

HOSTED BY



EFMS



7th EMIRATES FAMILY MEDICINE SOCIETY CONGRESS 2024

DUBAI | UAE | 22 to 24 APRIL

DUBAI WORLD TRADE CENTRE



Organized by

WirediV



Learning Objectives

In the pediatric population:

1. Implement an evidence-based screening strategy for prediabetes and diabetes
2. Review therapies to halt the progression from prediabetes to diabetes in the pediatric population
3. Review treatment strategies for Type 2 Diabetes in the pediatric population up to age 18 yo





Pediatric Diabetes





Worldwide incidence of Obesity: Selected countries, 2019-2022, Lancet

1	American Samoa	70.29	119	Italy	17.97
10	United States	41.64	131	South Africa	14.50
17	Saudi Arabia	38.13	132	Morocco	13.79
32	Bahrain	32.91	149	China	8.94
33	Egypt	32.48	161	Japan	7.63
48	United Arab Emirates	29.02	180	India	5.38
60	Turkey	26.22	200	Ethiopia	1.10
80	Germany	23.08			

Source: <https://data.worldobesity.org/rankings/>
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(23\)02750-2/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(23)02750-2/fulltext)





Epidemiology of Type 2 DM in children

- The incidence is increasing worldwide
- Directly related to an increase in obesity/overweight
- In the US:
 - 2002-2003: 9 cases/100,000
 - 2014-2015: 13.8 cases/100,000 (0.0138%)
- Similar data from Japan, Thailand, Argentina, and other countries
- Prediabetes – incidence in the US = 18% (1300x more common than DM)





Epidemiology and ethnicity of T2DM

- US data:
 - Non-Hispanic White youth – 4.5/100,000
 - Asian/Pacific Islander youth – 11.9/100,000
 - Hispanic youth – 20.9/100,000
 - Native American youth – 32.8/100,000
 - Non-Hispanic Black youth – 37.8/100,000
- Ethnicity and culture matters
- In UAE, diversity of people groups
 - Ride the Metro
 - “Beauty in the blend”





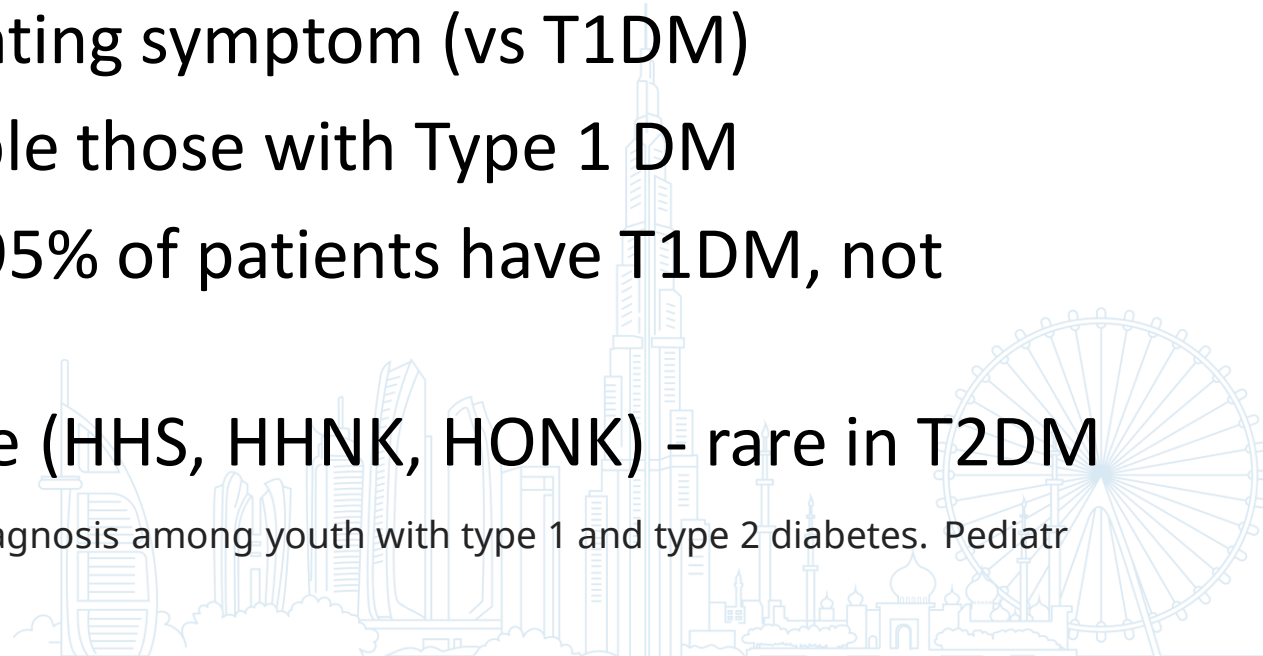
Risk factors for pediatric T2DM

- Obesity
 - US data – **80% of youth with T2DM** were obese
 - Additional 10% were overweight
- Genetic susceptibility
 - Purported to be polygenic
 - With monozygotic twins, 90% concordance with one twin having T2DM
 - In youth with T2DM, 50-75% have at least one affected parent
- Many pediatric patients present with T2DM with the onset of puberty.
 - Increased activity of growth hormone → decreased insulin sensitivity
- TODAY trial: 40% cases aged 10-14; 60% aged 15-19 yo



