Prevention of Type 2 Diabetes

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Introduction

Worldwide, a staggering number - an estimated 463 million people - have diabetes,\(^1\) 90–95% of which is type 2 diabetes. This has resulted in a significant burden, financially and in terms of population health and well-being.\(^1–3\) Additionally, a large population is at increased risk of developing type 2 diabetes; Approximately 374 million people have impaired glucose tolerance globally (IGT, a type of prediabetes),\(^1\) an underestimate of the true prediabetes burden as impaired fasting glucose (IFG), another type of prediabetes, occurs more frequently in some race/ethnic groups.\(^4,5\)

A reduction in the global burden of diabetes requires improved identification and treatment of diabetes and its complications but also an increased focus on implementing proven diabetes prevention programs in communities and clinics. Herein, we summarize the current evidence for type 2 diabetes prevention in the United States (U.S.) and globally. We consider lifestyle interventions, programs promoting diabetes risk reduction through diet improvement, increased physical activity, and/or weight loss, including efficacy trials

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Current Evidence

Efficacy of Lifestyle Interventions for Diabetes Prevention or Delay

Data from randomized controlled trials of individuals with IGT unequivocally show that lifestyle modification reduces diabetes incidence, improves glycemic control, and has beneficial effects on diabetes risk factors and its complications.\(^6\)\(^-\)\(^12\) In the largest diabetes prevention study (n=3234), the U.S. Diabetes Prevention Program (DPP), trained Lifestyle Coaches delivered on-on-one, individualized education and guidance to help participants improve health behaviors, overcome barriers, and reach study goals (≥7% weight loss and ≥150 minutes of weekly, moderate-level physical activity).\(^13\) The DPP reported a 58% reduction in diabetes incidence in intervention participants compared to controls.\(^9\) A meta-analysis of randomized controlled trials of diabetes prevention studies reported that lifestyle interventions were associated with a 39% reduction in diabetes risk compared to controls (Relative Risk = 0.61, 95% CI 0.54–0.68).\(^14\)

Lifestyle programs have proven effectiveness in a variety of settings and populations, with positive results reported in studies in the U.S., India, Europe, and China\(^9\),\(^10\),\(^15\),\(^16\) and within the DPP, across age, sex, BMI group, and race-ethnic identity.\(^9\) Studies have shown reductions in diabetes risk even among those at highest risk for conversion to diabetes, including older adults and participants with a history of gestational diabetes, the highest levels of insulin sensitivity, and increased genetic risk for diabetes.\(^9\),\(^17\),\(^18\)

Implementation of proven diabetes prevention programs could have wide-reaching impacts on public health. Efficacy trials have shown that effects of lifestyle intervention are long lasting. After 23 years of follow-up, Da Qing Diabetes Prevention Study participants had a 45% reduction in cumulative diabetes incidence (Hazard Ratio [HR]: 0.55, 95% CI 0.40–0.76) and reductions in both cardiovascular and all-cause mortality (HR: 0.59, 95% CI 0.36–0.96 and HR: 0.71, 95% CI 0.51–0.99, respectively).\(^19\) Participants in the DPP and the Da Qing Study whose glycemic levels returned to normal, even transiently, were less likely to develop diabetes\(^20\) and lower incidence of cardiovascular and microvascular diseases\(^21\),\(^22\) than participants who did not reach normoglycemia. In addition, the DPP, the Finnish Diabetes Prevention Study, and the Indian Diabetes Prevention Programme (IDPP) all reported that the lifestyle intervention in each program was cost effective.\(^23\)\(^-\)\(^25\)

Lifestyle intervention have resulting in diabetes prevention in some, but not all people with prediabetes. Studies in individuals with isolated IFG (iIFG) have not shown the same outcomes. A lifestyle intervention program in Japan was highly effective among individuals with IFG+IGT (HR, 0.41, 95% CI 0.24–0.69) but did not reduce diabetes risk among individuals with iIFG (HR: 1.17, 95% CI 0.50–2.74).\(^26\) Similarly, the Diabetes Community Lifestyle Improvement Program (D-CLIP) study in India reported only a 12% relative risk reduction for diabetes in the iIFG group compared to 31% and 39% relative risk...
reductions in the iIGT and IFG+IGT groups, respectively.\textsuperscript{27} Effective interventions for diabetes prevention among individuals with iIFG are needed.

