



MILKEN
INSTITUTE

Type 1 Diabetes Autoantibody Screening Implementation Roadmap: 2022 REPORT UPDATE

BY ERIN ROSS AND CARA ALTIMUS, PHD

THE LEONA M. AND HARRY B.
HELMSLEY
CHARITABLE TRUST

ABOUT THE MILKEN INSTITUTE

The [Milken Institute](#) is a nonprofit, nonpartisan think tank.

For the past three decades, the Milken Institute has served as a catalyst for practical, scalable solutions to global challenges by connecting human, financial, and educational resources to those who need them. Guided by a conviction that the best ideas, under-resourced, cannot succeed, we conduct research and analysis and convene top experts, innovators, and influencers from different backgrounds and competing viewpoints. We leverage this expertise and insight to construct programs and policy initiatives.

These activities are designed to help people build meaningful lives in which they can experience health and well-being, pursue effective education and gainful employment, and access the resources required to create ever-expanding opportunities for themselves and their broader communities.

About the Center for Strategic Philanthropy

The Milken Institute Center for Strategic Philanthropy advises philanthropists and foundations seeking to develop and implement transformative giving strategies.

©2022 Milken Institute

This work is made available under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs 3.0 Unported License, available at <https://creativecommons.org/licenses/by-nc-nd/3.0/>.

TABLE OF CONTENTS

- Introduction 1**
- New and Upcoming Initiatives Related to the Roadmap 1**
 - Goal 1: Develop and Refine Ambulatory Clinical Practice Guidelines 1
 - Goal 2: Promote the Continued Development, Validation, and Regulatory Authorization of Screening Assays 2
 - Goal 3: Build the Evidence Base for General Population Autoantibody Screening Design... 3
 - Goal 4: Support Efforts to Expand the Prevention–Therapeutic Pipeline..... 4
 - Supporting Goal 1: Increase Clinician Knowledge and Awareness of T1D Screening and Care Strategies 6
 - Supporting Goal 2: Improve Public Knowledge of T1D and Develop Tools to Convey Risk Accurately 6
- Additional Considerations for the Roadmap 8**
 - Access to Screening 8
 - Genetic Screening 8
 - Diversity in T1D Research 9
- Moving Forward..... 9**
 - Opportunities for Further Collaboration 9
 - Opportunities for Increased Focus 10
- Conclusion 10**
- Appendix: Essential Goals and Action Items for Achieving T1D Autoantibody Screening and Current and Upcoming Initiatives in the Community 11**
- References 14**
- Acknowledgments..... 15**
- About the Authors..... 15**



INTRODUCTION

In April 2021, the Milken Institute, with generous funding from The Leona M. and Harry B. Helmsley Charitable Trust, published a report focused on the implementation of type 1 diabetes (T1D) autoantibody screening in the general population. *Type 1 Diabetes Autoantibody Screening: A Roadmap for Pediatric Policy Implementation* contains four goals and two supporting goals, each with action items for the community to undertake (Milken Institute 2021). Although completion of the action items and achievement of the goals can each influence the field, the goals were not listed in any specific order of completion because of wide recognition in the field that progress will be iterative. Each goal stands on its own and can be undertaken at any point.

Many ongoing initiatives were working toward these goals at the time of publication, and the field has continued to make great strides within those initiatives and has launched new ones. In the second half of 2021, we conducted extensive follow-up research in the field. We interviewed 27 thought leaders and stakeholders, opened a public comment period, and hosted a public session to discuss the status of the goals and action items in the roadmap. Based on input from the field, this report update captures the continuing efforts of the community to continue toward T1D screening for the general population and identifies areas where further work or collaboration might be needed.

NEW AND UPCOMING INITIATIVES RELATED TO THE ROADMAP

GOAL 1: Develop and Refine Ambulatory Clinical Practice Guidelines

Clinical practice guidelines, developed through systematic evidence review to optimize clinical care and outcomes, do not exist for routine T1D screening for familial or for general populations. Autoantibody screening for T1D currently and typically occurs in the context of a research setting. Developing guidelines for screening in ambulatory clinical practice will aid ongoing efforts to expand current screening initiatives and implement new large-scale general population screening. Guidelines should include what age(s) to test, how many times to test, where and how sample collection occurs, how results are communicated to the family, and what happens after results are communicated.

