

Addressing Cardiometabolic Risk in Children and Adolescents: CHALLENGES AND SOLUTIONS





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Type 2 Diabetes in Children and Adolescents: Screening, Diagnosis, and Management

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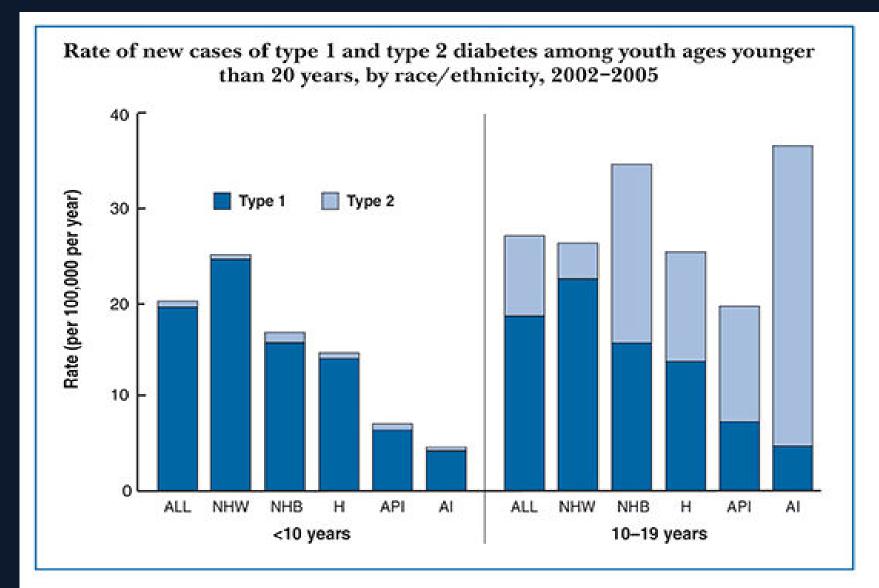


Goals

- Review the evolving epidemiology of type 2 diabetes in children and adolescents
- Review screening recommendations
- Discuss diagnostic criteria for children
- Compare and contrast treatment methods for type 2 diabetes in children and adolescents

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Source: SEARCH for Diabetes in Youth Study

NHW=non-Hispanic whites; NHB=non-Hispanic blacks; H=Hispanics/Latinos;

API=Asian/Pacific Islander Americans; AI=American Indians



From: Youth-Onset Type 2 Diabetes Consensus Report: Current Status, Challenges, and Priorities

