Virtual Provider Course Reference Guide

Course Overview

Virtual Provider Course: 20 CME hours across 3 days
Training Manual: Science-Based Clinical Evaluation and Treatment of Diabesity
Structure: 10 Sessions corresponding to 10 Sections

Sponsored by the Diabesity Institute

DAY 1: FOUNDATIONS

SESSION 1: Reframing the Issue

Corresponds to: Section 1 - Developing Awareness of Metabolic Function and Dysfunction
Time: 8:00 - 10:00 AM (2.0 CME credits)

Key Topics Covered:

- Past and present concepts in obesity treatment
- Why metabolic system is underemphasized
- Evidence base for understanding obesity as a metabolic disorder
- Historical perspective on calorie restriction

Most Pertinent References:

1. 1. **Friedman J.** (2012). Leading the charge in leptin research: an interview with Jeffrey Friedman. Dis Model Mech. 5(5):576-579.
   Relevance: Discovery of leptin - fundamental to understanding metabolic feedback loop
2. 2. **Sumithran P, Prendergast LA, Delbridge E, et al.** (2011). Long-term persistence of hormonal adaptations to weight loss. N Engl J Med. 365:1597-1604.
   Relevance: Critical evidence showing hormonal adaptations persist long after calorie restriction ends
3. 3. **Bowers CY.** (2012). History to the discovery of ghrelin. Methods Enzymol. 514:3-32.
   Relevance: Understanding orexigenic signals that drive hunger
4. 4. **Müller TD, Finan B, Clemmensen C, et al.** (2017). The new biology and pharmacology of glucagon. Physiol Rev. 97:721–766.
   Relevance: Modern understanding of metabolic hormones and therapeutic targets
5. 5. **Kumar N, Puri N, Marotta F, et al.** (2017). Diabesity: an epidemic with its causes, prevention and control with special focus on dietary regime. Functional Foods in Health and Disease 2017; 7(1):1-16.
   Relevance: Comprehensive overview of the diabesity epidemic

SESSION 2: Diabesity: Medical, Surgical, and Combined Approaches

Corresponds to: Section 2 - Importance of Individualized Decision-Making
Time: 10:30 AM - 12:30 PM (2.0 CME credits)

Key Topics Covered:

- Evidence base for surgical vs. pharmacological treatment
- Types of bariatric surgery
- Post-surgical pharmacological care
- Treatment duration and metabolic rehabilitation

Most Pertinent References:

6. 1. **Bray GA, Frühbeck G, Ryan DH, Wilding JPH.** (2016). Management of obesity. Lancet. 387(10031):1947-1956.
   Relevance: Comprehensive overview of obesity management approaches
7. 2. **Yumuk V, Tsigos C, Fried M, et al.** (2015). European guidelines for obesity management in adults. Obes Facts. 8:402–424.
   Relevance: Guidelines for surgical intervention criteria
8. 3. **van Beek AP, Emous M, Laville M, et al.** (2017). Dumping syndrome after esophageal, gastric or bariatric surgery: pathophysiology, diagnosis, and management. Obes Rev. 18(1):68–85.
   Relevance: Understanding post-surgical complications and management
9. 4. **US Food and Drug Administration.** Safety Alerts for Human Medical Products. Liquid-filled intragastric balloon systems: letter to healthcare providers - potential risks.
   Relevance: Safety considerations for endoscopic devices
10. 5. **Westergaard H.** (2007). Bile acid malabsorption. Curr Treat Options Gastroenterol. 10(1):28-33.
    Relevance: Post-operative metabolic concerns

SESSION 3: The Metabolic Feedback Loop

Corresponds to: Section 3 - Systemic and Central Influence / Importance of Neuroendocrine Autoregulation
Time: 1:30 - 3:30 PM (2.0 CME credits)

Key Topics Covered:

- Peripheral and central metabolic pathways
- Adipose as endocrine organ
- Gut-brain signaling
- Neuroendocrine autoregulation
- Genetic vulnerability