The field has made multiple efforts to expand language included in guidance documents from specialist societies and voluntary health organizations. For example, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) led an effort to develop language suggesting screening for all first-degree relatives to be included in the upcoming 2022 American Diabetes Association (ADA) Standards of Care. This notable endeavor convened several stakeholders in the field to work together and reach a consensus on the suggested language presented to ADA. Additionally, the next issue of the International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines is currently being drafted and may include broader recommendations for autoantibody screening.

Broadening T1D autoantibody screening recommendations in guidance documents is a crucial step in developing clinical practice guidelines for the general population. Experts have agreed that utilizing a quality improvement (QI) process will ensure that the guidelines are ultimately put into practice. The T1D Exchange currently manages a Quality Improvement Collaborative aimed at gathering data on T1D treatment and outcomes to help guide providers in improving quality of care in a real-world setting (T1D Exchange Quality Improvement Collaborative n.d.). The potential exists to expand the scope of the collaborative to include screening and follow-up care. Doing so would offer an opportunity to expand evidence on screening protocols and iteratively improve upon them.

As of this writing, TrialNet will sponsor an upcoming longitudinal observational study with an aim to implement and evaluate practice guidelines for screening. The study will use comparative effectiveness methods to assess clinical practice guidelines and their impact on clinical outcomes. Results from this study could greatly influence ambulatory clinical practice guidelines moving forward.

These new activities highlight the variety of stakeholders working to expand and develop clinical practice guidelines for T1D autoantibody screening. The T1D community largely views this work as an important step on the pathway to a recommendation for general population screening. It is important to note that development must often be done in tandem with efforts to iterate and evaluate practice guidelines to ensure that the recommendations reflect best practice and the evidence base.

GOAL 2: Promote the Continued Development, Validation, and Regulatory Authorization of Screening Assays

Significant strides are being made in the development of autoantibody screening assays, and efforts to harmonize and standardize these assays are being undertaken by groups such as the Islet Autoantibody Standardization Program and the Critical Path Institute's Type 1 Diabetes Autoantibody Workshop. However, although several different assays are being used successfully in screening research studies, they have varying specifications for sensitivity and specificity. It is difficult to achieve both high sensitivity and specificity in a single assay because the specifications typically exist in a state of balance, with higher sensitivity resulting in lower specificity and vice versa. Experts believe that the availability of scalable, fit-for-purpose, Food and Drug Administration (FDA)-authorized assays for both screening and confirmation of diagnosis will accelerate the issuance of a recommendation for pediatric general population screening by policy groups and specialist societies.

To this end, the Critical Path Institute is coordinating a multistakeholder effort to develop analytical parameters for assays suitable for screening. Additionally, an ongoing comparison assay study coordinated by TrialNet is investigating seven assay platforms with blind sample testing at academic centers. Janssen Pharmaceuticals is leading industry involvement in this area. They are investing in novel assay development and implementing them into central labs with consideration of training, workflow, equipment needs, and reimbursement process.

The Enable Antibody Detection by Agglutination (ADAP) assay is being used by the T1Detect screening program and is being considered for use in the upcoming JDRF-funded Australian general population screening pilot program. This multiplex assay can be performed on dried blood spot samples and has shown high sensitivity when tested on known T1D samples. Implementing use of the assay in these programs will enable important iterative refinement of the assay and development and optimization of protocols for its usage in the general population.

Stakeholders agree that identifying scalable and fit-for-purpose assays for T1D autoantibody screening is crucial to implementing general population screening. The current work to compare existing assays and develop analytical parameters will support this goal. The concurrent use and field testing of the assays provide important opportunities for feedback and assay improvement.

GOAL 3: Build the Evidence Base for General Population Autoantibody Screening Design

To issue a recommendation for general population autoantibody screening, policy groups such as the US Preventive Services Task Force or the American Academy of Pediatrics will require data on the proposed intervention, in this case, screening in the general population in the United States. Although large general population cohort screening studies in Europe and smaller studies in the US are being conducted, current screening for T1D in the US has mainly focused on family members of people with T1D in the context of research studies. These studies have contributed instrumentally to advances in screening and therapeutics. However, these studies alone cannot build the evidence base needed to support a universal screening recommendation in the US because the evidence derived is not from the general population. In addition, familial screening is estimated to capture only approximately 15 percent of T1D cases; the other 85 percent are people with no family history of the disease (Tuomilehto 2013). Larger general population screening studies are needed to assess the long-term harms and benefits of screening in the general population. Although data from international studies are important, data from US studies will be weighted more strongly by organizations that issue recommendations for the US.

