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Cost-Effectiveness of Population Screening for T1D: USA Application

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Trade-offs between health benefit and cost in the United States

- Budget impact analysis (BIA): *affordability,* e.g., incremental cost per person vs. standard of care
- Cost-effectiveness analysis (CEA): *value for money,* e.g., *cost per* health benefit gained vs. standard of care
- Both inform coverage and reimbursement negotiations[1-3]

1 Pearson SD, et al. Assessment of Barriers to Fair Access. Institute for Clinical and Economic Review, November 3, 2023. https://icer.org/policy-papers/fair-access- coverage-policies-in-2023/
2 Chambers JD, Chenoweth MD, Neumann PJ. Mapping US commercial payers' coverage policies for medical interventions. Am J Manag Care. 2016 Sep 1;22(9):e323-8
3 Zemplenyi A, et al. Using Real-World Data to Inform Value-Based Contracts for Cell and Gene Therapies in Medicaid. Pharmacoeconomics. 2024 Mar;42(3):319-328

Cost-effectiveness analysis

- **Quantitative evidence synthesis** method often calculated as the ratio of difference in cost to difference in effectiveness

BIM estimates often presented as "per member per month" in cost terms only

Incremental cost-effectiveness ratio (ICER) $= \Delta C / \Delta E$

$$= (C_{new\ approach} - C_{usual\ care}) / (E_{new\ approach} - E_{usual\ care})$$

- As we add resources in the numerator, ***continued spread in the denominator for efficient use of limited resources***

Economics of type 1 diabetes detection

- Screening and monitoring programs reduce DKA at onset[1-3]
- Avoiding DKA at onset alone may not be cost-effective at current spending[4]
- DKA at onset may have lifelong impact on disease course[5]
- ***What clinical benchmarks are needed to meet commonly cited cost-effectiveness thresholds?[6]***

1 Jacobsen et al. Heterogeneity of DKA Incidence and Age-Specific Clinical Characteristics in Children Diagnosed With Type 1 Diabetes in the TEDDY Study. Diabetes Care. 2022 Mar 1;45(3):624-633
2 Wentworth et al. Decreased occurrence of ketoacidosis and preservation of beta cell function in relatives screened and monitored for type 1 diabetes in Australia and New Zealand. Pediatr Diabetes. 2022 Dec;23(8):1594-1601
3 Ziegler et al. Yield of a Public Health Screening of Children for Islet Autoantibodies in Bavaria, Germany. JAMA. 2020 Jan 28;323(4):339-351
4 Meehan et al. Screening for T1D risk to reduce DKA is not economically viable. *Pediatr Diabetes.* 2015;16(8)
5 Duca et al. Diabetic Ketoacidosis at Diagnosis of Type 1 Diabetes Predicts Poor Long-term Glycemic Control. *Diabetes Care* 40(9): 1249-1255; AND Shalitin, S., et al. Ketoacidosis at onset of type 1 diabetes is a predictor of long-term glycemic control. *Pediatric diabetes*. 2018; 19(2): 320-328.
6 McQueen et al. Cost and Cost-Effectiveness of Large-Scale Screening for Type 1 Diabetes in Colorado. Diabetes Care 2020 Jul;43(7):1496-1503

Reductions in DKA and glycemic control improvements lead to cost-effectiveness

Table 4—Incremental lifetime population-level cost and clinical outcomes on the basis of projected reductions in DKA events and resulting improved HbA_{1c} from screening and follow-up

Percent reduction in DKA events (screening vs. no screening)	Proportion of patients with DKA events in screening arm	Incremental population average HbA_{1c} for patients with type 1 diabetes	Incremental DKA treatment costs at diagnosis§	Incremental other diabetes complication costs over a lifetime†	Incremental effectiveness, QALYs	Incremental total costs (ASK screening vs. no screening)‡	Incremental total costs (routine screening vs. no screening)‡
0%	46%	0.0%	$0	$0	0	$560,000	$1,641,000
20%	37%	−0.1%	−$37,000	−$506,000	17	$18,000*	$1,098,000*
40%	28%	−0.3%	−$73,000	−$965,000	33	−$478,000**	$602,000*
60%	18%	−0.4%	−$110,000	−$1,384,000	49	−$934,000**	$147,000*
80%	9%	−0.5%	−$146,000	−$1,769,000	64	−$1,355,000**	−$274,000**

§All costs are in 2018 USD and rounded to the nearest $1,000. †Other diabetes complication costs include treatment and management of annual hypoglycemic events and long-run diabetes-related complications. ‡Total costs include screening costs for 10,029 children and adolescents, DKA treatment costs for case patients diagnosed with type 1 diabetes and experience a DKA event, and all other diabetes complication costs over a lifetime for the predicted case patients who convert to diabetes. *Costs of screening offset enough for screening to be cost-effective at ≤$150,000 per QALY. **Costs of screening offset completely, resulting in a cost savings scenario.

