Yes, current evidence suggests that **combining genetic risk scoring with autoantibody screening** can improve **early detection of type 1 diabetes** and may be **cost-effective** at the population level, but **implementation barriers** such as assay costs, logistics, and psychosocial impacts remain significant.

1. Introduction

Early detection and prevention of type 1 diabetes (T1D) have become increasingly feasible due to advances in genetic risk scoring (GRS) and islet autoantibody (IA) screening. Recent studies highlight that while most T1D cases occur in individuals without a family history, combining GRS with IA screening can enhance risk stratification and enable timely intervention, potentially reducing disease severity and healthcare costs (Khine & Quandt, 2025; Rewers, 2025; Calderone et al., 2026; Bonifacio & Ziegler, 2025; So et al., 2021; Narayan et al., 2025). Population-based programs such as DIPP, BABYSCREEN, GPPAD, Fr1da, ASK, CASCADE, and PLEDGE have piloted these approaches internationally (Khine & Quandt, 2025; Rewers, 2025; Calderone et al., 2026). Health-economic analyses indicate that such combined screening strategies can be cost-effective if they reduce diabetic ketoacidosis (DKA) at diagnosis and long-term complications (Rewers, 2025; Calderone et al., 2026). However, challenges persist regarding implementation logistics, assay standardization, cost-effectiveness across diverse populations, and psychosocial impacts of early diagnosis (Khine & Quandt, 2025; Rewers, 2025; Bonifacio & Ziegler, 2025; Johnson et al., 2025). This review synthesizes the clinical and economic evidence for population-level genetic risk scoring combined with autoantibody screening for early T1D detection and prevention, explicitly addressing implementation barriers.

Is population-level genetic risk scoring combined with autoantibody screening effective and cost-effective for early detection of type 1 diabetes? N = 6

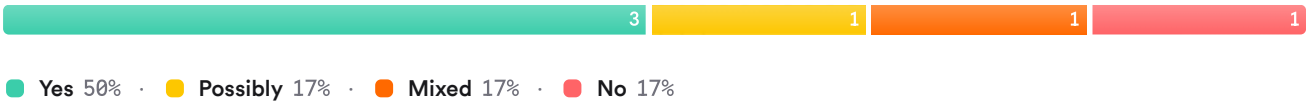

FIGURE 0 Consensus meter: Effectiveness and cost-effectiveness of combined genetic risk scoring and autoantibody screening for early T1D detection.

2. Methods

A comprehensive literature search was conducted across over 170 million research papers in Consensus—including Semantic Scholar, PubMed, and other sources—using targeted queries on genetic risk scoring, islet autoantibody screening, health-economic evaluation, implementation barriers, and related terms. A total of 3580 papers were identified; after multi-phase filtering for relevance and quality (including citation graph traversal), 86 papers were screened for eligibility. The final review includes the top 50 most relevant papers.

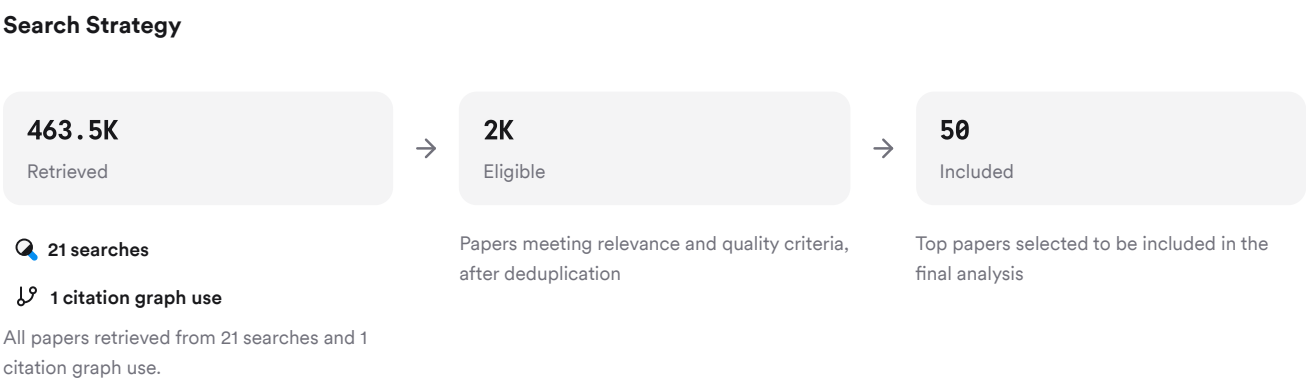

FIGURE 1 Flow diagram of paper identification to inclusion in this review.

Six unique search strategies were executed to capture foundational concepts, clinical evidence synthesis, health-economic evaluation, implementation barriers, alternative terminology use (e.g., 'polygenic risk scores'), and critiques/limitations.