In early 2021, JDRF launched T1Detect, which offers autoantibody screening at low or no cost to anyone, education and awareness resources, and the opportunity for individuals to connect with TrialNet and potentially participate in clinical research (T1Detect—JDRF n.d.). Currently, most participants have some current connection to T1D, but the program strives to expand its reach. In addition to existing general population studies that screen all individuals for islet autoantibodies, such as Autoimmunity Screening for Kids (ASK) (run by the Barbara Davis Center) and T1Detect, other studies employ a layered testing approach that conducts genetic testing then follows up with autoantibody testing based on genetic risk score.

Support for screening programs in Europe is increasing, which will build the evidence base. For example, Novo Nordisk supports screening efforts in Scandinavia through bolstering national screening programs and increasing clinical trial participants. Although these efforts will not build

evidence specific to the US population, they will build the broader evidence base and identify opportunities to improve the procedures and technology in use.

Groups that review and make policy recommendations also consider not only the feasibility and efficacy of screening to identify individuals at risk for T1D but also the harms and benefits of the screening process, including risk identification, the screening test, a confirmatory diagnosis, physiological stress and anxiety, and treatment options. In order for there to be a recommendation for screening from policy groups and payors, there will need to be additional data on the harms and benefits of screening for T1D autoantibodies. Several stakeholders expressed the need for a tool to capture and measure this type of information, and researchers are beginning to address this need in current and upcoming studies. T1D Exchange believes that it can generate data on long-term harms and benefits of screening via its patient registry by augmenting the current scope and expanding the data that the registry captures.

The ongoing and new general population screening studies in the US and Europe will expand the evidence base for the feasibility and efficacy of screening for T1D. They will also provide important insight into the design and implementation of future large-scale screening programs, collecting data on the long-term harms and benefits of screening.

GOAL 4: Support Efforts to Expand the Prevention–Therapeutic Pipeline

Currently, there are no FDA-approved T1D prevention or cure therapies to offer to people who are positive for multiple T1D autoantibodies. Voluntary health organizations such as ADA and other groups that write policy have indicated that this lack of prevention therapies precludes recommendations for general population screening. When a therapy(ies) becomes available, the incentive to recommend screening will increase because disease progression can be halted or significantly delayed.

Provention Bio is working to address the FDA's complete response letter to its application to bring teplizumab to market, which offers promise for the field. This therapeutic has been shown to delay the clinical onset of T1D by a median of three years after a single course, which the FDA Advisory Committee deemed clinically significant—confirming the belief that delay of symptomatic T1D can yield measurable health outcomes (Herold 2019). The submission is in the final stage of the Biologics License Application (BLA), and a decision is expected in mid-2022. Additionally, Novartis is evaluating a therapeutic for new onset T1D in clinical trials, and like other industry stakeholders, has expressed a potential desire to move into the stage 1 and 2 prevention space. There is hope that the teplizumab data and FDA analysis will streamline future therapeutic development focused on prevention through enabling more efficient clinical trial designs.

Crucial to this pipeline for the development and refinement of prevention therapeutics is adequate participation in clinical trials. T1D Exchange and its partners have launched initiatives to accelerate clinical trial enrollment, which will eventually include prevention trials. Patient advocacy groups play

a critical role in bridging communication between clinical research and people living with T1D and their families.

Most stakeholders agree that an FDA-approved therapeutic for prevention will transform the field. Further, the efforts to increase clinical trial participation may lead to a swell of activity as more industry stakeholders move into the stage 1 and 2 T1D prevention space.

