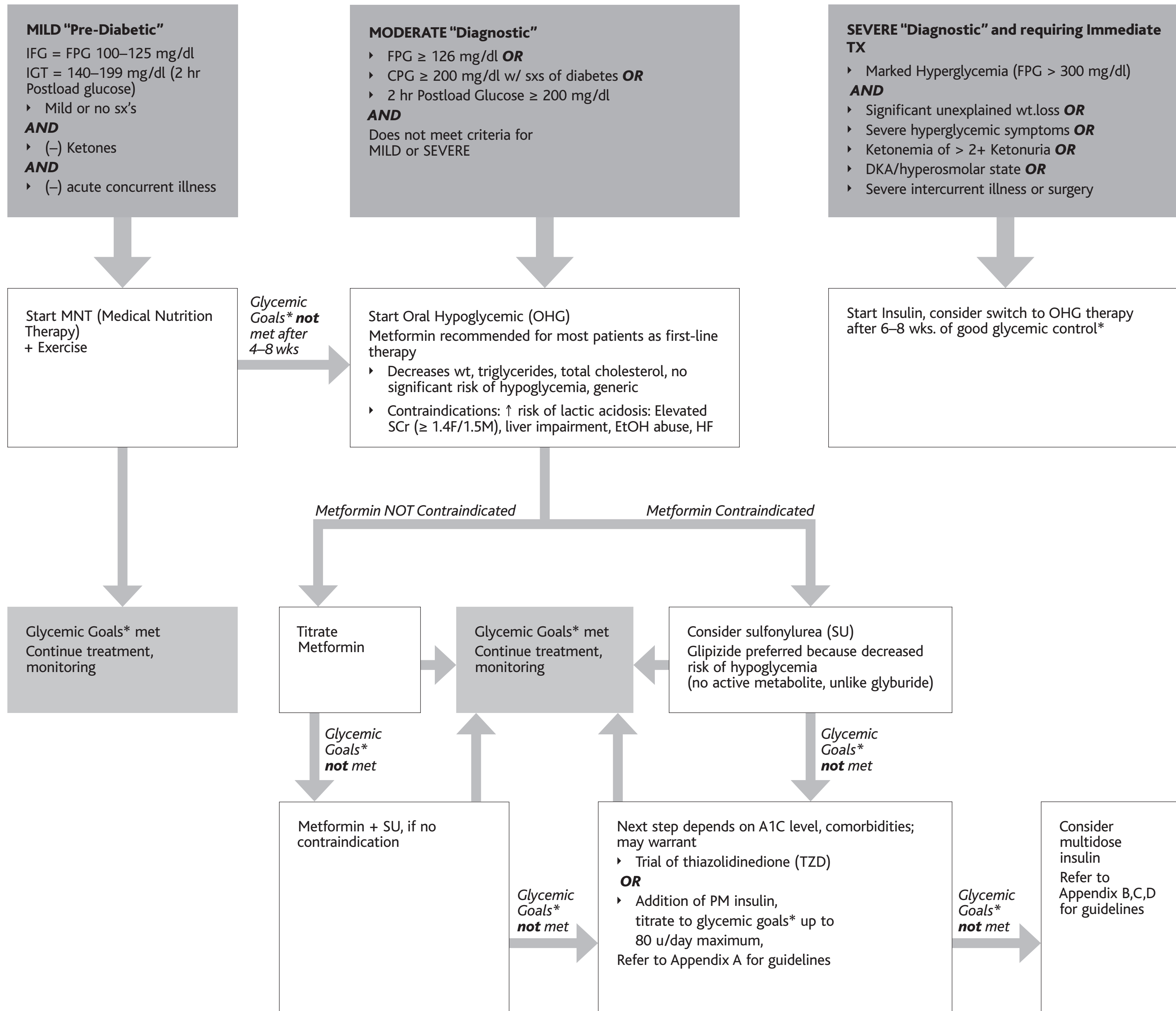
Type 2 Diabetes Treatment Algorithm



Diabetic Goals

*Glycemic Goals	
A1C	< 7.0%
Peak postprandial capillary plasma glucose	< 180 mg/dl
Preprandial capillary plasma glucose	90–130 mg/dl
Other Goals	
Blood pressure	< 130/80 mmHg
Triglycerides	< 150 mg/dl
LDL	< 100 mg/dl
HDL	> 40 mg/dl