Clinical presentation

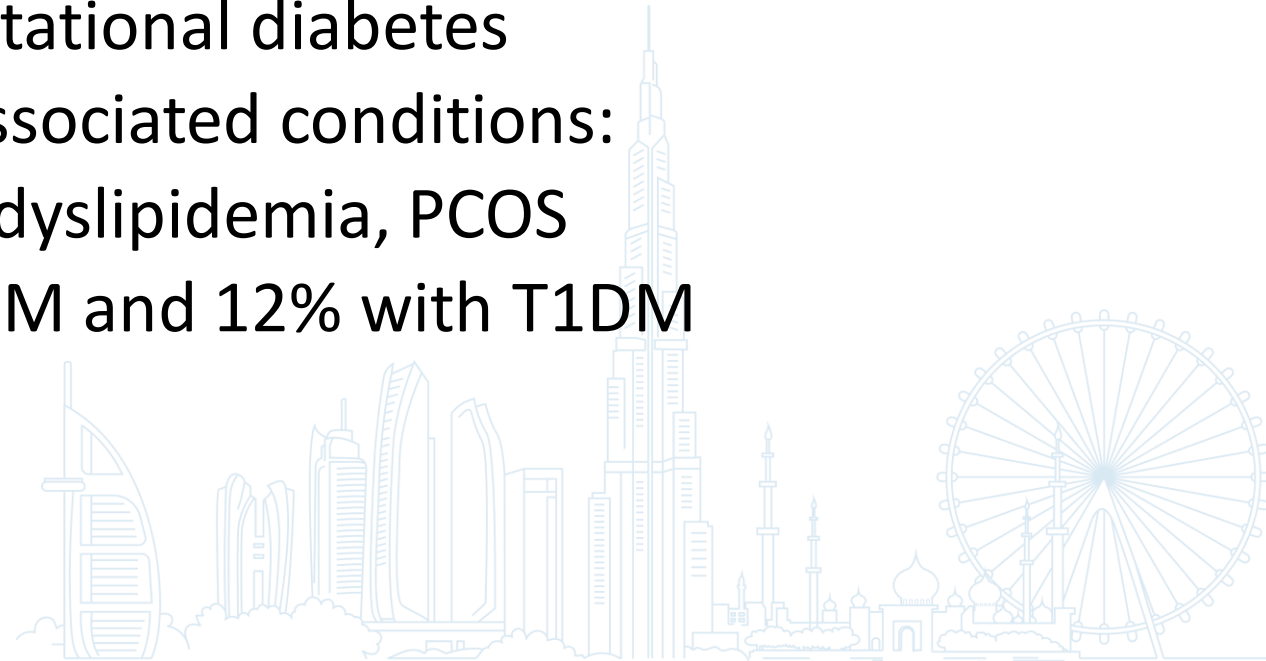
- Asymptomatic – 40%
- Symptoms due to hyperglycemia – 60%
 - Polyuria
 - Polydipsia
 - Nocturia
- Weight loss not a common presenting symptom (vs T1DM)
- Symptomatic patients can resemble those with Type 1 DM
- In patients presenting with DKA, 95% of patients have T1DM, not T2DM
- Hyperosmolar hyperglycemic state (HHS, HHNK, HONK) - rare in T2DM





Initial screening for T2DM

- Overweight or obese (BMI \geq 85th %-ile), **AND**
- One or more of the following:
 - T2DM in a 1st/2nd degree relative
 - Member of a high-risk ethnic group
 - Hx of maternal diabetes or gestational diabetes
 - Signs of insulin resistance or associated conditions:
 - Acanthosis nigricans, HTN, dyslipidemia, PCOS
 - US: 50-90% youth with T2DM and 12% with T1DM
 - Use of antipsychotic drugs





Acanthosis Nigricans

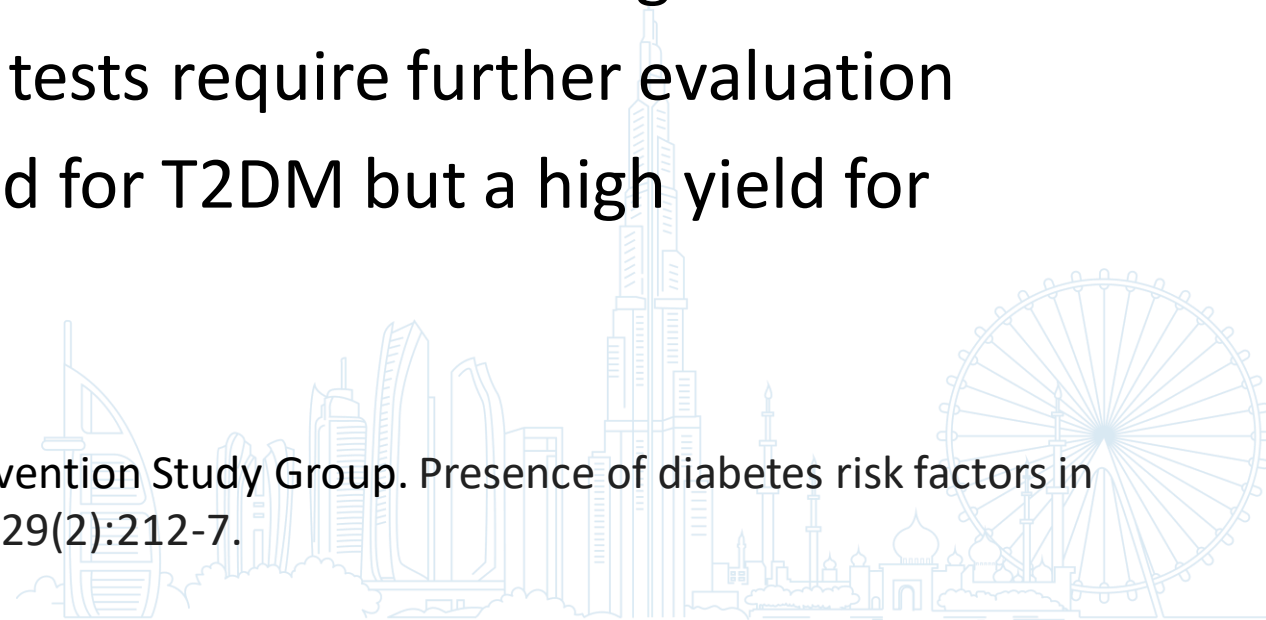




Timing of screening

- Start screening at the onset of puberty or age 10 yo, whichever is sooner
- Test of choice for screening: Hgb A1c and/or FBS
- Repeat annually in patients with marked obesity, evidence of insulin resistance (acanthosis nigricans), or abnormal screening tests
- Patients with abnormal screening tests require further evaluation
- Screening for T2DM has a low yield for T2DM but a high yield for preDM (0.5% vs 43%)

T Baranowski, D M Cooper, J Harrell, et al; STOPP-T2D Prevention Study Group. Presence of diabetes risk factors in a large U.S. eighth-grade cohort. *Diabetes Care*. 2006 Feb;29(2):212-7.