Diabetes Care. 2016;39(9):1635-1642. doi:10.2337/dc16-1066

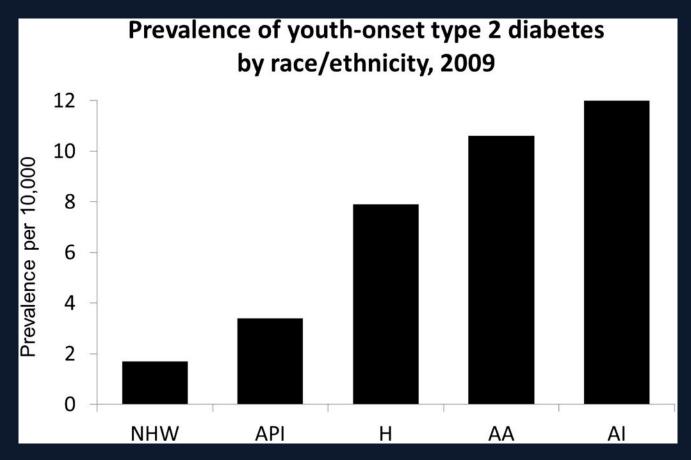


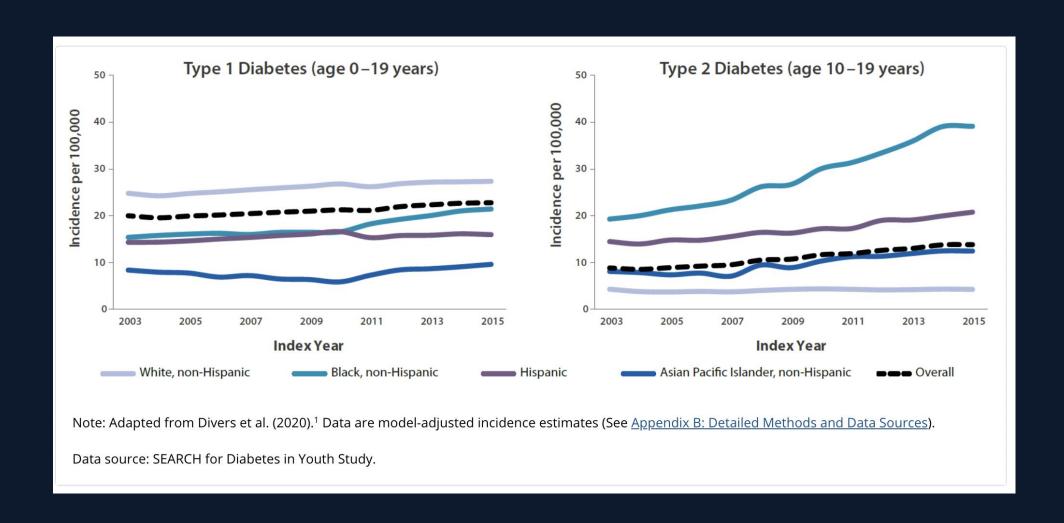
Figure Legend:

Prevalence of youth-onset type 2 diabetes by race/ethnicity. 2009 prevalence of type 2 diabetes among youth, as published by the SEARCH for Diabetes in Youth study (4). Prevalence is reported per 10,000 population at risk for type 2 diabetes (ages 10–19 years). AA, African American; AI, American Indian; API, Asian Pacific Islander; H, Hispanic; NHW, non-Hispanic white.

Type 2 Diabetes in Youth

- 33% of all adolescents in US with DM have TYPE 2 (1)
 - Over-representation from ethnic and racial minorities
 - Hispanic/Latino
 - African American
 - First American
 - Filipino
- Uncommon before puberty
 - Increased 35% in US 2001-2009 (2)
 - Increased 109% 2011-2015 (3)
 - Rates much higher in females (2)
- Closely tied to Family History and Obesity
- 1. Alberti G, et al. IDF Workshop Type 2 Diabetes in the young. An evolving Epidemic. Diabetes Care 2004.27(7):1798-1811.
- 2. Diabelea D et al. Incidence of diabetes in youth in the US. JAMA 2007.297(24):2716-2724.
- 3. Obesity and T2DM as Documented in Private Claims Data. A FAIR Health White Paper. FAIR Health Inc. January 2017. 1-16.

Trends in Type 1 and Type 2 diabetes in youth



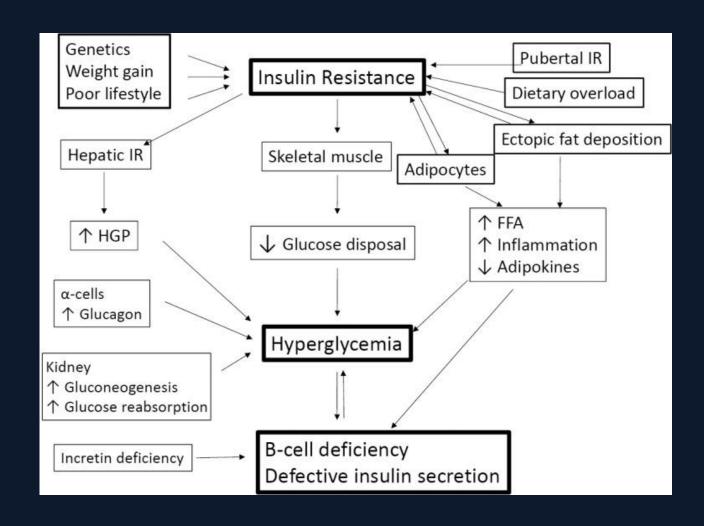
Risk Factors for T2DM in kids

- Excessive body weight
 - >85% of BMI for age and gender
- First American, Black, Hispanic,
 Pacific Islander, Asian
- FH of T2DM in first or second degree relatives
- Age 12-16 years

- Low Birth weight OR High Birth weight
- Maternal Gestational DM
- No breastfeeding
- Use of antipsychotics (increased risk x 3)

Pathophysiology of Type 2 diabetes in children and adolescents

 Valaiyapathi B, Gower B, Ashraf AP. Pathophysiology of Type 2 Diabetes in Children and Adolescents. Curr Diabetes Rev. 2020;16(3):220-229.