Even so, based on the strong data from randomized controlled trials supporting lifestyle intervention for diabetes prevention, expert organizations including the American, European, and Canadian Diabetes Associations recommend lifestyle programs for diabetes prevention in high-risk groups.\textsuperscript{28–30} In the U.S. and globally, there is a growing body of implementation and translation research describing the successes and challenges of delivering these proven programs at the clinic and community levels. Although these implementation studies show lower impact than efficacy studies, they do show that implementation of proven diabetes prevention programs in real-world settings can lead to improvements in participants’ weight, glucose, and physical activity and reductions in diabetes risk.\textsuperscript{31–33}

**Implementation/Dissemination in the U.S.**

The Centers for Disease Control and Prevention (CDC) created the National DPP (NDPP) to disseminate the DPP broadly in the U.S.\textsuperscript{33} The evidence-based curriculum materials, developed in collaboration with partners, are available to the public in multiple languages free of charge. The NDPP focuses on four key components to reach large-scale implementation: (1) training to increase the delivery workforce; (2) a recognition program to for quality assurances (Diabetes Prevention Recognition Program, DPRP); (3) health marketing to improve uptake of the program; and (4) intervention sites and payment models to support sustainability, including the U.S.’s largest private health insurer, United Health Group, and the YMCA.\textsuperscript{34}

Participant-level analysis of the first 4 years of NDPP implementation through CDC-recognized sites demonstrated clinically meaningful findings. Participants attended a median of 14 sessions, and 35.5% achieved the 5% weight loss goal (average weight loss 4.2%, median 3.1%). Participants reported a weekly average of 152 min of physical activity with over 40% meeting the physical activity goal (≥150 min/week).\textsuperscript{33}

Even with these efforts, NDPP dissemination remains low. National survey data analyses shows very low referral rates to CDC-recognized DPPs (<5%) and general weight loss programs (~20%) among at-risk individuals, and of those referred to programs, less than 40% report engaging.\textsuperscript{35} In the NDPP, retention was low with less than half of participants continuing the program for more than 6 months.\textsuperscript{33} Other studies have reported similar results, with low and dropping rates of participant engagement during the intervention period.\textsuperscript{36,37} Given that participants who remain in the DPP for 6 months or more are more likely to achieve weight loss and activity goals,\textsuperscript{33} there is an imperative need to better understand and address challenges to participant engagement.

**Community-based and virtual adaptations**—Although scaling proven interventions to real-world settings with diverse populations has been challenging with inconsistent outcomes, there are several examples of successful implementation of such programs. For example, participants in the DEPLOY Pilot Study at YMCAs showed significant reductions in weight, cholesterol and blood pressure compared to baseline,\textsuperscript{38} while the PREDICT...
Study, a church-based DPP program for African-Americans, demonstrated feasibility yet no difference in weight loss between groups that did and did not receive the intervention.\textsuperscript{39}

Cultural and linguistic adaptations have greatly improved the reach of the DPP,\textsuperscript{40} and several studies have taken a community-based participatory research approach and/or sought stakeholder or community feedback to inform DPP adaptations in hopes of improving outcomes.\textsuperscript{41} Resulting adaptations have included curriculum changes (e.g., incorporation of faith-based content,\textsuperscript{42} reducing session number,\textsuperscript{40} incorporating additional hands-on exercise or cooking/food education\textsuperscript{43}), group/family-based approaches,\textsuperscript{44,45} or use of community health workers (CHW)/peer coaches.\textsuperscript{40} Not all adaptations have been successful. For example curriculum updates to reflect the psychosocial stressor of historical trauma did not increase success in a DPP translation for American Indian and Alaska Natives.\textsuperscript{46}