FIGURE 1: CURRENT AND UPCOMING INITIATIVES RELATED TO ORIGINAL ROADMAP GOALS 1-4

<p>GOAL 1</p> <p>Develop and refine ambulatory clinical guidelines</p>	<p>GOAL 2</p> <p>Promote the continued development, validation, and regulatory authorization of screening assays</p>	<p>GOAL 3</p> <p>Build the evidence base for general population autoantibody screening design</p>	<p>GOAL 4</p> <p>Support efforts to expand the prevention-therapeutic pipeline</p>
<p>Potential to expand scope of existing Quality Improvement Collaborative managed by the T1D Exchange</p>	<p>Critical Path Institute is coordinating a multistakeholder effort to develop analytical assay parameters for assays suitable for screening</p>	<p>JDRF launched T1Detect, which offers autoantibody screening at low or no cost to anyone and provides education and awareness resources.</p>	<p>Prevention Bio is working to bring teplizumab to market to delay onset of clinical T1D</p>
<p>NIDDK led an effort to develop language suggesting screening for all first-degree relatives to be included in the ADA Standards of Care</p>	<p>Ongoing comparison assay study investigating seven assay platforms with blind sample testing</p>	<p>Novo Nordisk supports screening efforts in Scandinavia, national screening programs, and increasing clinical trial participation</p>	<p>Many therapeutics for new onset T1D are being evaluated in clinical trials</p>
<p>Janssen is developing a mock RUSP application for genetic screening for T1D</p>	<p>The Australian general population screening program is considering use of the Enable ADAP assay</p>	<p>T1D Exchange has potential to augment the current scope and expanding the data that the patient registry captures to generate data on long-term harms and benefits of screening</p>	
<p>Next ISPAD guidelines may include broader recommendations for autoantibody screening</p>	<p>Janssen invests in novel assay development and implementation into central labs</p>		
<p>TrialNet sponsored study with aim to implement and evaluate clinical practice guidelines for screening and follow-up</p>			

Source: Milken Institute 2022

SUPPORTING GOAL 1: Increase Clinician Knowledge and Awareness of T1D Screening and Care Strategies

Currently, pediatricians and other child-health providers do not routinely screen or test for T1D or monitor at-risk individuals for disease progression. This practice reduces the chance of detecting early T1D symptoms, resulting in the possible onset of diabetic ketoacidosis (DKA) and severe illness. Increased clinician awareness of T1D, symptoms, and current screening opportunities would lead to more rapid and less traumatic diagnosis for many patients. In addition, clinicians' close contact with patients positions them to identify people with familial risk and educate all families on T1D, screening opportunities, and available therapies.

Many continued and new efforts to raise awareness of the early T1D symptoms and the importance of T1D autoantibody screening are under way. For example, JDRF offers accredited and non-accredited awareness resources through Med-IQ and will begin pilot programs to raise clinician awareness of screening and provide insight on clinical practice guidelines. A parent advocate secured grant funding through the Pennsylvania Department of Health to develop continuing medical education (CME) modules for early childhood educators and daycare providers. Across the country in California, EASE T1D successfully advocated for the inclusion of its T1D symptom awareness video in a Kaiser Permanente internal newsletter. Further, the Barbara Davis Center's "ASK the Experts" platform serves as a central resource for both providers and families about screening, risk, and next steps for care and monitoring (Ask the Experts n.d.). Industry stakeholders are contributing to these efforts. Provention Bio developed a website for providers to learn about T1D and screening for autoantibodies.

Although these efforts represent progress toward this critical supporting goal, they are largely happening independently; their positive effects would be compounded if coordinated by a single or fewer larger campaigns. The increased focus of multiple types of stakeholders on increasing clinician awareness and resources for T1D is notable and indicative of the community's acknowledgment of the importance of achieving this goal.

SUPPORTING GOAL 2: Improve Public Knowledge of T1D and Develop Tools to Convey Risk Accurately

General public awareness of diabetes is heavily skewed toward T2D, leading to many misconceptions about T1D, its causes, and who is affected. General public awareness and knowledge of screening and monitoring procedures are also needed to increase the acceptance of screening.

Patient advocacy groups continue their vital work and ongoing campaigns to raise awareness about T1D symptoms and screening opportunities. In addition to supporting people living with diabetes and their families during and after diagnosis, JDRF is funding the development of an online calculator to determine the risk of T1D based on genetics, autoantibody status, and family history. Beyond Type 1 aims to reduce the stigma associated with T1D and increase public awareness of T1D symptoms. It has received funding to begin the next phase of its Warning Signs Awareness campaign to reduce DKA by increasing public awareness of T1D signs and symptoms.

