Update in Diabetic Nephropathy

Innovations and Updates in Diabetes Care

American Diabetes Association

Chicago, IL

Standards of Medical Care in Diabetes

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Disclosures

• Financial
  • Research support from Novartis, Novo Nordisk, Bayer
  • Consulting with Pfizer, Novartis, Novo Nordisk, Lilly, Merck, Janssen
Incident counts & adjusted rates, by primary diagnosis

Incident ESRD patients; rates adjusted for age, gender, & race.

USRDS - 2008
Incidence of Diabetic End-Stage Renal Disease per 100,000 People with Diabetes, U.S., 1980 – 2008

**We are making a difference!**

[Graph showing incidence of diabetic end-stage renal disease from 1981 to 2007]

**ESRD Rates per 100,000 People with Diabetes**

*National Diabetes Surveillance System, U.S. Renal Data System, National Health Interview Survey*
Natural History of Diabetic Nephropathy

- **GFR (ml/min/m²)**
- **Albumin**
- **Microalbuminuria**
- **Albuminuria**
- **Urinary albumin (mg/24h)**

**Duration of Diabetes (years)**

0  5  10  15  20  25  30
## Risk Categories for Kidney and Mortality Outcomes

<table>
<thead>
<tr>
<th>GFR Stage</th>
<th>Range (ml/min/1.73m²)</th>
<th>Optimal</th>
<th>High Normal</th>
<th>High</th>
<th>Very High</th>
<th>Nephrotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≥ 90</td>
<td>&lt;10 mg/g</td>
<td>10-29 mg/g</td>
<td>30-299 mg/g</td>
<td>300-1999 mg/g</td>
<td>&gt; 2000 mg/g</td>
</tr>
<tr>
<td>2</td>
<td>60 - 89</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>45 – 59</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>30 – 44</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>15 – 29</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>&gt; 15</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Optimal: Albuminuria < 10 mg/g
- High Normal: 10-29 mg/g
- High: 30-299 mg/g
- Very High: 300-1999 mg/g
- Nephrotic: > 2000 mg/g

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Levey et al., Ann Intern Med 2011;154:65
DCCT: Effect of Glycemic Control

MICROALBUMINURIA

Primary Prevention

Secondary Intervention

DCCT Research Group
NEJM 1993;342:381
### Primary & Secondary GFR Outcomes in DCCT/EDIC

<table>
<thead>
<tr>
<th>eGFR Category</th>
<th>Number of Events</th>
<th>Relative Risk Reduction (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intensive Therapy</td>
<td>Conventional Therapy</td>
<td>Risk Reduction (%, 95% CI)</td>
</tr>
<tr>
<td>eGFR &lt; 60*</td>
<td>24</td>
<td>46</td>
<td>50 (18, 69)</td>
</tr>
<tr>
<td>eGFR &lt; 45</td>
<td>24</td>
<td>39</td>
<td>40 (1, 64)</td>
</tr>
<tr>
<td>eGFR &lt; 30</td>
<td>13</td>
<td>23</td>
<td>44 (-9, 72)</td>
</tr>
<tr>
<td>ESRD</td>
<td>8</td>
<td>16</td>
<td>51 (-14, 79)</td>
</tr>
<tr>
<td>eGFR &lt; 60 or death</td>
<td>53</td>
<td>80</td>
<td>37 (10, 55)</td>
</tr>
</tbody>
</table>

* Sustained eGFR < 60 mL/min/1.73m² (primary outcome of this study)

Risk reduction is relative difference in risk of impaired GFR (in percent) comparing intensive to conventional diabetes therapy

DeBoer et al., NEJM 2011;365:2366
Annual Transition Rates In Patients with Type 2 Diabetes in the UKDPS

- No Nephropathy: 1.4%
- Microalbuminuria: 3.0%
- Albuminuria: 4.6%
- Elevated Creatinine or Renal Replacement Rx: 19.2%

Adler et al., Kidney Intl 2003;63:225
10-Year Excess Mortality in Type 2 Diabetes by Kidney Disease Status in NHANES III (n=15,046)