Format adaptations to include peer support, lay health educators, and community leaders have demonstrated feasibility and acceptability in minority communities, without significant differences in outcomes.\textsuperscript{31,47} The PREVENT-DM trial which compared a CHW-led DPP translation for Hispanic women to metformin-only or control reported the greatest weight loss in the CHW-led group.\textsuperscript{48} Other implementation studies have sought to optimize limited community resources by reducing DPP session number with some studies showing similar weight loss and HbA1c outcomes in shorter programs\textsuperscript{49} and other studies reporting higher weight loss in programs with fewer modifications.\textsuperscript{50}

DPP implementation trials are often shorter duration and lack data on diabetes outcomes, instead relying on intermediate outcomes like weight. Among these, weight loss is low, potentially due in part to lower retention and engagement of participants in community-based programs.\textsuperscript{51–53} Retention is markedly low in younger participants and racial/ethnic minorities.\textsuperscript{41,51} Among African Americans in DPP translation studies attendance ranges from 33\%–72\%, and weight loss is markedly less.\textsuperscript{54} Similarly, a NDPP study from Colorado found that Latinx, Blacks, young adults, and uninsured individuals were less likely to achieve the 5\% weight loss goal.\textsuperscript{55} These findings support the need for continued cultural adaptation of diabetes prevention interventions but also the importance of implementation process evaluation to understand the factors contributing to reduced effectiveness in these populations.

As efforts to adapt and implement the DPP have grown, so have the exploration and the need to incorporate novel technology and formats to meet the needs of various populations at risk for diabetes. One of the earliest adaptations was the use of telehealth to deliver the DPP curriculum. In partnership with local health systems, Montana’s Department of Public Health implemented a version of the DPP using video conferencing. The completed study of 894 participants, comparing participation in the video conference format to in-person delivery of the NDPP, reported no significant differences between study arms in the number of sessions attended or percentage of participants reaching weight loss goals of 5\% or 7\%.\textsuperscript{56}

With the growth of mobile technology, the use of smart-phone applications, online programs, and wearable devices has been a growing area of research to address the challenges related to participant adherence in the DPP. \textit{Prevent}, developed by Omada Health,
is a DPP-based group lifestyle intervention integrating a private online social network, weekly lessons, health coaching, and a wireless scale and pedometer. This model has shown meaningful weight loss and HbA1c change among participants after 1 year.\textsuperscript{57} Later iterations have also shown feasibility of online platforms to reach underserved communities, including Latinx, elderly, and rural populations.\textsuperscript{56,58} Another study comparing an app-based DPP with virtual coaching to a group receiving a paper-based DPP curriculum with regular medical care with no formal intervention, reported significantly better improvement in weight among the group receiving the mobile app-based program (−2.64kg [SE 0.71; \(P<.001\)]).\textsuperscript{59}

The creation and implementation of the NDPP has led to successful uptake and adaptations of the DPP including in-person, community, web-based, mobile delivery, and mixed interventions reporting weight loss of 3% or more.\textsuperscript{31,40,60,61} While various methods have been shown to be feasible, barriers at the participant-level (e.g. digital access, health literacy, behavior log burden, transportation, and activation), program-level (e.g. location, platform, class format); and system-level (e.g. payment model and marketing) must be addressed to achieve successful implementation and clinically meaningful outcomes.

**Implementation/Dissemination Globally**

The recent Global Burden of Disease Study estimates that the prevalence of diabetes will increase by almost 20% from 2019 to 2030 with most of the increase occurring in low- and middle-income countries (LMICs). With over 80% of people with diabetes living in LMICs and 1 million deaths a year due to diabetes alone, lower income countries do not have the capacity to manage this rising burden of disease.\textsuperscript{62} Diabetes prevention in LMICs is imperative. Most of the evidence for the effectiveness of diabetes prevention interventions comes from high-income countries. LMICs present a very different context, with differences at the provider-, participant-, and community-level; as well as limited availability of both human and material resources that impact translation of interventions. In the last several years, there has been a growing realization of the importance of considering context in implementation of interventions and the translation of evidence generated in high income countries to LMICs. Effective translation must consider adaptation, implementation outcomes, innovative and appropriate implementation strategies, and sustainability for the LMIC context.\textsuperscript{63,64}

