

## APPROACH TO MANAGEMENT OF TYPE 2 DIABETES

### Nonpharmacologic Therapy

- ◆ **Lifestyle Modifications & Patient Education** are important at all levels!!!<sup>1,2</sup>

If individualized goals for glucose are not achieved in 2-4 months,  
 ⇒ reassess; advance to next level of therapy

See Health Canada's  
 Food & Fitness Guides

### Oral Hypoglycemic Monotherapy

- ◆ **If obese (BMI ≥30)**

⇒ start **metformin (MF) 500mg po OD or BID** (↑dose over 3-4 weeks; usual ≤2,000mg/day; lower doses in elderly-see Table 2)  
 ⇒ alternative agents used if metformin contraindicated/not tolerated (e.g. acarbose, sulfonylureas, repaglinide, "glitazones"; see chart)

MF target dose in UKPDS (age ≤65):  
 1700mg am + 850mg @supper (↓ mortality)

- ◆ **If non-obese**

⇒ start sulfonylurea (SU) or metformin (↑dose over 3-4 weeks)  
 ⇒ consider acarbose or repaglinide if main target is **PPBG**  
 ⇒ alternative agents such as "glitazones" may also be considered (note these agents can take a long time before effect seen (8-16 weeks). There are theoretical advantages to early use, but await studies on morbidity and mortality outcomes  
 Repeat A1C; Reassess lifestyle modifications in 2-4 months,  
 ⇒ If targets for glucose control not achieved, advance combination therapy (Combination therapy will be required in most Type 2 patients)

### Oral Combination Therapy

- ◆ a variety of 2-drug combinations may be considered esp. if A1C ≥9% initially (see Table 7)
- ◆ combination of repaglinide and sulfonylureas not usually recommended  
 Repeat A1C; Reassess lifestyle modifications in 2-4 months,  
 ⇒ If targets for glucose control not achieved, advance to next level of therapy

### Add Insulin Therapy +/- Oral Agents

- ◆ **Option 1: Bedtime insulin** (e.g. Humalin N/Novolin N) + daytime oral hypoglycemics

⇒ if on SU + other oral agent, may consider discontinuing / reducing the SU  
 - add intermediate acting insulin, 5-15units at HS (initial ~0.1units/kg; max 0.25units/kg)  
 - ↑ insulin dose by 2 units every 3-4 days until fasting glucose of 4-7  
 - may result in better control, lower insulin dose, less weight gain than insulin alone  
 - if target BG not achieved at 30units/day, or if daytime BG rises, may switch to split-mixed insulin or a more intensive regimen (usual range: 0.25-1unit/kg/d)

- ◆ **Option 2: Switch to insulin therapy 1-4x/day**

⇒ may discontinue certain oral hypoglycemics (see Table 7)  
 - adjust insulin dose and frequency to achieve target levels  
 e.g. **Split-mixed insulin regimen**  
 - estimate total starting daily dose (0.3-0.6 units/kg)  
 - divide daily dose: 2/3 in morning before breakfast; 1/3 in evening before supper  
 - divide each dose: 2/3 intermediate-acting & 1/3 short-acting insulin (or 30/70 mix)

Some patients may eventually require very high doses of insulin due to insulin resistance (max 400U/day in UKPDS)

(Note: insulin temporarily indicated in any pt with metabolic decompensation, severe fasting hyperglycemia, or severe illness.)

| GLUCOSE TARGETS                    | Canadian 2003 | Target for most | Normal range | →consider achieving if can be done | Note: role for individualizing targets (ie. less aggressive in frail elderly <sup>29</sup> ; more aggressive in younger candidates). |
|------------------------------------|---------------|-----------------|--------------|------------------------------------|--|
| A1C q3-6 mon (calibrate meter qyr) | ≤7            | ≤6              |              |                                    |  |
| FPG (mmol/L)                       | 4-7           | 4-6             |              | safely without                     |  |
| PPBG (mmol/L) 2hr post             | 5-10          | 5-8             |              | hypoglycemia etc..                 |  |