1 McQueen et al. Cost and Cost-Effectiveness of Large-Scale Screening for Type 1 Diabetes in Colorado. Diabetes Care 2020 Jul;43(7):1496-1503

Where are we now?

- Global investment driving evidence for the "numerator"[1] (i.e., resources for screening, monitoring, treatment) with varying degrees of clarity on the "denominator" (i.e., net health benefit)
- ***What is the most efficient way to combine screening (e.g., age and frequency, IAB and GRS with combinations), monitoring, and interventions to achieve maximum health benefits?***[2]

1 Diabetic Ketoacidosis Trends and Resource Utilization at Diagnosis of Type 1 Diabetes in the United States Funded by The Leona M. and Harry B. Helmsley Charitable Trust. Grant reference number: 2202-05760. Co-PI: G. Todd Alonso, MD.
2 Clinical and Economic Optimization Platform for Type 1 Diabetes Screening Funded by Breakthrough T1D. Grant Key 2-SRA-2022-1261-S-B.

Rationale for a model

- Links intermediate outcomes (e.g., HbA1c) to long-run outcomes (e.g., survival)[1]
- Machine learning extensions "solve" for 1000s of screening strategies with multiple objectives

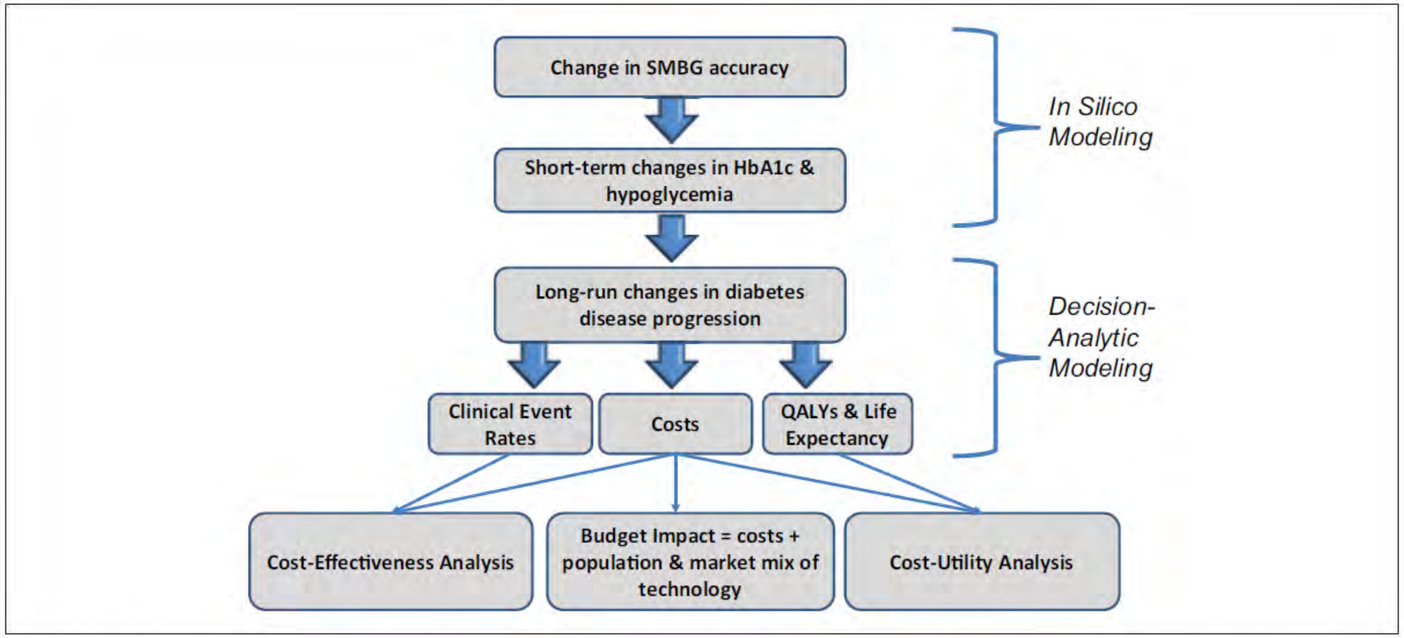

Figure 1. Evidence flow chart. Differences in the accuracy of self-monitoring blood glucose devices (SMBG) are associated with changes in HbA1c and hypoglycemia.[3] The analysis links these changes in hemoglobin A1c (HbA1c) and hypoglycemia to long-run diabetes disease progression. Disease progression in turn impacts costs, clinical event rates, and quality-adjusted life years (QALYs). Cost-effectiveness, budget impact, and cost-utility analyses are performed to investigate the long-run impact of accuracy differences in blood glucose monitoring devices.

