INSULIN THERAPY

Rungnapa Laortanakul, MD
Maharat Nakhon Ratchasima hospital
Case

- Somsak is a 64-year-old man was diagnosed with T2DM, HT, and dyslipidemia 9 years ago.
- No history of hypoglycemia and cardiovascular disease

- Glipizide (5) 2 tab bid.ac
- Metformin (500) 2 tab bid.pc
- Pioglitazone (30) 1 tab OD

- Losartan (100) 1 tab OD
- Simvastatin (10) 1 tab hs
Case

Laboratory
- Fasting plasma glucose 154 mg/dL
- HbA1C 8.9%
- Cholesterol 145 mg/dL
- Triglyceride 130 mg/dL
- HDL 45 mg/dL
- LDL 88 mg/dL
- Creatinine 1.0 mg/dL

What would you recommend to improve his glycemic control?
Benefits of tight glycemic control

- **Intensive glycemic control** reduces the risk of microvascular complications of type 2 diabetes, but the effect of strict glycemic control on the risk of macrovascular disease (especially in well-established type 2 diabetes) is less certain.

- A **near-normal glycemic target** range (6.0 to 6.5%), if implemented safely, could be considered for otherwise healthy patients with recently diagnosed type 2 diabetes and a long life expectancy.

Tight Glycemic Control Reduces Complications

Epidemiological extrapolation showing benefit of a 1% reduction in mean HbA$_{1c}$

- Deaths related to diabetes*: 21%
- Microvascular complications (eg, kidney disease and blindness)*: 37%
- Heart attack*: 14%
- Amputation or fatal peripheral blood vessel disease*: 43%
- Stroke**: 12%

*P<0.0001
**P=.035
Complications Risk in Diabetes
The Impact of Intensive Glycemic Control

Relative Risk of Complications

HbA\textsubscript{1c}
eAG (mmol/L)

6.9 8.5 10.1 11.7 13.2 14.8 16.4

EAG = estimated average glucose.
“Legacy Effect”

GUIDELINE
# Glycemic Treatment Targets

*Treatment targets for non-pregnant adults. AACE = American Association of Clinical Endocrinologists; FPG = fasting plasma glucose; IDF = International Diabetes Foundation; PPG = postprandial plasma glucose.

**Thai Guideline**

<table>
<thead>
<tr>
<th>การควบคุมเป้าหมาย</th>
<th>ควบคุมเข้มงวดมาก</th>
<th>ควบคุมเข้มงวด</th>
<th>ควบคุมไม่เข้มงวด</th>
</tr>
</thead>
<tbody>
<tr>
<td>ระดับน้ำตาลในเลือดขณะอดอาหาร</td>
<td>70-110 มก./ดล.</td>
<td>90-&lt;130 มก./ดล.</td>
<td>ใกล้เคียง 130 มก./ดล.</td>
</tr>
<tr>
<td>ระดับน้ำตาลในเลือดหลังอาหาร 2 ชั่วโมง</td>
<td>&lt;140 มก./ดล.</td>
<td>-</td>
<td>&lt;180 มก./ดล.</td>
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<tr>
<td>ระดับน้ำตาลในเลือดสูงสุดหลังอาหาร</td>
<td>&lt;180 มก./ดล.</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>HbA1C</td>
<td>&lt; 6.5%</td>
<td>&lt; 7.0%</td>
<td>7.0-8.0%</td>
</tr>
</tbody>
</table>

แนวทางประพฤติสำหรับโรคเบาหวาน 2554
GENERAL THERAPY RECOMMENDATIONS
ADA/EASD Joint Position Statement:

Summary of ADA/EASD Consensus Statement

- Achievement and maintenance of near normoglycemia (HbA$_{1c}$ <7.0%)

- Initial therapy with lifestyle intervention and metformin

- Rapid addition of medications and transition to new regimens when target glycemic goals not achieved or sustained*
  - Target glycemic goals can only be sustained by appropriate dose escalation and/or addition of other glucose-lowering medications