BP<sup>2004</sup> Diabetes → 130/80 if no proteinuria; 125/75 if proteinuria >1g/d. **LIPID**<sup>2003</sup> Diabetes → LDL <2.5 Total Chol/HDL <4

| RENAL                            | Normal                | Microalbuminuria            | Macroalbuminuria        |
|----------------------------------|-----------------------|-----------------------------|-------------------------|
| Albuminuria                      | <30mg/day (<20ug/min) | 30-300mg/day (20-200ug/min) | >300mg/day (>200ug/min) |
| Albumin mg/Creatinine mmol Ratio | Male <2; Female <2.8  | Male 2-20; Female 2.8-28    | Male >20; Female >28    |

| BMI (kg/m <sup>2</sup> ) | WEIGHT (Kg; lbs) |    |     |     |     |     |     |     |    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|--------------------------|------------------|----|-----|-----|-----|-----|-----|-----|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|                          | 45               | 50 | 55  | 60  | 65  | 70  | 75  | 80  | 85 | 90  | 95  | 100 | 105 | 110 | 115 | 120 | 125 | 130 | 99  | 110 | 121 | 132 | 143 | 154 | 165 | 176 | 187 | 198 | 209 | 220 | 231 | 242 | 253 | 264 | 275 | 286 |     |     |     |     |
| HEIGHT (Cm; inches)      | 150              | 59 | 20  | 22  | 24½ | 26½ | 29  | 31  | 33 | 35½ | 38  | 40  | 42  | 44½ | 46½ | 49  | 51  | 53  | 55½ | 58  | 155 | 61  | 18½ | 21  | 23  | 25  | 27  | 29  | 31  | 33  | 35½ | 37½ | 39½ | 41½ | 43½ | 46  | 48  | 50  | 52  | 54  |
|                          | 160              | 63 | 17½ | 19½ | 21½ | 23½ | 25½ | 27  | 29 | 31  | 33  | 35  | 37  | 39  | 41  | 43  | 45  | 47  | 49  | 51  | 165 | 65  | 16½ | 18½ | 20  | 22  | 24  | 26  | 27½ | 29½ | 31  | 33  | 35  | 36½ | 38½ | 40½ | 42  | 44  | 46  | 48  |
|                          | 170              | 67 | 15½ | 17  | 19  | 21  | 22½ | 24  | 26 | 27½ | 29½ | 31  | 33  | 34½ | 36  | 38  | 40  | 41½ | 43  | 45  | 175 | 69  | 14½ | 16  | 18  | 19½ | 21  | 23  | 24½ | 26  | 28  | 29½ | 31  | 32½ | 34½ | 36  | 37½ | 39  | 41  | 42½ |
|                          | 180              | 71 | 14  | 15½ | 17  | 18½ | 20  | 21½ | 23 | 24½ | 26  | 28  | 29  | 31  | 32½ | 34  | 35½ | 37  | 38½ | 40  | 185 | 73  | 13  | 14½ | 16  | 17½ | 19  | 20½ | 22  | 23½ | 25  | 26  | 28  | 29  | 30½ | 32  | 33½ | 35  | 36½ | 38  |
|                          | 190              | 75 | 12½ | 14  | 15  | 16½ | 18  | 19½ | 21 | 22  | 23½ | 25  | 26  | 27½ | 29  | 30½ | 32  | 33  | 34½ | 36  | 195 | 77  | 12  | 13  | 14½ | 16  | 17  | 18½ | 19½ | 21  | 22½ | 23½ | 25  | 26  | 27½ | 29  | 30  | 31½ | 33  | 34  |

Underweight = <18.5kg/m<sup>2</sup>; Normal = 18.5-24.9kg/m<sup>2</sup>; Overweight = 25-29.9kg/m<sup>2</sup>; Obese = ≥30kg/m<sup>2</sup>

Table 6: Individualization of Drug Therapy: Special Considerations

| Patient Factor                     | Consider ⇒   |
|------------------------------------|--|
| Renal failure *                    | "Glitazones", repaglinide; also tolbutamide or gliclazide <sup>3</sup>                     |
| Hepatic disease                    | Insulin, repaglinide, acarbose (Caution: glyburide, metformin & glitazones)                |
| Hypoglycemia                       | Metformin, "Glitazones", Acarbose; also repaglinide, nateglinide, gliclazide & glimepiride |
| Obese                              | Metformin; Acarbose; also "Glitazones"   |
| Irregular mealtimes                | Repaglinide (may be preferred over SU)   |
| PPBG >10mmol/l & FPG minimally ↑'d | Repaglinide or Acarbose<br>Insulin lispro HUMANLOG (if PPBG very high)                     |