From: Youth-Onset Type 2 Diabetes Consensus Report: Current Status, Challenges, and Priorities

Diabetes Care. 2016;39(9):1635-1642. doi:10.2337/dc16-1066

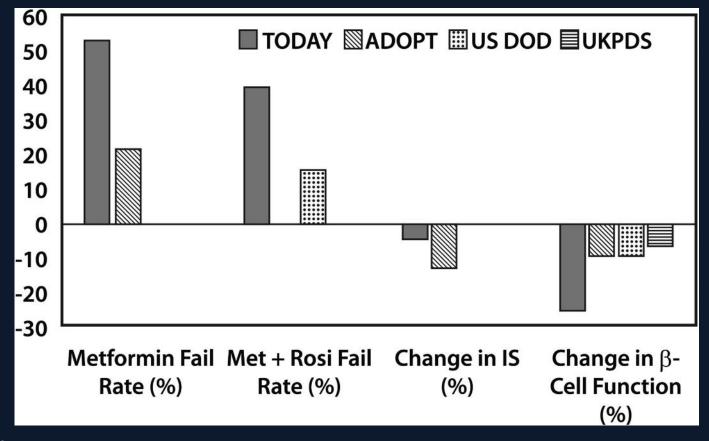
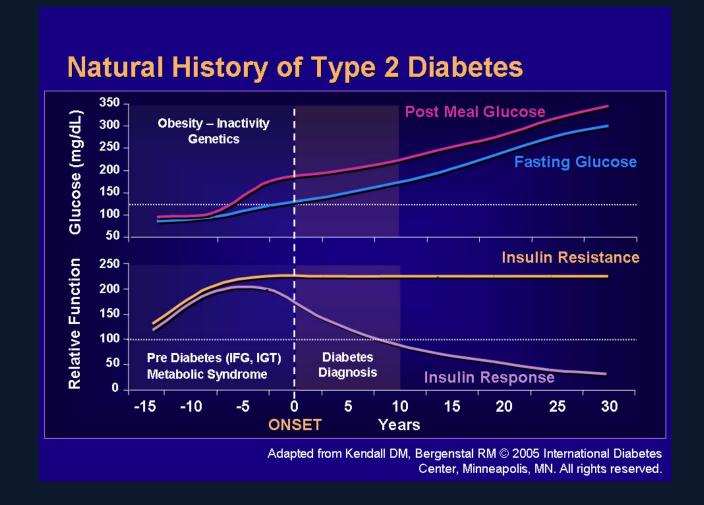


Figure Legend:

β-Cell failure rates in adults versus youth with type 2 diabetes. A comparison of medication treatment failure rates and percent change in surrogate measures of insulin sensitivity and β-cell function as reported in the TODAY study (youth) versus adult studies (A Diabetes Outcome Progression Trial [ADOPT], U.S. Department of Defense Database [US DOD], and UK Prospective Diabetes Study [UKPDS]). Note that the studies had different primary end points and therefore this is an approximate comparison, as there have been no head-to-head comparisons (11,12,14–16,67,68). Met, metformin; Rosi, rosiglitazone.

Type 2 DM Progression

- Lose 15% of beta cell function/year
- No change in insulin sensitivitymaximally resistant
 - 31% loss of insulin medicated glucose disposal
 - 78% loss of acute insulin response



Gungor N et all Progressive beta cell failure in T2DM of youth. J Pediatrics 2004.144(5):656-659.

Weyer C et al. The natural history of insulin secretory function and insulin resistance in the pathogenesis of T2DM. J Clin Invest 1999.104(6):787-794.

