Update in Diabetes 2014
SGIM National Meeting

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Update in Diabetes

Disclosures

Dr. Dugdale - None
Dr. DeWitt - None

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Physicians of the UW Diabetes Care Center
Physicians of the UW GIM Center
Learning Goals

• Review new research in diabetes that is likely to change practice in GIM/Hospitalist care:
  – Diagnosis and pathogenesis of diabetes
  – Prevention of diabetes
  – Innovations in the management of diabetes
Overview of Session

- 11:00 – 11:05: Introductory material
- 11:05 – 12:05: Review of “top 10” articles
- 12:05 – 12:20: Questions and discussion
- 12:20 – 12:25: Brief comments about our “2nd top 15” articles
- 12:25 – 12:30: Session evaluation
Method of Paper Selection

- Recommendations solicited from UW DCC and GIMC physicians
- References of 2014 ADA standards of care
- Review of tables of contents for Annals Internal Medicine, NEJM, JGIM, Diabetes Care
- Review of guidelines search
Overview of “Top Ten”

- Diagnosis
- Prevention
- Management
  - Blood sugar
  - Other targets
  - Innovations
• Traditional dx criteria for diabetes
  – Fasting plasma glucose $> 126$ mg/dL
    • (minimum 8 hour fast)
  – 2 hour post-prandial PG $> 200$ mg/dL
    • (75 gram oral GTT)
  – Random PG $> 200$ mg/dL
    • (accompanied by sx of hyperglycemia)

• A1c criterion to dx diabetes
  – A1c $> 6.5$
    • Recommended in 2009 by expert panel
    • Method must be certified by the National Glycohemoglobin Standardization Program using and “standardized or traceable” to the DCCT reference assay

The pros and cons of diagnosing diabetes with A1C. Diabetes Care 2011.
Use of HBA1c to Diagnose Diabetes

• Pros of using A1c to dx diabetes
  – Fasting is not required
  – Not affected by “acute perturbations” such as stress and illness, that can affect PG
  – Greater pre-analytical stability than PG
    • Pre-analytical variability of PG is ~5-10%
    • Analytical variability of A1c and PG are both ~2%
  – Less biological variability than PG
    • Biological variability of A1c is < 1% while it is 4% for PG
  – Better associated with diabetes cardiovascular complications than FPG

The pros and cons of diagnosing diabetes with A1C. Diabetes Care 2011.
Use of HBA1c to Diagnose Diabetes

- Cons of using A1c to dx diabetes
  - Diabetes is clinically defined by high BG not glycation of proteins
  - A1c is less sensitive for a diabetes dx than PG measurements
    - A1c ~ 30%
    - FPG ~ 45%
    - 2 hr PP PG ~ 90%
  - 2 hour post-prandial PG is better associated with diabetes cardiovascular complications than A1c
  - The A1c-glucose correlation is unreliable in ~ 20% of people
    - Anemia
    - RBC turnover
    - Liver and kidney disease
    - Hemoglobinopathy
    - Transfusion

The pros and cons of diagnosing diabetes with A1C. Diabetes Care 2011.
Use of HBA1c to Diagnose Diabetes: Our Clinical Bottom Line

- Plasma glucose remains the preferred method for diagnosing diabetes
- Post prandial testing is more sensitive
- The “poor man’s GTT”: check glucose 2 hours after 2 cans (12 ounces each) of sugared soda!

The pros and cons of diagnosing diabetes with A1C. Diabetes Care 2011.
• Systematic review and meta-analysis
  – Clinical trials that assessed the effect of a multifaceted lifestyle intervention on patient-important outcomes:
    • Progression to T2DM for patients at high-risk of developing it
    • Microvascular and macrovascular outcomes, including CVD for patients with T2DM.
  – Four trials included high-risk patients
  – Two trials included patients with diabetes

Effect of Lifestyle Interventions

• For high risk patients
  – Participation in a comprehensive lifestyle intervention reduced the risk for type 2 diabetes in persons who are at increased risk
    • All used diet and exercise interventions
    • DPP: 7% weight loss in first 24 weeks; 150 min/wk of moderate physical activity

