Optimal Care for People: Why Cut Off ??

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Speaker:

Syed Abbas Raza, FACE

• Has disclosed that he serves as a Speaker on the Panel of Experts for Novo Nordisk, Servier, Eli Lilly and Aventis

• Will not be discussing the off-label or investigational use of products
I have Sooooo Much Information that I don’t know what to do with that....
Waiting for What ???
WHY
126 ?????
Standards of Medical Care in Diabetes 2016:
Diabetes Care 2016;39(Suppl. 1):S4–S5

- The order and discussion of diagnostic tests (fasting plasma glucose, 2-h plasma glucose after a 75-g oral glucose tolerance test, and A1C criteria) were revised to make it clear that no one test is preferred over another for diagnosis.
- "Foundations of Care: Education, Nutrition, Physical Activity, Smoking Cessation, Psychosocial Care, and Immunization”
- To reflect the changing role of technology in the prevention of type 2 diabetes, a recommendation was added encouraging the use of new technology such as apps and text messaging to affect lifestyle modification to prevent diabetes.
- This new section, which incorporates prior recommendations related to bariatric surgery, has new recommendations related to the comprehensive assessment of weight in diabetes and to the treatment of overweight/obesity with behavior modification and pharmacotherapy. This section also includes a new table of currently approved medications for the long-term treatment of obesity.
- Bariatric surgery was removed from this section and placed in a new section entitled “Obesity Management for the Treatment of Type 2 Diabetes.”
Standards of Medical Care in Diabetes 2016:
Diabetes Care 2016;39(Suppl. 1):S4–S5

- A new recommendation for pharmacological treatment of older adults was added. To reflect new evidence on ASCVD risk among women, the recommendation to consider aspirin therapy in women aged ≥60 years has been changed to include women aged ≥50 years. A recommendation was also added to address antiplatelet use in patients aged ≥50 years with multiple risk factors.

- A recommendation was made to reflect new evidence that adding ezetimibe to moderate-intensity statin provides additional cardiovascular benefits for select individuals with diabetes and should be considered.

- “Nephropathy” was changed to “diabetic kidney disease” to emphasize that, while nephropathy may stem from a variety of causes, attention is placed on kidney disease that is directly related to diabetes.

- Diabetic retinopathy: guidance was added on the use of intravitreal antiVEGF agents for the treatment of center-involved diabetic macular edema, as they were more effective than monotherapy or combination therapy with laser.

- The scope of this section is more comprehensive, capturing the nuances of diabetes care in the older adult population. This includes neurocognitive function, hypoglycemia, treatment goals, care in skilled nursing facilities/nursing homes, and end-of-life considerations.
A new recommendation was added to highlight the importance of discussing family planning and effective contraception with women with preexisting diabetes. A1C recommendations for pregnant women with diabetes were changed, from a recommendation of ≤6% (42 mmol/mol) to a target of 6–6.5% (42–48 mmol/mol), although depending on hypoglycemia risk the target may be tightened or relaxed. Glyburide in gestational diabetes mellitus was deemphasized based on new data suggesting that it may be inferior to insulin and metformin.
Current criteria for the diagnosis of type 2 diabetes

- HbA$_1^C$ $\geq 6.5\%$
- Fasting plasma glucose (FPG) $\geq 126$ mg/dl (7.0 mmol/l)
- Two-hour plasma glucose $\geq 200$ mg/dl (11.1 mmol/l) during an OGGT
- A random plasma glucose $\geq 200$ mg/dl (11.1 mmol/l)

Diabetes Control and Complications Trial (DCCT) of 1,441 patients with type 1 diabetes with either no retinopathy (n=715) or mild retinopathy (n=726) at baseline randomly assigned to intensive therapy or conventional therapy. Results shown: intensive therapy group.

Risk of Progression of Microvascular Complications vs A1C

A1C=hemoglobin A$_{1c}$

Prevalence of Retinopathy (Hisayama Study)

Relationship Between CVD, FPG and 2-HR PG

WHY SCREEN FOR RETINOPATHY
ADA Recommendation…

- **Adults with type 1 diabetes**: Eye examination by an ophthalmologist or optometrist within 5 years after the onset of diabetes.