Goals

- Review the evolving epidemiology of type 2 diabetes in children and adolescents
- Review screening recommendations
- Discuss diagnostic criteria for children
- Compare and contrast treatment methods for type 2 diabetes in children and adolescents versus adults

There are no reliable "classic symptoms" to diagnose T2DM in youth

We must rely on evidence based national screening programs

Pre-Diabetes/Diabetes Diagnostic Criteria

| <u>Normal</u> | <u>Pre-Diabetes</u> | <u>Diabetes</u> |
|--------------------------------|--|---|
| Fasting glucose < 100 mg/dl | Impaired fasting glucose ≥ 100 - 125 mg/dl | Fasting glucose ≥ 126 mg/dl |
| 2-h PG < 140 mg/dl | Impaired glucose tolerance 2-h PG <u>></u> 140 - 199 mg/dl | 2-h post meal glucose ≥ 200 mg Random PG ≥ 200 + symptoms |
| A1C < 5.7% | 5.7% to 6.4% | ≥ 6.5% |

Which kids should we screen for T2DM?

- Start at age 10 or onset of puberty in:
 - Any child who is overweight or obese (BMI >85%)
 - Family history in 1 or 2 degree relative
 - First American, Black, Hispanic. Asian, Pacific Islander
 - Any sign of insulin resistance:
 - Acanthosis
 - Hypertension
 - Dyslipidemia
 - PCOS
- Repeat screening every 3 years
- Fasting glucose is preferred
- Consider looking for other forms of diabetes

Case: Adolescent with dirty neck

- A 14-year-old AA female presents with concerns about a rash on her neck that will not wash away.
- Has been present for a couple years but seems to be worse.
- Child does not like it nor do parents.
- Does not seem to wash away
- Teacher said he was going to report to Children Services if nothing was done



Case: History and Physical

History

- Always obese, late menarche, bilateral knee pain
- Rash was seen by mom at event- no quick changes, nothing seems to make it better or worse
- No meds, no allergies
- FH- hypertension in both parents, DM in mom, CRF in dad
- Social- doing fair in school, some friends, lives with mom and brother, Shared custody with dad

Physical

- Obese adolescent (> 95% for gender, age and Ht)
- Truncal obesity
- Bp 148/92 (HIGH)

Case: labs

- A1c 9.2%. (high)
- Glucose 138 mg/dl (fasting) (high)
- AST 56 (high)
- ALT 62 (high)
- Lipid panel
 - Total chol 258 mg/dl (high)
 - HDL 30 mg/dl (low)
 - LDL 172 mg/dl
 - Trigs 380 mg/dl (high)

Where do we begin with this kid?

- Problem List
 - Insulin resistance syndrome
 - Metabolic syndrome
 - Diabetes- probably T2
 - Possible fatty liver disease
 - Dyslipidemia
 - Suspect hypertension
 - Obesity
- Where do we start?

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Management—Lifestyle Management (Type 2)

- 14.55 All youth with type 2 diabetes and their families should receive comprehensive diabetes self management education and support that is specific to youth with type 2 diabetes and is culturally appropriate. B
- 14.56 Youth with overweight/obesity and type 2 diabetes and their families should be provided with developmentally and culturally appropriate comprehensive lifestyle programs that are integrated with diabetes management to achieve 7–10% decrease in excess weight. C
- 14.57 Given the necessity of long-term weight management for children and adolescents with type 2 diabetes, lifestyle intervention should be based on a chronic care model and offered in the context of diabetes care. E

Management—Glycemic Targets (Type 2)

- 14.60 Blood glucose monitoring should be individualized, taking into consideration the pharmacologic treatment of the patient. E
- 14.61 Real-time continuous glucose monitoring or intermittently scanned continuous glucose monitoring should be offered for diabetes management in youth with type 2 diabetes on multiple daily injections or continuous subcutaneous insulin infusion who are capable of using the device safely (either by themselves or with a caregiver). The choice of device should be made based on patient circumstances, desires, and needs. E
- 14.62 Glycemic status should be assessed every 3 months. E

