Diversity in Pediatric Type 2 Diabetes (T2D) Trials

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Disclosure

The contents of this presentation represent the views of the speaker and do not necessarily reflect FDA policy

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Overview

- Introduction to Youth-onset Type 2 diabetes (T2D)
- FDA's approach to encouraging representative studies through regulations impacting pediatric trials (PREA/BPCA) and new guidance related to diversity action plans
- Highlight unique challenges in conducting clinical trials in youth-onset T2D
- Assessment of representativeness for a sample of pediatric T2D clinical trials
- Lessons Learned & Future Directions

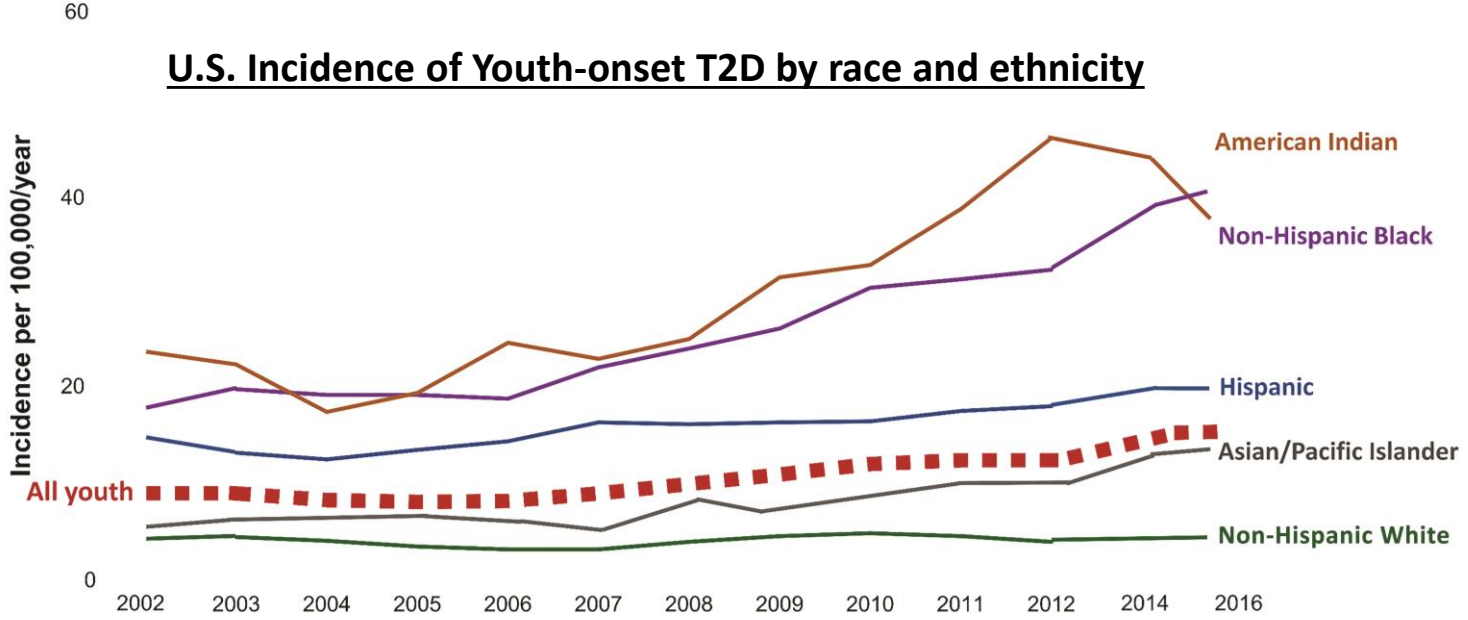
Youth-onset Type 2 Diabetes (T2D)

- Type 2 diabetes (T2D) in youth is a serious disease
  - Complications of diabetes develop rapidly in children, with a high risk of debilitating complications by young adulthood
  - Mortality in children with T2D is ~2-3x higher than the general population
- Diabetes is common (1:10 in U.S., 90-95% T2D)
- However, **Youth-onset T2D** is relatively rare
  - **Prevalence:** 1 in 1,500 U.S. youth <20y
    Of ~43 mill U.S. youth (10-19y) in the US, ~**28,800** have T2D*
  - **Incidence:** Each year, ~5,300 youth <20y are diagnosed with T2D
    In contrast, >3x as many youth are diagnosed with type 1 diabetes
    (SEARCH 2017-2018 Wagenknecht LE et al. Lancet Diabetes Endocrinol. 2023)
  - Impacts **female** > male youth **(Perng W et al Diabetes Care. 2023)**