Many other initiatives are occurring. T1D Exchange is interested in using its patient registry and online community to expand the reach of public messaging and is partnering with other stakeholders to develop this messaging. Provention Bio has developed a companion website to its provider website for individuals to learn about screening for autoantibodies. EASE T1D successfully advocated for a state bill in California that requires public schools to send T1D awareness information to every parent with children in the public school system. The literature will be developed in conjunction with experts and provided electronically to reduce costs (EASE T1D n.d.). Finally, ADA is considering options, such as a smartphone application, to make its Standards of Medical Care more accessible to the public.

These efforts to reach the general public could raise awareness of screening opportunities, reduce the incidence of DKA, and identify individuals eligible for clinical trials. Patient advocacy groups already working in this space are being joined by industry and other new initiatives. Increased coordination among them could facilitate progress toward achieving this goal.

FIGURE 2: CURRENT AND UPCOMING INITIATIVES RELATED TO ORIGINAL ROADMAP SUPPORTING GOALS 1 AND 2

SUPPORTING GOAL 1 Increase clinician knowledge and awareness of T1D screening and care strategies	SUPPORTING GOAL 2 Improve public knowledge of T1D and develop tools to convey risk accurately
JDRF offers accredited and non-accredited awareness resources through Med-IQ	T1D Exchange is partnering with other stakeholders to build T1D screening messaging
JDRF will begin pilot programs to raise clinician awareness of screening and provide insight on clinical practice guidelines	T1D Exchange is interested in using its patient registry to expand reach of public messaging
CME modules were developed through PA Dept of Health grant funding	JDRF educates the public about T1D and T1D screening opportunities
Provention Bio developed a website to share more information on T1D and screening for autoantibodies with providers	Provention Bio has developed a website for individuals to learn about screening for autoantibodies
EASE T1D awareness video is included in internal newsletter for KP	EASE T1D advocated for a state bill in CA to require distribution of T1D awareness information to parents
The Barbara Davis Center “ASK the Experts” platform provides answers to clinicians’ and families’ questions about screening, risk, and care	JDRF to fund development of online calculator for determining T1D risk
	Beyond Type 1 to begin next phase of Warning Signs Awareness campaign
	ADA is looking for ways to increase the public’s access to the Standards of Medical Care

Source: Milken Institute 2022

ADDITIONAL CONSIDERATIONS FOR THE ROADMAP

Our follow-up interviews and additional outreach to stakeholders in the community highlighted a few more areas for the field to consider. These topics are covered briefly or tangentially in the original roadmap, but they bear further examination in the current landscape.

Access to Screening

The original roadmap acknowledged the key role of payers. For pediatric services, in particular, individual insurers have varying requirements. Affordable Care Act (ACA) marketplace insurance plans are required to cover essential pediatric preventive care services outlined in the Bright Futures Periodicity Schedule. Medicaid plans are required to provide Early Periodic Screening, Diagnosis, and Treatment services and follow a nationally recognized pediatric periodicity schedule (Early and Periodic Screening, Diagnostic and Treatment | Medicaid n.d.). Public and private insurers can add and cover additional services. To make these decisions, payers require evidence in specific data sets and must consider many aspects of the service. These considerations include cost/benefit analysis, what can be offered to individuals who screen positive for a condition, and resources needed to start and implement a service. Multiple groups are evaluating cost-effectiveness models, and early learnings indicate that thinking on this topic needs to shift from just cost savings at diagnosis to assurance against negative outcomes for the duration of the disease. The next steps for this work on cost effectiveness will require collaboration across programs to apply the modeling frameworks effectively. Although experts agree on the need for additional research in these areas, efforts are under way to engage payers in the space. JDRF is discussing screening and disease modifying therapies with payers. Enable is submitting test claims to various payers to learn more about the landscape.