Impaired GFR = <60 ml/min/1.73m²

Afkarian M et al., JASN 2013;24:302
Albuminuria and Decreased GFR have Additive Risks for Cardiovascular Disease in Diabetes: Potential Links

- Common Genetic Predisposition
- Endothelial Dysfunction
- Associated Hypertension
- Insulin Resistance
- Atherogenic Dyslipidemia
- Hyperglycemia
- Volume overload
Glycemic Management in the Patient with Progressing CKD
Sulfonylurea Use in CKD

- **Glyburide**
  - Glyburide clearance not affected but renal clearance of metabolites is reduced with CKD
  - Risk of hypoglycemia high with CKD and should not be used with eGFR < 60

- **Glimepiride**
  - Glimepiride clearance not affected but renal clearance of metabolites is reduced with CKD
  - Risk of hypoglycemia increased and should be used with caution with eGFR < 60 and avoided with eGFR < 30

- **Glipizide**
  - Less than 10% renally cleared
  - Use with caution with eGFR < 30

Rosencranz et al., Diabetologia 1996;39:1617  Ferreira et al., Diabetes Care 2012 doi:10.2337/dc12-1365/-/DC1
Nateglinide, Repaglinide and CKD

- Nateglinide does not accumulate with CKD but metabolite M1 is metabolically active and its clearance is greatly delayed with CKD
  - Nateglinide should not be used for eGFR < 60 ml/min/1.73m²

- Repaglinide does not accumulate and no dose change is needed in CKD

Nagai et al., Diab Res Clin Pract 2003;59:191
Inoue et al., Clin Nephrol 2003;60:90
Metformin Dosing
What to Do?

<table>
<thead>
<tr>
<th>eGFR (ml/min/1.73m²)</th>
<th>Metformin Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 60</td>
<td>No limitation of dosing</td>
</tr>
<tr>
<td>≥ 45 – &lt;60</td>
<td>Caution with dosing Monitor eGFR every 3 – 6 mos</td>
</tr>
<tr>
<td>≥ 30 - &lt;45</td>
<td>Maximum dose 1000 mg/day Monitor eGFR every 3 – 4 mos</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>Stop metformin</td>
</tr>
</tbody>
</table>

- Stop metformin in inpatients if:
  - Unstable
  - Hypotensive
  - Hypoxic
  - Septic
  - Acute worsening of renal function

Lipska et al., Diabetes Care 2011;34:1431
KDIGO Controversies, In preparation
Thiazolidinediones and CKD

• Pioglitazone and Rosiglitazone
  – Clearance not affected by kidney function
    • No dose reduction needed in CKD
  – Potential problems with fluid retention
  – Bone disease - ? Additive to renal osteodystrophy
  – Slight increased risk of bladder cancer (??)

Budde et al., Br J Clin Pharmacol 2003;55:368
Panchapakesan et al., Nephrology 2009;14:298
Colmers et al., CMAJ 2012;184:E675
Betteridge, Diabetic Medicine 2011;28:759
Alpha-Glucosidase Inhibitors
Acarbose and Miglitol

- Acarbose
  - Minimal absorption with < 2% of drug and active metabolites appearing in urine
  - Package insert states that in patients with eGFR < 25 ml/min/1.73m², the peak concentration is increased 6x and the AUC is increased 5X but no long-term trials in patients with serum creatinine > 2 mg/dL
  - Should not be used if serum creatinine > 2 mg/dL

- Miglitol
  - 50-70% absorption with >95% excreted in urine
  - Package insert states that in patients with eGFR < 25 ml/min/1.73m², the peak concentration is increased 2x and no long-term trials in patients with serum creatinine > 2 mg/dL
  - Should not be used if serum creatinine > 2 mg/dL
Incretins

- **GLP-1 receptor agonists**
  - Exenatide – discontinue for eGFR < 30
  - Liraglutide – no dose adjustments
  - Dulaglutide – no dose adjustments
  - Albiglutide – no dose adjustments