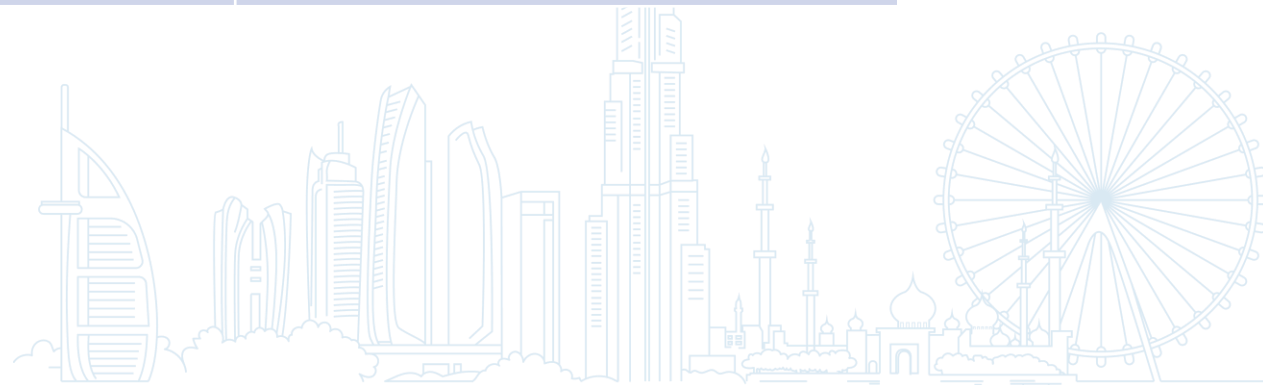




Dx of Prediabetes and Diabetes

- Same as adult population

	FBS	A1c
Normal	<100	≤5.7
Prediabetes	100-125	5.7 – 6.5
Diabetes	≥126	≥6.5





Dx of Diabetes – four pathways

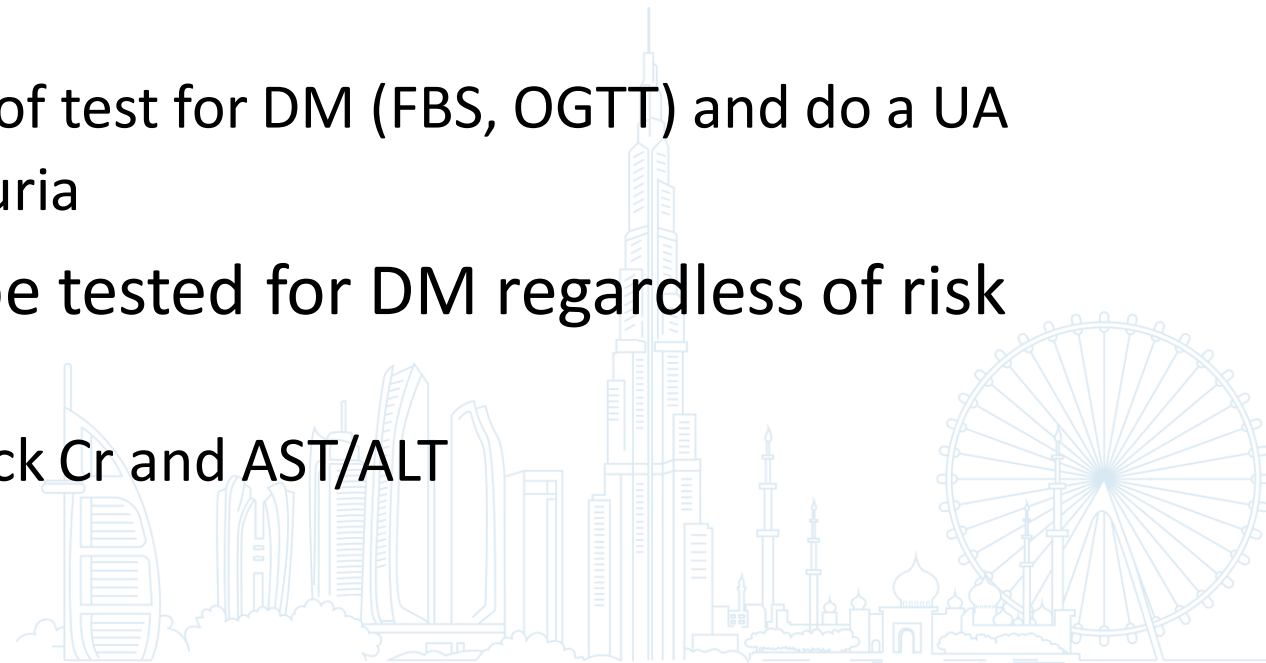
- FBS > 125 mg/dL
 - Confirm with results from a clinical laboratory, not just point-of-care testing
- Hgb A1c > 6.5%
 - Confirm with results from a clinical laboratory, not just point-of-care testing
- Random glucose > 200 in a patient with symptoms of hyperglycemia
- OGTT > 200
 - The 2 hour oral glucose tolerance test
 - 75 gram glucose load (1.75 g/kg in children up to 75 gms)
 - Measure serum glucose in 2 hours
 - > 200 → confirms dx of diabetes
 - 140 – 200 → confirms dx of prediabetes





Follow up of abnormal screening tests

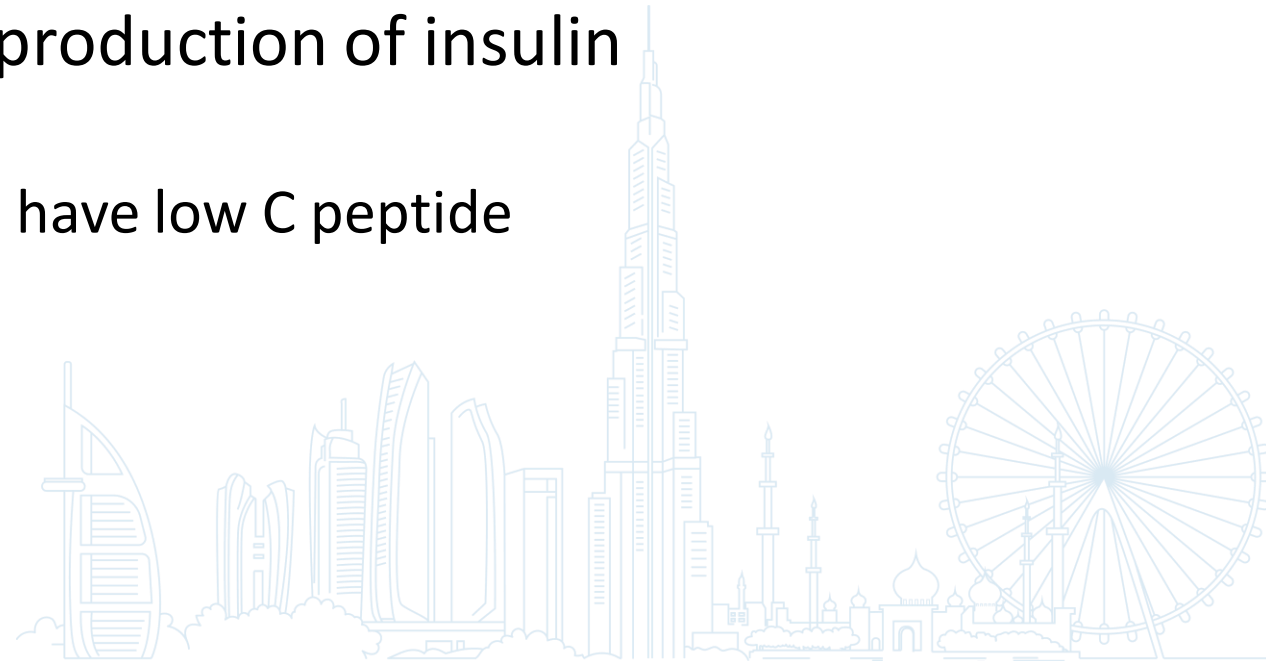
- Asymptomatic patients with prediabetes
 - Repeat testing in 3-6 months
 - If there is a high degree of clinical suspicion:
 - Repeat the screening test earlier, or
 - Proceed to 2-hour OGTT
- Asymptomatic and A1c > 6.5
 - Repeat the A1c and/or at least one of test for DM (FBS, OGTT) and do a UA
 - The UA checks for ketones, proteinuria
- Symptomatic patients should all be tested for DM regardless of risk factors
 - A1c, FBS, UA. Consider CMP to check Cr and AST/ALT