Table 1 summarizes key studies of implementation and effectiveness of diabetes prevention initiatives in LMICs with a focus on studies in China (highest number of people with diabetes), India (the second highest number of people with diabetes and the largest population with prediabetes), and Sub-Saharan Africa (largest projected growth in number of people with diabetes).\textsuperscript{1} Understanding how and why components of the original evidence-based intervention were adapted is important for informing diabetes prevention in other settings. D-CLIP,\textsuperscript{27} Lifestyle Africa,\textsuperscript{65} and the Kerala Diabetes Prevention Program (K-DPP)\textsuperscript{66} detail adaptations to the original diabetes prevention programs for the Indian and South African cultural context. These studies highlight the importance of engaging key stakeholders and people living with chronic disease in the process to understand barriers and facilitators to partaking in healthy lifestyle.
Implementation research engages key stakeholders to understand critical implementation outcomes such as reach, adoption, acceptability, fidelity, and sustainability. Understanding these outcomes facilitates the process of taking the intervention to scale. The K-DPP study and Lifestyle Africa provide us with important information on these implementation outcomes that can inform larger nation-wide efforts. The K-DPP uses well known implementation frameworks to report on reach/penetration adoption, acceptability, and fidelity. Similarly, in Lifestyle Africa investigators report on reach, acceptability, adoption, fidelity, and sustainability.

Understanding the cost, cost-effectiveness, and cost-utility of diabetes prevention interventions is important for policy-makers in LMICs who have limited budgets, human resources, and many competing health-related priorities. Cost-effectiveness analysis of the IDPP showed it to be less cost-effective than Kerala-DPP. Cost in the D-CLIP study was slightly higher than the IDPP or Kerala-DPP. K-DPP showed a cost per diabetes case prevented of $295, while D-CLIP had a higher cost per diabetes case prevented at $2604.

These studies also provide great examples of innovative implementation strategies that can increase the reach of interventions. The use of mobile technology and text messaging in India is one example of a program component that lessens the requirement for more costly and time-intensive in-person sessions. Virtual tools also overcome transportation barriers often cited for missing sessions. Phone-based messaging was successfully used in two studies in India. In Lifestyle Africa, the US-DPP was modified to include video-assisted sessions, which required less training and experience for individuals delivering the intervention. While encouraging, the use of innovative delivery methodologies to facilitate scale-up of interventions in LMICs still require comparative studies to understand the effectiveness and cost-effectiveness of these approaches compared to more traditional, in-person delivery.

The increased reporting of implementation outcomes, adaptation, and cost-analysis for diabetes prevention interventions in LMICs is encouraging. However, as the evidence base for implementation of diabetes prevention interventions in different LMIC contexts increases, there is a need to ensure that there is a parallel effort to translate these findings into effective and sustainable scale-up (implementing programs at the subnational/national level) and scale-out (implementing programs in similar contexts) initiatives. For example, the state-wide scale-up of the K-DPP or scale-out of Lifestyle Africa to in other sub-Saharan Africa countries with high diabetes and prediabetes burdens such as Nigeria. Studies must also consider longer-term follow-up to understand the factors that impact sustainability of and adherence to interventions.

**Discussion**

Despite strong evidence for lifestyle interventions for diabetes prevention, implementation of these programs at the community level, particularly in LMIC settings, is lagging and there are significant gaps in the available literature to guide these efforts. There is need for research to identify successful methods to overcome challenges seen within diabetes prevention studies, including loss of program gains over time (e.g., weight gain, decreases in
physical activity) and identification of successful interventions for individuals with non-IGT prediabetes or normal weight individuals with prediabetes. Novel intervention methods for diabetes prevention, for example a Health at Every Size approach or high intensity interval training exercise should be tested within the context of diabetes prevention studies to determine their efficacy within different populations. Behavioral Nudges, small changes in the environment that nudge an individual to make certain choices, and financial incentives should be tested more widely in the context of improving health behaviors and participant outcomes in diabetes prevention research.