- Individualised treatment
  - Balance HbA$_{1c}$ reduction and long-term benefit with specific safety issues, side effects, ease of use, long-term adherence, expense, and nonglycemic effects of medications

*In selected clinical settings, therapeutic agents in the second-tier consensus may be considered. For example, exenatide is a reasonable option when hypoglycaemia is particularly undesirable, or if promotion of weight loss is a major consideration and the HbA$_{1c}$ is close to target (<8%). Nathan DM, et al. Diabetes Care. 2009;32(1):193-203.
Selecting the Appropriate Agent for Individual Patients

Selecting Specific Diabetes Interventions

Glycemic effects

- Reduction in HbA$_{1c}$
- Risk of hypoglycemia
- Insulin secretory capacity
- Safety profile

Nonglycemic effects

- Changes in body weight
- CV risk factors
- Safety profile
- Tolerability
- Ease of use
- Cost

CV = cardiovascular.
Somsak is a 64-year-old man diagnosed with T2DM, HT, and dyslipidemia 9 years ago. He has no history of hypoglycemia and cardiovascular disease.

His current medications include:
- Glipizide (5) 2 tab bid.ac
- Losartan (100) 1 tab OD
- Metformin (500) 2 tab bid.pc
- Simvastatin (10) 1 tab hs
- Pioglitazone (30) 1 tab OD

His laboratory results show:
- Fasting plasma glucose: 154 mg/dL
- HbA1C: 8.9%
<table>
<thead>
<tr>
<th>Day</th>
<th>ac</th>
<th>pc</th>
<th>ac</th>
<th>pc</th>
<th>ac</th>
<th>pc</th>
<th>hs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>157</td>
<td>260</td>
<td>188</td>
<td>291</td>
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<td>145</td>
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<td>365</td>
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<td>4</td>
<td>167</td>
<td>255</td>
<td>232</td>
<td>301</td>
<td>276</td>
<td>345</td>
<td>344</td>
</tr>
</tbody>
</table>

Pre/post-prandial hyperglycemia
HbA$_{1c}$ Is a Combination of FPG and PPG

- The relative contribution of PPG and FPG varies with HbA$_{1c}$
- The clinical significance of improvement in postprandial hyperglycemia has not been established

As patients’ HbA$_{1c}$ level approaches the healthy range, PPG takes on greater importance in determining HbA$_{1c}$.

FPG = fasting plasma glucose.
Pathophysiological Alterations leading to hyperglycemia in type 2 DM

Increased Hepatic Glucose Production
- Weight loss, exercise, biguanides, insulin, thiazolidinediones, possibly bile acid sequestrants

Increased Insulin Resistance
- Weight loss, exercise, biguanides, thiazolidinediones, D2 dopamine–receptor agonists

Increased Rate of Gastric Emptying
- GLP-1–receptor agonists, amylin mimetics

Increased Glucagon Secretion
- GLP-1–receptor agonists, DPP-IV inhibitors, amylin mimetics

Increased Appetite
- GLP-1–receptor agonists, amylin mimetics

Decreased Insulin Secretion
- Sulfonylureas, meglitinides, GLP-1–receptor agonists, DPP-IV inhibitors

Impaired Incretin Effect
- GLP-1–receptor agonists, DPP-IV inhibitors, possibly bile acid sequestrants