Tests to distinguish Type 1 from Type 2 DM

- Pancreatic autoantibodies
 - Anti-glutamic acid decarboxylase (GAD)
 - Tyrosine phosphatase insulinoma-associated antigen 2 (IA2)
- Insulin autoantibodies
 - Patient not yet on insulin or on insulin for only 1-2 weeks
- C-peptide – measures pancreatic production of insulin
 - Low – supports dx of T1DM
 - However, some T2 patients can also have low C peptide





Ketoacidosis

- Present at diagnosis in 30% children with T1DM
- Only present in 5-10% of children with T2DM at diagnosis
- Use the UA to screen for ketonuria
- Can check the anion gap (BMP/CMP) and venous pH
- Hospitalize for presence of ketoacidosis





Management of T2DM in children and adolescents





Goals of therapy

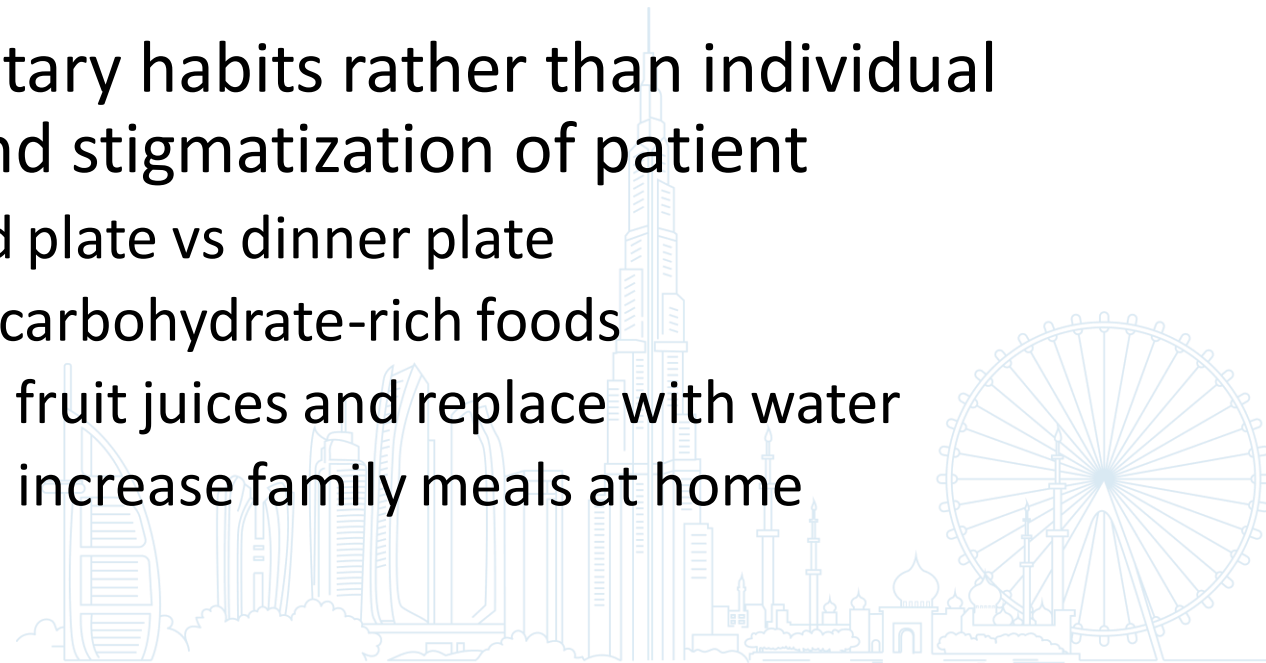
1. Achieve and maintain near-normal glycemic control
2. Improve insulin sensitivity and secretion
3. Identify and treat comorbidities
 - HTN, dyslipidemia, MAFLD/MASH (NAFLD/NASH)
4. Prevent vascular complications of T2DM
 - Microvascular: nephropathy, neuropathy, retinopathy
 - Macrovascular: ASCVD, Stroke, PAD
5. Avoid unplanned pregnancies with their attendant high risk of adverse outcomes





Nonpharmacologic therapy

- Nutrition
- Physical activity
- Weight goals:
 - 7-10% decrease in body weight with those who have completed linear growth
 - BMI < 85th %-ile for youth still growing
- Focus on individual and family dietary habits rather than individual dietary treatment: avoid blame and stigmatization of patient
 - Decrease portion size – eat off salad plate vs dinner plate
 - Substitute vegetables and fruits for carbohydrate-rich foods
 - Eliminate high-caloric drinks: sodas, fruit juices and replace with water
 - Reduce frequency of eating out and increase family meals at home