*** Based on data obtained from U.S. census bureau (2023) & pediatric T2D prevalence from SEARCH 2017-2018**

Burden of youth-onset T2D

- While youth-onset T2D is still relatively rare, there is a rising number of diagnoses in children every year
  - Yearly diagnoses almost doubled from 2002 → 2018
- In the US, racial and ethnic minority populations carry the largest burden of this increase in youth-onset T2D



Perng W, Conway R et al; Diabetes Care 2023

Representation in pediatric trials

- Evaluating the safety and effectiveness of medical care and treatments for a representative and diverse population is critical to advancing health equity
- For pediatric T2D, there is a disproportionate impact on youth of ethnic/racial minorities:
  - higher rate of new diagnoses
  - differences in both health outcomes and differences in risk factors for health outcomes observed by race and ethnicity
    (Bacha F, Cheng P, et al Diabetes Care. 2021)
- Representation in youth-onset T2D trials is important in ensuring that positive health outcomes from treatments being investigated apply to all patients

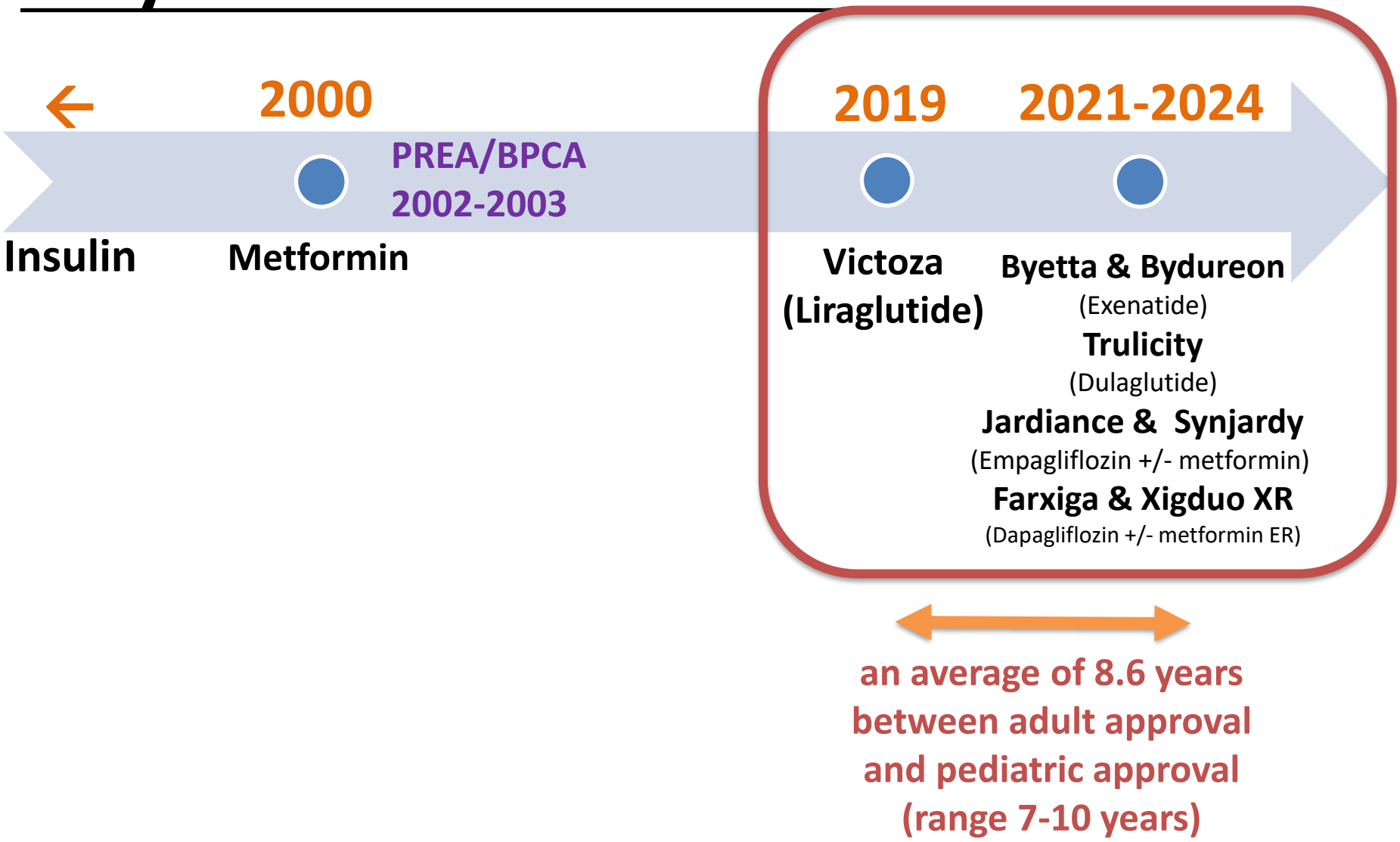
FDA Regulations: Pediatric Trials

- **Pediatric Research and Equity Act (PREA) 2003**
  - A ***requirement*** to submit a pediatric study plan at the time of the completion of Phase 2 Trials in adults
- **Best Pharmaceuticals for Children Act (BPCA) 2002**
  - A ***request*** to conduct pediatric clinical studies by issuing a Written Request
  - If terms of Written Request fulfilled, may add 6 months of market exclusivity
