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Review Article

Lifestyle Modification Versus Pharmacotherapy in Prediabetes: An Evidence-Based Review

Abdare Manjusha*, Bhadange Vaishnavi, Magar Disha, Kharat Shreya, Dr. P. N. Kelgoankar

Department of pharmacy practice, Channabasweshwar Pharmacy College (Degree), Kava Road, Basweshwar Chowk, Latur- 413512

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ABSTRACT

Prediabetes is an intermediate metabolic state characterized by impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or elevated glycated hemoglobin (HbA1c). Without intervention, many individuals progress to type 2 diabetes mellitus (T2DM), increasing the risk of cardiovascular disease, chronic kidney disease, and other complications. Lifestyle modification remains the cornerstone of diabetes prevention, whereas pharmacotherapy is recommended for selected high-risk individuals. This evidence-based review evaluates the comparative effectiveness, safety, cost-effectiveness, and long-term outcomes of lifestyle interventions and pharmacological therapies in prediabetes. Findings from major randomized controlled trials indicate that intensive lifestyle modification reduces diabetes incidence more effectively than metformin in most populations, although metformin is beneficial in younger individuals with obesity or women with prior gestational diabetes. Current guidelines recommend individualized treatment strategies emphasizing lifestyle modification as first-line therapy.

INTRODUCTION

Prediabetes is a high-risk metabolic condition in which blood glucose levels are above normal but below the diagnostic threshold for diabetes mellitus. It affects millions of adults worldwide and represents an important opportunity for early intervention. Without preventive measures,

approximately 5–10% of people with prediabetes progress to type 2 diabetes annually. Lifestyle modification and pharmacotherapy are the two major preventive approaches. This review compares these interventions using current evidence and international guideline recommendations.

***Corresponding Author:** Abdare Manjusha

Address: Channabasweshwar Pharmacy College (Degree), Kava Road, Basweshwar Chowk, Latur- 413512

Email ✉: manjushaabdare@gmail.com

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2. DEFINITION OF PREDIABETES

According to the American Diabetes Association (ADA), prediabetes is diagnosed by:

- Fasting plasma glucose: 100–125 mg/dL
- 2-hour plasma glucose (OGTT): 140–199 mg/dL
- HbA1c: 5.7–6.4%

Individuals with prediabetes have increased insulin resistance and impaired pancreatic β -cell function, placing them at greater risk of developing T2DM.

3. PATHOPHYSIOLOGY

Major mechanisms include:

- Insulin resistance
- Progressive β -cell dysfunction
- Chronic low-grade inflammation
- Obesity
- Genetic susceptibility
- Sedentary lifestyle

Persistent insulin resistance eventually leads to hyperglycemia and progression to diabetes.

4. LIFESTYLE MODIFICATION

Lifestyle intervention consists of:

Dietary modification

- Mediterranean diet
- DASH diet
- High-fiber foods
- Reduced refined carbohydrates
- Calorie restriction
- Reduced sugary beverages

Physical activity

- ≥ 150 minutes/week of moderate aerobic exercise
- Resistance training 2–3 days/week

Weight reduction

A weight loss of 5–10% significantly reduces diabetes risk.

Behavioral intervention

- Smoking cessation
- Stress management
- Sleep optimization
- Regular counseling

Lifestyle modification improves insulin sensitivity, lipid profile, blood pressure, and overall cardiovascular health.

5. PHARMACOTHERAPY

Drug therapy is mainly reserved for high-risk individuals.

Metformin

- Decreases hepatic glucose production
- Improves insulin sensitivity
- Most evidence among preventive medications

GLP-1 receptor agonists

- Promote weight loss
- Improve insulin secretion
- Reduce progression to diabetes

Other medications

- Acarbose
- Pioglitazone
- Voglibose (selected populations)



Drug therapy should complement—not replace—lifestyle modification.

6. EVIDENCE FROM MAJOR CLINICAL TRIALS

Diabetes Prevention Program (DPP)

- Lifestyle modification reduced diabetes incidence by 58%.
- Metformin reduced incidence by 31%.
- Lifestyle intervention showed greater benefit than metformin in the overall study population.

DPP Outcomes Study (DPPOS)

Long-term follow-up demonstrated sustained diabetes prevention with both interventions, although lifestyle modification remained the preferred first-line strategy.

Systematic Reviews

Recent meta-analyses conclude that lifestyle modification has the strongest evidence for reversing prediabetes, while medications such as metformin, GLP-1 receptor agonists, and α -glucosidase inhibitors also reduce progression in selected patients.

7. COMPARISON OF LIFESTYLE MODIFICATION AND PHARMACOTHERAPY

Parameter	Lifestyle Modification	Pharmacotherapy
First-line treatment	Yes	Selected patients
Effectiveness	Excellent	Moderate to High
Weight reduction	Significant	Drug dependent
Adverse effects	Minimal	GI and drug-specific adverse effects
Cost	Low	Moderate to High
Long-term sustainability	High	Depends on continued treatment
Guideline recommendation	Strong	Adjunctive

8. CURRENT GUIDELINE RECOMMENDATIONS

The ADA recommends:

- Lifestyle modification for all individuals with prediabetes.
- Consider metformin in high-risk adults, particularly those with BMI ≥ 35 kg/m², age <60 years, or a history of gestational diabetes.
- Individualize therapy according to patient characteristics and risk profile.

9. DISCUSSION

Current evidence consistently demonstrates that lifestyle modification remains the most effective strategy for preventing progression from prediabetes to type 2 diabetes. Intensive dietary intervention, increased physical activity, and sustained weight loss improve insulin sensitivity and reduce cardiovascular risk. Pharmacotherapy, particularly metformin, offers additional benefit for carefully selected high-risk individuals but should not replace lifestyle intervention. Future research should focus on personalized treatment strategies and the role of newer agents such as GLP-1 receptor agonists in diabetes prevention.



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