *388, 30 wks*	SC, QW 0.25, 0.5, 1, 2 mg	A1C 8.0 BMI 32.9	↓ A1c 1.5 ↓ BW 3.5
Semaglutide *(Rybelsus)*	ioneer−1 *703, 26 wks*	Oral, OD 3, 7, 14 mg	A1C 8.0 BMI 31.8	↓ A1c 1.1 ↓ BW 2.3
Tirzepatide *** *(Mounjaro)*	urpass−1 *478, 40 wks*	SC, QW 0.25, 0.5, 0.75, 10, 12.5. 15 mg	A1C 7.9 BMI 31.9	↓ A1c 2.3 ↓ BW 8.8

Bailey CJ, Flatt PR, Conlon JM. Multifunctional incret associated comorbidities. Peptides 2025:187;171380

Incretin Peptides 'Primer'

- Targeted therapies for managing obesity

C.J. Bailey et al.

Table 1
Efficacy of currently available incretin-based peptide agents in phase 3 trials that assessed lowering of A1C and body weight.

Agent *(Brand)*	Trial name *n number* *Duration (wks)*	Route, timing Dose(s)	Efficacy in phase 3 randomised control trial*	
Obesity				
			Baseline BW kg BMI kg/m^2	**Efficacy** ↓ BW kg (%)
Liragluride *(Saxenda)*	Scale−1 *n 3731, 56 wks*	SC, OD 3 mg	BW 106.2 BMI 38.3	↓ BW 5.6 (5.2 %)
Semaglutide *(Wegovy)*	Step−1 *N 1961, 68 wks*	SC, QW 2.4 mg	BW 105.4 BMI 37.8	↓ BW 12.7 (12.4 %)
Semaglutide *(Rybelsus)*	Oasis−1 *n 667, 68 wks*	Oral, OD 50 mg	BW 105.4 BMI 37.5	↓ BW 13.0 (12.7 %)
Tirzepatide *(Zepbound)*	Surmount−1 *n 2539, 72 wks*	SC, QW 5, 10, 15 mg	BW 105.6 BMI 38.1	↓ BW 21.2 (17.8 %)

Bailey CJ, Flatt PR, Conlon JM. Multifunctional incretin peptides in therapies for type 2 diabetes, obesity and associated comorbidities. Peptides 2025:187;171380.