Key Concepts In Setting Glycemic Goals

- A1C is the primary target for glycemic control
- Goals should be individualized; Certain populations (children, pregnant women, and elderly) require special considerations
- More stringent glycemic goals (i.e., a normal A1C < 6%) may further reduce complications at the cost of increased risk of hypoglycemia
- Less intensive glycemic goals may be indicated in patients with severe or frequent hypoglycemia
- Postprandial glucose may be targeted if A1C goals are not met, despite reaching preprandial glucose goals
- For primary prevention patients > 40 yrs, consider statin at dose sufficient to reduce LDL by 30–40% and low-dose ASA to reduce risk of CV events.

Adapted from: Table 6, Standards of medical care in diabetes. Diabetes Care (2006);29(suppl 1):510, 518.

Legend

Abbreviation	Meaning
CPG	Casual Plasma Glucose
FPG	Fasting Plasma Glucose
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance
SMBG	Self-Monitoring Blood Glucose

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Guidelines for Conservative Titration of Insulin in Type 2 Diabetes

APPENDIX A: Adding PM Insulin to an OHG Regimen: Indicated When FPG/Fasting SMBG Consistently (>60% Readings) ≥ 140 mg/dl and A1C ≥ 8% Despite Max Dose of OHG

On METFORMIN: Start / continue metformin 1000mg BID; Stop all other OHG

- Add NPH HS:
  10u (16u if BMI ≥ 30)
  if no recent hypoglycemia
  5u (10u if BMI ≥ 30)
  if recent hypoglycemia

On GLIPIZIDE or GLYBURIDE and DO NOT include METFORMIN: Start / continue glipizide 20mg or glyburide 10mg BID; Stop all other OHG

- Add NPH HS:
  10u (16u if BMI ≥ 30)
  if no recent hypoglycemia
  6u (10u if BMI ≥ 30)
  if recent hypoglycemia

1 Adjust insulin dose based on AM fasting SMBG reading: Follow-up at least weekly until insulin dose titrated to ≥ 80% *fasting* SMBG readings between 80–120 mg/dl:

If ≥ 60% of AM SMBG readings ≥ 140 mg/dl: ↑ HS NPH x 2u (4u if BMI ≥ 30)

If ≥ 60% of AM SMBG readings ≤ 80 mg/dl: ↓ HS NPH dose x 2u (4u if BMI ≥ 30)

- If receiving sulfonylurea and AC supper SMBG readings are < 80 mg/dl x3, reduce AM SU dose by 50%.

2 Adjust OHG based on AC and HS SMBG readings: Patient to perform QID SMBG testing (AC & HS) x 3–5 days

- Titrate / add OHG to achieve AC and fasting SMBG readings 80–120 mg/dl. Dose ↑ indicated if ≥ 60% of AC & HS SMBG readings ≥ 140mg/dl.
- If patient receives 2 or 3 OHG + HS insulin AND AC and fasting SMBG readings are still above goal, consider BID insulin therapy.

APPENDIX B: Initiation / Titration of 70/30 Insulin

1 Initiation of 70/30 insulin: 10u AM, 5u PM AC breakfast & supper (if BMI ≥ 30, double each dose)

- Dose adjustment: Patient to perform QID SMBG testing (AC & HS). Follow-up at least wkly until insulin dose titrated to ≥ 80% fasting & AC SMBG readings are 80–140 mg/dl . When goal has been reached, reduce SMBG to AC breakfast & supper one day alternating with AC lunch and before bedtime the other day.

SMBG consistently high (≥ 60% of readings ≥ 140mg/dl) w/o hypoglycemia:

- AC breakfast &/or pre-HS readings high: ↑ PM 70/30 dose x 2u (4u if BMI ≥ 30)
- AC lunch &/or AC supper readings high: ↑ AM 70/30 dose x 2u (4u if BMI ≥ 30)

SMBG consistently low (≥ 60% of readings ≤ 80mg/dl):

- AC breakfast &/or pre-HS readings low:↓ PM 70/30 dose x 2u (4u if BMI > 30)
- AC lunch &/or AC supper readings low: ↓ AM 70/30 dose x 2u (4u if BMI > 30)