- **DPP4 Inhibitors**

<table>
<thead>
<tr>
<th></th>
<th>Sitagliptin</th>
<th>Saxagliptin</th>
<th>Alogliptin</th>
<th>Linagliptin</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFR &gt; 50</td>
<td>100 mg/d</td>
<td>5 mg/d</td>
<td>25 mg/d</td>
<td>5 mg/d</td>
</tr>
<tr>
<td>GFR 30 – 50</td>
<td>50 mg/d</td>
<td>2.5 mg/d</td>
<td>12.5 mg/d</td>
<td>5 mg/d</td>
</tr>
<tr>
<td>GFR &lt; 30</td>
<td>25 mg/d</td>
<td>2.5 mg/d</td>
<td>6.25 mg/d</td>
<td>5 mg/d</td>
</tr>
</tbody>
</table>
SGLT2 Inhibitors

- Increase urinary glucose excretion, thereby lowering blood glucose
- Less effective with eGFR < 60 ml/min/1.73m²
- Possibly more adverse effects (volume loss, hyperkalemia) with eGFR < 45 ml/min/1.73m²
  - For eGFR < 60 ml/min/1.73m²: Canagliflozin should be kept at 100 mg/day and higher dose (300 mg) avoided
  - Canagliflozin and Empagliflozin currently not approved for use with eGFR < 45 ml/min/1.73m²
  - Dapagliflozin not approved for use with eGFR < 60 ml/min/1.73m³
Primary outcome: 3-point MACE

HR 0.86
(95.02% CI 0.74, 0.99)
p = 0.0382*

Cumulative incidence function. MACE, Major Adverse Cardiovascular Event; HR, hazard ratio.

* Two-sided tests for superiority were conducted (statistical significance was indicated if p≤0.0498)
Empa-Reg: Kidney Outcomes

- Entire study: Empagliflozin 4687 subjects
  Placebo 2333 subjects
  - Outcome of Doubling of Creatinine, ESRD, or Renal Death: HR 0.54, p<0.0002
  - Outcome of new-onset or worsening of nephropathy: HR 0.61, p<0.001

<table>
<thead>
<tr>
<th>A</th>
<th>Empagliflozin</th>
<th>Placebo</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. subjects with eGFR &lt;60 (ml/min/1.73m²)</td>
<td>1212</td>
<td>607</td>
<td></td>
</tr>
<tr>
<td>Primary Outcome (MACE 3)</td>
<td>171 (15%)</td>
<td>99 (16%)</td>
<td>0.88</td>
</tr>
<tr>
<td>All Cause Mortality</td>
<td>115 (9%)</td>
<td>72 (12%)</td>
<td>0.80</td>
</tr>
<tr>
<td>Cardiovascular Death</td>
<td>75 (6%)</td>
<td>48 (8%)</td>
<td>0.78</td>
</tr>
</tbody>
</table>

MACE 3: Cardiovascular death, MI, Stroke

Empa-Reg: Kidney Outcomes

Glycemic Management in CKD: Summary

- **eGFR < 60 ml/min/1.73m²:**
  - Reduce dose of canagliflozin, stop dapagliflozin
  - Avoid glyburide

- **eGFR < 45 ml/min/1.73m²:**
  - Reduce doses of Insulin
  - Reduce doses of metformin, sitagliptin, saxagliptin, alogliptin
  - Restrict sulfonylureas to glipizide
  - Stop acarbose, miglitol, nateglinide, canagliflozin, & empagliflozin

- **eGFR < 30 ml/min/1.73m²:**
  - Stop metformin and exenatide
  - Reduce doses of sitagliptin, saxagliptin, alogliptin further
Control of BP Slows Decline of GFR in Patients with Diabetic Nephropathy

ΔGFR: 0.94 ml/min/month
Start of antihypertensive treatment
ΔGFR: 0.29 ml/min/month

Parving et al., 1987
Relationship Between Achieved BP and GFR

MAP (mm Hg)

GFR (ml/min/year)

130/80

140/90

r=0.69; p < 0.05

Untreated Hypertension

Parving et al., 1989
Viberti et al., 1993
Klahr et al., 1993
Hebert et al., 1994
Lebovitz et al., 1994