Effect of Lifestyle Interventions

• For high risk patients
  – Effect on diabetes prevention persisted up to 10 years after intervention
    • End of intervention RR = 0.35
    • 4 yrs after end of intervention RR = 0.56
    • 10 yrs after end of intervention RR = 0.80
    • DPPOS plans additional analysis in 2014
  – Two trials reported on cardiovascular outcomes in high-risk patients, but neither found benefit with lifestyle interventions

Effect of Lifestyle Interventions: Our Clinical Bottom Line

- FOR PATIENTS AT HIGH RISK FOR DEVELOPING DIABETES
  - Use the Diabetes Prevention Project Protocol
  - 7% weight loss in first 24 weeks; 150 min/wk of moderate physical activity

Effect of Lifestyle Interventions: Our Clinical Bottom Line

- FOR PATIENTS WITH DIABETES
  - Participation in a comprehensive lifestyle intervention did not reduce mortality or a composite CV endpoint in people with type 2 diabetes: RR = 0.75 (95% CI: 0.53-1.06)
    - All studies included diet and exercise components plus at least 1 additional component—for some it was orlistat or other weight loss meds
    - Steno-2 trial used multiple medications in addition to lifestyle; studied patients with albuminuria—so a higher risk group
    - Look AHEAD trial studied overweight or obese patients
      - Composite CV endpoint RR = 0.95 (95% CI 0.83-1.09)
      - 1 yr weight loss was 8% vs. 0.5%; 10 yr weight loss 6% vs. 3.5%
      - There were similar differences in A1c and fitness

LEAD-2: Efficacy and Safety of Metformin + liraglutide vs. glimepiride vs. placebo

- Liraglutide is a QD injectable (vs. exenatide BID) GLP-1 receptor agonist ("incretin")
  - N = 1091 patients with T2DM
  - Adults age 18-80
  - A1c 7-11%
  - BMI < 40 kg/m²
  - Each arm was study drug plus metformin
    - Liraglutide 0.6, 1.2 or 1.8 mg once-daily
    - Glimepiride
  - 26 weeks blinded ± 18 month open-label extension → 2 years

## LEAD-2: Efficacy and Safety of Metformin + liraglutide vs. glimepiride vs. placebo

<table>
<thead>
<tr>
<th>Study Arm</th>
<th>A1c</th>
<th>Weight</th>
<th>Hypo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liraglutide-Met</td>
<td>-0.4%*</td>
<td>-2.1kg*</td>
<td>&lt; 5%*</td>
</tr>
<tr>
<td>0.6 mg</td>
<td>-0.6%*</td>
<td>-3.0kg#</td>
<td></td>
</tr>
<tr>
<td>1.2 mg</td>
<td>-0.6%*</td>
<td>-2.9kg#</td>
<td></td>
</tr>
<tr>
<td>1.8 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glimep-Met</td>
<td>-0.5%</td>
<td>+0.7kg*</td>
<td>24%*</td>
</tr>
<tr>
<td>Metformin</td>
<td>+0.3%*</td>
<td>-1.8kg#</td>
<td>NS</td>
</tr>
</tbody>
</table>

*p < 0.001 in category

#p < 0.05 in category

**NOTE:** No added benefit with doses > 1.2 mg/day

Nauck, Diabetes Obes Metab, 2013.
• Liraglutide gives A1c reductions of ~1% (like major orals)
• Liraglutide promotes ~ 1 kg. weight loss
  – liraglutide + metformin ~2 kg vs. 1 kg met alone
  – GI side effects significant but improve over time

• Current ICER $33,086 more/lifetime than exenatide
• Cost-effective per UK study as an add-on to MET vs. glimepiride or sitagliptin

