What is the best strategy for impaired glucose tolerance in nonpregnant adults?

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EVIDENCE-BASED ANSWER

The best treatment strategy for impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) is lifestyle intervention with a structured weight loss program of diet and exercise (strength of recommendation [SOR]: **B**, based on high-quality randomized controlled trials [RCTs] for disease-oriented outcomes). Patients with IGT and IFG should be counseled to lose 5% to 7% of their body weight and instructed on moderate intensity physical activity for ~150 minutes per week.

Metformin (Glucophage), acarbose (Precose), and troglitazone (Rezulin) are also effective, but lifestyle interventions appear superior (**TABLE**) (SOR: **B**, based on single high quality randomized controlled trials). The American Diabetes Association defines IFG as a fasting glucose of between 100 and 125 mg/dL, and IGT as glucose between 140 and 199 mg/dL after a 2-hour oral glucose challenge.

Adults with IGT or IFG should have laboratory screening for diabetes every 1 to 2 years (SOR: C, based on expert opinion), using the fasting plasma glucose (FPG) as a screening test (SOR: **C**, based on expert opinion). For individuals whose FPG exceeds 125 mg/dL, oral glucose tolerance testing is considered superior to glycohemoglobin testing for ruling out progression to diabetes (SOR: **C**, based on expert opinion).

CLINICAL COMMENTARY

Lifestyle modification clearly works; medication may have a role as well

While lifestyle interventions are clearly efficacious, clinicians will need appropriate resources to help patients exercise and maintain weight loss if they are to achieve similar results. This Clinical Inquiry helps practitioners realize that diabetes mellitus, impaired fasting glucose, impaired glucose tolerance, and obesity probably constitute a spectrum disorder and that we should treat all of these patients more aggressively. This is particularly true considering the epidemic proportion of obesity in the United States. Physicians' attitudes towards obese patients might be a barrier to effective care. It is important for clinicians to realize that monitoring hemoglobin A_{1c} levels is not recommended for IGT and IFG. Putting evidence into practice will mean that physicians need to be aware of the efficacy of both lifestyle and medical interventions in IGT and IFG.

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Evidence Summary

Both IGT and IFG are associated with a significant risk of developing diabetes and its associated cardiovascular comorbidities; thus, the primary goal for treatment is to prevent or delay the onset of diabetes. Recent well-designed studies have demonstrated benefits of lifestyle interventions for patients with IGT.

In the US Diabetes Prevention Program (DPP), 3234 patients with IGT and a body-mass index (BMI) of at least 24 kg/m^2 were randomly assigned to one of the following groups: placebo, metformin, or intensive lifestyle modification. After an average follow-up of 2.8 years, there was a 14% absolute risk reduction in the progression to diabetes in the lifestyle intervention group compared with placebo (number needed to treat [NNT]=7).[1] In the Finnish Diabetes Prevention Study, the lifestyle intervention group had a 12.5% absolute risk reduction compared with the control group (NNT=8).[2] Successful lifestyle interventions in these studies included

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TABLE

Comparison of major lifestyle and pharmacologic trials in IGT and IFG

INTERVENTION	RELATIVE RISK REDUCTION IN INCIDENCE OF DIABETES MELLITIS (95% CI)	NUMBER NEEDED TO TREAT	ABSOLUTE RISK REDUCTION
Lifestyle[1]	58% (48%–66%)	7	14%
Lifestyle[2]	58% (hazard ratio 0.4; 95% CI, 0.3%–0.7%)	8	12.5%
Metformin 850 mg twice daily (Glucophage)[1]	31% (17%–43%)	14	7%
Acarbose 100 mg three times daily (Precose)[3]	25% (10%–37%)	11	9%
Troglitazone 400 mg daily[4] (Rezulin [withdrawn])	56% (17%–75%)	6	16.7%

NNT, number needed to treat; ARR, absolute risk reduction.
Adapted from Davies et al, *Diabetic Medicine* 2004.[9]

FAST TRACK

The best treatment strategy for impaired glucose tolerance is a structured weight loss program of diet and exercise

weight loss of 5% to 7%, decreased fat intake, increased fiber intake, and 150 minutes of exercise per week.[1–2]

Drug therapy with metformin, acarbose, and troglitazone has also been successful in preventing or delaying diabetes in people with IGT.[1,3,4] In the placebo-controlled DPP trial, metformin use was associated with a reduction in progression to diabetes mellitus (NNT=14).[1] In the STOP-NIDDM trial of 1429 persons over 3.3 years of follow-up, acarbose 100 mg 3 times daily resulted in a 9% reduction of progression to diabetes, compared with placebo (NNT=11).[3]

In the TRIPOD study, troglitazone use was associated with a 17% absolute risk reduction in the incidence of diabetes in high-risk Hispanic women (NNT=6 over an average of 30 months).[4] The preventive effect of the drug was maintained more than 8 months after troglitazone therapy was discontinued (due to withdrawal from the US market). Current trials with other thiazolidinediones are underway.

Recommendations from others

The American Diabetes Association (ADA) recommends counseling on weight loss and instructing on increased physical activity in people with IGT.[5] The United States Preventive Services Task Force recommends intensive programs of lifestyle modification (diet, exercise, and behavior) for patients who have pre-diabetes.[6]

The ADA recommends regular monitoring (every 1 to 2 years) for the development of diabetes in people with prediabetes, and prefers FPG to screen for diabetes since it is faster, cost-effective, and more reproducible than the more sensitive 2-hour oral glucose tolerance test.[5,7] The ADA also recommends that if the FPG is <126 mg/dL and there is a high suspicion for diabetes, a 2-hour oral glucose tolerance test should be performed.

Glycosylated hemoglobin (HbA_{1C}) is not recommended as a screening tool, because individuals with IFG or IGT may have normal or near-normal HbA_{1C} levels; these individuals often manifest hyperglycemia only when challenged with

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the oral glucose load use in the standardized oral glucose tolerance test.[8]

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