- **Patients with type 2 diabetes**: Initial dilated and comprehensive eye examination by an ophthalmologist or optometrist shortly after the diagnosis of diabetes.

- **If there is no evidence of retinopathy** for one or more eye exams: Then exams every 2 years may be considered.

- **High-quality fundus photographs** can detect most clinically significant diabetic retinopathy. While retinal photography may serve as a screening tool for retinopathy, it is not a substitute for a comprehensive eye exam.

- **Women with preexisting diabetes who are planning pregnancy or who have become pregnant**: Eye examination should occur in the first trimester with close follow-up throughout pregnancy and for 1 year postpartum.
Why Treat Early...
The Importance of Early Detection: Higher FPG at Presentation Are Associated with Greater Risk of Microvascular Disease

Comparison of glycemic control and clinical and surrogate outcomes for 5,088 UKPDS participants according to presenting fasting plasma glucose (FPG): low (140 mg/dl [7.8 mmol/l]), intermediate (140 to 180 mg/dl [7.8 to 10.0 mmol/l]), or high (180 mg/dl [10 mmol/l]).
Why Intervene with Life Style Modification.....
Lifestyle Changes Can Prevent the Onset of Diabetes: DPP Study

Incidence of diabetes over 4 years for intensive lifestyle intervention (i.e., weight loss and exercise) vs. control

58% lower onset of diabetes (p<0.001)
3-Year NNT = 6.9

Lifestyle Changes Can Prevent the Onset of Diabetes: Finnish Diabetes Prevention Study

Incidence of diabetes over 6 years for intensive lifestyle intervention (i.e., weight loss and exercise) vs. control

Prevention of Type 2 Diabetes
Diet + Exercise Intervention for IGT

Reduction in progression to diabetes (%)

• Diabetes Prevention Program
  N=3234, 2.8 years
  Low-fat diet + exercise 58

• Finnish Study
  N=522, 3.2 years
  Low-fat diet + exercise 58

• Da Qing Study
  N=577, 6.0 years
  Diet and/or exercise 31–46

Pan XR et al. *Diabetes Care.* 1997;20:537-544
Prevention of Type 2 Diabetes
Diet + Exercise Intervention for IGT

• Nutrition
  - Seek 5% to 7% weight reduction
    (50% and 43% achieved this in Diabetes Prevention Program and Finnish trials, respectively)
  - <30% calories from fat

• Physical activity
  - Moderate exercise, 150 to 210 min/week
    (equivalent to 30-min sessions 5 to 7 days/week; 74% and 86% achieved this in Diabetes Prevention Program and Finnish trials, respectively)

Why look for Neuropathy ......
ADA Recommendation...

- All patients should be screened for distal symmetric polyneuropathy (DPN) starting at diagnosis of type 2 diabetes and 5 years after the diagnosis of type 1 diabetes and at least annually thereafter, using simple clinical tests.

- Electrophysiological testing or referral to a neurologist is rarely needed, except in situations where the clinical features are atypical.

- Screening for signs and symptoms of CAN should be instituted at diagnosis of type 2 diabetes and 5 years after the diagnosis of type 1 diabetes.

- Medications for the relief of specific symptoms related to painful DPN and autonomic neuropathy are recommended because they may reduce pain and improve quality of life.
Why consider with Medication.....
# Prevention of Type 2 Diabetes Pharmacotherapy for IGT

<table>
<thead>
<tr>
<th>Study</th>
<th>Reduction in progression to diabetes (%)</th>
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<tbody>
<tr>
<td><strong>Diabetes Prevention Program</strong></td>
<td></td>
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<tr>
<td>N=3234, 2.8 years</td>
<td>31</td>
</tr>
<tr>
<td>Metformin 850 mg bid</td>
<td></td>
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<tr>
<td><strong>STOP-NIDDM trial</strong></td>
<td></td>
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<tr>
<td>N=1429, 3.3 years</td>
<td>25</td>
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<tr>
<td>Acarbose 100 mg tid</td>
<td></td>
</tr>
<tr>
<td><strong>CANOE study</strong></td>
<td></td>
</tr>
<tr>
<td>N=207, 3.9 years</td>
<td>66</td>
</tr>
<tr>
<td>Rosiglitazone 2 mg qd</td>
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</table>

Zinman et al. *Lancet* 2010
Why Treat Aggressively.....
DCCT: Lower Risk of Progression of Retinopathy with Intensive Therapy

Diabetes Control and Complications Trial (DCCT) of 1,441 patients with type 1 diabetes with either no retinopathy at baseline (n=726) or mild retinopathy at baseline (n=715) randomly assigned to intensive therapy or conventional therapy.