ORIGIN- Basal Insulin Outcomes

- RCT of 12,537 patients: IFG, IGT, T2DM
- 573 sites in 40 countries: median 63.5 yrs; 35%F
- 11% IFG or IGT; Prior diabetes mean ~5.5 years
  - Insulin glargine to FPG ≤ 95mg/dL vs. “Standard care”
  - n-3 fatty acids
- Sponsored by *Sanofi* before glargine cancer scare

Assessed CV events, diabetes outcomes, weight, hypoglycemia, cancer

Good randomization with median f/u 6.2 years (5.8-6.7)

At 1 year

- Insulin glargine 0.4U/kg, FPG 94 mg/dL
- Standard care-few on insulin, FPG 123 mg/dL
- Overall ~30% on MET and/or SU in both arms during trial
ORIGIN- Basal Insulin Outcomes

- CV events: MI, CVA or death
  - ~2.9/100 person-yrs (NS)
- CV events + revascularization or hospital for CHF
  - ~5.4/100 py
- Glargine stopped → new DM dx in 30-35%
- Glargine ↑ weight (+1.6kg vs. -0.5 kg)
- Glargine ↑ hypos (1.0 vs. 0.3/100py)
- Cancer- no difference H.R. 1.00

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Insulin Glargine (N=6264)</th>
<th>Standard Care (N=6273)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st coprimary outcome</td>
<td>(no. (%))</td>
<td>(no. (%))</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First coprimary outcome</td>
<td>1041 (16.6)</td>
<td>1013 (16.1)</td>
<td>1.02 (0.94–1.11)</td>
<td>0.63</td>
</tr>
<tr>
<td>Second coprimary outcome</td>
<td>1792 (28.6)</td>
<td>1727 (27.5)</td>
<td>1.04 (0.97–1.11)</td>
<td>0.27</td>
</tr>
<tr>
<td>Microvascular outcomes</td>
<td>1323 (21.1)</td>
<td>1363 (21.7)</td>
<td>0.97 (0.90–1.05)</td>
<td>0.43</td>
</tr>
<tr>
<td>Total mortality</td>
<td>951 (15.2)</td>
<td>965 (15.4)</td>
<td>0.98 (0.90–1.08)</td>
<td>0.70</td>
</tr>
<tr>
<td>Total myocardial infarctions</td>
<td>336 (5.4)</td>
<td>326 (5.2)</td>
<td>1.02 (0.88–1.19)</td>
<td>0.75</td>
</tr>
<tr>
<td>Total strokes</td>
<td>331 (5.3)</td>
<td>319 (5.1)</td>
<td>1.03 (0.89–1.21)</td>
<td>0.69</td>
</tr>
<tr>
<td>Death from cardiovascular causes</td>
<td>580 (9.3)</td>
<td>576 (9.2)</td>
<td>1.00 (0.89–1.13)</td>
<td>0.98</td>
</tr>
<tr>
<td>Hospitalization for congestive heart failure</td>
<td>310 (4.9)</td>
<td>343 (5.5)</td>
<td>0.90 (0.77–1.05)</td>
<td>0.16</td>
</tr>
<tr>
<td>Revascularization</td>
<td>908 (14.5)</td>
<td>860 (13.7)</td>
<td>1.06 (0.96–1.16)</td>
<td>0.24</td>
</tr>
<tr>
<td>Angina</td>
<td>709 (11.3)</td>
<td>743 (11.8)</td>
<td>0.95 (0.85–1.05)</td>
<td>0.29</td>
</tr>
<tr>
<td>Unstable</td>
<td>238 (3.8)</td>
<td>261 (4.2)</td>
<td>0.91 (0.76–1.08)</td>
<td>0.28</td>
</tr>
<tr>
<td>New</td>
<td>100 (1.6)</td>
<td>138 (2.2)</td>
<td>0.72 (0.56–0.93)</td>
<td>0.01</td>
</tr>
<tr>
<td>Worsening</td>
<td>455 (7.3)</td>
<td>446 (7.1)</td>
<td>1.02 (0.89–1.16)</td>
<td>0.80</td>
</tr>
<tr>
<td>Limb or digit amputation</td>
<td>47 (0.8)</td>
<td>53 (0.8)</td>
<td>0.89 (0.69–1.21)</td>
<td>0.55</td>
</tr>
<tr>
<td>Cardiovascular hospitalization</td>
<td>2081 (33.2)</td>
<td>2071 (33.0)</td>
<td>1.00 (0.94–1.07)</td>
<td>0.90</td>
</tr>
<tr>
<td>Noncardiovascular hospitalization</td>
<td>2339 (37.3)</td>
<td>2349 (37.4)</td>
<td>0.99 (0.94–1.05)</td>
<td>0.85</td>
</tr>
<tr>
<td>Any cancer</td>
<td>476 (7.6)</td>
<td>477 (7.6)</td>
<td>1.00 (0.88–1.13)</td>
<td>0.97</td>
</tr>
<tr>
<td>Death from cancer</td>
<td>189 (3.0)</td>
<td>201 (3.2)</td>
<td>0.94 (0.77–1.15)</td>
<td>0.52</td>
</tr>
</tbody>
</table>