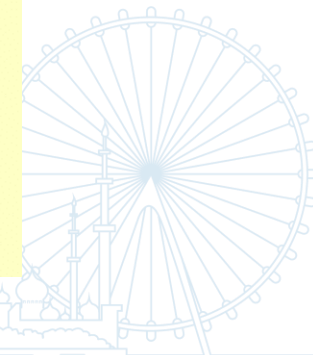
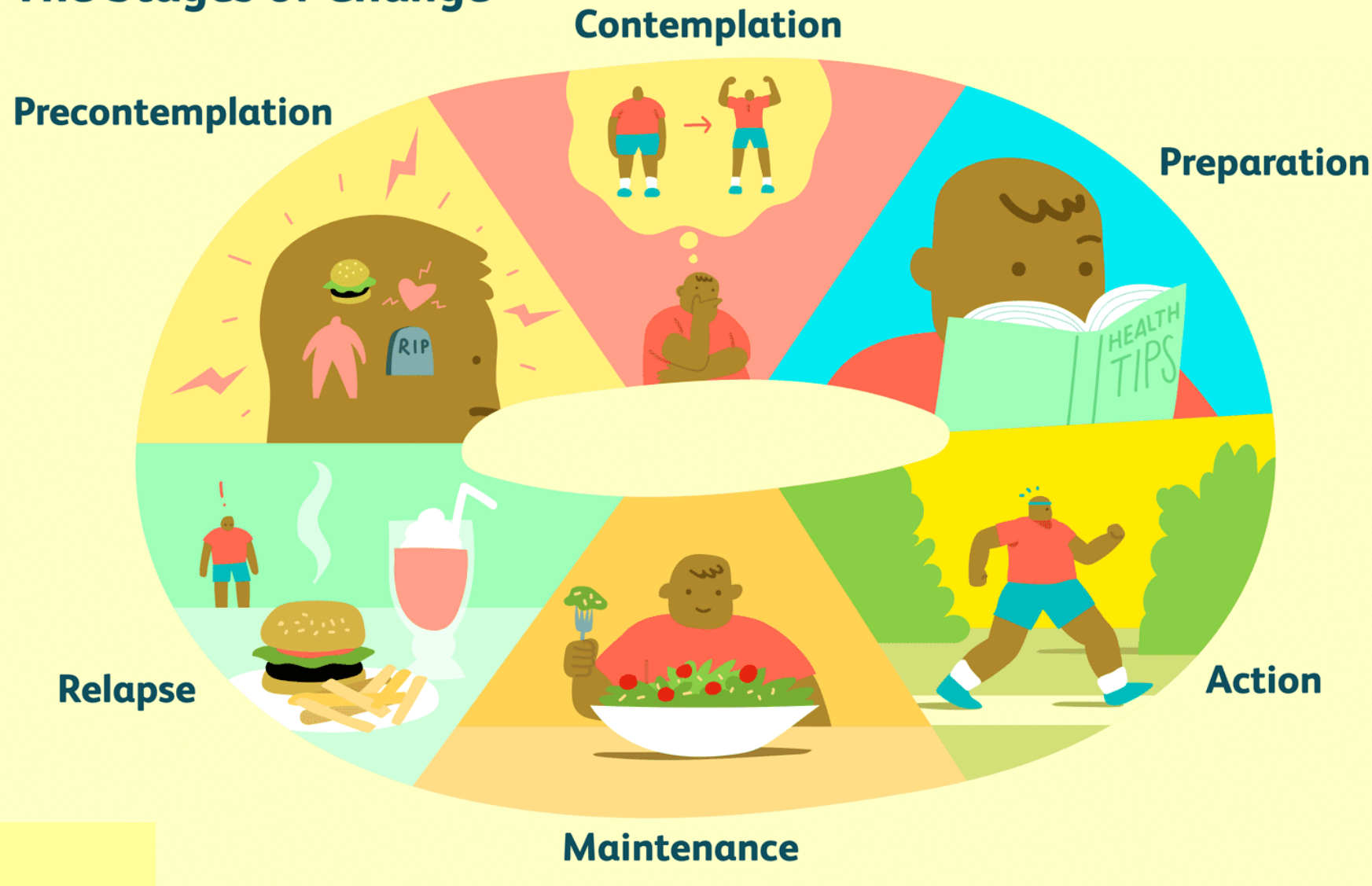


Lifestyle Medicine, patient education

- Studies show at least 26 hours of patient education is required to have a meaningful impact in outcomes (1)
- Stages of change model
- Motivational interviewing
 - Explore and determine what motivates a patient to change behavior
 - Suggest and encourage therapies that align with patient motivators
- Stimulus control
 - Uncouple environmental clues that lead to undesired behavior
 - Eating potato chips while watching a TV/movie
 - Getting home from school, playing video games in room eating candy

1. Hampl SE, Hassink SG, Skinner AC, et al. Executive Summary: Clinical Practice Guideline for the Evaluation and Treatment of Children and Adolescents With Obesity. *Pediatrics* 2023; 151.

The Stages of Change





“Vegetables and fruits”

Rather than “Fruits and vegetables”



Physical Activity

- One hour daily
- Limit nonacademic screen time < 2 hours daily:
 - Television
 - Video games
 - Mobile devices
 - Computer
- Join a sport with an encouraging coach
- Playground time with other families
- Parents – model desired behaviors