Diabetes Control and Complications Trial (DCCT) of 1,441 patients with type 1 diabetes with either no retinopathy at baseline (n=726) or mild retinopathy at baseline (n=715) randomly assigned to intensive therapy or conventional therapy.

DCCT: Lower Risk of Developing Neuropathy with Intensive Therapy

Diabetes Control and Complications Trial (DCCT) of 1,441 patients with type 1 diabetes with either no retinopathy at baseline (n=726) or mild retinopathy at baseline (n=715) randomly assigned to intensive therapy or conventional therapy. Analysis included all patients from either cohort who did not have the abnormality in question at baseline.

UKPDS: Reducing HbA$_{1c}$ Associated with Reduction in Risk of Microvascular Endpoints

Risk of microvascular endpoints by HbA$_{1c}$ level

Reference category (HR 1.0) is HbA$_{1c}$ <6% with log linear scales. P value reflects contribution of glycemia to multivariate model. Data adjusted for age at diagnosis of diabetes, sex, ethnic group, smoking, presence of albuminuria, systolic blood pressure, HDL-C, and triglycerides.

UKPDS: Reducing HbA$_{1c}$ Associated with Reduction in Risk of Fatal / Non-Fatal MI

Risk of fatal and non-fatal MI by HbA$_{1c}$ level

MI, myocardial infarction. Reference category (HR 1.0) is HbA$_{1c}$ <6% with log linear scales. P value reflects contribution of glycemia to multivariate model. Data adjusted for age at diagnosis of diabetes, sex, ethnic group, smoking, presence of albuminuria, systolic blood pressure, HDL-C, and triglycerides.

14% decrease per 1% reduction in HbA$_{1c}$

Why treat Both Fasting and Post Prandial...
What Is More Important:

• Fasting vs. Post Prandial
Relative Risk for Death Increases with 2hour Blood Glucose Regardless of the FPG Level

Relative Risk of Death*

Fasting Plasma Glucose (mg/dL)

*Adjusted for age, sex, study center
Why Now ??

Is Benefit going it last long Enough
DCCT/EDIC: Incidence of Any Cardiovascular Disease Outcome

DCCT = Diabetes Control and Complications Trial.
EDIC = Epidemiology of Diabetes Interventions and Complications.

DCCT/EDIC: Incidence of Nonfatal MI, Stroke, or Death

MI = myocardial infarction.
DCCT = Diabetes Control and Complications Trial.
EDIC = Epidemiology of Diabetes Interventions and Complications.

A Broader View of CVD and Diabetes: Implications of ACCORD, ADVANCE and VADT

<table>
<thead>
<tr>
<th>Study</th>
<th>Microvascular</th>
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<tbody>
<tr>
<td>UKPDS</td>
<td>↓</td>
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<tr>
<td>DCCT/EDIC</td>
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<tr>
<td>ACCORD</td>
<td>TBD</td>
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<tr>
<td>ADVANCE</td>
<td>↓</td>
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<tr>
<td>VADT</td>
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Partners in Crime…..