There is a need for more detailed reporting and evaluation of implementation processes to guide further implementation, scale-up, and dissemination. Few diabetes prevention implementation studies describe what adaptations were made or document the reasons for these changes. Providing this granular data would be highly beneficial to guide additional tailoring of proven diabetes prevention programs across settings. There is need for data from implementation trials assessing longer-term outcomes including diabetes incidence, a deeper understanding of barriers to participant engagement and retention paired with methods to improve these metrics, and additional work testing novel methods for cultural adaptation. A greater number of implementation studies should be designed to assess fidelity, cost and cost-effectiveness, acceptability, and sustainability.

Future diabetes prevention efforts within communities should focus on delivering programs to overcome barriers to attendance; for example, worksite-based interventions can ease participation barriers to reaching at-risk individuals at a location where they already spend much of their time. Similarly, mobile or online programs can be delivered anywhere and maybe more appealing to some populations; however, barriers to digital access or digital literacy may prevent the reach and uptake of such models. Additional research is needed to understand how to best leverage and utilize digital tools (e.g., wearable fitness trackers, continuous glucose monitoring) and platforms to support diabetes prevention. This attention to digital DPP delivery is particularly appropriate currently, as the COVID-19 pandemic necessitated that on-going DPP programming adapt to comply with social distancing measures. Studies are needed to understand how existing programs responded to the global COVID-19 crisis and use this knowledge to create more nimble diabetes prevention programming that can quickly respond to similar breaks in delivery in the future (e.g., during a natural disaster).

**Summary**

Randomized control trials provide strong evidence for the efficacy of lifestyle interventions focused on increasing physical activity, improving diet quality and quantity, and/or weight loss for reducing diabetes incidence and improving cardiometabolic health among individuals at elevated risk for type 2 diabetes. Implementation studies, both in the U.S. and globally, have successful applied these models at the community level. However, additional research is needed to better guide community implementation and dissemination, understand diabetes prevention across different prediabetes groups, and improve participant engagement and retention in diabetes prevention programs.
Acknowledgments

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References


Synopsis

The global diabetes burden is staggering and prevention efforts are needed to reduce the impact on individuals and populations. There is strong evidence from efficacy trials showing that lifestyle interventions promoting increased physical activity, improvements in diet, and/or weight loss significantly reduce diabetes incidence and improve cardiometabolic risk factors. Implementation research assessing the feasibility, effectiveness, and cost-effectiveness of delivering these proven programs at the community level has shown success, but more research is needed to overcome barriers to implementation in different settings globally. New avenues of research should be considered to combat this public health issue.
**Key Points**

- There is strong evidence for the efficacy and effectiveness of lifestyle interventions for diabetes prevention.
- Lifestyle interventions are not equally effective for all types of prediabetes, with the strongest evidence of effectiveness among those with impaired glucose tolerance or impaired glucose tolerance + impaired fasting glucose. Further research is needed to identify if and/or which lifestyle interventions are effective for reducing risk among individuals with isolated impaired fasting glucose.
- Implementation of proven programs face unique challenges both in the U.S. and globally.
- Well-designed implementation studies that consider the needs and realities of different communities, populations, and settings and clearly describe program adaptations are needed to increase successful scaling and dissemination of diabetes prevention interventions at the community level.
Clinic Care Points

- There is strong evidence that diabetes can be prevented or delayed in high risk adults by increasing physical activity, reducing weight, and improving diet quality and quantity.

- Clinicians should consider the cultural appropriateness of lifestyle advice and work with patients to find solutions to barriers, both personal and cultural, to achieve the needed behavior change.

- Clinicians should regularly screen individuals at risk for prediabetes to identify patients who could benefit from proven diabetes prevention programs.