1 McQueen RB et al. Economic value of improved accuracy for self-monitoring of blood glucose devices for type 1 diabetes in Canada. JDST 2015.

Methods overview:

Category	Description
Model	Patient-level microsimulation with multi-objective optimization (Non-dominated Sorting Genetic Algorithm [NSGA-II]) in Python
Setting and Perspective	Routine screening from a United States payer perspective
Population size simulated	100,000
Cycle length and discount rate	Annual cycle and 3% discount rate (costs and outcomes)
Time horizon	15 year time horizon for prediction of type 1 diabetes; lifetime for forecasting glycemic control benefits
Outcomes	Cost per child* as per member per month, lifetime incremental costs, and life years gained

***Cost per child are average per 100,000 children inclusive of early detection, missed cases, monitoring among high risk cases, costs for DKA events, and cost offsets from avoiding DKA events**

Key Inputs

Evidence Input Category	Strategies/sub-categories	Mean value (uncertainty included in model analyses)	Mean estimate (uncertainty included in analyses)
IAB and GRS testing costs	1. Islet autoantibody screening reimbursement ($ for 4 panel) 2. Genetic risk score testing ($)	**1. $92 (reimbursement)** **2. $50 (cost to produce)**	McQueen et al. Cost and Cost-Effectiveness of Large-Scale Screening for Type 1 Diabetes in Colorado. Diabetes Care 2020 Jul;43(7):1496-1503 Centers for Medicare & Medicaid Services. Clinical laboratory fee schedule. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/index.html. Published 2017. Accessed November, 2018
Monitoring market basket (applied to high risk)	• Coordination and communication with families and providers • Continuous glucose monitoring • HbA1c testing • Fingerstick monitoring • Primary care visits	Weighted average ranging from **$200** per year with ability to update to **$1000** per year until onset for high-risk patients	Steck AK et al. ASK Study Group. Diabetes Care. 2022 Feb 1;45(2):365-371.; Market rates for home-based glucose monitoring testing; Simmons KMW, Frohnert BI, O'Donnell HK, Bautista K, Geno Rasmussen C, Gerard Gonzalez A, Steck AK, Rewers MJ. Historical Insights and Current Perspectives on the Diagnosis and Management of Presymptomatic Type 1 Diabetes. Diabetes Technol Ther. 2023 Nov;25(11):790-799
Screening treatment effects	1. Diabetic ketoacidosis (DKA) at onset without screening 2. DKA at onset with screening, testing, monitoring strategies 3. HbA1c improvements after onset	**1. 58%** 2. Varies with **lower end fixed at 5%** 3. Varies between **0.1%-0.5%**	Alonso G et al. Diabetic Ketoacidosis at Diagnosis of Type 1 Diabetes in Colorado Children, 2010-2017. Diabetes Care. 2020 Jan;43(1):117-121; Jacobsen et al. Heterogeneity of DKA Incidence and Age-Specific Clinical Characteristics in Children Diagnosed With Type 1 Diabetes in the TEDDY Study. Diabetes Care. 2022 Mar 1;45(3):624-633; Duca LM et al.. Diabetic Ketoacidosis at Diagnosis of Type 1 Diabetes Predicts Poor Long-term Glycemic Control. Diabetes Care. 2017 Sep;40(9):1249-1255

Budget impact results

Screening strategy	DKA ratio	Screening and monitoring costs	DKA costs at diagnosis[1]	Incremental Budget Impact (per member per month)[2]
No screening	58%	$0	$6,870,000	**Reference**
Ages 2 and 6 IAB only	29.5%	$21,250,000	$3,520,000	**$1.40**
Ages 2 and 6 IAB + GRS high risk	33.7%	$5,200,000	$4,000,000	**$0.53**

[1] All costs are in 2024 USD

[2] Incremental budget impact includes onset costs with and without DKA events and screening costs based on **N=100,000** children and adolescents from ages 0-15; **N=504 T1D** cases eventually diagnosed within the first 15 years

Results are preliminary and subject to change

Lifetime cost-effectiveness results

Screening strategy	DKA ratio	Incremental population average HbA1c per patient	Other diabetes complication costs over a lifetime[1]	Incremental Effectiveness (life years)	Incremental total cost-effectiveness ratio (Screening vs. No Screening)[1,2]
No screening	58%	Reference	$284,000,000	Reference	**Reference**
Ages 2 and 6 IAB only	29.6%	-0.24%	$282,000,000	363	**$50,000 per life year gained**
Ages 2 and 6 IAB + GRS high risk	33.7%	-0.21%	$283,000,000	363	**$6,000 per life year gained**

Both cost effective at <$100,000 per life year gained[3]

[1] All costs are in 2024 USD

[2] Total costs include screening costs for **N=100,000** children and adolescents aged 0-15, T1D onset costs (with and without DKA), and lifetime diabetes complication-related costs for **N=504 T1D** cases eventually diagnosed within the first 15 years and followed for a lifetime.