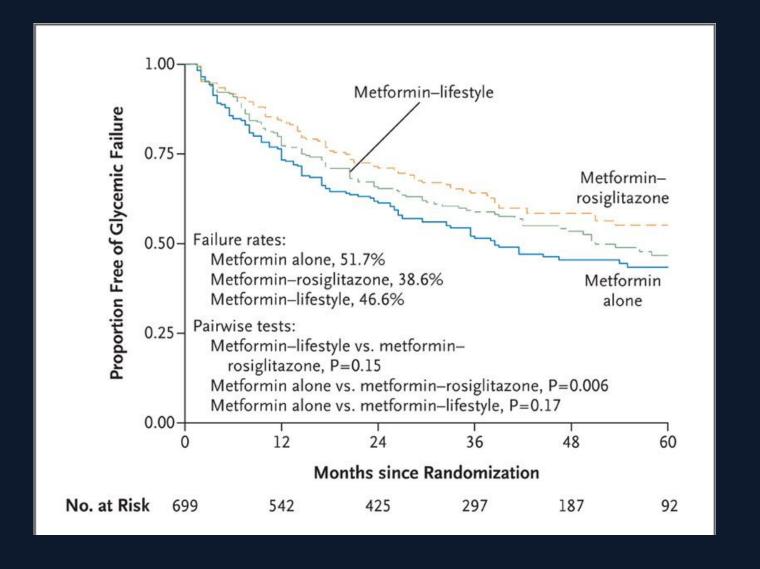
Pharmacologic Management (Type 2)

- 14.66 Initiate pharmacologic therapy, in addition to behavioral counseling for healthful nutrition and physical activity changes, at diagnosis of type 2 diabetes. A
- 14.67 In incidentally diagnosed or metabolically stable patients (A1C <8.5% [69 mmol/mol] and asymptomatic), metformin is the initial pharmacologic treatment of choice if renal function is normal. A
- 14.68 Youth with marked hyperglycemia (blood glucose ≥250 mg/dL [13.9 mmol/L], A1C ≥8.5% [69 mmol/mol]) without acidosis at diagnosis who are symptomatic with polyuria, polydipsia, nocturia, and/or weight loss should be treated initially with basal insulin while metformin is initiated and titrated. B

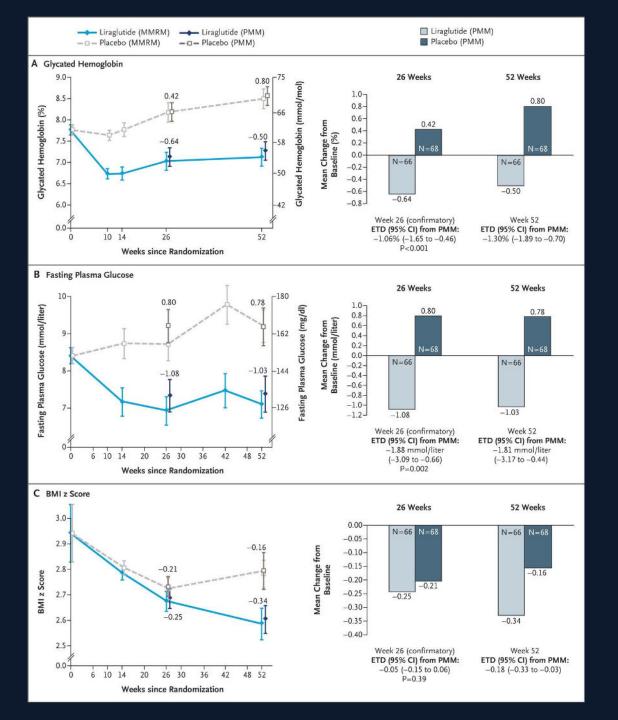
TODAY Trial (Treatment Options for T2DM in Adolescents and Youth)

- A Clinical Trial to Maintain Glycemic Control in Youth with Type 2 Diabetes
- Compared Treatment of Youth with:
 - A) Metformin
 - B) Metformin + Lifestyle changes
 - C) Metformin + Rosiglitazone
- Failure rate declined 13.1% with addition of rosiglitazone

TODAY study results



Zeitler P, Hirst K, Pyle L, et al; TODAY Study Group. A Clinical Trial to Maintain Glycemic Control in Youth with Type 2 Diabetes. N Engl J Med. 2012; 366(24):2247-2256.