Pharmacologic agents in 2024

Metformin

Insulin

Glucagon-like peptide 1 (GLP-1) agonists

Sodium glucose cotransporter 2 (SGLT2) inhibitors

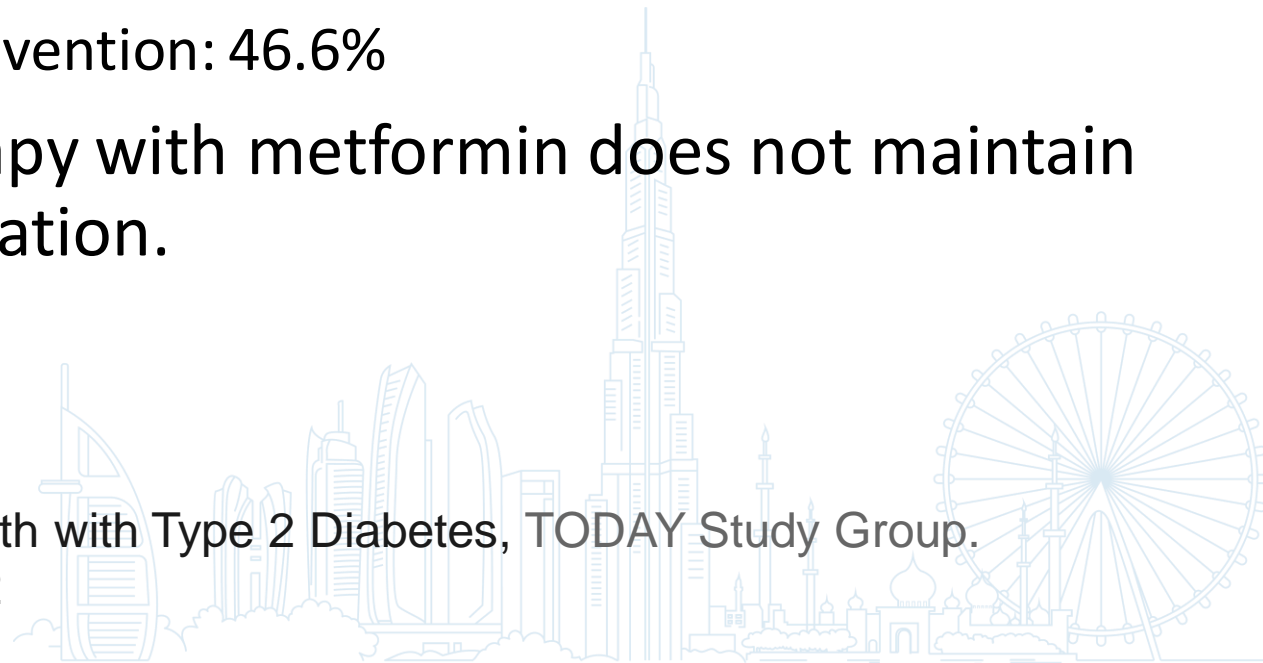




TODAY Study - 2012

- Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY)
- 699 youths, mean duration 3.8 years
- Primary outcome – loss of glycemic control, A1c >8.0 for 6 months
 - Metformin alone (titrated up to 1000mg bid): 51.7%
 - Metformin + rosiglitazone (not longer available): 38.6%
 - Metformin + intensive lifestyle intervention: 46.6%
- Conclusion: oral agent monotherapy with metformin does not maintain glycemic control in half this population.

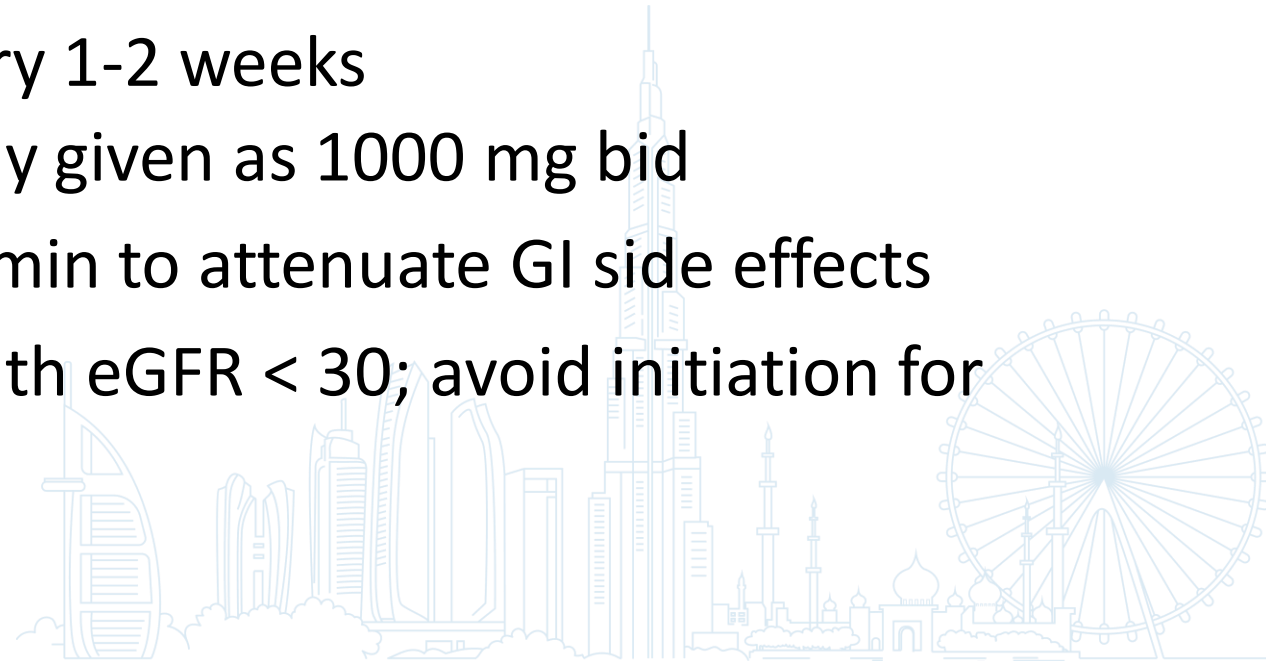
A Clinical Trial to Maintain Glycemic Control in Youth with Type 2 Diabetes, TODAY Study Group.
N Engl J Med 2012;366:2247-2256, June 14, 2012





Metformin

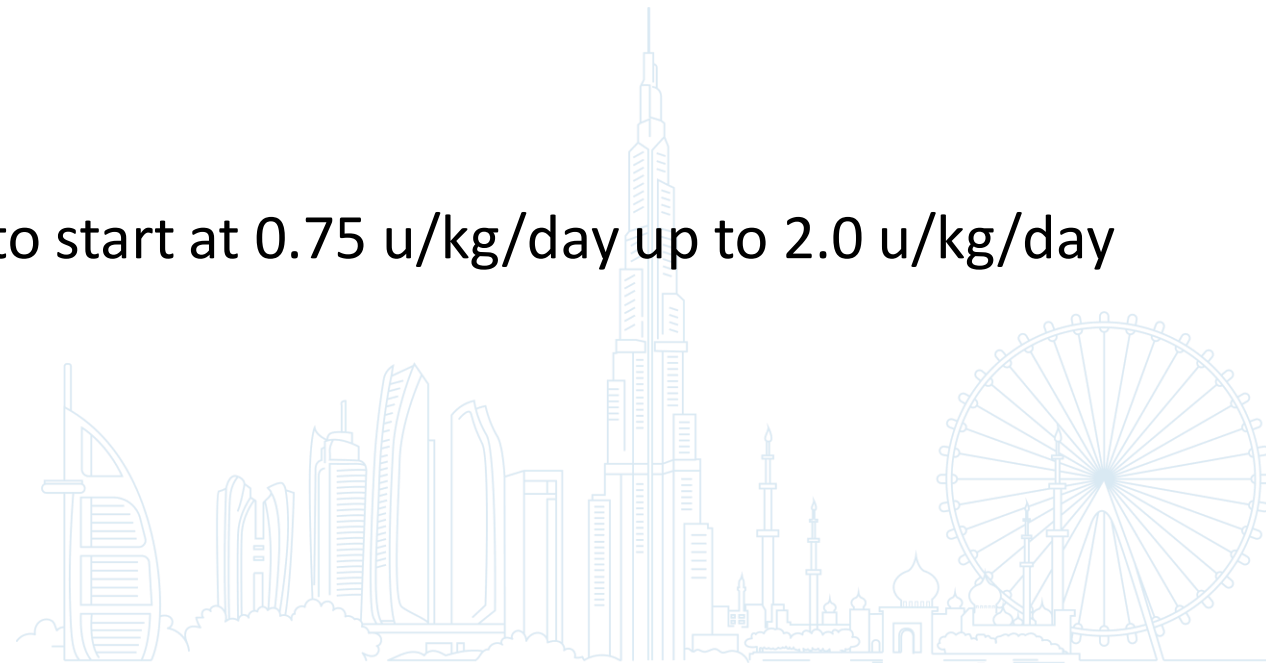
- First-line for most patients in conjunction with lifestyle therapy
 - Improves insulin sensitivity
 - Decreases hepatic gluconeogenesis
 - Modest weight loss
- Dosing: start at 500 mg daily
 - Titrate up by 500 mg daily every 1-2 weeks
 - Max dose 2000 mg daily usually given as 1000 mg bid
- Can use extended-release metformin to attenuate GI side effects
- Lactic acidosis; contraindicated with eGFR < 30; avoid initiation for eGFR 30-44 mL/min