Figure 1. Hazard Ratios for the Coprimary and Other Outcomes.

Hazard ratios are adjusted for the factorial allocation, baseline diabetes status, and the presence or absence of a history of a cardiovascular event before randomization, as described in the protocol.
• Glargine used to treat to normal fasting glucose is overall no better or worse for CV, DM or Cancer outcomes than “standard care”
• Only 1 CV outcome was better—but this is within statistical “accident”
Inpatient Management
Basal-Bolus Therapy: Background

- Previous **Medical** trial (Umpierrez, 2007)
  - Basal-Bolus better control than NPH/Reg or Sliding Scale without increasing severe hypoglycemia
- **University Health System Consortium (90 hospitals)**
  - Diabetes control in hospital is poor
  - Only 45% of in-patients (12-77%) get insulin
- Trial supported by Sanofi-Aventis

Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes undergoing general surgery (RABBIT 2 Surgery). Diabetes Care, 2011.
**Inpatient Management Basal-Bolus Therapy**

- Randomized multi-center trial in T2 surgical patients (n = 211)
- Basal-Bolus glargine plus glulisine before meals (n = 104)
- Sliding Scale regular insulin 4 times daily for BG > 140 (n = 107)

<table>
<thead>
<tr>
<th>Hospital Goal BG: 72 to 180</th>
<th>Basal-Bolus</th>
<th>Sliding Scale</th>
<th>Significance - P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean after 1 day</td>
<td>145 ± 32</td>
<td>172 ± 47</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Insulin dose after 1 day</td>
<td>33.4 units</td>
<td>12.3 units</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BG &gt; 180 mg/dL</td>
<td>35.3%</td>
<td>20.5%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BG &lt; 140 mg/dL</td>
<td>55%</td>
<td>31%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BG &lt; 70 mg/dL</td>
<td>23.1%</td>
<td>4.7%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BG &lt; 40 mg/dL</td>
<td>3.8%</td>
<td>0</td>
<td><strong>NS</strong> P = 0.057</td>
</tr>
<tr>
<td>Composite BG &lt; 140 mg/dL</td>
<td>24.3%</td>
<td>8.6%</td>
<td>&lt; 0.003; OR 3.39</td>
</tr>
<tr>
<td>Total complications</td>
<td>9</td>
<td>26</td>
<td>&lt; 0.003</td>
</tr>
</tbody>
</table>

Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes undergoing general surgery (RABBIT 2 Surgery). Diabetes Care, 2011.
Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes undergoing general surgery (RABBIT 2 Surgery). Diabetes Care, 2011.
Inpatient Management
Basal-Bolus Therapy

Will it work in my patients?

• Age ~58 with T2DM x ~6 years
• Mean admission BG ~190
  – Most on oral agents (158) and ~ 20 each on diet/insulin/insulin + OA
  – Women = Men; Black > White > Other
  – BMI ~30-31
  – Did not include new hyperglycemia without prior DM dx

*Excluded cardiac surgery patients, Cr > 3, patients on high-dose insulin, Hx DKA

Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes undergoing general surgery (RABBIT 2 Surgery). Diabetes Care, 2011.
Inpatient Management
Basal-Bolus Therapy

Will it work in my patients?