Change from Baseline during the 52-Week Trial Period in the Primary and Two Secondary End Points

Tamborlane WV, et al. Ellipse Trial Investigators. Liraglutide in Children and Adolescents with Type 2 Diabetes. N Engl J Med. 2019 Aug 15;381(7):637-646

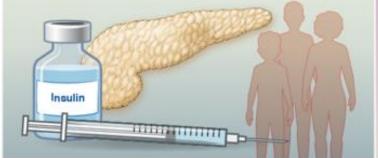
Tamborlane WV et al. N Engl J Med 2019;381:637-646



Liraglutide in Children with Type 2 Diabetes

MULTICENTER, RANDOMIZED TRIAL

134 Children and adolescents receiving metformin with or without insulin



Liraglutide + Metformin



Placebo + Metformin



Change in glycated hemoglobin at 26 wk

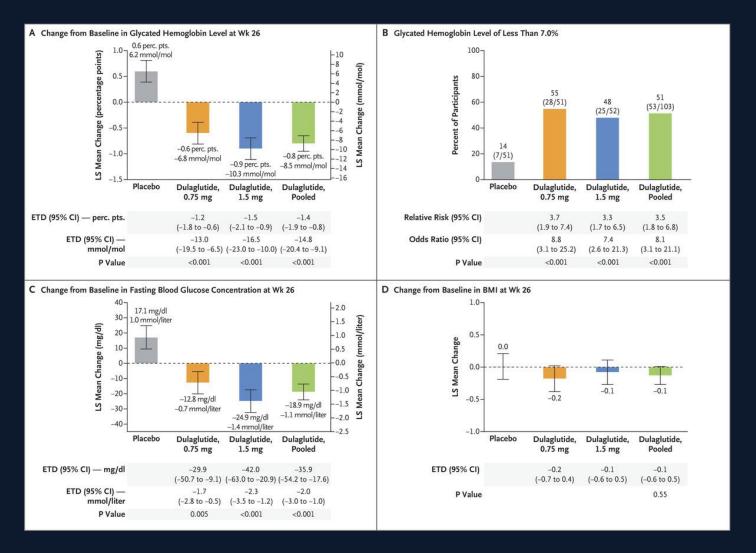
-0.64 percentage points

0.42 percentage points

(Treatment difference, -1.06; 95% CI, -1.65 to -0.46; P<0.001)

Liraglutide added to metformin with or without insulin improved glycemic control

Change in the **Glycated Hemoglobin** Level, a Glycated **AWARD-PEDS Trial-**Hemoglobin Level of Less Than 7.0%, and Changes in the Fasting **Blood Glucose** Concentration and Body-Mass Index (BMI) at Week 26.