  - section 505A(d)(1)(A) of the Federal Food, Drug and Cosmetic Act states that in issuing a Written Request, the FDA shall ***"take into account adequate representation of children of ethnic and racial minorities"***

June 2024: *Draft guidance for industry,*

Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials

FDA-Approved Treatments for youth-onset T2D



Challenges: youth-onset T2D trials

- Longer time required to complete trials in pediatric T2D due to slow enrollment
  - From an analysis of U.S. Phase 3/4 pediatric T2D trials (2000-2020): 5/17 (30%) met enrollment targets in < 4 years

Currie BM, Howell TA, et al. Diabetes Ther. 2021

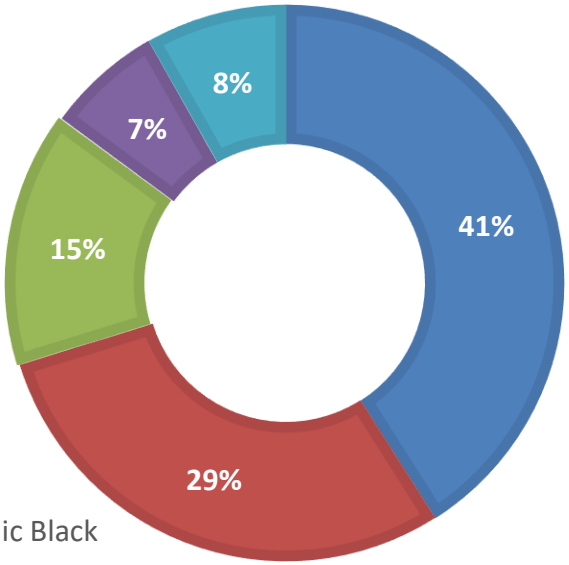
Longer enrollment times contribute to longer timelines to approval of drugs in pediatric T2D

Pediatric T2D Assessment

- **Goal:** compare the race and ethnicity breakdown of pediatric T2D trials submitted to the diabetes division versus the known race and ethnicity breakdown of youth with T2D in the US
  - 5 clinical trials identified (limited to FDA approvals)
- **Source of Representativeness Benchmark:**

  SEARCH For Diabetes in Youth study
  - CDC-funded, NIH-supported study that surveilled physician-diagnosed diabetes in 5 U.S. states plus select American Indian reservations, from 2000 to 2020
  - population selected to represent, or overrepresent youth thought to be at greatest risk for youth-onset T2D
  - CDC's prevalence & incidence estimates for youth onset T2D come from the SEARCH study (CDC.gov, National Diabetes Statistics Report)