• Insulin Glargine + glulisine (Sanofi-Aventis)
  – 0.5U/kg: 50% basal and 50% bolus
    • Decreased to 0.3U/kg if age > 70 or Cr > 2.0 mg/dL

• Regular insulin (Novo Nordisk)
  – Four times daily (before meals and bedtime) for glucose > 140 mg/dL
  – If uncontrolled (> 240 x 3 or mean) → switched to BB

• After 24 Hours
  – BB 33.4 U/day vs. SS 12.3 U/day (p < 0.001)

Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes undergoing general surgery (RABBIT 2 Surgery). Diabetes Care, 2011.
• Basal-Bolus is “better” than SS in general surgery patients with T2DM
• *May be better than insulin infusion once dosing is established*
• Dosing of 0.3-0.5U/kg divided 50/50 is safe in *most* T2DM and findings are probably generalizable
  – Adjust for age, creatinine, prior treatment

Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes undergoing general surgery (RABBIT 2 Surgery). Diabetes Care, 2011.
Safety and Effectiveness: Glucose Monitoring and Insulin Delivery

- Self-monitoring of blood glucose (SMBG) vs.
- Real-time Continuous Glucose Monitoring (rt-CGM)

- Similar for A1C and rates of severe hypoglycemia
- Both T1DM* and T2DM
  - *One study showed significantly lower A1C

Safety and Effectiveness: Glucose Monitoring and Insulin Delivery

- Multiple Daily Injections (MDI) vs.
- Continuous Subcutaneous Insulin Infusion (CSII)
- Similar for A1C and rates of severe hypoglycemia
- Both T1DM* and T2DM
  - *One study showed significantly lower A1C

Safety and Effectiveness: Glucose Monitoring and Insulin Delivery

- 2012 Systematic review and Meta-analysis
- Mostly industry-sponsored
- No language restrictions
- Many small studies; mostly white patients
- Cost of CSII- $2839 USD/year
  - 2010 pub cost of £1700 with similar 2014 exchange rate of $1.67
  - Better across all outcomes but compared to NPH-based MDI!
- Cost of rt-CGMS- /CGMS

Glucose Monitoring and Insulin Delivery: Our Clinical Bottom Line

- CGMS improves glycemic control and reduces hypoglycemia significantly
- CSII with insulin analogues is “better” and is probably cost-effective; but for many patients with T2DM, MDI, or simpler, is enough

Angiotensin Inhibition for Diabetic Nephropathy

- **Patient population:**
  - Veterans with T2DM
  - Urine ACR $> 300$ mg/g (median $\sim 850$ mg/g)
  - eGFR 30.0-89.9 mL/min/1.73 m$^2$

Intervention:
- 4346 patients screened; 1448 randomized
- Initial treatment with losartan 50 mg then 100 mg per day
- Patients randomized to add lisinopril or placebo
- Dose was 10, then 20, then 40 mg as long as K < 5.5 mmol/L and creatinine did not rise by > 30%
- BP drugs adjusted to target SBP 110-130, and DBP < 80.
- Median follow-up = 2.2 yrs

## Angiotensin Inhibition for Diabetic Nephropathy

<table>
<thead>
<tr>
<th>Category</th>
<th>ARB + ACEI</th>
<th>ARB only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drop in eGFR of 30 or more</td>
<td>18.2%</td>
<td>21.0%</td>
</tr>
<tr>
<td>ESRD</td>
<td>5.9%</td>
<td>3.7%</td>
</tr>
<tr>
<td>Death</td>
<td>8.7%</td>
<td>8.3%</td>
</tr>
<tr>
<td>MI, HF, or CVA</td>
<td>18.5%</td>
<td>18.8%</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>18.0%</td>
<td>11.0%</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>9.9%</td>
<td>4.4%</td>
</tr>
</tbody>
</table>