3. Results

3.1 Clinical Utility of Combined Genetic Risk Scoring and Autoantibody Screening

Multiple studies confirm that combining GRS with IA testing improves identification of individuals at high risk for T1D compared to either method alone (Khine & Quandt, 2025; Calderone et al., 2026; Bonifacio & Ziegler, 2025; So et al., 2021; Narayan et al., 2025; Aamodt & Powers, 2025). Prospective cohort studies (e.g., TEDDY, DIPP) show that nearly all individuals with multiple autoantibodies progress to clinical disease; adding GRS further refines prediction by identifying those most likely to seroconvert or progress rapidly (So et al., 2021; Narayan et al., 2025; Aamodt & Powers, 2025). General population programs like Fr1da (Germany), ASK (USA), GPPAD (Europe), CASCADE/PLEDGE/PRiMeD (USA), and pilot studies in Australia demonstrate feasibility at scale (Khine & Quandt, 2025; Rewers, 2025; Calderone et al., 2026).

3.2 Health-Economic Evidence & Cost-Effectiveness

Cost-effectiveness analyses suggest that population-level screening is justified if it reduces DKA incidence at diagnosis and long-term complications (Rewers, 2025). For example, Fr1da reduced DKA at diagnosis by 61% in Germany; US estimates suggest hundreds of thousands could be identified presymptomatically (Rewers, 2025). Combining T1D screening with other conditions (e.g., celiac disease) further improves cost-effectiveness (Rewers, 2025). However, economic viability depends on test costs (HLA/GRS/IA), prevalence rates, healthcare system efficiency, follow-up protocols, and integration into existing public health services (Rewers, 2025; Calderone et al., 2026).

3.3 Implementation Barriers

Key barriers include logistical challenges integrating screening into routine care (e.g., primary care time constraints), assay standardization across labs/countries, psychological impacts on families/children identified as "at-risk," need for ongoing monitoring/counseling resources, disparities in predictive accuracy across ancestries/populations due to PRS limitations or HLA diversity, ethical concerns about labeling asymptomatic children as "pre-diabetic," data privacy issues with genetic information storage/use, and lack of clear guidelines for follow-up management (Khine & Quandt, 2025; Bonifacio & Ziegler, 2025; Johnson et al., 2025).

3.4 Advances & Limitations

Technological advances have improved IA assay sensitivity/specificity (e.g., multiplex platforms), while PRS models now incorporate ancestry-specific variants to improve generalizability (Narayan et al., 2025; Ortega et al., 2025). However, predictive accuracy remains lower in non-European populations due to underrepresentation in GWAS datasets (Ortega et al., 2025; Wang et al., 2022). The psychosocial impact—especially anxiety from being labeled "at-risk"—is a major concern among providers/families (Johnson et al., 2025), highlighting the need for education/interventions alongside technical solutions.

Results Timeline

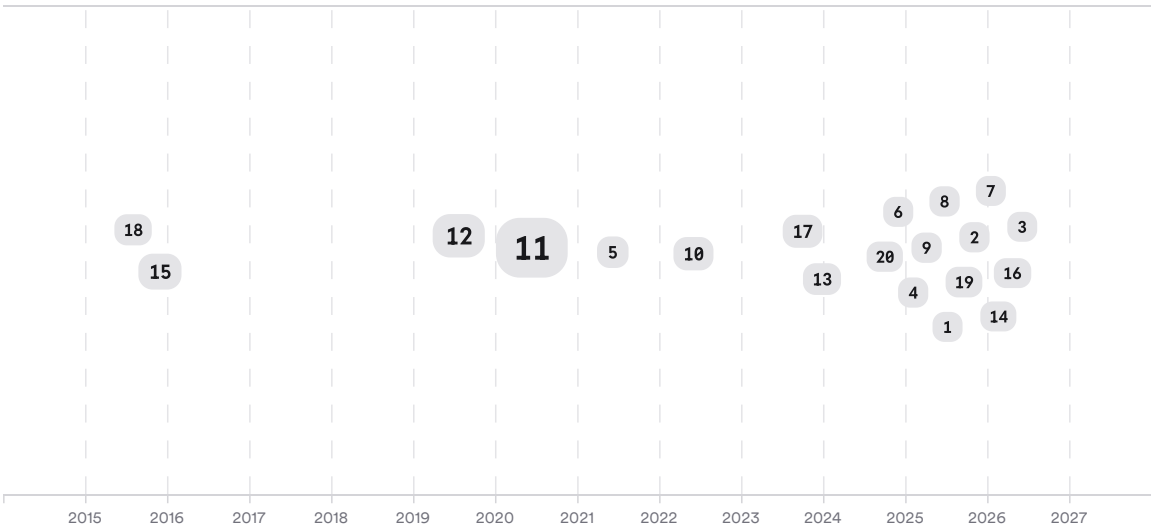

FIGURE 2 Timeline showing evolution of clinical utility studies and health-economic evaluations for combined genetic/autoantibody T1D screening. Larger markers indicate more citations.