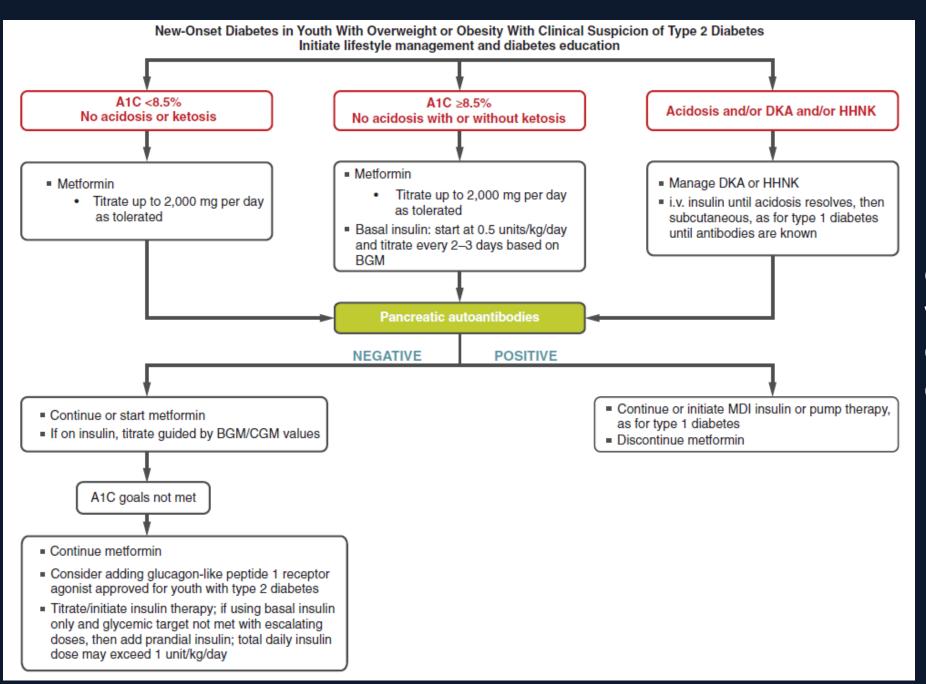


Figure 14.1—
Management of newonset diabetes in youth with overweight or obesity.

Children &
Adolescents:
Standards of
Medical Care in
Diabetes - 2022.
Diabetes Care
2022;45(Suppl. 1)

Management—Metabolic Surgery (Type 2)

- 14.75 Metabolic surgery may be considered for the treatment of adolescents with type 2 diabetes who have severe obesity (BMI >35 kg/m2) and who have uncontrolled glycemia and/or serious comorbidities despite lifestyle and pharmacologic intervention. A
- 14.76 Metabolic surgery should be performed only by an experienced surgeon working as part of a well-organized and engaged multidisciplinary team including a surgeon, endocrinologist, dietitian nutritionist, behavioral health specialist, and nurse. A

Other important issues in Peds T2DM

- Mood disorders (Depression, Anxiety)
- Disordered Eating
- Challenges for the Emerging Adult (leaving home, independence, sex, drugs, responsibility, relationships)
- Need a transition team
 - Helps to provide goals for independence
 - Introduce child to new provider
 - Helps to support in gaps of care
 - College
 - Job
 - Lack of insurance/underinsurance
 - Rebel years
- The Primary Care Pediatrician can be a VERY valuable resource for these kids-

Importance of Family-Centered Care

- Addressing cultural issues within family
- Peer-enhanced activities
- Engaging the family helps in younger ages:
 - Adherence to meds
 - Lifestyle changes
 - Provides support system

Summary

- Type 2 DM in children is on the rise
- Type 2 diabetes is MORE progressive and harder to treat in children
- Treat diabetes like you would treat cancer
 - Use treatments as early as possible
 - Use a comprehensive team-based approach



Questions?

Website

tu.edu/mobec

diabetesprevention.tu.edi

Social Media

Facebook: @DiabetesDREAMTeam

Twitter: @DiabetesTUCA

Instagram: Diabetestuca

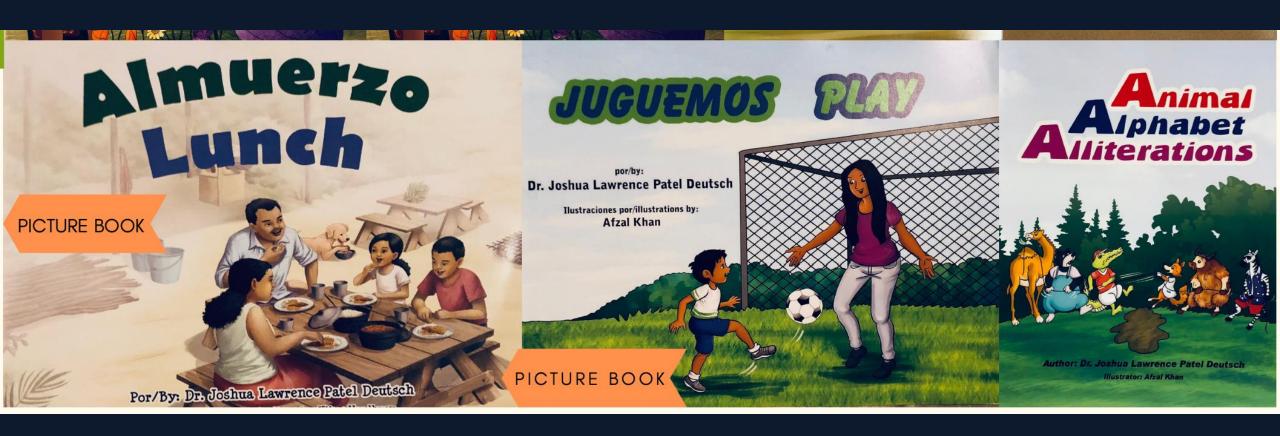




MOBEC programs







Fingerprint Asymmetry as Indicator for Diabetes





Fingerprint Asymmetry Discriminates between Individuals with and without Diabetes