Genetic Screening

Genetics has been identified as a key factor in predicting the risk of T1D. Many stakeholders suggested expanding the roadmap scope to include the role of genetic screening in the path to general population screening for T1D. Several general population studies utilize a layered screening approach. In these studies, participants undergo genetic screening, and those with a high genetic risk score receive follow-up autoantibody testing. Genetic screening may be more efficient and less costly than autoantibody screening, and a model is already in place: Nearly all states screen newborns for all conditions on the Recommended Uniform Screening Panel (RUSP) (Recommended Uniform Screening Panel n.d.). It is believed that a layered screening approach could increase payer uptake because of lower costs. However, genetic screening alone will miss a proportion of individuals at risk for T1D. Janssen Pharmaceuticals is examining the layered screening approach as a pathway to general population screening and is developing a mock RUSP application for genetic screening for T1D. Further study is needed of the financial impact of this approach and its viability for payers.

Additionally, genetic screening can help identify participants for specific trials, such as primary prevention trials, and can serve as a tool for precision medicine for T1D care. Experts have noted that the time between identification of risk and progression to clinical T1D underscores the importance of access to follow-up education and monitoring programs and materials. Finally, the appetite of parents and patients for additional genetic screening should be considered as concerns about sensitive medical information ending up in the public domain increase.

Diversity in T1D Research

T1D has a genetic component, and the field must seek genetic diversity in clinical trials. Racial/ethnic representation in clinical trials should reflect racial/ethnic representation in the general population. Research has shown inequity in racial representation in randomized controlled trials for diabetes technology (Halis K. Akturk 2021) and poorer glycemic control and diabetes technology use in minority populations (Shivani Agarwal 2020).

Studies on screening and other aspects of diabetes care must enroll a diverse population of patients and give patients and their families more control of participation and data—not only to prioritize equity but also to yield greater insight into disease progression. Further, education should consider the needs of underrepresented minority populations to a greater extent, potentially by tailoring interventions and campaigns.

MOVING FORWARD

Our follow-up research clearly illustrates the community's continued and even increased activity toward general population autoantibody screening. When layered against the original roadmap, this research identifies two important findings: 1. there are places where this increased activity could lend itself to further collaboration and 2. there are places where increased activity has emphasized the need for increased focus.

Opportunities for Further Collaboration

Many efforts to increase clinician and public awareness of T1D symptoms and screening opportunities (Supporting Goals 1 and 2) are under way. While large and/or multiple stakeholders have undertaken some efforts, many are individual efforts siloed into a geographical region or audience. Often, groups that undertake these efforts have limited funding and reach. Increased endeavors by larger groups in the T1D community to pull together these efforts and include evidence-based behavior change techniques and strategies in their initiatives could result in more streamlined initiatives, consistent messaging, and even greater outcomes.

Experts agree that field-tested clinical practice guidelines will be necessary for payers to cover autoantibody screening (Goal 1). Several groups are modeling and field-testing clinical practice guidelines. Increased collaboration among these groups could result in the use of existing screening opportunities to perform QI on practice guidelines for screening and follow-up education and monitoring. The community could benefit from a neutral party driving this type of work.

Payers will also consider the cost-effectiveness of screening beyond the known cost savings of DKA prevention. Researchers are gathering, modeling, and determining the implications of health economics data for T1D screening. If the field can reach a consensus on a publicly available, global model to assess the cost-effectiveness of screening, then payers will have valuable evidence to inform their deliberations. Stakeholders know that different types of evidence will likely play different roles in health economics decisions. The community could streamline efforts through prioritizing questions and modeling to enable more intentional building of the evidence base.

Opportunities for Increased Focus

While all goals included on the original roadmap have seen additional or increased activity, some areas within the original roadmap would benefit from increased focus. The field acknowledges that multiple screening assays will likely be in use as general population screening for autoantibodies is implemented and scaled up. Experts have indicated that clinical and analytical parameters need further refinement and development. A collaboration led by clinical experts to establish goals for the community and develop and implement standardization efforts would help ensure the field's readiness to implement screening in the general population screening.

Many ongoing screening studies are building the evidence base needed to evaluate general population screening recommendations. Increased coordination among studies and increased reach will enhance the development of approaches to scaling up screening, as well as of standardized protocols and data analysis.

CONCLUSION

The T1D community consists of stakeholders from many different fields committed to diabetes care, cure, and prevention. One goal is to screen for autoantibodies in the general population to prevent DKA and achieve better health outcomes. Autoantibody screening will also identify clinical trial participants and drive the development of disease-modifying therapeutics. The action items identified in our original March 2021 report for achieving autoantibody screening in the general population are multifaceted and require stakeholder engagement from across the community. The follow-up research we conducted illustrates the many initiatives under way and planned. The community has been making great strides toward this goal, and continued collaboration and coordination will ensure that the field continues to move forward.