Top Contributors

Type	Name	Papers
Author	E. Bonifacio	(So et al., 2021)
Author	Anette-Gabriele Ziegler	(So et al., 2021)
Author	Marian J. Rewers	(Rewers, 2025)
Journal	*Diabetes Obesity & Metabolism*	(Rewers, 2025; So et al., 2021)
Journal	*Current Diabetes Reports*	(Khine & Quandt, 2025)
Journal	*Children*	(Calderone et al., 2026)

FIGURE 3 Authors & journals that appeared most frequently in the included papers.

4. Discussion

The literature demonstrates strong support for the clinical value of combining GRS with IA screening to identify individuals at high risk for T1D before symptom onset—enabling earlier intervention with therapies like teplizumab or structured education to prevent DKA/severe onset (Khine & Quandt, 2025; Rewers, 2025; Bonifacio & Ziegler, 2025). Cost-effectiveness is context-dependent but generally favorable when programs are well-integrated into public health systems or combined with other screenings (Rewers, 2025). However, real-world implementation faces substantial hurdles: logistical integration into primary care workflows; ensuring assay quality/standardization; addressing disparities in predictive accuracy across ancestries; managing psychosocial consequences; providing adequate counseling/follow-up resources; navigating ethical/data privacy concerns; and establishing clear guidelines for action after positive screens (Khine & Quandt, 2025; Bonifacio & Ziegler, 2025; Johnson et al., 2025).

The evidence base is strongest from European/North American cohorts—limiting generalizability globally—and there are gaps regarding long-term outcomes/costs beyond DKA reduction or initial diagnosis stage. While technological advances continue to improve feasibility/costs of both GRS/IA assays—and new therapies may shift cost-benefit calculations—the field must address equity/access issues before recommending universal adoption.

Claims & Evidence Table

Claim	Evidence Strength	Reasoning	Papers
Combined GRS + IA screening improves early detection vs either alone	Strong	Multiple large-scale cohort/program data show improved identification/prediction	(Khine & Quandt, 2025; Calderone et al., 2026; Bonifacio & Ziegler, 2025; So et al., 2021)
Population-level screening reduces DKA/severe onset	Strong	Programs like Fr1da show >60% reduction in DKA at diagnosis	(Rewers, 2025)
Cost-effectiveness depends on test costs/prevalence/system efficiency	Moderate	Economic models show favorable results only under certain cost/prevalence assumptions	(Rewers, 2025)
Implementation faces major logistical/psychosocial barriers	Moderate	Multiple reviews cite workflow integration challenges/anxiety/resource needs	(Khine & Quandt, 2025; Bonifacio & Ziegler, 2025; Johnson et al., 2025)
Predictive accuracy lower outside European ancestry	Moderate	PRS models less validated/generalizable in non-European populations	(Ortega et al., 2025; Wang et al., 2022)
Universal adoption not yet justified globally	Moderate	Most data from Europe/North America; limited global outcome/cost data	(Ortega et al., 2025)

FIGURE Key claims and support evidence identified in these papers.

5. Conclusion

Combining genetic risk scoring with islet autoantibody screening enhances early detection of type 1 diabetes at the population level—with growing evidence supporting its clinical utility and potential cost-effectiveness when implemented efficiently within public health systems. However, significant implementation barriers remain—including logistical integration into routine care settings; ensuring equity across diverse populations; managing psychosocial impacts; standardizing assays; providing adequate counseling/follow-up resources; addressing ethical/data privacy concerns; and establishing clear guidelines for post-screening management.

Research Gaps

Topic/Outcome	European ancestry children	Non-European ancestry children	Adults/general population	Cost-effectiveness analysis	Psychosocial impact
Early detection efficacy	10	2	4	4	4
Cost-effectiveness	4	GAP	GAP	7	GAP
Implementation barriers	6	GAP	4	GAP	7
Long-term outcomes	4	GAP	GAP	GAP	GAP

FIGURE Matrix showing research coverage by topic/outcome versus study attribute/population.

Open Research Questions

Future research should focus on optimizing predictive models across ancestries/populations; evaluating long-term outcomes/costs beyond initial diagnosis/DKA reduction; developing scalable counseling/support frameworks; refining ethical/data privacy protocols; integrating new therapies into cost-benefit analyses; and establishing global best-practice guidelines.

Question	Why
How can predictive models be optimized for diverse populations?	Current PRS/IA models perform best in European ancestry groups—improving generalizability is essential for equity.
What are the long-term health-economic outcomes beyond DKA reduction?	Most analyses focus on short-term benefits—understanding lifetime costs/savings will inform policy decisions.
How can psychosocial harms from early 'at-risk' labeling be minimized?	Anxiety/resource needs are major barriers—effective interventions could improve uptake/success of population programs.

FIGURE Open questions guiding future research directions.

In summary: Combined genetic risk scoring plus autoantibody screening shows promise for early T1D detection/prevention but requires further optimization—especially regarding equitable implementation—and robust long-term outcome data before universal adoption can be recommended.

These search results were found and analyzed using Consensus, an AI-powered search engine for research. Try it at https://consensus.app. © 2026 Consensus NLP, Inc. Personal, non-commercial use only; redistribution requires copyright holders' consent.

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