APPENDIX C: Initiation and Titration of NPH and Regular Insulin

1 Initiation of NPH insulin: 10u AM, 6u PM AC breakfast & supper (BMI ≥ 30: 20u AM, 10u PM). Patient to perform fasting AM and AC supper SMBG daily

2 NPH dose adjustment: Follow-up at least weekly until insulin dose titrated to ≥ 80% fasting and AC SMBG readings are 80–140 mg/dl

SMBG consistently high (≥ 60% of readings ≥ 140mg/dl) without hypoglycemia:

- Pre-breakfast readings high: ↑ PM NPH dose x 2u (4u if BMI > 30)
- Pre-supper readings high: ↑ AM NPH dose x 2u (4u if BMI > 30)

SMBG consistently low (≥ 60% of readings ≤ 80mg/dl):

- Pre-breakfast readings low: ↓ PM NPH dose x 2u (4u if BMI > 30)
- Pre-supper readings low: ↓ AM NPH dose x 2u (4u if BMI > 30)

3 Regular insulin initiation & dose adjustment

- When goal reached, patient to perform QID SMBG testing (pre-meals & HS) x 3–5 days. Add/adjust regular insulin 30 min AC as follows.

Follow-up at least weekly until insulin dose titrated to ≥ 80% of SMBG readings between 80–140 mg/dl

SMBG consistently high (≥ 60% of readings ≥ 140mg/dl) without hypoglycemia:

- AC lunch readings high: Add or ↑ AM R dose x 2 u (4 u if BMI > 30)
- Pre-HS readings high: Add or ↑ PM R dose x 2 u (4 u if BMI > 30)

SMBG consistently low (≥ 60% of readings < 80mg/dl):

- AC lunch readings low: ↓ AM R dose x 2 u (4 u if BMI > 30)
- Pre-HS readings low: ↓ PM R dose x 2 u (4 u if BMI > 30)

APPENDIX D: Initiation and Titration of Long-Acting (QD or BID) + Rapid-Acting (Pre-Meal) Insulins

1 Initiation of long-acting insulin: Patient to perform AC breakfast (FPG) testing daily; if using NPH or detemir BID, also perform SMBG testing AC dinner.

- NPH 10u HS to 10u BID
- Glargine 10–14u QD, usually QHS. When converting patient from NPH, glargine dose same as total daily dose of NPH if NPH is given QD and is 20% less if NPH is given BID
- Detemir 10u QD (QPM with dinner or HS) to 10u BID (Note: When converting from NPH, total daily dose is same as total daily NPH dose).

2 NPH or detemir BID dose adjustment: Follow-up at least weekly until insulin dose titrated to ≥ 60% FPG and AC dinner readings are 80–140 mg/dl

SMBG consistently ↑ (≥ 60% of readings ≥ 140mg/dl) without hypoglycemia:

- AC breakfast readings high: ↑ PM NPH or detemir dose x 2u (4u if BMI > 30)
- AC supper readings high: ↑ AM NPH or detemir dose x 2u (4u if BMI > 30)

SMBG consistently low (≥ 60% of readings ≤ 80mg/dl):

- AC breakfast readings low: ↓ PM NPH or detemir dose x 2u (4u if BMI > 30)
- AC supper readings low: ↓ AM NPH or detemir dose x 2u (4u if BMI > 30)

3 NPH, detemir (less common) or glargine once daily dose adjustment: Follow-up at least weekly until insulin dose titrated to ≥ 60% FPG readings are 80–140 mg/dl

FPG consistently ↑ (≥ 60% of readings ≥ 140mg/dl) without hypoglycemia:

- ↑ NPH or detemir dose x 2u (4u if BMI > 30)

FPG consistently low (≥ 60% of readings ≤ 80mg/dl):

- ↓ NPH or detemir dose x 2u (4u if BMI > 30)

4 Rapid-acting insulin initiation & dose adjustment: Start with ~1u for every 10–15 gm carbohydrates in each meal (most meals consist of 60 gm CHO). Inject within 15 minutes AC or within 20 minutes of starting meal. Follow-up at least wkly until insulin dose titrated to ≥ 80% of AC SMBG readings are 80–140 mg/dL. When goal reached, reduce SMBG to AC breakfast & supper one day alternating w/ AC lunch & before bedtime the other day.