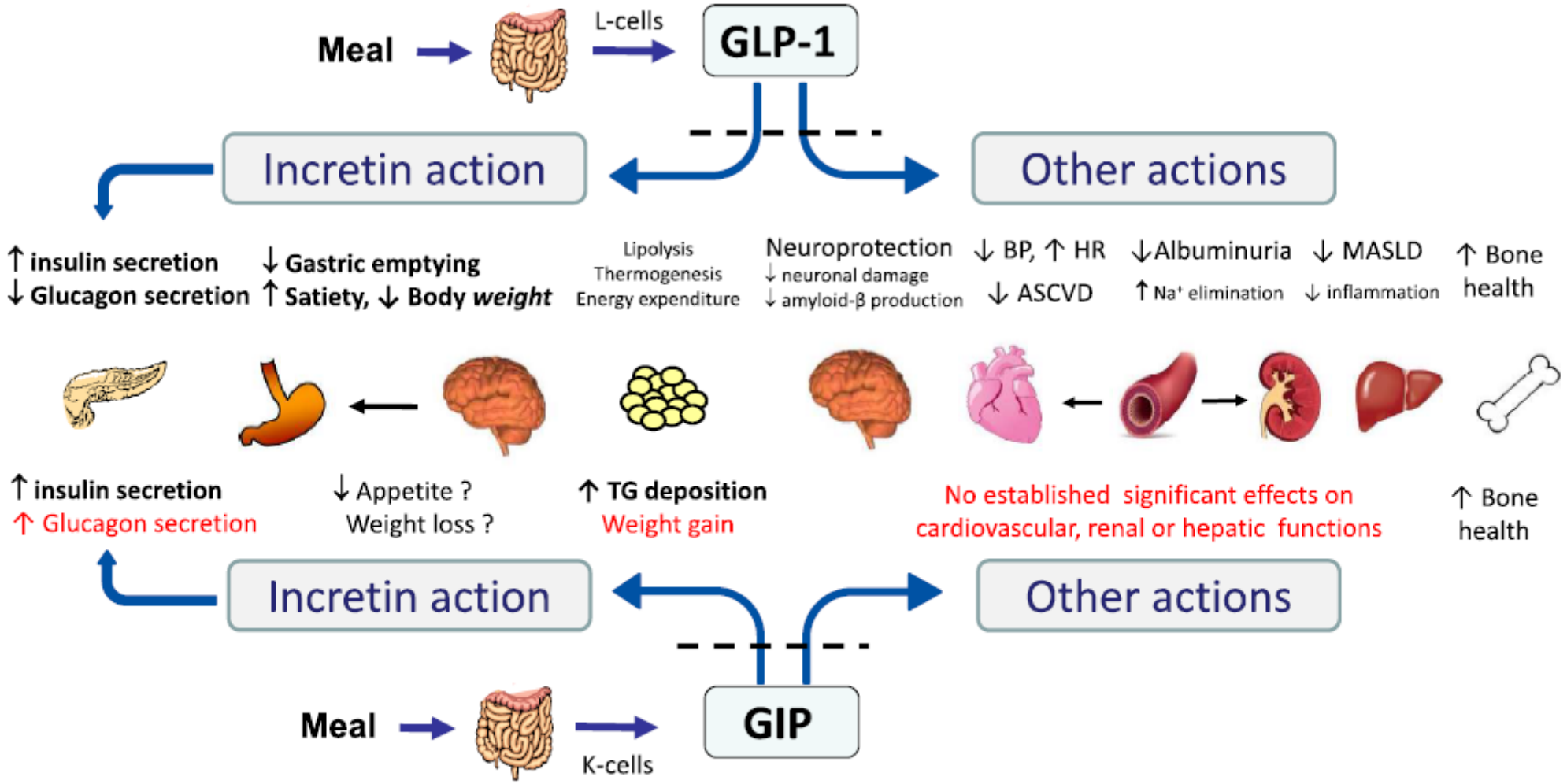


Fig. 1. An illustration of the diverse actions of glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) with therapeutic significance. ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; heart rate; MASLD, metabolic dysfunction-associated steatotic liver disease; TG, triglyceride. ↑, increase; ↓, decrease. The dashed line indicates that GLP-1 and GIP are susceptible to rapid degradation by the enzyme dipeptidyl peptidase-4.

Bailey CJ, Flatt PR, Conlon JM. Multifunctional incretin peptides in therapies for type 2 diabetes, obesity and associated comorbidities. Peptides 2025:187;171380.

Managing Obesity in Older Adults

- Obesity prevalence in older individuals increasing (~20% and rising)
- Complications of obesity include increased risk of T2DM, liver and CV disease and malignancy with added risks in older individuals including functional decline, worsening cognition, and lowered quality of life
- Complications of unintended weight loss in older individuals includes reduced skeletal muscle and bone mass (vs. the 'obesity paradox')
- Lifestyle interventions remain cornerstone of management (resistance training to maintain muscle strength and bone mineral density)
- Add pharmacotherapy (AOMs) when refractory to lifestyle interventions:
  - GLP-1RAs (liraglutide, Semaglutide, tirzepatide) currently primary focus

Henney AE, Wilding JPH, Alam U, Cuthbertson DJ. Obesity pharmacotherapy in older adults: a narrative review of evidence. Int J Obesity 2025;49:369-380.

