

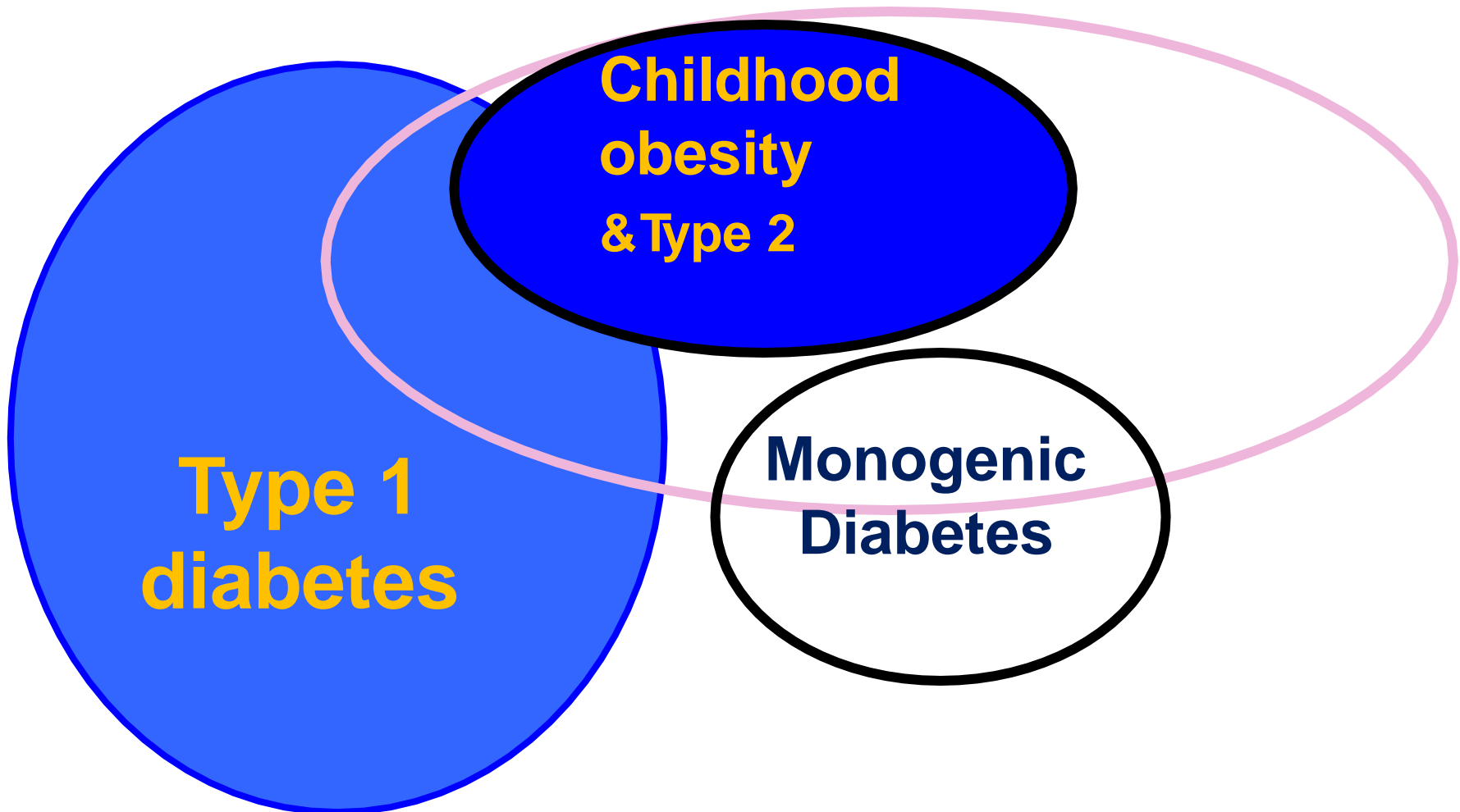
# Type 2 DM in Children & Adolescents: Management Overview

Abdulmoein Al-Agha, FRCPCH (UK)  
Professor & Head of Pediatric Endocrinology,  
King Abdulaziz University Hospital, Jeddah, KSA  
[aagha@kau.edu.sa](mailto:aagha@kau.edu.sa)

# Discussion Points

- Obesity prevalence has been increasing steadily resulting in an increased prevalence of type 2 DM in children.
- Management options for type 2 DM including lifestyle modifications versus pharmacological interventions.
- Metformin/Insulin/ GLP-1 receptor agonist.
- Bariatric surgery indications in children.
- Summery.