\* Metformin dosing in elderly: lactic acidosis assoc. with metformin is rare (<1:10,000 treated pts)<sup>4,5,6</sup>  
 Maximum Metformin Dose<sup>7</sup>: For CrCl 60 ml/min → 1700mg/d; 30 ml/min → 850mg/d; <30 ml/min → contraindicated

Table 7: Combination Therapy/Insulin Therapy in Type 2 Diabetes<sup>8,9</sup>

| Drug combination                           | ↓ in A1C         | hypo-glyc. | Wt  | Comments (long-term outcomes not well studied!)  |
|--|------------------|------------|-----|--|
| SU + MF                                    | ↓↓↓              | ↑↑         | ↑   | ◆ if SU initial agent, may add MF or a TZD; (SU+MF may ↓A1C by additional 1.7%; one study found ↑mortality with combination <sup>10</sup> )<br>◆ if MF initial agent, may add SU or repaglinide<br>◆ MF combos generally result in less weight gain than SU combinations; ◆ MF+pioglitazone had positive lipid effects; ◆ MF+acarbose: ↓ weight / PPBG but ↑GI SEs; ◆ for hypoglyc. on acarbose: must treat with glucose as sucrose not absorbed |
| SU + TZD <sup>11</sup>                     | ↓↓               | ↑↑         | ↑↑  |  |
| SU + acarbose                              | ↓                | ↑↑         | ↑   |  |
| MF+ repaglinide <sup>12</sup>              | ↓↓               | ↑          | ↑   |  |
| MF+ TZD <sup>13,14</sup>                   | ↓↓               | ↑          | ↑   |  |
| MF+ acarbose <sup>15</sup>                 | ↓                | -          | ↓   |  |
| TZD + acarbose                             | ↓                | ↑          | ↑   |  |
| Insulin monotherapy                        | ↓↓↓              | ↑↑↑        | ↑↑↑ | ◆ tight BG control but hypoglycemia/weight gain  |
| Insulin + SU                               | ↓↓↓              | ↑↑         | ↑↑  | ◆ may improve glycemic control over insulin alone; caution in elderly due to hypoglycemia  |
| Insulin + MF (FINFAT STUDY <sup>16</sup> ) | ↓↓↓              | ↑          | ↑   | ◆ overcomes insulin resistance; MF has positive effect on wt & lipids; preferred in obese patient; superior to insulin+SU; insulin sparing ~20-25%   |
| Insulin+ pioglitazone or rosiglitazone*    | ↓↓ <sup>17</sup> | ↑↑↑        | ↑↑↑ | ◆ overcomes insulin resistance; effective but more study needed (e.g. ↑ risk of edema/HF <sup>18</sup> ),  |
| Insulin+ repaglinide                       | ↓↓               | ↑↑         | ↑↑  | ◆ option to ↓ PPBG   |
| Insulin + acarbose                         | ↓                | ↑↑↑        | ↑↑↑ | ◆ recommended to ↓ PPBG when diet high in CHOs; may also ↓ weight & triglycerides  |

◆ some 3-drug regimens useful for glycemic control but not well studied (e.g. Insulin+SU+MF)












A1C = glycosylated hemoglobin BG = blood glucose CHO = carbohydrate FPG = fasting plasma glucose HF = heart failure MF = metformin PPBG = postprandial blood glucose SE = side effects SU = sulfonylurea TZD = pioglitazone & rosiglitazone Wt = weight \*official labeling: "not indicated"