APPENDIX: Essential goals and action items for achieving T1D autoantibody screening and current and upcoming initiatives in the community

GOAL	ACTION ITEM	CURRENT AND UPCOMING INITIATIVES
<p>Goal 1: Develop and refine ambulatory clinical practice guidelines</p>	<ol style="list-style-type: none"> 1. Initiate quality improvement (QI) for T1D autoantibody screening 2. Strengthen the relationship between clinical communities and groups that issue guidelines 3. Model, develop, and field-test clinical practice guidelines 	<ul style="list-style-type: none"> • Potential to utilize existing Quality Improvement Collaborative housed within the T1D Exchange • Multiple stakeholders joined an NIDDK-led effort to develop language that suggests inclusion of screening for all first-degree relatives in the ADA standards of care • Janssen is developing a mock RUSP application for genetic screening for T1D • Next ISPAD guidelines may expand recommendations for autoantibody screening • TrialNet to sponsor a study with an aim to implement and evaluate clinical practice guidelines for screening and follow-up
<p>Goal 2: Promote the continued development, validation, and regulatory authorization of screening assays used for ambulatory care</p>	<ol style="list-style-type: none"> 4. Evaluate quality assurance parameters for autoantibody screening assays 5. Initiate key stakeholder assay coalition to prioritize features of diagnostic and screening assays 6. Support development of assay technologies 7. Support refinement of assays through current screening studies 	<ul style="list-style-type: none"> • Critical Path Institute is coordinating a multistakeholder effort to develop analytical assay parameters for assays suitable for screening • An ongoing comparison assay study is investigating seven assay platforms with blind sample testing at academic centers • The Australian general population screening pilot program is considering use of the Enable ADAP assay • Janssen is investing in novel assay development and implementing them into central labs.

<p>Goal 3: Build the evidence base for general population autoantibody screening design</p>	<p>8. Design and implement a large-scale, general population cohort screening study model</p> <p>9. Coordinate partnerships and develop improved infrastructure for RCTs for therapeutics</p>	<ul style="list-style-type: none"> • JDRF launched T1Detect, which offers autoantibody screening at low or no cost to anyone and provides education and awareness resources • Novo Nordisk is supports screening efforts in Scandinavia, national screening programs, and increasing clinical trial participants • T1D Exchange believes that it can generate data on long-term harms and benefits of screening via its patient registry by augmenting the current scope and expanding the data that the registry captures.
<p>Goal 4: Support efforts to expand the prevention-therapeutic pipeline</p>	<p>10. Support development and refinement of disease-modifying therapeutics for T1D</p>	<ul style="list-style-type: none"> • Provention Bio is working to bring teplizumab to market to delay onset of clinical T1D • Multiple therapeutics for new onset T1D are being evaluated in clinical trials
<p>Supporting Goal 1: Increase clinician knowledge and awareness of T1D screening and care strategies</p>	<p>11. Develop T1D clinician awareness campaign</p>	<ul style="list-style-type: none"> • JDRF offers accredited and non-accredited awareness resources through Med-IQ • JDRF will begin pilot programs to raise clinician awareness of screening and provide insight on clinical practice guidelines • CME modules were developed through PA Dept of Health grant funding • Provention Bio developed a website to share with providers more information about T1D and screening for autoantibodies • The EASE T1D awareness video is included in internal newsletter for Kaiser Permanente • The Barbara Davis Center “ASK the Experts” platform provides answers to clinicians’ and families’ questions about screening, risk, and care
<p>Supporting Goal 2: Improve public knowledge of T1D and develop tools to convey risk accurately</p>	<p>12. Pilot infrastructure to support clinician awareness of screening opportunities</p> <p>13. Coordinate partnerships between clinician groups and current screening programs</p> <p>14. Develop consensus on T1D public messaging</p>	<ul style="list-style-type: none"> • T1D Exchange is partnering with other stakeholders to develop public messaging • T1D Exchange is interested in using its patient registry to expand the reach of public messaging