# Various types of diabetes in children



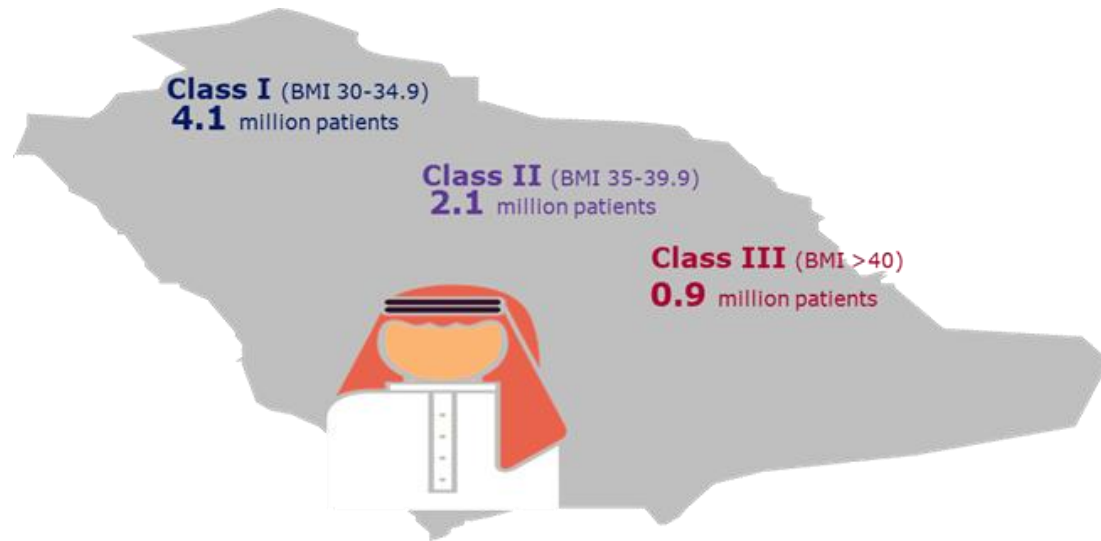
As obesity prevalence has increased,  
Type 2 diabetes in children and  
adolescent becomes more and more  
relevant

# Obesity Prevalence & Burden



**671**

**million people**  
live with obesity<sup>2,3</sup>



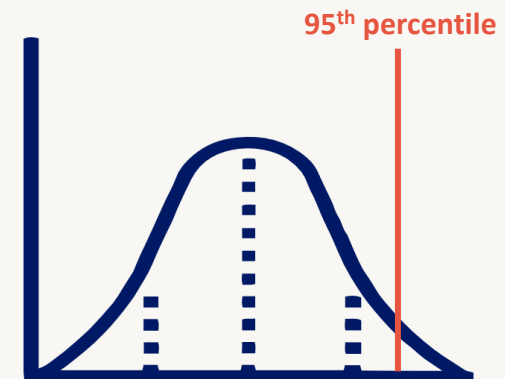
Obesity Map in Saudi Arabia

1. WHO. Global Health Observatory (GHO) data. Prevalence of obesity among adults. Available from [https://www.who.int/gho/ncd/risk\\_factors/overweight\\_obesity/obesity\\_adults/en/](https://www.who.int/gho/ncd/risk_factors/overweight_obesity/obesity_adults/en/). Accessed May 2020; 2. World Obesity Federation. Obesity: missing the 2025 targets. Executive summary. Available [here](#). Accessed June 2020; 3. NCD Risk Factor Collaboration. *The Lancet* 2017;390:2627–2642. Database available at: [www.ncdrisc.org](http://www.ncdrisc.org). Accessed June 2020. WHO (2018) Fact sheet. Available [here](#); Accessed on January 17, 2020, Alfadda A, et al. ACTION-IO. The First International Conference of the Saudi Society for Clinical Nutrition. Riyadh. October 2019.