Carbohydrate Absorption
- Alpha-glucosidase inhibitors

Decreased Amylin Secretion
- Amylin mimetics

Hyperglycemia in Type 2 Diabetes

## Antidiabetic interventions as monotherapy

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Expected decrease in HbA1c (%)</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lifestyle interventions</strong></td>
<td></td>
<td>Low cost, many benefits</td>
<td>Fails for most in first year</td>
</tr>
<tr>
<td><strong>Metformin</strong></td>
<td>1.5</td>
<td>Weight neutral, inexpensive</td>
<td>GI side effects, rare lactic acidosis</td>
</tr>
<tr>
<td><strong>Insulin</strong></td>
<td>1.5-2.5</td>
<td>No dose limit, inexpensive, improved lipid profile</td>
<td>Injections, monitoring, hypoglycaemia, weight gain</td>
</tr>
<tr>
<td><strong>Sulfonylureas</strong></td>
<td>1.5</td>
<td>Inexpensive</td>
<td>Weight gain, hypoglycaemia</td>
</tr>
<tr>
<td><strong>TZDs</strong></td>
<td>0.5-1.4</td>
<td>Improved lipid profile</td>
<td>Fluid retention, weight gain, expensive</td>
</tr>
<tr>
<td><strong>DPP IV inhibitor</strong></td>
<td>0.5-0.8</td>
<td>No hypoglycemia, Well tolerated</td>
<td>Urticaria/angioedema ? Pancreatitis</td>
</tr>
<tr>
<td><strong>α-Glucosidase inhibitors</strong></td>
<td>0.5-0.8</td>
<td>Weight neutral</td>
<td>Frequent GI side effects, three times/day dosing, expensive</td>
</tr>
<tr>
<td><strong>Exenatide</strong></td>
<td>0.5-1.0</td>
<td>Weight loss</td>
<td>Injections, frequent GI side effects, expensive, little experience</td>
</tr>
<tr>
<td><strong>Glinides</strong></td>
<td>1.0-1.5</td>
<td>Short duration</td>
<td>Three times/day dosing, expensive</td>
</tr>
</tbody>
</table>
The steps of insulin treatment

- Setting glucose control goal
- Initiating insulin therapy
- Titration of insulin dose
- Intensification of treatment regimen
## Glycated Hemoglobin Range

<table>
<thead>
<tr>
<th>Most Intensive Level, Approximately 6.0%</th>
<th>Factors</th>
<th>Least Intensive Level, Approximately 8.0%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highly motivated, adherent, knowledgeable, strong self-care capability</td>
<td>Psychosocial considerations</td>
<td>Less motivated, nonadherent, less knowledge, weak self-care capability</td>
</tr>
<tr>
<td>Adequate</td>
<td>Resources or support systems</td>
<td>Inadequate</td>
</tr>
<tr>
<td>Low</td>
<td>Risk of hypoglycemia</td>
<td>High</td>
</tr>
<tr>
<td>Short</td>
<td>Duration of type 2 diabetes</td>
<td>Long</td>
</tr>
<tr>
<td>Long</td>
<td>Life expectancy</td>
<td>Short</td>
</tr>
<tr>
<td>None</td>
<td>Microvascular disease</td>
<td>Advanced</td>
</tr>
<tr>
<td>None</td>
<td>Cardiovascular disease</td>
<td>Established</td>
</tr>
<tr>
<td>None</td>
<td>Coexisting conditions</td>
<td>Multiple, severe, or both</td>
</tr>
</tbody>
</table>

Basal vs Mealtime Hyperglycemia in Diabetes

Plasma Glucose (mmol/L) vs Time of Day

- Basal hyperglycemia
- Mealtime hyperglycemia

Type 2 Diabetes
Healthy

AUC = area under the curve.
# Pharmacokinetic Profiles of Insulin Therapies

<table>
<thead>
<tr>
<th>Insulin type</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-acting</td>
<td>2 hr</td>
<td>No peak</td>
<td>16-24</td>
</tr>
<tr>
<td>• Detemir</td>
<td>2–4 hr</td>
<td>No peak</td>
<td>20-24</td>
</tr>
<tr>
<td>• Glargine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate-acting</td>
<td>1-3 hr</td>
<td>4-10</td>
<td>10-20</td>
</tr>
<tr>
<td>• NPH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-acting</td>
<td>15 to 30 min.</td>
<td>30 to 90 min.</td>
<td>3 to 5 hr</td>
</tr>
<tr>
<td>• Aspart/Glulisine/Lispro</td>
<td>30 to 60 min.</td>
<td>2 to 4 hr</td>
<td>5 to 8 hr</td>
</tr>
<tr>
<td>• Regular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>15 to 30 min.</td>
<td>Dual</td>
<td>14 to 24 hr</td>
</tr>
<tr>
<td>• NPH/lispro or aspart</td>
<td>30 to 60 min.</td>
<td>Dual</td>
<td>14 to 24 hr</td>
</tr>
<tr>
<td>• NPH/regular</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Am Fam Physician. 2011;84(2):183-190
## Insulin