**HYPOGLYCEMIC AGENTS - Comparison Chart**

19-20-21-22-23-24-25-26-27-28-29-30

Prepared by: Loren Regier, Sharon Downey, Brent Jensen—www.RxFiles.ca

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| NAME /DOSAGE FORMS   | KINETICS   | EFFECTS ON   |      |         |         |     |     |     | DRUG INTERACTION   | COMMENTS  | INITIAL & (Max.) DOSE   | USUAL DOSE RANGE   | \$  /100 day  |  |
|--|--|--|------|---------|---------|-----|-----|-----|--|---|---|--|--|--|
|  |  | FPG  | PPBG | A1C     | LDL     | HDL | TGs | Wt  |  |   |   |  |  |  |
| <b>SULFONYLUREAS (SU) – stimulate insulin release from β cell; increase peripheral glucose utilization (↑ #/sensitivity of insulin receptors?); reduce hepatic gluconeogenesis</b>                         |  |  |      |         |         |     |     |     |  |   |   |  |  |  |
| <b>Chlorpropamide</b><br><b>DIABINESE</b><br>(100, 250mg scored tabs)  | P = 6-8h<br>D = 24-72h                                   | ↓  | ↓    | ↓       | ↓       | ↓   | ↓   | ↓   | <b>Numerous:</b><br>• ↑ Hypoglycemic effect with: EtOH, NSAIDs, salicylates, sulfonamides, MAOIs, cimetidine.<br>• β-Blockers may mask hypoglycemia<br>• Disulfiram rx. with EtOH, mostly with chlorpropamide<br>• rifampin ↓ effect | Does not correct impaired 1st phase insulin response; many (~75%) require 2 <sup>nd</sup> agent for adequate control (e.g. + metformin or TZD); ~1 <sup>st</sup> choice option for lean patient<br><b>Hypoglycemia:</b> most with chlorpropamide & glyburide (see note below); <b>least:</b> tolbutamide, glimepiride <sup>31,32</sup> & gliclazide <sup>33</sup><br>Caution in elderly (hypoglycemia risk) & obese (wt gain).<br><b>Require consistent food intake</b> to avoid problems with hypoglycemia (↑risk: elderly, debilitated, malnourished)<br><b>SE: Wt gain, headache, dizziness, sulfa skin reactions</b> (rash/photosensitivity ~1%), GI side effects in 1-3%; concerns with cardiac toxicity and hyperinsulinemia.<br>Reduce dose if hypoglycemia or renal/hepatic dysfx<br><b>Dose titration q1-2 weeks</b> | 100mg od<br>(500mg od)  | 100mg po od<br>250mg po od   |  16<br> 13   |  |
| <b>Gliclazide</b> ✕ ▼<br><b>DIAMICRON</b> 80 <sup>5</sup> mg tab<br><b>DIAMICRON MR</b><br>30 <sup>5</sup> mg  | P = 4-6h<br>D = 10-24h                                   | ↓  | ↓    | ↓ 1-1.5 | -       | -   | -   | ↑↑  |  |   | 40mg (160mg bid)<br>30mg (120mg od)   | 80mg po bid<br>60mg MR po od   | 95<br>95   |  |
| <b>Glyburide</b><br><b>DIABETA</b><br>(2.5, 5mg scored tabs)   | O = 15-60min<br>P = 2-4h<br>D = 12-24h                   | Total Wt gain with glyburide >4kg vs >6kg insulin (UKPDS-33)   |      |         |         |     |     |     |  |   | • Disulfiram rx. with EtOH, mostly with chlorpropamide<br>• rifampin ↓ effect | 1.25-2.5mg od<br>(10mg bid)  | 5mg po od<br>5mg po bid<br>7.5mg po bid  |  15<br> 20<br> 26 |
| <b>Tolbutamide</b><br><b>ORINASE</b> (500mg scored tab)  | P = 3h<br>D = 6-12h                                      | Glimepiride <b>AMARYL</b> ✕ ⊗ (1,2,4mg scored tab)<br>1mg od (\$90); 2mg od (\$90); 4mg od (\$90) /100days  |      |         |         |     |     |     |  |   |   | 250mg od<br>(1000mg tid)   | 500mg po bid<br>500mg po tid   | 27<br>37   |
| <b>BIGUANIDES – increase insulin sensitivity and cellular glucose uptake &amp; utilization; reduce hepatic glucose production; ↓ morbidity &amp; mortality in obese patients (UKPDS-34)</b>                |  |  |      |         |         |     |     |     |  |   |   |  |  |  |
| <b>Metformin (MF)</b><br><b>GLUCOPHAGE</b><br>(500 <sup>5</sup> , 850mg tab)   | P = 3h<br>D = 8-12h                                      | ↓  | ↓    | ↓ 1-1.5 | ↓       | ↑   | ↓   | -/↓ | • EtOH and cimetidine ↑ effect<br>• contrast media (long-term ↓ B <sub>12</sub> & folate absorption)<br>{ Caution if CrCl ≤ 60ml/min }<br>• ↑ effect on lipids & weight  | Does not by itself cause hypoglycemia<br>Possible <b>wt loss</b> vs wt gain; → <b>DOC for OBESITY!</b><br><b>SE:</b> To avoid GI SEs, <b>start low &amp; titrate up q2-4wk</b><br>Anemia 6-8:100 (due to B <sub>12</sub> malabsorption)<br>Avoid if <b>severe renal dysfx/CHF</b> or hepatic disease (lactic acidosis 1:10,000) <sup>7</sup> . +SU, TZD, Ins., CMBA<br><b>Elderly: dose reduction required.</b> <sup>34</sup> May prevent NIDDM <sup>35</sup> DPP   | 250-500mg od<br>(850mg tid)   | 500mg po bid<br>850mg bid<br>1g po bid   |  23<br> 46<br> 37<br> 66 |  |