[3] David J. Vanness, James Lomas, Hannah Ahn. A Health Opportunity Cost Threshold for Cost-Effectiveness Analysis in the United States. Ann Intern Med.2021;174:25-32.

Results are preliminary and subject to change

Next steps

- Online version will inform implementation and budget impact scenarios feasible to health systems around the world
- Application suggesting range of reimbursements that meet cost-effective and affordability thresholds in the U.S.[1]
- Screen and treat scenarios with use of teplizumab in practice[1]

https://t1dpredictor.diabetesgenes.org

1 Improving the Uptake and Applicability of the Clinical and Economic Optimization Platform for Type 1 Diabetes Screening. Breakthrough T1D Grant Reference 2-SRA-2024-1620-S-B.

Strengths and limitations

- Model platform “solves” for multiple objectives relevant to insurance and public health decision makers
  - Subject to inputs and data sources
- Screening effectiveness estimates from around the world will inform future iterations of the model[1-6]

1 https://www.healio.com/news/endocrinology/20240327/hybrid-closedloop-may-be-more-costeffective-than-immune-therapies-for-type-1-diabetes
2 Mital S, Nguyen HV. Cost Effectiveness of Teplizumab for Prevention of Type 1 Diabetes Among Different Target Patient Groups. Pharmacoeconomics. 2020 Dec;38(12):1359-1372
3 Sims EK et al. Screening for Type 1 Diabetes in the General Population: A Status Report and Perspective. Diabetes. 2022 Apr 1;71(4):610-623
4 https://www.kidsdiabetesscreen.com.au/#:~:text=Every%20day%20three%20children%20are,families%20in%20every%20way%20possible.
5 https://www.diabetes.org.uk/diabetes-the-basics/types-of-diabetes/type-1/type-1-diabetes-screening
6 Florian M. Karl, Christiane Winkler, Anette-Gabriele Ziegler, Michael Laxy, Peter Achenbach; Costs of Public Health Screening of Children for Presymptomatic Type 1 Diabetes in Bavaria, Germany. Diabetes Care 1 April 2022; 45 (4): 837–84

Overall summary

- Various type 1 diabetes detection strategies are cost-effective if and only if long-term benefits are demonstrated
- Incremental budget impact estimates range from $0.50 to $1.40 per member per month in added costs
- Volume-based discounts and “bundles” are expected and will improve affordability estimates

Contact information

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Other inputs

Evidence Input Category	Strategies/sub-categories	Study population	Mean estimate (uncertainty included in analyses)	Evidence Sources (key citations not inclusive of all evidence used in model)
Variation in screening method	Examples include • IAB screening without GRS or human leukocyte antigen (HLA) • IAB screening with high GRS or HLA • GRS screening alone	• The Environmental Determinants of Diabetes in the Young (TEDDY) • Ongoing validation in Type 1 Diabetes TrialNet and Type 1 Diabetes Prediction and Prevention (DIPP)	Transition probabilities vary by strategy	Ferrat, L.A., Vehik, K., Sharp, S.A. et al. A combined risk score enhances prediction of type 1 diabetes among susceptible children. Nat Med 26, 1247–1255 (2020).; Locke JM et al. Methods for quick, accurate and cost-effective determination of the type 1 diabetes genetic risk score (T1D-GRS). Clin Chem Lab Med 2020;58:e102-e4.
Optimal age and frequency of screening	Number of screenings before age 15	• Diabetes Autoimmunity Study in the Young (DAISY) • Diabetes Prediction in Skåne (DiPiS) • DIPP	Performance varies by age and frequency	Ghalwash, M. et al. (2022). "Two-age islet-autoantibody screening for childhood type 1 diabetes: a prospective cohort study." Lancet Diabetes Endocrinol 10(8): 589-596.
Diabetes-related complication costs and health benefits	• Total DKA events and DKA events avoided • Total DKA events, DKA events avoided, long-term complications, life years, and quality-adjusted life years	DCCT, EDIC, Pittsburgh Epidemiology of Diabetes Complications Studies; diabetes incidence evidence	Varies by complication	Tieder JS et al. Variation in resource use and readmission for diabetic ketoacidosis in children's hospitals. Pediatrics. 2013:peds. 2013-0359.; Shrestha et al.. Medical expenditures associated with diabetes among privately insured US youth in 2007. *Diabetes Care.* 2011;34(5):1097-1101.; Ward A et al. Direct medical costs of complications of diabetes in the United States: estimates for event-year and annual state costs (USD 2012). *Journal of medical economics.* 2014;17(3):176-183.