AC SMBG consistently high:
Increase prior meal dose of rapid-acting insulin x 1–2 u

AC SMBG consistently low:
Decrease prior meal dose of rapid-acting insulin x 1–2 u

CPG	Casual Plasma Glucose	FPG	Fasting Plasma Glucose	IFG	Impaired Fasting Glucose	IGT	Impaired Glucose Tolerance	SMBG	Self-Monitoring Blood Glucose

Oral Hypoglycemic Agents

Medication/Brand, Maker	Available Strengths	Starting Dose (E = elderly)	Dose Adjustment[1]	Dosing Interval	Maximum Daily Dose[2]	Comments	Generic
Second Generation Sulfonylureas (SU)							
Glimepiride/Amaryl, Aventis	1, 2, 4mg	1–2 mg/d (E: 1 mg/d)	2mg/d Q1–2 weeks	QD w/ breakfast	8mg		✓
Glipizide/Glucotrol, Pfizer	5, 10mg	2.5–5 mg/d; may start up to 40mg/d if mod–severely symptomatic (E: 2.5 mg/d)	Double dose Q–week	QD 30 minutes AC (BID if > 20mg/d)	40mg	‣ No active metabolites	✓
Glipizide/Glucotrol XL, Pfizer	5, 10mg	5mg/d (E: 5mg/d)	5mg/d Q1–2 weeks	QD w/ breakfast	20mg		✓
Glyburide/Diabeta, Sanofi-aventis; **Micronase,** Pharmacia	1.25, 2.5, 5mg	2.5–5 mg/d; may start up to 20mg/d if mod–severely symptomatic (E: 1.25 mg/d)	Double daily dose Q1–2 weeks	QD w/ breakfast (BID if > 10mg/d)	20mg	‣ Active metabolites; sulfonylurea with highest incidence of hypoglycemia	✓
Glyburide, micronized/ Glynase, Pfizer	1.5, 3, 4, 5, 6mg	1.5–3mg/d (E: 0.75–1.5 mg/d)	Double daily dose Q1–2 weeks	QD w/ breakfast (BID if > 10mg/d)	12mg		
Biguanides/Biguanide Combinations							
Metformin, BMS	500, 850, 1000mg	500mg QD w/ dinner x 1 week; if tolerated, ↑ to 500mg BID w/ food	500mg/d Q1–2 weeks	QD-TID (usually BID) with meals	2550mg	‣ May initiate w/ 850mg/day and ↑ x 850mg Q1–2 weeks, but may be less GI-tolerable. ‣ Maximum effective dose appears to be 2000mg/d	✓
Metformin XR, BMS	500 mg	500mg QD	500mg/d Q–week	QD w/ evening meal	2000mg		✓
Glyburide-Metformin/ Glucovance, BMS	1.25/250, 2.5/500, 5/500mg	1.25/250mg QD-BID	1 tab/d Q–week	BID w/ meals	20/2000mg		✓
Glipizide-Metformin/ Metaglip, BMS	2.5/500, 2.5/500, 5/500mg	2.5/250mg QD w/ meal Consider 2.5/500mg BID if FPG 280–320	1 tab/d Q1–2 weeks	BID w/ meals	10/2000mg		
Thiazolidinediones (TZD) and Combinations							
Pioglitazone Actos, Takeda	15, 30, 45mg	A1C <9: 15mg QAM A1C ≥ 9: 30mg QAM	15mg/d Q2–3 months (based on A1C)	QD	45mg	‣ Check LFTs at baseline and periodically (Q3–6 mon) **Do not** initiate /continue if ALT > 2.5 upper limits of normal. ‣ HF: Use only in stable patients; not recommended for NYHA Class III or IV. TZD-induced fluid retention may exacerbate HF.	
Rosiglitazone Avandia, GSK	2, 4, 8mg	4mg QAM	4mg/d Q2–3 months (based on A1C)	QD (may be given BID)	8mg		
Piogliatzone-Metformin/ Actoplus Met, Takeda	15/500mg 15/850mg	15/500 mg or 15/850mg QD-BID	Q2–3 months (based on A1C)	QD-BID	45/2550 mg	‣ See individual comments for pioglitazone and metformin.	
Rosiglitazone-Metformin/ Avandamet, GSK	1/500mg, 2/500mg, 4/500mg, 2/1000mg, 4/1000mg	Usually 2/500 to 4/500mg BID	• Rosiglitazone component: Q2–3 months (based on A1C) • Metformin component: Q1–2wks	BID	8/2000mg	‣ See individual comments for rosiglitazone and metformin.	
Rosiglitazone-glimepiride / Avandaryl, GSK	4/1mg, 4/2mg, 4/4mg	4/1mg or 4/2mg QD (E: 4/1mg QD)	• Rosiglitazone component: Q2–3 months (based on A1C) • Glimepiride component: Q1–2wks	QD w/ first meal of day	8/4mg	‣ See individual comments for rosiglitazone and glimepiride.	