| <b>Metformin/Rosiglitazone</b> <b>AVANDAMET</b> ✕ ⊗ tabs<br>(500mg/1,2,4mg BID = \$150, \$260, \$445 /100day tab; 1gm/2,4mg = \$280, \$470)  |  |  |      |         |         |     |     |     |  |   |   | 1700mg po am, 850mg po pm: <b>UKPDS</b><br>TID dosing option for larger doses to ↓ GI intolerance (dyspepsia, nausea & diarrhea) |  |  |
| <b>α GLUCOSIDASE INHIBITORS –inhibit α-glucosidases in brush border of small intestine; prevent hydrolysis &amp; delay carbohydrate digestion (Tx hypoglycemia with glucose/Insta-gluc, honey or milk)</b> |  |  |      |         |         |     |     |     |  |   |   |  |  |  |
| <b>Acarbose</b><br><b>PRANDASE</b><br>(50,100mg scored tabs)   | Meal-time dosing; may take several weeks for max. effect | acarbose minimally absorbed; monitor 2hr PPBG  |      |         |         |     |     |     | • ↓ digoxin effect<br>• Cholestyramine & cathartics ↑ effect<br>• amylase & pancreatic enzymes ↓ effect<br>• ↓ Fe <sup>++</sup> ? (sucrose not absorbed)   | Does not by itself cause hypoglycemia<br>↑ Liver enzymes = 3% with acarbose; monitor.<br>(Caution as may accumulate in chronic renal failure.)<br><b>SE: GI intolerance: flatulence &gt;41%, diarrhea &gt;28%.</b><br>Maximal effect takes weeks; ↑ dose q4-8wks<br><b>ROLE:</b> useful in pts with ↑ PPBG; + SU, MF; (+Ins.?)  | 25mg od<br>(100mg tid)<br>STOP-NIDDM <sup>36</sup>                            | 50mg po tid<br>100mg po tid  | 92<br>124  |  |
| <b>Miglitol</b> (not yet available in Can.) ✕ ⊗<br><b>GLYSET</b> (25,50,100mg tab)   |  | miglitol well absorbed   |      |         |         |     |     |     |  |   |   | 25mg od<br>(100mg tid)   | 25mg po tid<br>50mg po tid   | n/a<br>n/a   |
| <b>THIAZOLIDINEDIONES (TZDs) or “GLITAZONES” – insulin sensitizers: ↓ hepatic output of glucose &amp; ↑ peripheral insulin uptake; ~ 4+ weeks before effect (adjust dose at ~3 months)</b>                 |  |  |      |         |         |     |     |     |  |   |   |  |  |  |
| <b>Pioglitazone</b><br><b>ACTOS</b><br>(15, 30, 45 mg tab)   | Delayed action...<br>Onset ~3wks                         | ↓  | ↓    | ↓       | -       | ↑   | ↓   | -/↑ | • Cholestyramine ↓ absorption ~70%<br>• Hepatic CYP <sub>2C8</sub><br>• rosigl. not CYP <sub>3A4</sub><br>• ↓ effect of oral contraceptives?<br>• rosigl. ↑ by gemfibrozil   | More effective in obese or hyperinsulinemia patients<br>Does not by itself cause hypoglycemia; resumption of ovulation in anovulatory premenopausal women<br><b>SE: Edema 4.8% (HF<sup>37,38</sup>.HTN); Wt gain; 1% mild anemia</b> (due to hemodilution?); monitor liver fx (ALT) q2mo in 1 <sup>st</sup> yr; pioglitazone may have more +ve lipid effects <sup>39,40</sup><br><b>ROLE:</b> + MF,SU; (possibly alone or + Ins. but ↑HF risk)  | 15mg od<br>(45mg/day)   | 15mg po od<br>30mg po od<br>45mg po od   | 241<br>326<br>475  |  |
| <b>Rosiglitazone</b><br><b>AVANDIA</b><br>(2, 4, 8mg tab)  |  | Max effect in 8-16 wks   | ↓    | ↓       | ↓ 1-1.5 | 41  | 42  | -/↑ |  |   | -/↑   | 4mg od<br>(4mg bid)  | 4mg po od<br>4mg po bid<br>8mg po od   | 236<br>446<br>326  |
| <b>CARBAMOYL BENZOIC ACID DERIVATIVES (CMBAs) – short-acting insulin secretagogue; bind to β cell to stimulate insulin release at different site than SUs; (adjust dose at ~7days)</b>                     |  |  |      |         |         |     |     |     |  |   |   |  |  |  |
| <b>Nateglinide</b><br><b>STARLIX</b><br>(60, 120, 180mg tab)   | O = <20min<br>P = 60-120min<br>D = ~4h                   | ↓  | ↓    | ↓ .5    | -       | -   | -   | -/↑ | • CYP inhibitors ↑ effect:<br>azole-antifungals, erythromycin, gemfibrozil<br>• CYP inducers ↓ effect:<br>barbs, carbamaz & rifampin   | Restores 1 <sup>st</sup> phase insulin release - (↓ PPBG)<br>Rapid, short duration ⇒ ↓ risk of hypoglycemia vs SUs<br>∴ option in elderly; {Flexibility with food intake:<br>skip dose if skip meal; take extra dose if add meal}<br>If stop other hypoglycemics begin next day & watch for hypoglycemia.<br><b>ROLE:</b> alone or + MF, TZD, or insulin  | 60mg tid ac<br>(180mg po tid)   | 60mg po tid<br>120mg po tid<br>180mg po tid  | } 200  |  |
| <b>Repaglinide</b><br><b>GLUCONORM</b><br>(0.5, 1, 2mg tab)  | O = 15-60min<br>P = 60-90min<br>D = ~4-6h                | ↓  | ↓    | ↓ 1-1.5 | -       | -   | -   | -/↑ |  |   | 0.5mg tid ac {if no prev tx or A1C <8%}<br>(4mg qid)                          | 0.5mg po tid<br>1-2mg po tid<br>4mg po tid   | } 105<br>210   |  |