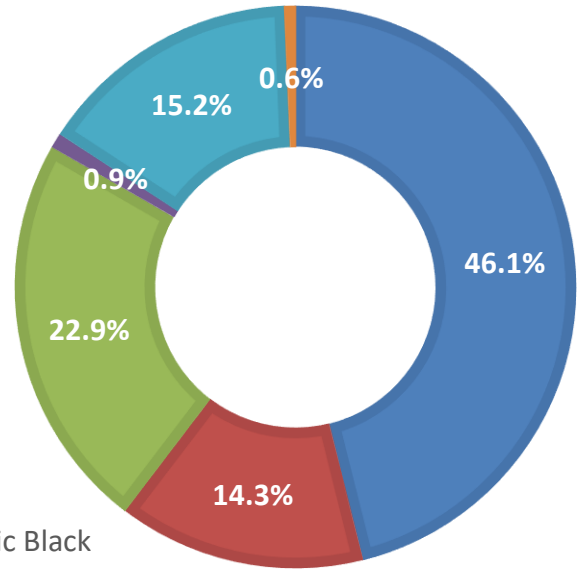
2017 SEARCH N=1,230



- Hispanic
- Non-hispanic Black
- Non-hispanic White
- Non-hispanic American Indian or Alaska Native
- Non-hispanic Asian*

*** includes Native Hawaiian or Other Pacific Islander**

5-study Analysis N=811 **(Global)**



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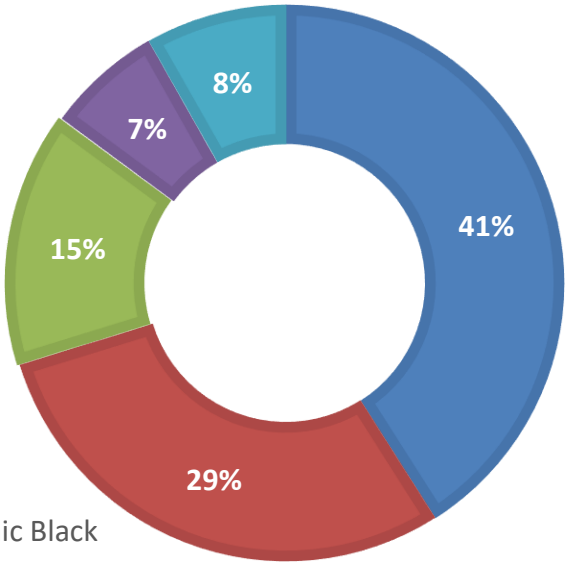
Note: Global trials included 42% US vs. 58% Non-US subjects (US subjects made up 15-68% of the study populations)

Lawrence JM, Divers J, et al, JAMA. 2021

2017 SEARCH N=1,230



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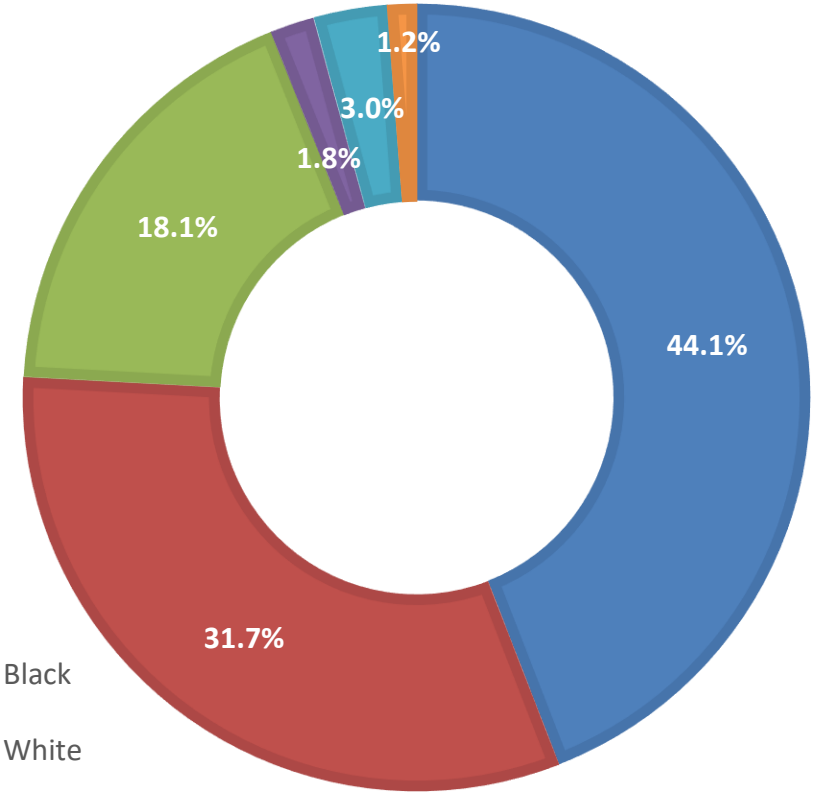
5-study Analysis N=339 **(US)**



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Lawrence JM, Divers J, et al; JAMA 2021