[1] Frequency listed is the soonest that the dose should be changed based on drug pharmacokinetics and pharmacodynamics; more time (e.g., 2-4 weeks) may be appropriate to evaluate the impact of concomitant MNT and exercise.
[2] For SU, dosing beyond half of maximum daily dose provides minimal benefit.

Notes: Non-Sulfonylurea Secretagogues (repaglinide/Prandin, nateglinide/Starlix) were not included because of lack of efficacy in patients who fail SU therapy and relative lower efficacy than the sulfonylureas. Alpha-Glucosidase Inhibitors (acarbose/Precose, miglitol/Glyset) also not included due to limited impact on glycemic control, although these may be useful for patients with significant postprandial hyperglycemia.

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Insulins

Insulin / Brand, Maker	Onset	Peak	Duration	Dosage Timing	Appearance	Compatibility
Rapid Acting						
Insulin Lispro / Humalog, Eli Lilly	15 min	30 min–1.5 hrs	4–5 hrs	15 min AC–15 min PC	Clear	‣ Can mix w/ NPH or U (draw lispro first) ‣ **Do not** mix with glargine
Insulin Aspart / Novolog, Novo	15 min	40–50 min	3 –5 hrs	5–10 min AC		
Insulin glulisine/Apidra, Sanofi-aventis	15 min	1 hr	4–5 hrs	15 min AC–15 min PC		
Short Acting						
Regular Insulin / Humulin R, Eli Lily	30–60 min	1–2 hrs	5–8 hrs	30 min AC	Clear	‣ Can mix w/ NPH
Regular Insulin / Novolin R, Novo						
Intermediate Acting						
NPH Insulin (Isophane insulin suspension; w/ Zinc and protamine) / Humulin N, Eli Lilly	1–3 hrs	6–14 hrs	16–24 hrs	‣ w/in 15 min AC if mixed w/ rapid ‣ w/in 30 min AC if mixed w/ short ‣ individualized based on SMBG	Cloudy	‣ Can mix with aspart or lispro (draw rapid first and inject immediately) ‣ Can mix w/ reg (draw reg first) ‣ **Do not** mix w/ L, U, or glargine
NPH Insulin (Isophane insulin suspension; w/ Zinc and protamine) / Novolin N, Novo						
Long Acting						
Insulin detemir/Levemir, Novo Nordisk	Not specified by manufacturer	6–8 hrs	6–23 hrs (dose dependent)	QD or BID	Clear	‣ **Do not** mix w/ other insulins
Insulin glargine / Lantus, Aventis	1 hr	none	24 hrs	QD usually dosed HS		
Insulin Combinations						
30% ins. aspart, 70% ins. aspart protamine / Novolog Mix 70 /30, Novo	Faster than Novolin 70/30, about equal to insulin aspart	Mean 2.4 hrs Range 1–4 hrs	15–18 hrs, max up to 24 hrs	15 min AC	Cloudy	N/A
25% ins. lispro, 75% ins. lispro protamine / Humalog Mix 75/25, Eli Lilly	Faster than Humulin 75/25, about equal to insulin lispro	Mean 2.6 hrs Range 1–6.5 hrs	Up to 24 hrs (similar to Hum 70/30)			
30% regular, 70% NPH / Novolin 70/30, Novo	30 to 60 min	2–12 hrs	Effective 10–16 hrs Max up to 18–24 hrs	30 min AC, based on individual response		
30% regular, 70% NPH / Humulin 70/30, Eli Lilly		Mean 4.4 hrs Range 1.5–16 hrs				
50% regular, 50% NPH / Humulin 50/50, Eli Lilly		Mean 3.3 hrs. Range 2–5.5 hrs				

Note: All pork insulins, Lente and Ultralente (Humulin L and Humulin U) preparations discontinued as of end calendar year 2005

References:

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