Moschino et al., 1996
Bakris et al., 1996
Bakris et al., 1997
GISEN Group, 1997

MAP=[SBP + 2xDBP])/3

Am J Kidney Dis 2000;36:646
Relative Risk of Reaching a Renal End Point (doubling of serum creatinine or SCr $\geq 6.0$ or RRT) by Level of Achieved SBP in the Irbesartan Diabetic Nephropathy Trial (IDNT)

Pohl et al., JASN 2005;16:3027
Relative Risk of Reaching a Renal End Point (doubling of serum creatinine or SCr ≥ 6.0 or RRT) and All Cause Mortality by Level of Achieved SBP in the Irbesartan Diabetic Nephropathy Trial (IDNT)

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Relative Risk of Reaching a Renal End Point (doubling of serum creatinine or SCr ≥ 6.0 or RRT) and All Cause Mortality by Level of Achieved SBP in the Irbesartan Diabetic Nephropathy Trial (IDNT)

Pohl et al., JASN 2005;16:3027
ACCORD BP Study: Primary and Secondary Outcomes

- Patients with T2D and hypertension (N = 4733)
- Random assignment
  - Intensive therapy: target SBP < 120 mm Hg
  - Standard therapy: target SBP < 140 mm Hg
- 1° outcome: nonfatal MI, nonfatal stroke, death from CV causes
- Mean follow-up = 4.7 y

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive</th>
<th>Standard</th>
<th>HR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP after 1 year (mmHg)</td>
<td>119.3</td>
<td>133.5</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>1° outcome (annual rate)</td>
<td>1.87</td>
<td>2.09</td>
<td>0.88</td>
<td>.20</td>
</tr>
<tr>
<td>Death from any cause (annual rate)</td>
<td>1.28</td>
<td>1.19</td>
<td>1.07</td>
<td>.55</td>
</tr>
<tr>
<td>Stroke (annual rate)</td>
<td>0.32</td>
<td>0.53</td>
<td>0.59</td>
<td>.01</td>
</tr>
<tr>
<td>AEs (rate)</td>
<td>3.3</td>
<td>1.3</td>
<td>NR</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

INVEST Study – Secondary Analysis in Subjects with Type 2 Diabetes

- 6400 subjects with type 2 DM and CAD over age 50
- Treated with Verapamil or Trandolapril followed by an ACE inhibitor, a diuretic or both to achieve BP < 130/85
- Current analysis compared:
  - “Tight” control - SBP < 130  (n=2175)
  - “Usual” control – SBP 130-140  (n=2255)
  - “Uncontrolled” – SBP > 140  (n=1970)
- Primary Outcome: first occurrence of all-cause mortality, nonfatal MI or nonfatal stroke

Cooper-DeHoff, R. M. et al. JAMA 2010;304:61-68
INVEST: Cumulative Event Rate for Primary Outcome (first occurrence of all-cause mortality, nonfatal MI or stroke)

Overall log-rank $P < .001$
Tight control vs usual control log-rank $P = .19$

Cumulative Event Rate, %

Systolic blood pressure control
- Uncontrolled
- Tight
- Usual

No. of patients at risk

<table>
<thead>
<tr>
<th>Systolic blood pressure control</th>
<th>0.5</th>
<th>1.0</th>
<th>1.5</th>
<th>2.0</th>
<th>2.5</th>
<th>3.0</th>
<th>3.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncontrolled</td>
<td>2175</td>
<td>2037</td>
<td>1981</td>
<td>1918</td>
<td>1801</td>
<td>1289</td>
<td>821</td>
</tr>
<tr>
<td>Tight</td>
<td>2255</td>
<td>2203</td>
<td>2144</td>
<td>2087</td>
<td>1970</td>
<td>1153</td>
<td>538</td>
</tr>
<tr>
<td>Usual</td>
<td>1970</td>
<td>1918</td>
<td>1876</td>
<td>1834</td>
<td>1730</td>
<td>1175</td>
<td>668</td>
</tr>
</tbody>
</table>

Cooper-DeHoff, R. M. et al. JAMA 2010;304:61-68.
INVEST: Adjusted Risk of All-Cause Mortality