Managing Obesity in Older Adults

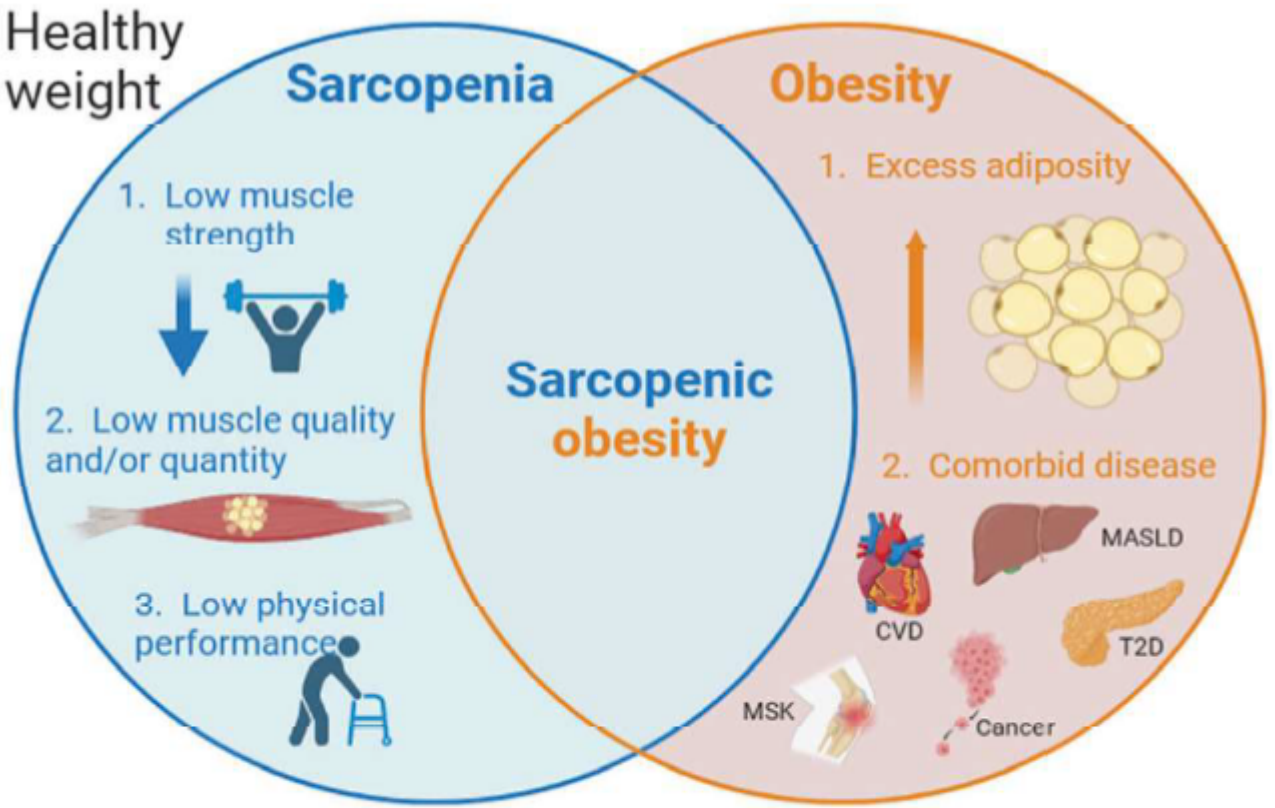


Fig. 1 Venn diagram exploring the four body composite phenotypes in older adults (including healthy weight). The triad of sarcopenia, as defined by The European Working Group on Sarcopenia in Older People (EWGSOP), is illustrated [35]. Co-morbid complications related to obesity include, but are not limited to, cardiovascular disease (CVD), metabolic dysfunction associated steatotic liver disease (MASLD), type 2 diabetes (T2D), hormone-dependant cancers, and musculoskeletal (MSK) issues such as osteoarthritis.

Henney AE, Wilding JPH, Alam U, Cuthbertson DJ.Obesity pharmacotherapy in older adults: a narrative review of evidence.
Int J Obesity 2025;49:369-380.

Oral Semaglutide for Type 2 Diabetes

- Mean HbA1c and weight significantly decreased over 6 months in 101 elderly patients (mean age almost 75 years old)
- Number achieving target HbA1c (≤7%) increased from 36.6% to 61.7%
- 9.6% achieved ≥1% reduction in HbA1C and ≥5% reduction in weight
- Average weight loss of 3.1 kg (nearly 7 lbs)
- Significant reductions in BMI, waist circumference, total cholesterol and LDL , and systolic BP
- Approximately 10% of patients noted ADRs with 7% discontinuing therapy

Fiore V, Carbotta G, Barraco S, et. al. Real-world retrospective study in elderly patients aged 65 years and older with type 2 diabetes mellitus treated with daily oral Semaglutide (SEMA-elderly). Diabetes Obes Metab. 2025;27:1805-1814.