Insulin

- Start insulin in patients with ketosis or severe hyperglycemia
- Plasma glucose > 250
- A1c > 9%
- Long-acting insulin can be used as a second agent should metformin monotherapy fail
 - Glargine, detemir, or degludec
 - 0.2 units/kg/day at bedtime
 - If severe hyperglycemia, may need to start at 0.75 u/kg/day up to 2.0 u/kg/day





GLP-1s

- No long-term studies in adolescents, no head-to-head trials vs insulin
- **Liraglutide** - ELLIPSE trial(1): **decrease in A1c = 0.64** when added to metformin
 - 86% completed trial w/o insulin rescue vs 67% metformin only
 - **Daily subcutaneous injections** 0.6 mg, may increase every 1-2 weeks to 1.8 mg daily
- **Extended-release exenatide** – trial (2): **decrease in A1c = 0.36**
 - **Once weekly subcutaneous injection** = 2mg
- **Dulaglutide** (dose = 0.75mg/1.5mg) trial (3): **decrease in A1c = 0.6/0.75**
 - **Once weekly dose titration:** start at 0.75 mg, may increase to 1.5 mg weekly
- If patient on insulin, decrease insulin dose by 20% when starting GLP-1

1. Tamborlane WV, Barrientos-Pérez M, Fainberg U, Ellipse Trial Investigators. Liraglutide in Children and Adolescents with Type 2 Diabetes. N Engl J Med. 2019;381(7):637. Epub 2019 Apr 28.

2. Tamborlane WV, Bishai R, Geller D, et al. Once-Weekly Exenatide in Youth With Type 2 Diabetes. Diabetes Care. 2022;45(8):1833.

3. Arslanian SA, Hannon T, Zeitler P, et al. Once-Weekly Dulaglutide for the Treatment of Youths with Type 2 Diabetes. N Engl J Med 2022; 387:433.



GLP-1s

- GLP-1s potential CV benefits vs insulin
- Weight loss vs weight gain from insulin
- Cost – GLP-1s \$\$\$ vs insulin \$
- Side effects – GI, common
- When to avoid:
 - Renal insufficiency
 - H/o pancreatitis
 - H/o medullary thyroid cancer or MEN 2





SGLT2s

- **Oral agents** vs subcutaneous injections → better adherence?
- CV and renal benefits
- Expensive \$\$\$ vs insulin \$
- **Empagliflozin** – approved in USA/FDA for pediatric population
 - DINAMO study (1), **decrease in A1c = 0.84**
 - Start at 10 mg, may increase to 25 mg at 12 weeks
 - **Comes in combination with metformin** (5/500, 5/1000, 12.5/500, 12.5/1000)
- Dapagliflozin – approved by the European Medicines Agency (2)
 - Decrease in A1c = 0.75 but CI (-1.65 to 0.15) → not clinically significant
 - Start at 5 mg, may increase to 10 mg at 12 weeks

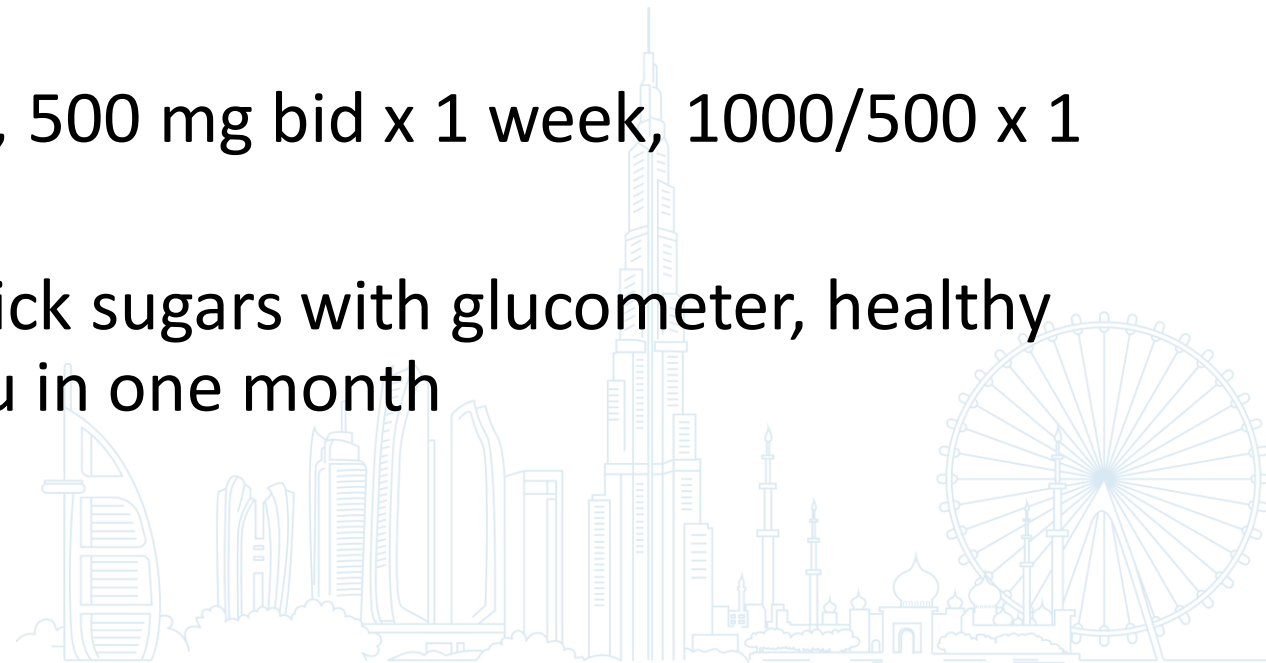
1. Laffel LM, Danne T, Klingensmith GJ, et al, DINAMO Study Group. Efficacy and safety of the SGLT2 inhibitor empagliflozin versus placebo and the DPP-4 inhibitor linagliptin versus placebo in young people with type 2 diabetes (DINAMO): a multicentre, randomised, double-blind, parallel group, phase 3 trial. *Lancet Diabetes Endocrinol.* 2023;11(3):169. Epub 2023 Feb 1.