Most Pertinent References:

11. 1. **Myers MG, Heymsfield SB, Haft C, et al.** (2012). Defining clinical leptin resistance - challenges and opportunities. Cell Metab. 15(2):150–156.
    Relevance: Central to understanding metabolic dysfunction
12. 2. **Toni R.** (2004). The neuroendocrine system: organization and homeostatic role. J Endocrinol Invest. 27(6 Suppl):35-47.
    Relevance: Foundational understanding of neuroendocrine signaling
13. 3. **Hayes MR.** (2014). Brain-gut-periphery axis integration: GLP-1 receptor signaling. Trends Endocrinol Metab.
    Relevance: Understanding peripheral-central signaling mechanisms

14. 4. **Bastard JP, Maachi M, Lagathu C, et al.** (2006). Recent advances in the relationship between obesity, inflammation, and insulin resistance. Eur Cytokine Netw. 17(1):4-12.
Relevance: Adipose tissue as active endocrine organ
15. 5. **Farooqi IS, O'Rahilly S.** (2008). Mutations in ligands and receptors of the leptin-melanocortin pathway that lead to obesity. Nat Clin Pract Endocrinol Metab. 4(10):569-577.
Relevance: Genetic vulnerabilities in metabolic pathways
16. 6. **Drucker DJ, Habener JF, Holst JJ.** (2017). Discovery, characterization, and clinical development of the glucagon-like peptides. J Clin Invest. 127(12):4217-4227.
Relevance: GLP-1 pathway - critical for understanding incretin-based therapies
17. 7. **Trayhurn P, Bing C.** (2006). Appetite and energy balance signals from adipocytes. Phil. Trans. R. Soc. B 361(1471):1237-1249.
Relevance: Adipokine signaling in metabolic regulation

DAY 2: ASSESSMENT & DIAGNOSIS

SESSION 4: Anthropometrics and Metabolic Testing

Corresponds to: Section 4 - Comprehensive Assessment Beyond Traditional Metrics
Time: 8:00 - 10:00 AM (2.0 CME credits)

Key Topics Covered:

- Body composition testing methods
- Lean mass deficits/excesses
- Contributors to metabolic expenditure
- Body-fat percentage guidelines
- Measuring body-fat composition and distribution

Most Pertinent References:

18. 1. **Heyward VH.** (2014). Advanced Fitness Assessment and Exercise Prescription.
    Relevance: Standards for body composition assessment
19. 2. **McArdle WD, Katch FI, Katch VL.** (2009). Exercise Physiology: Nutrition, Energy, and Human Performance.
    Relevance: Frame size and anthropometric standards
20. 3. **CDC.** (2010). Mean percentage body fat by age, sex, and ethnicity.
    Relevance: Population norms for body composition
21. 4. **Spalding KL, Arner E, Westermark PO, et al.** (2008). Dynamics of fat cell turnover in humans. Nature. 453(7196):783-787.
    Relevance: Understanding adipose tissue dynamics
22. 5. **McLaughlin T, Lamendola C, Liu A, et al.** (2011). Preferential fat deposition in subcutaneous versus visceral depots is associated with insulin sensitivity. J Clin Endocrinol Metab. 96(11):E1756–E1760.
    Relevance: Fat distribution and metabolic health
23. 6. **Westerterp KR.** (2004). Diet induced thermogenesis. Nutr Metab (Lond). 1(1):5.
    Relevance: Understanding metabolic expenditure components
24. 7. **Cichosz SL, Rasmussen NH, Vestergaard P, Hejlesen O.** (2021). Precise Prediction of Total Body Lean and Fat Mass From Anthropometric and Demographic Data: Development and Validation of Neural Network Models. J Diabetes Sci Technol. 15(5):1154-1162.
    Relevance: Limitations of predicted lean mass equations in obesity - "In obese participants, the prediction of FM was considerably reduced; this might be due to an increased interpersonal variation of fat distribution and difficulties in the accuracy of obtaining anthropometric measurements in obese people"