- Patients with prediabetes should be referred to existing diabetes prevention programs (community or payer-based programs) and clinicians should provide support and encouragement to help patients find programs that work for them; these include virtual or other remote applications that may improve acceptability for some patients. Resources for health professionals are available through the Centers for Disease Control and Prevention at https://www.cdc.gov/diabetes/prevention/info-hcp.html.

- Clinicians should be prepared to escalate therapy for patients with prediabetes struggling with weight loss or lifestyle behavior changes. This includes following up with patients regarding their prediabetes diagnosis and diabetes prevention program referral and helping them overcome resistance to joining and remaining engaged in these programs.
Table 1: Implementation of Diabetes Prevention Interventions Globally – Key Examples from China, India, and Sub-Saharan Africa

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Study Population</th>
<th>Intervention components</th>
<th>Mode of delivery of the intervention</th>
<th>Adaptation reported; implementation outcomes reported</th>
<th>Intervention cost (INR to prevent one case of diabetes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Da Qing Diabetes Prevention Study</td>
<td>China</td>
<td>Diet, exercise, or combined</td>
<td>In-person counseling sessions</td>
<td>N/A (original study)</td>
<td>Not reported</td>
</tr>
<tr>
<td>IDPP-1</td>
<td>India</td>
<td>Lifestyle modification only Metformin only Lifestyle + Metformin</td>
<td>Lifestyle modification delivered via</td>
<td>N/A (original study)</td>
<td>$1,052 Metformin $1,095 LSM+Metformin $1.359^{15}</td>
</tr>
<tr>
<td>IDPP mobile</td>
<td>India (men only)</td>
<td>Diet and physical activity recommendations Mobile phone messages tailored to trans-theoretical model stage (based on IDPP)</td>
<td>Phone messages and emails</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>LIMIT</td>
<td>India</td>
<td>Lifestyle modification recommendations</td>
<td>Phone messages and emails</td>
<td>Not reported</td>
<td>$137.29 to prevent one case of overweight/obesity</td>
</tr>
<tr>
<td>D-CLIP</td>
<td>India</td>
<td>Lifestyle modification modeled on DPP Metformin escalation</td>
<td>In-person group sessions Phone call follow up</td>
<td>Documented DPP curriculum adaptations</td>
<td>$2604.14^{16}</td>
</tr>
<tr>
<td>K-DPP</td>
<td>India</td>
<td>Lifestyle modification modeled on DPP</td>
<td>In-person group sessions delivered by peers</td>
<td>Documented DPP curriculum adaptations Implementation outcomes assessed: reach, adoption, fidelity</td>
<td>$295.1^{18}</td>
</tr>
<tr>
<td>Yoga-DP</td>
<td>India</td>
<td>Yoga-based exercises Program booklet</td>
<td>In-person; home video</td>
<td>Not reported</td>
<td>N/A</td>
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<tr>
<td>Lifestyle Africa</td>
<td>South Africa</td>
<td>Lifestyle modification modeled on DPP Video-based sessions modeled on DPP Sessions facilitated by CHWs</td>
<td>Video-based sessions modeled on DPP Sessions facilitated by CHWs</td>
<td>Documented adaptations on content, literacy/numeracy. Implementation outcomes assessed: reach, fidelity, participant satisfaction</td>
<td>N/A</td>
</tr>
<tr>
<td>SA-DPP</td>
<td>South Africa</td>
<td>Lifestyle modification modeled on the Finnish Diabetes Prevention Study</td>
<td>In-person sessions plus informational booklet</td>
<td>Documented adaptations</td>
<td>N/A</td>
</tr>
</tbody>
</table>

* IDPP = Indian Diabetes Prevention Study; LIMIT = Lifestyle Modification in Information Technology; D-CLIP = Diabetes Community Lifestyle Improvement Program; K-DPP = Kerala Diabetes Prevention Program; Yoga-DP = Yoga Programme for Type 2 Diabetes Mellitus Prevention; SA-DPP = South African Diabetes Prevention Program