2. Tamborlane WV, Laffel LM, Shehadeh N, et al. Efficacy and safety of dapagliflozin in children and young adults with type 2 diabetes: a prospective, multicentre, randomised, parallel group, phase 3 study. *Lancet Diabetes Endocrinol.* 2022;10(5):341. Epub 2022 Apr 1.



Case 1

- 15 yo male, weight = 100 kg, BMI 37
- A1c = 8.7, FBS = 188, UA – negative for ketones and protein
- Cr = 1.3, Anion gap normal at 10
- No symptoms
- Treatment options?
- Metformin 500 mg daily x 1 week, 500 mg bid x 1 week, 1000/500 x 1 week, then 1000 mg bid
- Pt education on lifestyle, finger stick sugars with glucometer, healthy nutrition, gentle daily exercise, f/u in one month





Case 1 continues:

- At f/u in 6 weeks:
- A1c = 8.5 (8.7), FBS 170 (188), urine ketones negative
- Challenges with GI upset from metformin
- Treatment options?
 - A. Start GLP-1 → decrease A1c and weight loss
 - Will this decrease A1c sufficiently?
 - Consider dulaglutide at 0.75 mg once weekly, phone call in 2 weeks
 - If not improving, increase to 1.5 mg weekly
 - B. Start basal insulin at 0.25 units/kg/day = 25 units at HS
 - Phone call in 2 weeks and reassess
 - C. Start empagliflozin/metformin 5/1000 → can ↑ to 12.5/1000



Treatment options

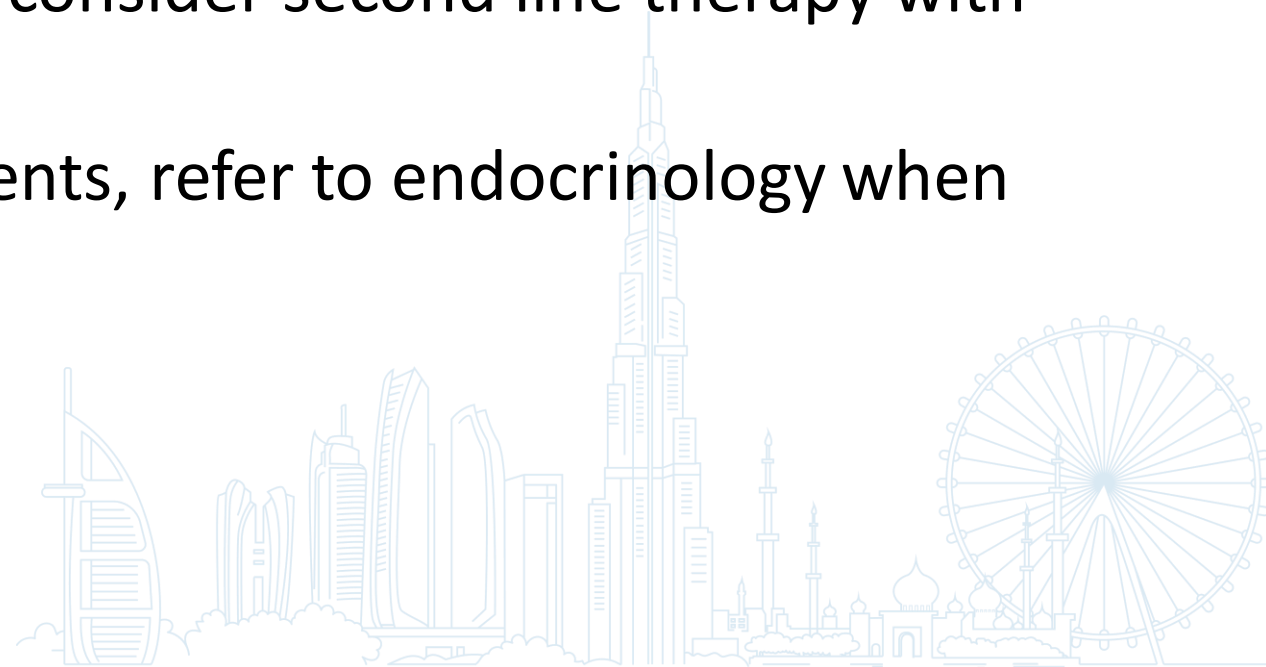
- Failure of dual therapy with metformin with basal insulin
 - Add GLP-1 or SGLT2 preferred over starting prandial insulin
- Patients not tolerating metformin
 - Consider extended-release metformin
 - Continue basal insulin
 - Add a GLP-1 and/or and SGLT2
- Referral to pediatric endocrinology is always a good consideration depending on availability
- Weight loss surgeries






Best practice guidelines

1. Screen at-risk patients for diabetes starting at age 10
2. Recommend lifestyle modifications for all at risk and affected patients
3. Prescribe metformin first line for most patients with T2DM
4. For patients not reaching goals, consider second line therapy with basal insulin, GLP-1s, or SGLT2s.
5. For most pediatric diabetic patients, refer to endocrinology when available



A serene sunset scene over a calm body of water. The sky is filled with soft, horizontal bands of color, transitioning from a pale blue at the top to deep oranges and yellows near the horizon. The sun is partially obscured by a line of dark, silhouetted trees along the shore. The water in the foreground is still, creating a clear reflection of the colorful sky and the dark trees. The overall mood is peaceful and contemplative.

Thank you for your time and attention
Eneedham7@gmail.com