Original Article

A New Method to Assess Asymmetry in Fingerprints Could Be Used as an Early Indicator of Type 2 Diabetes Mellitus

Journal of Diabetes Science and Technology I–8

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Molly R. Morris, PhD¹, Bjoern Ch. Ludwar, PhD², Evan Swingle¹, Mahelet N. Mamo², and Jay H. Shubrook, DO³

Permanence of fingerprints allows for assessment in cross-sectional study

Discriminative Accuracy for T2DM: AUC = 0.73

Discriminative Accuracy for T1DM: AUC = 0.85

Recommendations from ADA and AAP

- Youth-onset type 2 diabetes consensus report: Current Status, Challenges and Priorities. *Diabetes Care* 2016.39(9):1635-1642.
- Evaluation and Management of Youth-Onset Type 2 Diabetes: A Position Statement by the American Diabetes Association. *Diabetes Care* 2018 Dec;41(12):2648-2668. doi: 10.2337/dci18-0052. PMID: 30425094; PMCID: PMC7732108.
- Springer SC et al Technical report. Management of type 2 diabetes mellitus in children and adolescents. *Pediatrics*. 2013 Feb;131(2):e648-64. doi: 10.1542/peds.2012-3496. Epub 2013 Jan 28. Erratum in: Pediatrics. 2013 May;131(5):1014. PMID: 23359584.
- Copeland KC et al. Clinical Practice Guidelines. Management of Newly Diagnosed T2DM in children and adolescents. *Pediatrics* 2013. 131(2):364-382.
- Diabetes Care for Emerging Adults: Recommendations for Transition From Pediatric to Adult Diabetes Care Systems. Diabetes Care 2011. Diabetes Care 2011. 34(11): 2477-2485.

Landmark Articles

- SEARCH-Mayer-Davis EJ, et a. SEARCH for Diabetes in Youth Study. Incidence Trends of Type 1 and Type 2 Diabetes Among Youths, 2002-2012. *N Eng J Med* 2017;376:1419-1429. PMID: 28402773.
- TODAY-Zeitler P, Hirst K, Pyle L, et al; TODAY Study Group. A Clinical Trial to Maintain Glycemic Control in Youth with Type 2 Diabetes. *N Engl J Med.* 2012; 366(24):2247-2256.
- RISE Consortium: Impact of insulin and metformin versus metformin alone on beta cell functionin youth with impaired glucose tolerance or recently diagnosed type 2 diabetes. *Diabetes Care* 2018;41:1717-1725.

New Reference

 Molinari, Antonia M. and Shubrook, Jay H. "Treatment options and current guidelines of care for pediatric type 2 diabetes patients: a narrative review" *Journal of Osteopathic Medicine*, vol. 121, no. 4, 2021, pp. 431-440. https://doi.org/10.1515/jom-2020-0172.

Pharmacotherapy References

- Valaiyapathi B, Gower B, Ashraf AP. Pathophysiology of Type 2 Diabetes in Children and Adolescents. Curr Diabetes Rev. 2020;16(3):220-229. doi: 10.2174/1573399814666180608074510. PMID: 29879890; PMCID: PMC7516333.
- Tamborlane WV, et al. Ellipse Trial Investigators. Liraglutide in Children and Adolescents with Type 2 Diabetes. N Engl J Med. 2019 Aug 15;381(7):637-646. doi: 10.1056/NEJMoa1903822. Epub 2019 Apr 28. PMID: 31034184.
- Tamborlane WV, et al; Once-Weekly Exenatide in Youth With Type 2 Diabetes. *Diabetes Care* 2022; dc212275. https://doi.org/10.2337/dc21-2275