<table>
<thead>
<tr>
<th>Compound(s)</th>
<th>Primary physiological action(s)</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Human NPH</td>
<td>• ↑ Glucose disposal</td>
<td>• Universally effective</td>
<td>• Hypoglycemia</td>
</tr>
<tr>
<td>• Human Regular</td>
<td>• ↓ Hepatic glucose production</td>
<td>• Theoretically unlimited efficacy</td>
<td>• Weight gain</td>
</tr>
<tr>
<td>• Lispro</td>
<td></td>
<td>• ↓ Microvascular risk (UKPDS)</td>
<td>• ? Mitogenic effects</td>
</tr>
<tr>
<td>• Aspart</td>
<td></td>
<td></td>
<td>• Injectable</td>
</tr>
<tr>
<td>• Glulisine</td>
<td></td>
<td></td>
<td>• Training requirements</td>
</tr>
<tr>
<td>• Glargine</td>
<td></td>
<td></td>
<td>• “Stigma” (for patients)</td>
</tr>
<tr>
<td>• Detemir</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Premixed (several types)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Diabetes Care 2012;35:1364–1379
Pharmacokinetic Profiles

![Graph showing relative plasma insulin levels for different types of insulin, including Aspart, lispro (4–6 hr), Regular (6–10 hr), NPH (12–20 hr), Extended zinc insulin (18–24 hr), and Glargine (20–24 hr).]
Insulin

- Ideally, the principle of insulin use is the creation of as normal a glycemic profile as possible without unacceptable weight gain or hypoglycemia.

- As initial therapy, unless the patient is markedly hyperglycemic and/or symptomatic, a “basal” insulin alone is typically added.
Diabetes Care 2012;35:1364–1379
**Start** with bedtime intermediate-acting insulin, or bedtime or morning long-acting insulin; can initiate with 10 units or 0.2 units per kg

**Check** fasting CBG usually daily and increase dose,
- Typically by 2 unit every 3 days, until fasting CBG 70-130 mg/dl;
- Can increase dose in larger increments,
  e.g. by 4 units every 3 days, if fasting CBG > 180 mg/dl

**If Hypoglycemia** occurs, or fasting glucose level < 70 mg/dl, reduce bedtime dose by ≥ 4 units, or 10% if dose > 60 units
Initiating insulin therapy

- Basal insulin is preferable when adding insulin therapy to antidiabetes drugs.

3 exceptions ...

- Patients with relatively low fasting or preprandial glucose (<150 \text{mg/dL}) despite high HbA$_1$C
- Patients with difficulty in compliance with the high demands of basal-bolus treatment
- Patients in whom self-titration might not be feasible
Rationale for initiating basal versus premix insulin analogs
<table>
<thead>
<tr>
<th>Day</th>
<th>ac</th>
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<td><strong>229</strong></td>
<td>178</td>
<td><strong>257</strong></td>
<td>204</td>
</tr>
</tbody>
</table>
The steps of insulin treatment

- Setting glucose control goal
- Initiating insulin therapy
- Titration of insulin dose
- Intensification of treatment regimen
Insulin intensification

- When basal insulin fails to achieve the target in spite of titration, the physician should proceed to insulin intensification.

3 common regimens ...
- Premix
- Basal plus
  - Addition of rapid-acting insulin with one of the daily meals
- Basal bolus
  - Addition of rapid insulin with 2-3 daily meals
Once-daily glargine, detemir, or NPH therapy
Basal-bolus insulin

The diagram illustrates the insulin effect at different times of the day for different types of insulin:
- **Glargine**: Constant release throughout the day.
- **Aspart, lispro, or glulisine**: Bolus release at meals.
- **Detemir**: Basal release at bedtime.
- **NPH**: Basal release throughout the day with peak at bedtime.