Angiotensin Inhibition for Diabetic Nephropathy: Our Clinical Bottom Line

- Dual angiotensin inhibition with an ARB and ACEI is not helpful, **AND** is harmful

Antihypertensive Timing in Patients with T2DM

- Patient population:
  - Spanish hypertensive patients with T2DM
  - HTN defined by ABPM: awake mean BP $> 135/85$ OR asleep mean BP $> 120/70$
  - Mean duration of DM = 8.8 yrs; for HTN = 7.5 yrs
  - Previous CVD event $\sim 9\%$
  - Mean HBA1c 6.9%
  - Mean number of BP drugs = 2.5; 60% of pts took 3 or more

Influence of time of day of blood pressure–lowering treatment on cardiovascular risk in hypertensive patients with type 2 diabetes. Diab Care 2011.
Antihypertensive Timing in Patients with T2DM

- Intervention:
  - 480 patients screened; 448 randomized
  - Trial was randomized, open-label, blinded end point trial
  - Intervention was to take at least 1 of the BP drugs at bedtime vs. control taking all BP meds upon awakening
  - Median follow-up = 5.4 yrs

Influence of time of day of blood pressure–lowering treatment on cardiovascular risk in hypertensive patients with type 2 diabetes. Diab Care 2011.
### Antihypertensive Timing in Patients with T2DM

<table>
<thead>
<tr>
<th>Measure</th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controlled ambulatory BP</td>
<td>62%</td>
<td>51%</td>
</tr>
<tr>
<td>Controlled nocturnal BP</td>
<td>71%</td>
<td>55%</td>
</tr>
<tr>
<td>Primary end point: a CVD composite</td>
<td>23%</td>
<td>68%</td>
</tr>
<tr>
<td>Other primary end point: major CVD event</td>
<td>6%</td>
<td>22%</td>
</tr>
</tbody>
</table>

Influence of time of day of blood pressure–lowering treatment on cardiovascular risk in hypertensive patients with type 2 diabetes. Diab Care 2011.
Antihypertensive Timing in Patients with T2DM: Our Clinical Bottom Line

- Move at least 1 antihypertensive drug to bedtime (absent a reason not to do this)

Influence of time of day of blood pressure–lowering treatment on cardiovascular risk in hypertensive patients with type 2 diabetes. Diab Care 2011.
Bariatric Surgery: Weight loss and Glycemic Control

- Bariatric surgery better than medical for BMI > 35
- JAMA systematic review: What about BMI > 30-35?
- 32 surgical studies and 11 “medical” SRs + 11 “medical” studies published after the SRs
- Surgery better @ 1-2 years follow-up for
  - WL (14.4-24 kg)
  - Glycemic control (0.9-1.43% A1C)
  - Hospital death rate 0.3-1%
- No long term outcomes at this level

Bariatric Surgery: Related Studies

- 11 studies of BMI ≥ 30
- WL: -26 kg (95% CI -21 to -31)
- Remission of T2DM: RR 22.1 (3.2-154.3)
  - Conservative analysis RR 5.3 (1.8-15.8)
  - TG↓; LDL↑; HDL no change
  - BP no change
- Complications:
  - Fe deficiency anemia in 15% of malabsorptive surgeries
  - Re-operation in 8%

Bariatric Surgery: Cost-Effectiveness vs. Medical Therapy

- Cost-effectiveness ratios
- Severely obese patients > BMI 35 and T2DM
- Bypass surgery
  - $7 000 per QALY new dx
  - $12 000 per QALY chronic dx
- Gastric banding
  - $11 000 per QALY new dx
  - $13 000 per QALY chronic dx

Henteleff et al, Can J Surg, 2013 review
Bariatric Surgery: Our Clinical Bottom Line

- Bariatric surgery works: outcomes somewhat center and surgeon dependent
- DDW study in submission and experience-
  - Rapid decreases in medical tx post-op demonstrate carbohydrate intake → be prepared to decrease medical DM therapy or discontinue (in T2)
  - Patients will stop meds if you don’t tell them not to
  - Patient education and reinforcement of diet restrictions is crucial!