SESSION 5: Modern Approach to Diagnosis in Metabolic Dysfunction

Corresponds to: Section 5 - Advanced Diagnostic Frameworks for Personalized Treatment
Time: 10:30 AM - 12:30 PM (2.0 CME credits)

Key Topics Covered:

- TOFI phenotype
- Advanced lipid testing
- Inflammatory markers
- Thyroid, sex hormone, and cortisol assessment
- Nutrient deficiencies in metabolic syndrome

Most Pertinent References:

25. 1. **Després JP.** (2012). Body fat distribution and risk of cardiovascular disease: an update. Circulation. 126(10):1301-1313.
    Relevance: TOFI phenotype and metabolic risk
26. 2. **Marques-Vidal P, Pécoud A, Hayoz D, et al.** (2010). Normal weight obesity: relationship with lipids, glycaemic status, liver enzymes and inflammation. Nutr Metab Cardiovasc Dis. 20(9):669-75.
    Relevance: Metabolically unhealthy normal weight individuals
27. 3. **Mora S, Wenger NK, Cook NR, et al.** (2019). Evaluation of high-density lipoprotein particle number and size by nuclear magnetic resonance for cardiovascular risk assessment. JAMA Cardiol. 4(4):325-332.
    Relevance: Advanced lipid testing
28. 4. **Ridker PM, Everett BM, Thuren T, et al.** (2017). Antiinflammatory therapy with canakinumab for atherosclerotic disease. N Engl J Med. 377(12):1119-1131.
    Relevance: Inflammation and cardiovascular risk
29. 5. **Santini F, Marzullo P, Rotondi M, et al.** (2014). Mechanisms in endocrinology: the crosstalk between thyroid gland and adipose tissue. Eur J Endocrinol. 171(4):R137-152.
    Relevance: Thyroid-metabolism interaction

SESSION 6: Pharmacological Strategies for Metabolic Dysfunction

Corresponds to: Section 6 - Pharmacological Interventions and Treatment Algorithms
Time: 1:30 - 3:30 PM (2.0 CME credits)

Key Topics Covered:

- GLP-1 receptor agonists
- Dual and triple agonists
- Amylin analogs
- Combination therapy rationale
- Treatment algorithms
- Contraindications and side effect management

Most Pertinent References:

30. 1. **Drucker DJ, Habener JF, Holst JJ.** (2017). Discovery, characterization, and clinical development of the glucagon-like peptides. J Clin Invest. 127(12):4217-4227.
    Relevance: GLP-1 pathway fundamentals

31. 2. **Wilding JPH, Batterham RL, Calanna S, et al.** (2021). Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med. 384:989-1002.
Relevance: Clinical efficacy of GLP-1 receptor agonists
32. 3. **Jastreboff AM, Aronne LJ, Ahmad NN, et al.** (2022). Tirzepatide once weekly for the treatment of obesity. N Engl J Med. 387(3):205-216.
Relevance: Dual agonist clinical data
33. 4. **Garvey WT, Batterham RL, Bhatta M, et al.** (2022). Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial. Nat Med. 28:2083-2091.
Relevance: Long-term efficacy and safety
34. 5. **Tschöp MH, Finan B, Clemmensen C, et al.** (2016). Unimolecular polypharmacy for treatment of diabetes and obesity. Cell Metab. 24(1):51-62.
Relevance: Multi-agonist therapy rationale

DAY 3: INTEGRATION & APPLICATION

SESSION 7: Nutritional Strategies for Metabolic Health

Corresponds to: Section 7 - Evidence-Based Nutritional Interventions
Time: 8:00 - 10:00 AM (2.0 CME credits)

Key Topics Covered:

- Metabolic flexibility
- Meal timing and frequency
- Macronutrient distribution
- Low-carb vs. calorie restriction
- Fasting strategies
- Protein requirements

Most Pertinent References:

35. 1. **Goodpaster BH, Sparks LM.** (2017). Metabolic flexibility in health and disease. Cell Metab. 25(5):1027-1036.
    Relevance: Metabolic flexibility framework
36. 2. **Hall KD, Guo J.** (2017). Obesity energetics: body weight regulation and the effects of diet composition. Gastroenterology. 152(7):1718-1727.
    Relevance: Energy balance and diet composition
37. 3. **Gardner CD, Trepanowski JF, Del Gobbo LC, et al.** (2018). Effect of low-fat vs low-carbohydrate diet on 12-month weight loss. JAMA. 319(7):667-679.
    Relevance: Diet composition comparison
38. 4. **de Cabo R, Mattson MP.** (2019). Effects of intermittent fasting on health, aging, and disease. N Engl J Med. 381(26):2541-2551.
    Relevance: Intermittent fasting evidence
39. 5. **Phillips SM, Chevalier S, Leidy HJ.** (2016). Protein "requirements" beyond the RDA: implications for optimizing health. Appl Physiol Nutr Metab. 41(5):565-572.
    Relevance: Protein optimization

SESSION 8: Laboratory Testing and Metabolic Assessment

Corresponds to: Section 8 - Comprehensive Laboratory Evaluation
Time: 10:30 AM - 12:30 PM (2.0 CME credits)

Key Topics Covered:

- Comprehensive metabolic panel interpretation
- Continuous glucose monitoring
- HbA1c limitations
- Insulin testing
- HOMA-IR calculations
- Advanced metabolic markers

Most Pertinent References:

40. 1. **American Diabetes Association.** (2022). Standards of medical care in diabetes-2022. Diabetes Care. 45(Suppl 1):S1-S264.
    Relevance: Current diagnostic criteria
41. 2. **Battelino T, Danne T, Bergenstal RM, et al.** (2019). Clinical targets for continuous glucose monitoring data interpretation. Diabetes Care. 42(8):1593-1603.
    Relevance: CGM data interpretation guidelines
42. 3. **Nathan DM, Kuenen J, Borg R, et al.** (2008). Translating the A1C assay into estimated average glucose values. Diabetes Care. 31(8):1473-1478.
    Relevance: HbA1c interpretation
43. 4. **Wallace TM, Levy JC, Matthews DR.** (2004). Use and abuse of HOMA modeling. Diabetes Care. 27(6):1487-1495.
    Relevance: HOMA-IR utility and limitations
44. 5. **Beck RW, Bergenstal RM, Cheng P, et al.** (2019). The relationships between time in range, hyperglycemia metrics, and HbA1c. J Diabetes Sci Technol. 13(4):614-626.
    Relevance: Time in range vs HbA1c

SESSION 9: Interventions Beyond Diet and Exercise

Corresponds to: Section 9 - Lifestyle Factors and Environmental Influences
Time: Afternoon session (2.0 CME credits)

Key Topics Covered:

- Sleep optimization
- Stress management
- Environmental toxins
- Physical activity beyond exercise
- Circadian rhythm optimization

Most Pertinent References:

Sleep and Circadian Rhythm:

45. 1. **Spiegel K, Leproult R, Van Cauter E.** (1999). Impact of sleep debt on metabolic and endocrine function. Lancet. 354(9188):1435-1439.
    Relevance: Foundational sleep-metabolism research
46. 2. **Tasali E, Chapotot F, Wroblewski K, et al.** (2014). The effects of extended bedtimes on sleep duration and food desire in overweight young adults. Appetite. 80:220-224.
    Relevance: Sleep extension benefits
47. 3. **Depner CM, Stothard ER, Wright KP Jr.** (2014). Metabolic consequences of sleep and circadian disorders. Curr Diab Rep. 14(7):507.
    Relevance: Sleep architecture and metabolic risk
48. 4. **Knutson KL, Van Cauter E.** (2008). Associations between sleep loss and increased risk of obesity and diabetes. Ann N Y Acad Sci. 1129:287-304.
    Relevance: Sleep duration recommendations

Stress Management:

49. 5. **Sinha R, Jastreboff AM.** (2013). Stress as a common risk factor for obesity and addiction. Biol Psychiatry. 73(9):827-835.
    Relevance: Stress-metabolism interface
50. 6. **Goyal M, Singh S, Sibinga EM, et al.** (2014). Meditation programs for psychological stress and well-being: a systematic review and meta-analysis. JAMA Intern Med. 174(3):357-368.
    Relevance: Evidence-based stress interventions
51. 7. **Kim HG, Cheon EJ, Bai DS, Lee YH, Koo BH.** (2018). Stress and heart rate variability: a meta-analysis and review of the literature. Psychiatry Investig. 15(3):235-245.
    Relevance: Stress monitoring technology

Environmental Factors:

52. 8. **Grün F, Blumberg B.** (2009). Endocrine disrupters as obesogens. Mol Cell Endocrinol. 304(1-2):19-29.
    Relevance: Environmental obesogens
53. 9. **Baillie-Hamilton PF.** (2002). Chemical toxins: a hypothesis to explain the global obesity epidemic. J Altern Complement Med. 8(2):185-192.
    Relevance: Environmental modifications

Physical Activity:

54. 10. **Fletcher GF, Ades PA, Kligfield P, et al.** (2013). Exercise standards for testing and training: a scientific statement from the American Heart Association. Circulation. 128(8):873-934.
    Relevance: Exercise guidelines
55. 11. **Loucks AB, Thuma JR.** (2003). Luteinizing hormone pulsatility is disrupted at a threshold of energy availability in regularly menstruating women. J Clin Endocrinol Metab. 88(1):297-311.
    Relevance: Under-fueled exercise risks

SESSION 10: Neuroendocrine Integration and Clinical Management Strategies

Corresponds to: Section 10 - Advanced Clinical Applications and Long-term Management
Time: Afternoon session (2.0 CME credits)

Key Topics Covered:

- Hypothalamic-pituitary axis integration
- Clinical management strategies for common dysfunctions
- Post-prandial hypoglycemia management
- Genetic testing applications
- Pharmacological safety monitoring
- Long-term management protocols

Most Pertinent References:

56. 1. **Myers MG, Heymsfield SB, Haft C, et al.** (2012). Defining clinical leptin resistance - challenges and opportunities. Cell Metab. 15(2):150–156.
    Relevance: Leptin signaling dysfunction
57. 2. **Farooqi IS, O'Rahilly S.** (2008). Mutations in ligands and receptors of the leptin-melanocortin pathway that lead to obesity. Nat Clin Pract Endocrinol Metab. 4(10):569-577.
    Relevance: Genetic testing applications
58. 3. **Stanikova D, Surova M, Buzga M, et al.** (2015). Age of obesity onset in MC4R mutation carriers. Endocr Regul. 49(3):137-40.
    Relevance: MC4R mutations and clinical implications
59. 4. **Feuillan PP, Ng D, Han JC, et al.** (2011). Patients with Bardet-Biedl Syndrome have hyperleptinemia suggestive of leptin resistance. J Clin Endocrinol Metab. 96(3):E528–E535.
    Relevance: Syndromic obesity management
60. 5. **Trevaskis JL, Parkes DG, Roth JD.** (2010). Insights into amylin-leptin synergy. Trends Endocrinol Metab. 21(8):473-9.
    Relevance: Multi-modal treatment integration
61. 6. **Sandovala D, Sisley SR.** (2015). Brain GLP-1 and insulin sensitivity. Mol Cell Endocrinol. 418(Pt 1):27–32.
    Relevance: Central pathway integration
62. 7. **Varela L and Horvath TL.** (2012). Leptin and insulin pathways in POMC and AgRP neurons that modulate energy balance and glucose homeostasis. EMBO Rep. 13(12):1079-1086.
    Relevance: Hypothalamic integration mechanisms

Key Cross-Cutting References

These references are fundamental across multiple sessions:

Metabolic Feedback Loop (Sessions 1, 3, 6, 10):

Myers MG, Heymsfield SB, Haft C, et al. (2012). Defining clinical leptin resistance. Cell Metab. 15(2):150–156.