This type of insulin regimen is used to manage blood sugar levels in diabetes management.
Premix insulin

- 70/30 or 75/25 mix
- 70/30
- Lispro
- Regular
- NPH

Breakfast  Lunch  Dinner  Hs  Bedtime

Am Fam Physician. 2011;84(2):183-190
Insulin Regimens

• Most patients who begin a basal plus regimen will eventually need a basal-bolus regimen; therefore, basal plus regimen should be initiated if the treating physician decides that the patient will be able to adhere to a basal-bolus regimen.

• Basal bolus most closely resembles physiological insulin secretion

• Premix insulin analogs can be a good option with less complicated and demanding glucose monitoring and injection schedule
Which patient should be offered a premix vs basal-bolus/basal plus regimen?

<table>
<thead>
<tr>
<th>Premix insulin analogs</th>
<th>Basal plus/basal bolus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient preference</td>
<td>Type 1 DM</td>
</tr>
<tr>
<td>Older age</td>
<td>Younger age</td>
</tr>
<tr>
<td>Need assistance with injections</td>
<td>Highly motivated and compliance</td>
</tr>
<tr>
<td>Organized lifestyle</td>
<td>Active lifestyle</td>
</tr>
<tr>
<td>Two meals a day or evening main meal</td>
<td>High variability in eating habits</td>
</tr>
</tbody>
</table>

DIABETES CARE, VOLUME 36, SUPPLEMENT 2, AUGUST 2013
BASAL-BOLUS

Regimen
**Start** with bedtime intermediate-acting insulin, or bedtime or morning long-acting insulin; can initiate with 10 units or 0.2 units per kg

**Check** fasting CBG usually daily and increase dose,
- Typically by 2 unit every 3 days, until fasting CBG 70-130 mg/dl;
- Can increase dose in larger increments, e.g. by 4 units every 3 days, if fasting CBG > 180 mg/dl

If **Hypoglycemia** occurs, or fasting glucose level < 70 mg/dl, reduce bedtime dose by ≥4 units, or 10% if dose > 60 units

**HbA1C ≥ 7%** after 2-3 months

**Add second injection**
If fasting CBG in target 70-130 mg/dl, check CBG before lunch, dinner and bed; depending on CBG results, add second injection; can usually begin with ~4 units and adjust by 2 units every 3 days until CBG in range

**NO**

**YES**

Continue regimen; check HbA1C every 3 months

*Diabetologia (2006) 49:1711–1721*
Add second injection
If fasting CBG in target 70-130 mg/dl, check CBG before lunch, dinner and bed; depending on CBG results, add second injection; can usually begin with ~4 units and adjust by 2 units every 3 days until CBG in range

Pre-lunch CBG out of range: add rapid-acting insulin at breakfast
Pre-dinner CBG out of range: add NPH insulin at breakfast or rapid acting at lunch
Pre-bed CBG out of range: add rapid-acting insulin at dinner

NO
Continue regimen; check HbA1C every 3 months

YES
HbA1C ≥ 7% after 3 months?
Recheck pre-meal CBG and if out of range, check 2-h postprandial levels and adjust preprandial rapid-acting insulin

PREMIX
Regimen
Initiation and intensification of premix insulin analogs

Start with MIX 25/75 or 30/70 – 12 u with breakfast, 6 u with dinner (Or divide basal insulin to 2/3 dose in morning and 1/3 evening)

Fasting glucose: add 2-4 u to evening dose
Check glucose before bed and early morning to avoid hypoglycemia
Repeat until reach target

Evening glucose: Add 2-4 u to morning dose
Check glucose before lunch to avoid hypoglycemia
Repeat until reach target

If fail to reach target in 6 months, consult with diabetologist

DIABETES CARE, VOLUME 36, SUPPLEMENT 2, AUGUST 2013
Using Insulin with Oral Medications

- Insulin sensitizers have been proven safe and effective when combined with insulin therapy
- Metformin, Thiazolidinediones, Alpha-glucosidase inhibitors, DPP-IV inhibitor (Sitagliptin), etc.
Using Insulin with Oral Medications

• Insulin secretagogues (sulfonylureas and glitinides) can be combined with insulin, especially when only basal augmentation is being used.
  • However, there is a possible increased risk of hypoglycemia that needs to be monitored closely.