Group Medical Visits and Diabetes Care

- Systematic review and meta-analysis
  - Clinical trials that assessed the effect of group visits
    - Typically led by MD or NP, and inclusive of other disciplines
    - Typical size 12-15 patients
  - Could be aimed at either T1DM or T2DM
  - 26 studies met inclusion criteria; 20 done in the US
  - 13 studies were RCTs; these were the subject of the meta-analysis

• Among the RCTs
  – Session duration was 60 – 300 minutes
  – Session frequency was weekly to quarterly
  – Length of study was 4 - 48 months
  – Total number of sessions : 4 – 15 (mean 8.2)

• Among the RCTs
  – Patients were felt to have “poorly controlled” diabetes
  – Definition of this was variable
  – Most often, HBA1c was 8.0% or greater
  – Mean HBA1c ranged from 7.2% to 9.7%

Group Medical Visits and Diabetes Care

- Results (RCTs)
  - HBA1c effect size of intervention: 0% to -1.7%
  - Pooled HBA1c effect was -0.46% (95% CI -0.80% to -0.13%)
  - Pooled HBA1c effect was -0.58% for T2DM only
  - Session frequency did NOT predict HBA1c response
  - Duration of group visit intervention DID predict HBA1c response:
    - For each additional year that of intervention continued, HBA1c dropped by 0.25%
  - No ideal characteristics of the group visit could be identified

• Results (RCTs)
  – Pooled SBP effect size -2.8 mm Hg
  – Pooled DBP effect size -1.0 mm Hg
  – Pooled BMI effect size + 0.05
    • 95% CI included 0 for all of these measures
  – Diabetes related QOL improved in the 2 studies that reported it using the Diabetes QOL questionnaire
  – Positive outcomes were seen in other process measures:
    • Diabetes knowledge
    • Self-efficacy
    • Self-management
    • Setting and achievement of measurable goals

Group Medical Visits and Diabetes Care: Our Clinical Bottom Line

- Positive outcomes in other process measures may be possible with a short course of group visits
- A1c improvement is correlated with duration of program
- Effect on BP is promising

Set clear goals
Be sure the whole team buys into them
Be sure the patient knows them (and agrees)
SECOND BIG Clinical Bottom Line

Sliding Scale


References for Top Ten

References for Top Ten


**Clinical Bottom Line**-Intensive A1c goal < 6% resulted in > 5-yr mortality, H.R. 1.21 (but lower non-fatal MI) than goal of 7-7.9%. Intensive stopped at 3.37 years. End A1c 7.2%, with similar hypo rates overall in both arms. The question now is probably whether aiming for 6.5% (assuming reaching 6.5-7%) is safe since other studies support better neuro and renal outcomes below 7%.


**Clinical Bottom Line**- High-potency statins may increase risk of incident diabetes. Pts. > 66 without DM, no statin use x 1 year. Rate/1000-person-years. Pravastatin = 23 (= Fluvastatin & Lovastatin); Simvastatin = 26; Atorvastatin = 31; Rosuvastatin = 34 (but = pravastatin when adjusted for dose/potency).

*This study may have other implications given new lipid treatment guidelines!*

**Clinical Bottom Line:** Low-carb diet (aim for 20% carbs/kcal) decreased insulin requirements. Weight loss ~equal for low-carb vs. low fat (-4kg @ 6 mo and ~2.5kg @ 24 mo). Insulin dose decreased ~8-12U in low carb diet with a small decrease in A1c.


**Clinical Bottom Line:** Short-term US-Taiwan RCT in 120 pts confirms that gastric bypass results in more wt. loss and better DM/CV surrogate outcomes with fewer medications (3 less per pt) but more nutritional deficiencies.