![Graph showing adjusted hazard ratio vs systolic blood pressure]

Adjusted Hazard Ratio

Systolic Blood Pressure, mm Hg

- <110
- 110-<115
- 115-<120
- 120-<125
- 125-<130

No. at risk

- 35
- 98
- 306
- 757
- 1059

No. of deaths

- 12
- 17
- 38
- 69
- 112

Cooper-DeHoff, R. M. et al. JAMA 2010;304:61-68.
• Blood Pressure Targets
  – Systolic < 140
  – Diastolic < 90
  – <130/80 mmHg may be appropriate for certain individuals, such as younger patients, if it can be achieved without undue treatment burden

• Treatment
  – Confirmed BP > 140/90 mmHg should, in addition to lifestyle therapy, have prompt initiation and timely subsequent titration of pharmacological therapy to achieve blood pressure goals.
Effects of ACE Inhibitors and ARBs on Renal Events in Patients with Type 2 Diabetes – Meta-analysis

<table>
<thead>
<tr>
<th></th>
<th>RR (CI) vs. other drugs</th>
<th>RR (CI) vs. Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESRD</td>
<td>0.82 (0.64, 1.05)</td>
<td>0.80 (0.69, 0.93)</td>
</tr>
<tr>
<td>Doubling creatinine</td>
<td>0.66 (0.52, 0.83)</td>
<td>0.76 (0.69, 0.84)</td>
</tr>
<tr>
<td>Macroalbuminuria</td>
<td>0.71 (0.50, 1.00)</td>
<td>0.67 (0.54, 0.83)</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>0.84 (0.61, 1.15)</td>
<td>0.82 (0.64, 1.05)</td>
</tr>
</tbody>
</table>

- Consistent reno-protective effect of ACEI/ARB over other antihypertensive drugs in type 2 diabetes.
- Lack of any differences in BP decrease between ACEI/ARB and active comparators suggest this benefit is not due simply to the antihypertensive effect.

Vejakama et al., Diabetologia 2012;55:566
Effects of ACE Inhibitors and ARBs on Cardiac Events in Patients with Type 2 Diabetes – Meta-analysis

<table>
<thead>
<tr>
<th></th>
<th>ACEi vs. Control</th>
<th>ARB vs. Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Cause Mortality</td>
<td>RR 0.87 (0.78-0.98)</td>
<td>RR 0.94 (0.82-1.08)</td>
</tr>
<tr>
<td>CV Mortality</td>
<td>RR 0.83 (0.70-0.99)</td>
<td>RR 1.21 (0.81–1.80)</td>
</tr>
<tr>
<td>Major CV Events</td>
<td>RR 0.86 (0.77-0.95)</td>
<td>RR 0.94 (0.85-1.01)</td>
</tr>
</tbody>
</table>

Cheng et al., JAMA Intern Med 2014;174:773
Average Number of Antihypertensive Medications Needed per Patient to Achieve Target Systolic Blood Pressure (SBP) Goals in Various Trials

TRIAL (SBP Achieved)
- ALLHAT (138 mmHg)
- IDNT (138 mmHg)
- RENAAL (141 mmHg)
- UKPDS (144 mmHg)
- ABCD (132 mmHg)
- MDRD (132 mmHg)
- HOT (138 mmHg)
- AASK (128 mmHg)

Heart Protection Study
Cardiovascular Benefits of Simvastatin in those with Normal and Abnormal Renal Function

% of Patients with Cardiac Events

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Simvastatin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>23.9</td>
<td>19.5</td>
</tr>
<tr>
<td>No Diabetes</td>
<td>24.3</td>
<td>19.1</td>
</tr>
<tr>
<td>Creatinine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1.24 mg/dl †</td>
<td>168</td>
<td>142</td>
</tr>
<tr>
<td>GFR &gt;47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1.47 mg/dl ‡</td>
<td>515</td>
<td>504</td>
</tr>
<tr>
<td>GFR &gt;52</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4D Study: Primary Composite End Point (Cardiac Death, Nonfatal MI & Stroke)