 = ↓ dose for renal dysfx    ζ = scored tab    \$ Cost = total cost & markup in Sask;    ☞ = Exception Drug Status in SK    ✕ = Non-formulary in SK    ⊗ = prior approval for NIHB    ⊗ = not covered by NIHB    ▼ covered by NIHB;    '+' denotes combination options  
 A1C = glycosylated Hemoglobin (reflects glycemic control over prior 8-10 weeks)    BP= blood pressure    DOC= drug of choice    dysfx= dysfunction    EtOH= alcohol    FPG= fasting plasma glucose    GI= gastrointestinal    HDL= high density lipoprotein    HF= heart failure    Ins.= Insulin    KINETICS: O= onset    P= peak    D= duration;    LDL= low density lipoprotein    PPBG= postprandial blood glucose    SE= side effects    Wt= weight    ζ = scored tablet  
**Drug induced ↑ glucose:** antipsychotics, corticosteroids, cyclosporine, diuretics (thiazides e.g. >25mg HCTZ), estrogens, interferon<sup>alpha</sup>, nicotinic acid ↑ dose, phenytoin, sympathomimetics (decongestants), tacrolimus & thyroid meds.  
 Beta-blockers minimal risk of altering glucose control but may alter/mask hypoglycemic response.    **Pregnancy:** Encourage diet, moderate exercise; Avoid oral hypoglycemics; Add insulin as needed if FBG >5.3 & 2hr PPBG >8.9.  
**Hypoglycemia risk -UKPDS:** risk of ≥1 MAJOR hypoglycemic events/yr (ITT): chlorpropamide=1%, glyburide=1.4%, insulin 1.8%; risk of ANY hypoglycemic event/yr chlorprop.= 16%, glyburide=21%, insulin 28%.  
**Oral agents +/- insulin:** with progression of Type 2 diabetic disease, combo therapy with oral agents &/or addition of insulin to the regimen may eventually be required.  
**PPBG** may better reflect risk of cardiovascular disease & all-cause mortality than FBG<sup>44</sup>; FBG & A1C are greater predictors of microvascular complications.    •Consider: ASA 80-325mg/d, control of lipids, diet/exercise, orlistat, ↓ hypertension ACE inhibitor/ARB/thiazide & DC smoking!

- <sup>1</sup> Canada's food guide to healthy eating. Website: <http://www.hc-sc.gc.ca/hppb/nutrition/pube/foodguid/index.html>
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