**Clinical Bottom Line:** Cancer rates increase linearly with years of diabetes (p<0.001). T2DM > 15 years: prevalence is 1.6 for men and 1.8 for women vs. < 15 yrs. T2DM insulin-treated prevalence = 1.3 x higher, likely explained by insulin as a growth factor promoting tumor growth rather than causing cancer? But conflicts with ORIGIN results.


**Clinical Bottom Line:** 5145 US T2DM → intensive lifestyle; trial stopped early after median 9.6 years based on futility: despite wt. loss and decreased A1c in tx group, no difference in CV outcomes or mortality.

Clinical Bottom Line: Patients not on insulin do not benefit from SMBG. Meta-analysis shows no difference in metabolic or other outcomes (e.g. satisfaction), except cost (~150 USD/yr) with SMBG in patients not using insulin. Choosing Wisely #1 for SGIM.


Clinical Bottom Line: Intensive BP targets (<130/80) do not decrease mortality or MI risk but do decrease stroke slightly (absolute risk difference, -0.01; 95% CI, -0.02 to -0.00).

Clinical Bottom Line: Patients benefit from peer-coaching, but patients with “low self-management and medication adherence” at baseline benefit more (+0.5% A1c usual care vs. -0.8 A1c peer coaching) than those with high adherence. High adherence (-1.1 vs -1.3), RCT of 299 pts. With 6 month study period


Clinical bottom line: ≤ 0.6 U/kg seems to be a thresh-hold for hypoglycemia in non-critically ill patients (but there is a linear association with doses above this). Trend to NPH causing more hypos than other insulins. Case (glu < 70 mg/dL) vs. Control (non-hypoglycemic) on “day of hypoglycemia”, matched for BMI, age, sex.

Clinical Bottom Line: Mediterranean diet with extra-virgin olive oil, but no calorie restriction (vs MD with nuts or LF diet advice), decreased risk of T2DM (HR 0.6; 16.0 cases/1000 p-y vs. 23.6 cases in diet advice group) in a Spanish population. RCT of 3541 pts 55-80 with CRF.


Clinical Bottom Line: Saxagliptin does not improve 2-year CV outcomes and does not increase pancreatitis. RCT of 16,492 DM pts with CVD/risk. Saxagliptin is a DPP-4 inhibitor. No difference in composite CV outcomes but ↑hosp for CHF (HR 1.27; p<0.007).

**Clinical Bottom Line:** SGLT-2 inhibitors are a new class that inhibit renal glucose reabsorption and are effective. Some advantages but no significant reason to prefer them over metformin: ↓ A1c ~-0.66%; ↓ Wt. -1.8kg; ↓ BP -4.5 mmHg; ~= hypos. Downside- ↑ adverse renal events if ↓ GFR. ↑ UTIs. ↑ Bladder & Breast Ca with dapagliflozin; and cost.


**Clinical Bottom Line:** Pharmacist and nurse care management programs are both more effective than usual care. It is not clear if 1 model is superior. If pharmacists are involved, it is more effective if they can independently adjust medication doses.

**Clinical Bottom Line:** High fat meals increase glucose levels and insulin needs (highly individual) for a given amount of carbohydrate. Patients and clinicians may need to adjust accordingly.
References for New Guidelines


Clinical Bottom Line: For adults >65 with DM
1. No longer recommend ASA for 1° prevention of CVD
2. BP goal < 140/90 (not 130/90)- diuretics, ACEI, BB or CCB.
   1. Check Cr, lytes in 1-2 weeks
3. Treat dyslipidemias with statins
4. Lifestyle modification reinforced based on evidence

Clinical Bottom Line: Metformin first line, A1c goal < 7% or individualized. If A1c > 9%→ insulin may be 1st line.


Clinical Bottom Line: Most DFIs are polymicrobial (GPC esp. S.A. ± GNBs). If not 2 signs of infxn→ No abx (but beware mid-foot abscess). If 2 signs of infxn→ MRI→ tissue bx→ abx→ surgical debridement. Off-loading (>10 min/d of wt bearing negates off-loading) and appropriate (new) wound dressing critical.