Weight Gain and Hypoglycemia
Balancing Risk of Severe Hypoglycemia Against the Risk of Complications: DCCT

Weight Gain With Intensive Insulin Therapy: DCCT


*P<0.001 vs baseline
Why TO Differentiate between Type 1 vs Type 2
Types
# Type 1 vs Type 2 Diabetes

<table>
<thead>
<tr>
<th></th>
<th>Type 1 Diabetes</th>
<th>Type 2 Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual Clinical Course</td>
<td>Insulin-dependent</td>
<td>Usually only insulin requiring later in the disease</td>
</tr>
<tr>
<td>Usual Age of Onset</td>
<td>50% &lt;20 yrs/50% &gt;20 yrs</td>
<td>Mostly &gt;40 yrs but can occur younger</td>
</tr>
<tr>
<td>Body Weight</td>
<td>Usually lean</td>
<td>Usually obese</td>
</tr>
<tr>
<td>Clinical Onset</td>
<td>Acute</td>
<td>Often subtle, slow</td>
</tr>
<tr>
<td>Ketosis-prone</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Family History</td>
<td>≤15%</td>
<td>Common</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Mostly white</td>
<td>More common in minorities</td>
</tr>
<tr>
<td>Islet Antibodies</td>
<td>Often positive</td>
<td>Negative</td>
</tr>
</tbody>
</table>
Glycemic Control in Diabetes
A Brief History of Intervention Trials

- UGDP
- DCCT
- UKPDS
- EDIC
- SDIS
- BARI -2D
- VADT
- ADVANCE
- ACCORD
- RECORD
- PROactive
- Kumamoto
- VACS
- Oxford
- Steno
- Kroc
- Dallas
- Oslo

Why Screen for Thyroid and Other possible Deficiency ..........
Because of the increased frequency of other autoimmune diseases in type 1 diabetes:

- Screening for thyroid dysfunction
- Vitamin B\textsubscript{12} deficiency
- Celiac disease

should be considered based on signs and symptoms. Periodic screening in asymptomatic individuals has been recommended, but the effectiveness and optimal frequency are unclear.
Why Screen for Mental Health .....
ADA Recommendation

Key opportunities for routine screening of psychosocial status occur at diagnosis, during regularly scheduled management visits, during hospitalizations, with the discovery of complications, or when problems with glucose control, quality of life, or self-management are identified.

Patients are likely to exhibit psychological vulnerability at diagnosis and when their medical status changes, e.g., end of the honeymoon period, when the need for intensified treatment is evident, and when complications are discovered.

Depression affects about 20–25% of people with diabetes

Diabetes-related distress is distinct from clinical depression and is very common among people with diabetes and their family members. Prevalence is reported as 18–45%, with an incidence of 38–48% over 18 months. High levels of distress are significantly linked to A1C, self-efficacy, dietary and exercise behaviors.
Why keep a Vaccination Card.....
ADA Recomendation

• Annually provide an influenza vaccine to all diabetic patients ≥6 months of age.

• Administer pneumococcal polysaccharide vaccine to all diabetic patients ≥2 years of age. A one-time revaccination is recommended for individuals >65 years of age who have been immunized >5 years ago.

• Administer hepatitis B vaccination to unvaccinated adults with diabetes who are aged 19–59 years. Consider administering hepatitis B vaccination to unvaccinated adults with diabetes who are aged ≥60 years.
Why Use Aspirin ..
Risk Benefit ratio...
**ADA Recommendation:**

- Consider aspirin therapy (75–162 mg/day) as a primary prevention strategy in those with type 1 or type 2 diabetes at increased cardiovascular risk (10-year risk >10%).

- This includes most men aged >50 years who have at least one additional major risk factor (family history of CVD, hypertension, smoking, dyslipidemia, or albuminuria).

- **New Guidelines for Women:** Clinicians should consider prescribing aspirin therapy to women age 50 and older who have at least one additional major risk factor, such as family history of premature atherosclerotic cardiovascular disease, hypertension, smoking, dyslipidemia, or albuminuria, and are not at increased risk of bleeding.

- Aspirin **should not be recommended for CVD** prevention for adults with diabetes at low CVD risk (10-year CVD risk <5%, such as in men aged <50 years and women aged <60 years with no major additional CVD risk factors), since the potential adverse effects from bleeding likely offset the potential benefits.

- For patients with CVD and documented aspirin allergy, clopidogrel (75 mg/day) should be used.

- Dual antiplatelet therapy is reasonable for up to a year after an acute coronary syndrome.
Why Screen for Smoking and advise cessation...
ADA Recommendation..