• Usually by the time insulin is required for meals, insulin secretagogues are not effective or necessary.
  • However, it is recommended to continue oral medications while starting insulin to prevent rebound hyperglycemia.
  • After the diabetes is controlled, the patient may be weaned off of oral medications
How Should I Advance Insulin Therapy* for People with Type 2 Diabetes?

<table>
<thead>
<tr>
<th></th>
<th>Basal Insulin: When to dose and where to start</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Start with once daily intermediate or long-acting insulin</td>
</tr>
<tr>
<td></td>
<td>Initial dose should be 10 U or 0.2 U/kg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Basal Insulin: How to adjust</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.</td>
<td>Adjust by 2 U every 3 days until BG is in range</td>
</tr>
<tr>
<td></td>
<td>Use a pre-breakfast BG target range of 3.9-7.2 mmol/L</td>
</tr>
<tr>
<td></td>
<td>If after 3 months HbA$_{1c}$ is $\geq$7.0%, add a prandial insulin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Prandial Insulin: When to dose, where to start, and how to adjust</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.</td>
<td>Check PG before breakfast, lunch, dinner, and bedtime</td>
</tr>
<tr>
<td></td>
<td>Add rapid-acting insulin to the meal with the highest glucose excursion</td>
</tr>
<tr>
<td></td>
<td>Start with 4 U and adjust by 2 U every 3 days based on BG change</td>
</tr>
<tr>
<td></td>
<td>Add additional meal-time injections if HbA$_{1c}$ $\geq$7.0% after 3 months</td>
</tr>
</tbody>
</table>

BG = blood glucose.

*Insulin therapy regimens should be designed taking lifestyle and meal schedule into account; this algorithm provides a basic guideline for initiation and adjustment of insulin. Regimens with once- or twice-daily premixed insulins are also possible. Nathan DM, et al. *Diabetes Care.* 2009;32(1):193-203.
PREMIXED INSULIN ANALOGUES

PREMIXED HUMAN INSULIN
# Comparison of Premixed Insulin Analogues with Premixed Human Insulin

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Premixed insulin analogues or premixed human insulin</th>
<th>Strength of evidence*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting glucose level</td>
<td>Similar effectiveness</td>
<td>Moderate</td>
</tr>
<tr>
<td>PPG level</td>
<td>Favors premixed insulin analogues</td>
<td>High</td>
</tr>
<tr>
<td>HbA\textsubscript{1c} level</td>
<td>Similar effectiveness</td>
<td>High</td>
</tr>
<tr>
<td>Hypoglycaemia</td>
<td>Similar effectiveness</td>
<td>High</td>
</tr>
<tr>
<td>Weight</td>
<td>Similar effectiveness</td>
<td>Moderate</td>
</tr>
<tr>
<td>All-cause mortality, CVD mortality, and CVD morbidity</td>
<td>Cannot make a conclusion</td>
<td>Low</td>
</tr>
</tbody>
</table>

*The strength of evidence was defined as follows: High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

SUMMARY of Insulin trials in type2 DM

- Any insulin will lower glucose and HbA1C
- All insulins are associated with some weight gain and some risk of hypoglycemia.
- The larger the doses and the more aggressive the titration, the lower the HbA1C, but often with a greater likelihood of adverse effects.
- Generally, long-acting insulin analogs reduce the incidence of overnight hypoglycemia, and rapid-acting insulin analogs reduce postprandial glucose excursions as compared with corresponding human insulins (NPH, Regular), but they generally do not result in clinically significantly lower HbA1C.
“All treatment decisions, where possible, should be made in conjunction with the patient, focusing on his/her preferences, needs, and values”