Safety and Efficacy of Semaglutide in Elderly Individuals

- Pooled safety and efficacy in younger (n=3045) vs. older (n=854) study participants receiving weekly SQ semaglutide compared to placebo, sitagliptin, exenatide or insulin
- Mean HbA1c decreased by approximately 1.2 to 1.9% in both younger and older semaglutide participants
- Mean body weight reductions similar in both age groups
- Similar efficacy and safety profile in both younger and older participants

Warren M, Chaykin L, Trachtenbarg D, et al. Semaglutide as a therapeutic option for elderly patients with type 2 diabetes: Pooled analysis of the SUSTAIN 1-5 trials. Diabetes Obes Metab. 2018;20:2291-2297.

Safety and Efficacy of Semaglutide in Elderly Individuals ≥75 Years Old

- Safety and efficacy in younger (<60, n=549) vs old (60 to 74, n=932) and older (≥75, n=341) study participants receiving oral semaglutide
- Oral semaglutide use significantly reduced rate of use of sulfonylurea medications and use of both rapid and basal insulin
- HbA1c reduced in all participants by almost 0.9% and body weight by 2.78kg (about 6lbs) at 6 months and 3.89 kg (8.6 lbs) at 12 months
- Similar reductions in older population:
  - HbA1C reduced by >0.5%
  - Body weight reduced by 1.6kg (3.5 lbs) at 6 months and 2.7kg (6 lbs) at 12 months
- Significant improvements in CV outcomes (SBP, DBP, Lipids)

Baronti W, Lencioni C, Occhipinti M, et al. Real-world effectiveness of oral semaglutide: Focus on patients with type2 diabetes older than 75 years. Diabetes Res Clin Prac. 2024;218:111928.

Semaglutide and Accelerated Sarcopenia

- Retrospective study comparing outcomes of semaglutide use in 220 elderly patients with T2DM and 212 matched controls
- Sarcopenia prevalence in more that 1 in 4 participants (27.7%)
- Significant BMI and muscle mass reduction in semaglutide-treated participants
- Reduced gait speed and grip strength in semaglutide group
- Predictors of muscle loss included semaglutide dosage, baseline ASMI and gait speed.

Ren Q, Zhi L, Liu H. Semaglutide Therapy and Accelerated Sarcopenia in Older Adults with Type 2 Diabetes: A 24-Month Retrospective Cohort Study. Drug Design, Development and Therapy 2025;19:5645-5652.

Risk of Weight Loss with Semaglutide Treatment in Elderly Individuals with Type II Diabetes

- Pooled analyses from published semaglutide studies (approximately 22% were elderly) suggest weight loss risk is dose dependent
  - Significant wt loss (>5%) seen more commonly with semaglutide vs. sitagliptin
  - Results suggest (but don't prove) increased risk of weight loss in older individuals
- Unintended weight loss in elderly individuals treated with GLP-1 inhibitors carries concern for increased mortality, reduced ADLs, poorer quality of life, higher rates of hospital admission, and increased risk of hip fractures
- Wt loss of > 4 to 5% within 1 year increases morbidity and mortality
- Mortality increases from 9% to 38% within 1 to 2.5 years following significant weight loss.
- This retrospective study in elderly and nonelderly VA patients residing in North Texas reported no difference in weight loss risk between younger and older patients.
- Weight loss increased with length of therapy

Huynh G, Runeberg H, Weideman R. Evaluating Weight Loss With Semaglutide in Elderly Patients With Type II Diabetes. J Pharm Tech 2023;39(1):10-15.

Summary and Recommendations for Semaglutide Use in Long-Term Care

- Semaglutide use generally produces HbA1C reductions with added benefits of improved CV outcomes (reduced BP and Lipids)
- Shifting from ‘traditional’ hypoglycemic therapies (insulin & sulfonylureas) may reduce rates of significant hypoglycemia (and hospitalization)
- Modest yet significant weight loss and improved BMI may improve mobility and reduce debility
- Must differentiate between intended and unintended weight loss
- Concerns of increased sarcopenia in older and more frail individuals may preclude use in some
- Use may be precluded by ‘gate keepers’ (insurance plans and PBMs)