Atorvastatin in Diabetic Dialysis Patients

Placebo          636             532             383            252             136              51       29
Atorvastatin    619             515             378            252             136              58       19

Relative Risk Reduction 8 %
(95 % CI: 0.77-1.10, P=0.37)

Median follow-up time of 4 years

Wanner et al., NEJM 2005;353:238
Aurora Study

2776 Patients with ESRD (19.2% with DM) assigned to Rosuvastatin 10 mg vs. Placebo, Primary Endpoint: CVD death, nonfatal MI or nonfatal stroke

43% reduction in LDL

## SHARP: Major Atherosclerotic Events by renal status at randomization

<table>
<thead>
<tr>
<th></th>
<th>Eze/simv (n=4650)</th>
<th>Placebo (n=4620)</th>
<th>Risk ratio &amp; 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-dialysis (n=6247)</td>
<td>296 (9.5%)</td>
<td>373 (11.9%)</td>
<td></td>
</tr>
<tr>
<td>Dialysis (n=3023)</td>
<td>230 (15.0%)</td>
<td>246 (16.5%)</td>
<td></td>
</tr>
<tr>
<td>Any patient</td>
<td>526 (11.3%)</td>
<td>619 (13.4%)</td>
<td>16.5% SE 5.4 reduction (p=0.0022)</td>
</tr>
</tbody>
</table>

23% with Diabetes
Summary of Lipids and CKD

- Patients with diabetes and CKD are at very high risk of CVD
- CVD events can be significantly reduced with statins in patients with diabetes
- CVD events can be significantly reduced with statins in patients with CKD prior to dialysis
- CVD events cannot be reduced with statins in patients with diabetes undergoing dialysis
  - Reasons remain unclear - ? CVD too far progressed?
- CVD events can be reduced with statins in patients following renal transplantation
- Risks of rhabdomyolysis with statins are low - <0.1%
Steno-2: Multifactorial Intervention and CVD in Type 2 DM

INTENSIVE THERAPY

- Dietary intervention
  - Total fat <30% calories
  - Saturated fat <10% calories
- Exercise: 30 min 3-5x/w
- Smoking cessation
- All prescribed ACE-I/ARB
- Glycemic control: Metformin/SU/insulin
- Hypertension: ACE-I/ARB/diuretics/CCA/BB
- Lipid: Statins/fibrates

Composite endpoint of death from CV causes, nonfatal MI, CABG, PCI, nonfatal stroke, amputation, or surgery for peripheral arterial disease.
When to Refer to the Nephrologist

• If concern about diagnosis of diabetic nephropathy
  – No retinopathy
  – No albuminuria
  – Disproportionate proteinuria
  – Active sediment
• Blood pressure difficult to control despite 3 drugs
• Rapidly falling GFR
• GFR approaching 30 ml/min/1.73m²
• Lack of comfort in dealing with problems as they are progressing
  – Secondary Hyperparathyroidism
  – Anemia
  – Blood Pressure
  – Fluid Retention
  – Hyperkalemia
What is the Role of the Diabetologist Once the Patient is Referred to the Nephrologist? True Co-management Is Needed

- **Continued glucose management**
  - The nephrologist does not have our expertise in managing hyper- and hypoglycemia

- **Continued management of other complications of diabetes**
  - Neuropathy, peripheral and autonomic
  - Retinopathy
  - Macrovascular disease
  - Dyslipidemia

- **Dialysis: Hemo- and Peritoneal**
  - Nobody knows how to manage the glucose!

- **Transplantation (if kidney only)**
  - Worsened glucose control with immunosuppressive agents
    - Glucocorticoids
    - Tacrolimus
    - Sirolimus
    - Cyclosporine
Summary

- Prevent nephropathy with glycemic control
- Delay progression of nephropathy and CVD with glycemic, BP and lipid control and use of ACE inhibitors and ARBs
- Manage dyslipidemia and BP aggressively
- Treat 2° hyperparathyroidism and anemia
- Refer to nephrologist as disease progresses
- Continue to co-manage diabetes with nephrologist
Our Goal!

Thank You