# Strategies for initiating insulin in type 2 diabetes

Christina Korownyk MD CCFP Noah Ivers MD CCFP G. Michael Allan MD CCFP

## Clinical question

**What is the optimal regimen for initiating insulin in type 2 diabetes (T2D)?**

## Evidence

Four reasonably sized randomized controlled trials address initiating insulin in T2D with poor glucose control.

- The 4-T study[1] followed 708 patients for 3 years, comparing long-acting basal insulin once daily, biphasic mixed insulin twice daily, and prandial insulin with meals.[1]
  -Levels of glycated hemoglobin $A_{1c}$ ($HbA_{1c}$) were not significantly different among the 3 groups.
    —Significantly more patients in the basal and prandial groups attained $HbA_{1c}$ levels ≤7.0% (63% and 67%, respectively, vs 49% biphasic; $P<.001$).
  -Those taking basal insulin had significantly ($P<.05$) ...
    —less weight gain (3.6 kg) than patients using prandial (6.4 kg) or biphasic insulin (5.7 kg),
    —fewer confirmed symptomatic hypoglycemic events per year (1.7 basal vs 3.0 biphasic vs 5.7 prandial), and
    —higher total doses of insulin than biphasic patients.
  -More patients using basal insulin (82%) also required a second type of insulin (vs 74% prandial, 68% biphasic).
- The 3 other studies[2-4] followed 160 to 418 patients (total 811) for 6 months to 1 year and compared basal with prandial,[2] basal with biphasic,[3] and biphasic with prandial[4] insulin.
  -Levels of $HbA_{1c}$ were generally similar, except biphasic insulin improved $HbA_{1c}$ 0.5% more than basal insulin in 1 study and got more people to $HbA_{1c}$ levels ≤7.0%.[3]
  -Basal insulin had significantly less hypoglycemia than prandial ($P<.001$)[2] or biphasic ($P<.05$)[3] insulin and less weight gain than biphasic ($P<.01$)[3] insulin.

## Context

- The 4-T study[1] is given priority because it is the largest and longest and compares the 3 options. Fortunately, the remaining studies[2-4] generally support those findings.
- INSIGHT[5] found initiating basal insulin in poorly controlled T2D resulted in significantly lower $HbA_{1c}$ levels than continued oral hypoglycemic agents did ($P=.005$).
  -Mean $HbA_{1c}$ levels and rates of hypoglycemia were not different between patients of FPs and diabetes experts.[6]
- Specialists are 5 times more likely to initiate insulin.[7]

## Bottom line

**In T2D poorly controlled with oral agents, initiating basal insulin results in similar $HbA_{1c}$ reductions compared with prandial or biphasic insulin and might cause less weight gain and hypoglycemia. Family physicians who start insulin are as effective as specialists.**

## Implementation

While newer insulin products have theoretical advantages, a meta-analysis found that compared with neutral protamine Hagedorn (NPH), longer-acting insulin offers little or no benefit but costs much more.[8] Advantages from reductions in hypoglycemia are at high risk of bias.[9] To initiate basal insulin, prescribe NPH, 10 units daily at bedtime, increasing by 1 unit each night until fasting blood glucose is 4 to 7 mmol/L, remembering to educate the patient about hypoglycemia.[10] A printable document available online simplifies the process of prescribing insulin[11]: **www.ocfp.on.ca/local/files/Insulin Prescription_Rev1.pdf.**

**Dr Korownyk** is Assistant Professor and **Dr Allan** is Associate Professor in the Department of Family Medicine at the University of Alberta in Edmonton. **Dr Ivers** is a family physician at Women's College Hospital in Toronto, Ont.



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