Studies of individuals with diabetes consistently demonstrate that smokers (and persons exposed to second-hand smoke) have a heightened risk of CVD, premature death, and increased rate of microvascular complications of diabetes.

Smoking may have a role in the development of type 2 diabetes. One study in smokers with newly diagnosed type 2 diabetes found that smoking cessation was associated with amelioration of metabolic parameters and reduced blood pressure and albuminuria at 1 year.

- Advise all patients not to smoke or use tobacco products.
- Include smoking cessation counseling and other forms of treatment as a routine component of diabetes care.
Why Screen and Treat Blood Pressure in Diabetes.....
UKPDS: Comparison of Risk Reduction
Glycemic vs BP Control

Epidemiology of Blood Pressure and Complications in Type 2 Diabetes: UKPDS

~ 15% reduction in risk associated with each 10 mm Hg decrease in SBP

Why screen and Treat Dyslipidemia in Diabetes…..
A. Screening and Diagnosis:
Blood pressure should be measured at every routine visit. Patients found to have elevated blood pressure should have blood pressure confirmed on a separate day.

Goals Systolic Targets:
People with diabetes and hypertension should be treated to a systolic blood pressure goal of ,140 mmHg. Lower systolic targets, such as ,130 mmHg, may be appropriate for certain individuals with diabetes, such as younger patients, those with albuminuria, and/or those with hypertension and one or more additional atherosclerotic cardiovascular disease risk factors, if they can be achieved without undue treatment burden.

Diastolic Targets: Individuals with diabetes should be treated to a diastolic blood pressure goal of ,90 mmHg. Lower diastolic targets, such as ,80 mmHg, may be appropriate for certain individuals with diabetes, such as younger patients, those with albuminuria, and/or those with hypertension and one or more additional atherosclerotic cardiovascular disease risk factors, if they can be achieved without undue treatment burden.
B Treatment:

• Patients with blood pressure 120/80 mmHg should be advised on lifestyle changes to reduce blood pressure.
• Patients with confirmed office-based blood pressure 140/90 mmHg should, in addition to lifestyle therapy, have prompt initiation and timely subsequent titration of pharmacological therapy to achieve blood pressure goals.
• In older adults, pharmacological therapy to achieve treatment goals of 130/70 mmHg is not recommended; treating to systolic blood pressure 130 mmHg has not been shown to improve cardiovascular outcomes and treating to diastolic blood pressure 70 mmHg has been associated with higher mortality.
• Lifestyle therapy for elevated blood pressure consists of weight loss, if overweight or obese; a Dietary Approaches to Stop Hypertension (DASH)-style dietary pattern including reducing sodium and increasing potassium intake; moderation of alcohol intake; and increased physical activity.
• Pharmacological therapy for patients with diabetes and hypertension should comprise a regimen that includes either an ACE inhibitor or an angiotensin receptor blocker but not both. If one class is not tolerated, the other should be substituted.
• Multiple-drug therapy (including a thiazide diuretic and ACE inhibitor/angiotensin receptor blocker, at maximal doses) is generally required to achieve blood pressure targets.
• If ACE inhibitors, angiotensin receptor blockers, or diuretics are used, serum creatinine/estimated glomerular filtration rate and serum potassium levels should be monitored.
• In pregnant patients with diabetes and chronic hypertension, blood pressure targets of 110–129/65–79 mmHg are suggested in the interest of optimizing long-term maternal health and minimizing impaired fetal growth.
In adults not taking statins, it is reasonable to obtain a lipid profile at the time of diabetes diagnosis, at an initial medical evaluation, and every 5 years thereafter, or more frequently if indicated.

Obtain a lipid profile at initiation of statin therapy and periodically thereafter as it may help to monitor the response to therapy and inform adherence.

Lifestyle modification focusing on weight loss (if indicated); the reduction of saturated fat, trans fat, and cholesterol intake; increase of omega-3 fatty acids, viscous fiber, and plant stanols/sterols intake; and increased physical activity should be recommended to improve the lipid profile in patients with diabetes.