# Overweight and obesity definitions

Classification	Definitions
Overweight <sup>2,3</sup>	BMI $\geq$ 85 <sup>th</sup> percentile for age and sex
Obesity <sup>2,3</sup>	BMI $\geq$ 95 <sup>th</sup> percentile for age and sex
Obesity class II <sup>3,4</sup>	BMI $\geq$ 120% of 95th percentile* for age and sex or a BMI $\geq$ 35 kg/m <sup>2</sup>
Obesity class III <sup>3</sup>	BMI $\geq$ 140% of 95th percentile for age and sex <sup>†</sup> or a BMI $\geq$ 40 kg/m <sup>2</sup>

Most countries use BMI  $\geq$  the 90<sup>th</sup>/95<sup>th</sup>/97<sup>th</sup> percentile based on a local reference when defining obesity<sup>1</sup>



An inclusion criterion for ongoing paediatric clinical trials NN8022-4179 and NN8022-4180 is a BMI corresponding to  $\geq$ 30 kg/m<sup>2</sup> for adults and  $\geq$ 95th percentile for age and sex. \*Corresponds to 1.2x the BMI value for the 95th centile; <sup>†</sup>Corresponds to 1.4x the BMI value for the 95th percentile.

1. Middelkoop & de Wilde. *Public Health Nutr* 2018;21:2969–2971; 2. CDC Growth Charts. Available [here](#); 3. Skinner et al. *JAMA Pediatr* 2014;168:561–6; 4. Kelly et al. *Circulation* 2013;128:1689–71. BMI, body mass index.

# Goals of management of type 2 diabetes

- To achieve & maintain near-normal glycaemic control.
- To improve insulin sensitivity and potentially improve insulin secretion, which results in improved glycaemic control.
- To identify and treat, if necessary, comorbidities such as hypertension, dyslipidemia, and non-alcoholic fatty liver disease.
- To prevent the vascular complications of T2DM.

# Management Options

- Treatment of type 2 DM depends on:
  - Diet.
  - Exercise.
- Medications:
  - Metformin.
  - Insulin.
  - GLP-1 receptor agonist (approved for adolescents 12 years and above).



# Lifestyle & dietary interventions in children with Type 2 DM



Weight reduction improves glycaemic control & is a crucial component of the successful management of T2DM in youth.

Lifestyle modifications to reduce body weight should be initiated in all patients with this disorder.

# Nutrition therapy

## Nutritional goals include:

- Improve glycaemic control by balancing food intake with physical activity. This may include providing small meals to avoid wide glycaemic excursions.
- Provide a diet that reduces caloric intake but also improves dietary quality to meet the nutritional requirements for normal health and growth.
- The patient and family should consult with a registered dietitian with experience in Pediatric nutrition and diabetes if possible.

# Dietary recommendations in children and adolescents with obesity

## NHMRC recommendations



Listen to internal hunger cues and to eat to appetite



Have healthy foods readily available

## ENDO recommendations



Reduce consumption of fast foods, added table sugar, high-fructose corn syrup, fruit juices, high-fat, high-sodium or processed foods



Portion control education, timely, regular meals, and avoiding constant 'grazing' during the day, recognising eating cues in the child or adolescent's environment



Increased intake of dietary fibre, fruits and vegetables

# Weight Reduction Goals

- In children & adolescents with T2DM, the optimal goal is 7 - 10 % decrease in body weight.
- Although the goal is weight reduction, it is prudent to approach this goal stepwise.
- It may be appropriate to set an initial goal of weight reduction followed by weight maintenance.
- Dietary intervention can focus on gradual weight loss to reach a BMI <85<sup>th</sup> percentile.
- In a growing child, a weight loss rate of 0.5 - 1 kg / month is a reasonable goal for growing youth.
- In a pubertal adolescents, weight loss goal of approximately 0.5 to 1 kg / week. “same weight loss goal recommended for adults with T2DM”.