15. Implement a comprehensive communication strategy for screening

16. Develop and implement T1D education materials

- JDRF educates the public about T1D and T1D screening opportunities
- JDRF is funding development of an online calculator for determining risk of T1D based on genetics, autoantibody status, and family history
- Provention Bio has developed a website for individuals to learn about screening for autoantibodies
- EASE T1D advocated for a state bill in CA to require that every household with children in the public school system receive T1D awareness information
- ADA is looking for ways to increase the public's access to the Standards of Medical Care
- Beyond Type1 will begin next phase of Warning Signs Awareness campaign

REFERENCES

- n.d. *Ask the Experts*. Accessed November 2021. <https://www.askhealth.org/experts>.
- n.d. *Early and Periodic Screening, Diagnostic and Treatment | Medicaid*. Accessed November 2021. <https://www.medicaid.gov/medicaid/benefits/early-and-periodic-screening-diagnostic-and-treatment/index.html>.
- n.d. *EASE T1D*. Accessed November 2021. <https://www.easet1d.org/copy-of-ease-t1d-resolution>.
- Akturk, Halis K., Sivani Agarwal, Lillian Hoffecker, Viral N. Shah. 2021. "Inequality in Racial-Ethnic Representation in Randomized Controlled Trials of Diabetes Technologies in Type 1 Diabetes: Critical Need for New Standards." *Diabetes Care* e121-123.
- Herold, Kevan C., Brian N. Bundy, S. Alice Long, Jeffrey A. Bluestone, Linda A. DiMeglio, Matthew J. Dufort, Stephen E. Gitelman, et al. 2019. "An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes." *The New England Journal of Medicine* 603-613.
- n.d. *Recommended Uniform Screening Panel*. Accessed November 2021. <https://www.hrsa.gov/advisory-committees/heritable-disorders/rusp/index.html>.
- Ross, Erin and Cara Altimus. *Type 1 Diabetes Autoantibody Screening: A Roadmap for Pediatric Policy Implementation*. Milken Institute. 2021. <https://milkeninstitute.org/reports/diabetes-pediatric-autoantibody-screening>.
- Agarwal, Shivani, Lauren G. Kanapka, Jennifer K. Raymond, Ashby Walker, Andrea Gerard-Gonzalez, Davida Kruger, Maria J. Redondo, et al. 2020. "Racial-Ethnic Inequity in Young Adults with Type 1 Diabetes." *Journal of Clinical Endocrinology and Metabolism* e2960-e2969.
- n.d. *T1D Exchange Quality Improvement Collaborative*. Accessed November 2021. <https://t1dexchange.org/quality-improvement/collaborative/>.
- n.d. *T1Detect—JDRF*. Accessed November 2021. <https://www.jdrf.org/t1d-resources/t1detect/>.
- Tuomilehto, Jaako. 2013. "The Emerging Global Epidemic of Type 1 Diabetes." *Current Diabetes Reports* 795-804.

ACKNOWLEDGMENTS

We are grateful for the generous support of The Leona M. and Harry B. Helmsley Charitable Trust.

ABOUT THE AUTHORS

Cara Altimus is a senior director at the Milken Institute Center for Strategic Philanthropy, where she leads the Center's biomedical philanthropy practice. A PhD neuroscientist, Altimus has advised individual philanthropists and foundations on the state of research for various areas, including neurodegenerative disease and mental health, to identify opportunities where their capital can make the biggest impact. With more than a decade of experience in neuroscience research, including neurological devices, psychiatric illness, learning, and memory, as well as sleep and circadian rhythms, Altimus has led Center projects ranging from the development of a philanthropic drug development program for neurodegenerative disease to a large patient-perspectives study for depression and bipolar research. Altimus holds a bachelor's degree in genetics from the University of Georgia and a doctorate in biology from Johns Hopkins University.

Erin Ross is an associate director on the Center for Strategic Philanthropy's biomedical science team, currently leading the Center's work on type 1 diabetes screening implementation. She has significant experience developing survey classification matrices and coding and has contributed to multiple Milken Institute publications. With a degree in biochemistry, Ross worked in the life science industry for more than 17 years building strong skills in scientific research, writing, and communication. Her expertise in endotoxin detection assays and primary cell culture contributed to the growth and quality enhancement of multiple product lines during her time in the industry.



MILKEN
INSTITUTE