Hayes MR. (2014). Brain-gut-periphery axis integration: GLP-1 receptor signaling.

Hormonal Regulation (Sessions 3, 6, 7, 9):

Holst JJ. (2007). The physiology of glucagon-like peptide 1. Physiol Rev. 87(4):1409-1439.

Kojima M. (2010). Discovery of ghrelin and its physiological function. J Med Sci. 3(2):92-95.

Clinical Assessment (Sessions 4, 5, 8):

American Diabetes Association. (2022). Standards of medical care in diabetes-2022.

Battelino T, Danne T, Bergenstal RM, et al. (2019). CGM data interpretation guidelines.

Lifestyle Interventions (Sessions 7, 9):

Goodpaster BH, Sparks LM. (2017). Metabolic flexibility in health and disease. Cell Metab. 25(5):1027-1036.

Spiegel K, Leproult R, Van Cauter E. (1999). Impact of sleep debt on metabolic and endocrine function.

Metabolic Adaptation (Sessions 1, 3, 6, 7):

Fothergill E, Guo J, Howard L, et al. (2016). Persistent metabolic adaptation 6 years after "The Biggest Loser" competition. Obesity. 24(8):1612-1619.

Relevance: RMR remained ~500 kcal/d lower than expected 6 years post-weight loss, demonstrating long-term metabolic adaptation

Martins C, Roekenes J, Salamati S, et al. (2021). Metabolic adaptation is associated with less weight and fat mass loss in response to low-energy diets. Nutr Metab. 18:60.

Relevance: Individual variation in metabolic adaptation ranges from -337 to +352 kcal/day, significantly impacting weight loss outcomes

Additional Resources

Historical Timeline References

The training manual includes comprehensive timelines showing the evolution of metabolic science from:

- 1700s: Calorimetry invention
- 1921: Insulin discovery
- 1994: Leptin identification
- 1999: Ghrelin isolation
- 2016-2017: Multi-agonist clinical trials

Emerging Therapies to Monitor

1. Cagrisema (Amylin/GLP-1 Co-Agonist)
2. Retatrutide (GLP-1/GIP/Glucagon Tri-Agonist)
3. Survodutide (GLP-1/Glucagon Dual Agonist)
4. Maritide (GIP antagonist)
5. Bremelanotide-GLP1 (dual Mc4R-GLP agonist)

Additional References Related to Q&A Session Discussion

These references address specific questions and topics raised during course Q&A sessions:

GLP-1 Receptor Agonists and Body Composition

Jeromson S, Baranowski BJ, Waters BD, et al. (2025). Semaglutide impacts skeletal muscle to a similar extent as caloric restriction in mice with diet-induced obesity. J Physiol. 603(10):2123-2145.

Relevance: Pair-feeding study demonstrating that semaglutide-induced lean mass loss largely reflects caloric restriction rather than a unique pharmacological effect; weight loss was greater with semaglutide than caloric restriction despite matched energy intake

Pediatric ADHD Medication and Potential Future Metabolic Effects

Schwartz BS, Bailey-Davis L, Bandeen-Roche K, et al. (2014). Attention Deficit Disorder, Stimulant Use, and Childhood Body Mass Index Trajectory. Pediatrics. 133(4):668-676.

Relevance: Large longitudinal study showing initial BMI growth suppression with stimulant medications followed by rebound

Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC3966507/

Hasanpour Asli S, Shoar Y, Eslamdoust-Siahestalkhi F, et al. (2024). Body Mass Index Changes in Children and Adolescents Treated with Methylphenidate for Attention Deficit Hyperactivity Disorder. Iranian Journal of Child Neurology. 18(2):67-76.

Relevance: Demonstrates increased BMI with longer duration of methylphenidate treatment in pediatric populations

Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC11015723/