# Physical activity

- Increased physical activity, independent of its effect on body weight, improves insulin sensitivity.
- Children with T2DM should be encouraged to do the followings:
  - engage in moderate to vigorous physical activity for at least one hour daily
  - strength training at least three times weekly
  - decrease sedentary behaviours
  - limiting non-academic "screen time" (e.g., television, video game, and computer) to less than two hours daily.

# Pharmacological Therapy

# Pharmacological Therapy

Consensus guidelines suggest that the initial regimen should depend upon the degree of dysglycemia:

- **Metformin monotherapy:** For patients with A1C <8.5 % and no symptoms. In metabolically stable adolescents with T2DM and no contraindications, with nonpharmacologic therapy (diet and physical activity).
- **Combination therapy with basal insulin and Metformin:** For patients with A1C ≥8.5 percent and hyperglycaemic symptoms (polyuria, polydipsia, nocturia, or weight loss) and without ketoacidosis.
- **Insulin alone:** Patients who present with ketosis or ketoacidosis should initially be treated with insulin and not metformin.
- Metformin should be added to the regimen only after the ketosis has cleared and blood glucose values have returned to normal or near-normal concentrations with insulin therapy.
- **Glucagon-Like Peptide 1 Receptor Agonists.**



# Metformin

- Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization.
- Unlike sulfonylureas, metformin does not produce hypoglycemia in either patients with type 2 diabetes or normal subjects.
- With metformin therapy, insulin secretion remains unchanged while fasting insulin levels and daylong plasma insulin response may decrease.

# Metformin

- Metformin is started in children initially at an oral dose of 500 mg administered once a day.
- The dose can be gradually increased by 500 mg increments at one-week intervals until the maximal daily dose of 2000 mg is achieved after four weeks.
- Extended-release preparations of metformin administered once daily should be considered in patients who have difficulty adhering to twice-daily dosing.
- Metformin is contraindicated in patients with hepatitis, impaired renal function, cirrhosis, alcoholism, cardiopulmonary insufficiency, or mitochondrial disease because it can cause lactic acidosis.
- Patients taking Metformin are advised to take a daily multivitamin because the absorption of vitamin B12 & folic acid can be compromised.

# Insulin Therapy

- Insulin therapy for selected adolescents with T2DM and any of the following characteristics:
  - Patients with ketosis or ketoacidosis should be managed as inpatients, with intravenous therapy.
  - Patients with mixed features of T2DM & T1DM in whom the diagnosis is not clear.
  - some patients may have mixed features and are difficult to classify. Such patients usually should be treated with insulin therapy.
  - Patients with marked hyperglycaemia (plasma glucose  $\geq 250$  mg/dL or A1C  $\geq 8.5$  percent).
  - The rationale for insulin treatment in these patients is that severe hyperglycaemia is toxic to pancreatic beta cells and treatment with insulin can help to restore endogenous insulin production.

# Glucagon-Like Peptide 1 Receptor Agonists

- Incretins are peptides produced by the intestinal mucosa in response to oral intake of nutrients that enhance glucose-stimulated insulin secretion & lower blood glucose levels.
- Administration of GLP-1 receptor agonists stimulates GLP-1 receptors, thereby increasing insulin secretion in response to oral glucose.
- Several GLP-1 receptor agonists are now approved in the for the treatment of type 2 diabetes starting from age of 12 years.

# Glucagon-Like Peptide 1 Receptor Agonists



SFDA



Liraglutide 3.0 mg is recommended in children  $\geq 12$  years if patient has weight more than 60 Kg and an initial body mass index (BMI) corresponding to 30 kg/m<sup>2</sup> or greater for adults, as an adjunct to a reduced-calorie diet and increased physical activity.