Intensify lifestyle therapy and optimize glycemic control for patients with elevated triglyceride levels ($150 \text{ mg/dL} [1.7 \text{ mmol/L}]$) and/or low HDL cholesterol ($<40 \text{ mg/dL} [1.0 \text{ mmol/L}]$ for men, $<50 \text{ mg/dL} [1.3 \text{ mmol/L}]$ for women). For patients with fasting triglyceride levels $\geq 500 \text{ mg/dL} (5.7 \text{ mmol/L})$, evaluate for secondary causes of hypertriglyceridemia and consider medical therapy to reduce the risk of pancreatitis.

For patients of all ages with diabetes and atherosclerotic cardiovascular disease, high-intensity statin therapy should be added to lifestyle therapy.

For patients with diabetes aged $<40$ years with additional atherosclerotic cardiovascular disease risk factors, consider using moderate-intensity or high-intensity statin and lifestyle therapy.

For patients with diabetes aged $40–75$ years without additional atherosclerotic cardiovascular disease risk factors, consider using moderate-intensity statin and lifestyle therapy.
Lipids

- For patients with diabetes aged 40–75 years with additional atherosclerotic cardiovascular disease risk factors, consider using high-intensity statin and lifestyle therapy.

- For patients with diabetes aged 75 years without additional atherosclerotic cardiovascular disease risk factors, consider using moderate-intensity statin therapy and lifestyle therapy.

- For patients with diabetes aged 75 years with additional atherosclerotic cardiovascular disease risk factors, consider using moderate-intensity or high-intensity statin therapy and lifestyle therapy.

- In clinical practice, providers may need to adjust intensity of statin therapy based on individual patient response to medication (e.g., side effects, tolerability, LDL cholesterol levels).

- The addition of ezetimibe to moderate-intensity statin therapy has been shown to provide additional cardiovascular benefit compared with moderate-intensity statin therapy alone and may be considered for patients with a recent acute coronary syndrome with LDL cholesterol $50 mg/dL (1.3 mmol/L) or for those patients who cannot tolerate high-intensity statin therapy.

- Combination therapy (statin/fibrate) has not been shown to improve atherosclerotic cardiovascular disease outcomes and is generally not recommended. However, therapy with statin and fenofibrate may be considered for men with both triglyceride level $204 mg/dL (2.3 mmol/L) and HDL cholesterol level #34 mg/dL (0.9 mmol/L).

- Combination therapy (statin/niacin) has not been shown to provide additional cardiovascular benefit above statin therapy alone and may increase the risk of stroke and is not generally recommended.

- Statin therapy is contraindicated in pregnancy.
Screening for CAD

In asymptomatic patients, routine screening for coronary artery disease is not recommended as it does not improve outcomes as long as atherosclerotic cardiovascular disease risk factors are treated.

Consider investigations for coronary artery disease in the presence of any of the following: atypical cardiac symptoms (e.g., unexplained dyspnea, chest discomfort); signs or symptoms of associated vascular disease including carotid bruits, transient ischemic attack, stroke, claudication, or peripheral arterial disease; or electrocardiogram abnormalities (e.g., Q waves).

Treatment:

In patients with known atherosclerotic cardiovascular disease, use aspirin and statin therapy (if not contraindicated) A and consider ACE inhibitor therapy to reduce the risk of cardiovascular events. In patients with prior myocardial infarction, b-blockers should be continued for at least 2 years after the event. B c In patients with symptomatic heart failure, thiazolidinedione treatment should not be used. In patients with type 2 diabetes with stable congestive heart failure, metformin may be used if renal function is normal but should be avoided in unstable or hospitalized patients with congestive heart failure.
LDL Cholesterol Targets in Diabetes

Partners in Crime.....

Weight Gain and Hypoglycemia
Balancing Risk of Severe Hypoglycemia Against the Risk of Complications: DCCT

Weight Gain With Intensive Insulin Therapy: DCCT


*P<0.001 vs baseline
Right Time to refer to a specialist....
When in Doubt:

- Type 1 vs 2
- Controlled vs Uncontrolled
- Type 1 Diabetes
- Complication of Diabetes
- Recurrent Hypoglycemia / Weight gain
- Uncomfortable prescribing newer class of medication