Conclusion

This assessment identified several gaps in the representativeness of pediatric T2D trials submitted to DDLO, but also was generally encouraging

- American Indian and Alaska Native, Asian and Native Hawaiian or other Pacific Islander patients with youth-onset T2D from the US are underrepresented based on this analysis

Lessons Learned:

- This analysis strategy could be applied to other pediatric clinical trial programs to evaluate relative representativeness in order to establish gaps and ensure better representation in clinical trials going forward

Next Steps

- Additional opportunities moving forward to address barriers in representativeness as well as overcome other challenges in conducting efficient youth-onset T2D trials
  - Increase public and stakeholder engagement: Pediatric T2D Workshop (Spring 2025)
  - Integrate diversity action plans in pediatric trial conduct (draft 2024 guidance)
  - Further collaboration with ORISE fellow in Indigenous Knowledge Fellowship program to investigate pediatric T2D trial representativeness with a focus on American Indian and Alaska Native populations

Thank You!

References

- US Census Bureau Dataset: census.gov/data/datasets/time-series/demo/popest/2020s-national-detail.html
- Bacha F, Cheng P, Gal RL, Beaulieu LC, Kollman C, Adolph A, Shoemaker AH, Wolf R, Klingensmith GJ, Tamborlane WV. Racial and Ethnic Disparities in Comorbidities in Youth With Type 2 Diabetes in the Pediatric Diabetes Consortium (PDC). Diabetes Care. 2021 Sep 2:dc210143. doi: 10.2337/dc21-0143. Epub ahead of print. PMID: 34475033.
- Currie BM, Howell TA, Matza LS, Cox DA, Johnston JA. A Review of Interventional Trials in Youth-Onset Type 2 Diabetes: Challenges and Opportunities. Diabetes Ther. 2021 Nov;12(11):2827-2856. doi: 10.1007/s13300-021-01136-5. Epub 2021 Sep 23. PMID: 34554411; PMCID: PMC8519987.
- Dabelea D, Mayer-Davis EJ, Saydah S, Imperatore G, Linder B, Divers J, et al. Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009. JAMA. 2014;311(17):1778–1786. doi: 10.1001/jama.2014.3201.
- Lawrence JM, Divers J, Isom S, Saydah S, Imperatore G, Pihoker C, Marcovina SM, Mayer-Davis EJ, Hamman RF, Dolan L, Dabelea D, Pettitt DJ, Liese AD; SEARCH for Diabetes in Youth Study Group. Trends in Prevalence of Type 1 and Type 2 Diabetes in Children and Adolescents in the US, 2001-2017. JAMA. 2021 Aug 24;326(8):717-727. doi: 10.1001/jama.2021.11165. Erratum in: JAMA. 2021 Oct 5;326(13):1331. doi: 10.1001/jama.2021.16144. PMID: 34427600; PMCID: PMC8385600.
- Perng W, Conway R, Mayer-Davis E, Dabelea D. Youth-Onset Type 2 Diabetes: The Epidemiology of an Awakening Epidemic. Diabetes Care. 2023 Mar 1;46(3):490-499. doi: 10.2337/dci22-0046. PMID: 36812420; PMCID: PMC10090267.
- Tamborlane WV, Chang P, Kollman C, Klingensmith GJ, Ruedy K, Gal RL, Van Name M, Bacha F, Willi S, Beck RW; Pediatric Diabetes Consortium. Eligibility for clinical trials is limited for youth with type 2 diabetes: Insights from the Pediatric Diabetes Consortium T2D Clinic Registry. Pediatr Diabetes. 2018 Dec;19(8):1379-1384. doi: 10.1111/pedi.12763. Epub 2018 Oct 10. PMID: 30175440.
- Wagenknecht LE, Lawrence JM, Isom S, Jensen ET, Dabelea D, Liese AD, Dolan LM, Shah AS, Bellatorre A, Sauder K, Marcovina S, Reynolds K, Pihoker C, Imperatore G, Divers J; SEARCH for Diabetes in Youth study. Trends in incidence of youth-onset type 1 and type 2 diabetes in the USA, 2002-18: results from the population-based SEARCH for Diabetes in Youth study. Lancet Diabetes Endocrinol. 2023 Apr;11(4):242-250. doi: 10.1016/S2213-8587(23)00025-6. Epub 2023 Feb 28. PMID: 36868256; PMCID: PMC10091237.


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