# Glucagon-Like Peptide 1 Receptor Agonists

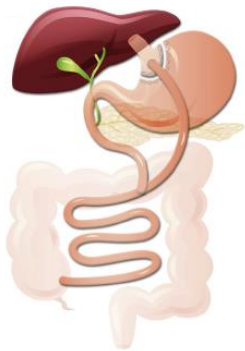
- These drugs are incretin mimetics that act to increase glucose-dependent insulin secretion from beta cells and help to ensure an appropriate insulin response following ingestion of a meal.
- They may have the additional benefit of promoting modest weight loss, probably due to delayed gastric emptying and possibly through central effects on appetite.
- Liraglutide is administered by subcutaneous injection once daily.
- Extended-release exenatide is a long-acting agent that is administered once weekly; this infrequent dosing reduces treatment burden compared with short-acting analogs, potentially leading to improved adherence.
- Other long-acting GLP-1 agonists that are used in adults include dulaglutide and Semaglutide.
- The oral preparation of Semaglutide is approved for use in adults with T2DM.

# Bariatric surgery in children and adolescents

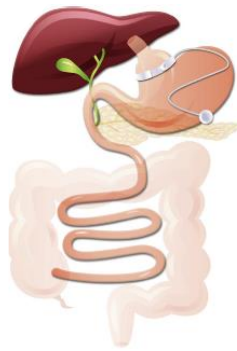


Three types of bariatric surgery are being commonly performed in the paediatric/adolescent population<sup>1-3</sup>

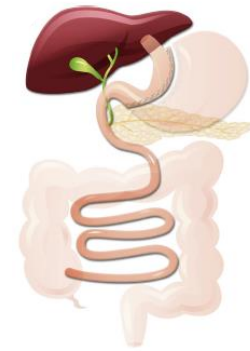
Laparoscopic Roux-en-Y gastric bypass (RYGB)



Laparoscopic adjustable gastric banding (LAGB)



Laparoscopic sleeve gastrectomy (LSG)



1. Piche et al. *Can J Cardio* 2015;31:153–66; 2. ASMBS *Bariatric Surgery Procedures* 2014. Available [here](#); 3. NHS England. Available [here](#); 4. Hofmann. *BMC Med Ethics* 2013;14:18.

# Candidates for bariatric surgery



**Class 2 obesity**, BMI  $\geq 35$  kg/m<sup>2</sup> or 120% of the 95<sup>th</sup> percentile for age and sex (whichever is lower) *with* clinically significant co-morbid condition (T2D, OSA, IIH, NASH, Blount disease, SCFE, GERD and hypertension)

OR

**Class 3 obesity**, BMI  $\geq 40$  kg/m<sup>2</sup> or 140% of the 95<sup>th</sup> percentile for age and sex, whichever is lower



**History of sustained efforts** to lose weight through changes in diet and physical activity



**Failure** of non invasive approaches



Eligibility should be determined through a thoughtful process that considers the **values of the patient and family**

1. Pratt et al. *Surg Obes Relat Dis* 2019; 14(7): 882-901; 2. Armstrong et al. *Pediatrics* 2019; 144(6): e20193223.

BMI, body mass index; GERD, gastroesophageal reflux disease; IIH, Idiopathic intracranial hypertension; NASH, non-alcoholic steatohepatitis; OSA, obstructive sleep apnoea; SCFE, slipped capital femoral epiphysis.



# Summary

Obesity treatment options for children are limited



Lifestyle treatments are centered in:

- Dietary interventions
- Physical activity & sedentary time
- Behavioural counselling
- Family-centred interventions

Current pharmacotherapy options include orlistat & phentermine



Bariatric surgery may be considered in exceptional cases



# Summary

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Lifestyle treatments are centered in:

- Dietary interventions
- Physical activity & sedentary time
- Behavioural counselling
- Family- centered interventions

Current pharmacotherapy options include Metformin &GLP-1 medications.



