Should We Count Fat and Protein in Bolus Insulin Dose Calculation: Does Carbohydrate Counting Work?

Howard A. Wolpert, MD
Carbohydrate to Insulin Ratio, circa 1935

10. How Many Grams of Carbohydrate Will One Unit Metabolize?—This question no one can answer. There are always adjustments required for exercise and diet. Even if these two factors are constant the improvement of the condition of the patient overthrows one’s calculations.

In general 1 unit of insulin will metabolize 1 or 2 grams of carbohydrate, and perhaps even 3 to 6 grams
Constraints: Eating had to be organized around the insulin profiles.

Nutrition education: Meal planning was based on exchanges: 3 meals/3 snacks.

Trade-off: Less lifestyle flexibility → often poorer adherence.
Basal-Bolus/Flexible Insulin Therapy: Past 2 decades

Milestones in the evolution of intensive insulin therapy:
- 1993: DCCT
- 1995: Introduction of 1st analog insulin (Lispro)
- 2003: Introduction of 1st pump with bolus calculator (Deltec Cozmo)
The Current Approach

Carbohydrate quantity \times \text{Insulin-to-Carb ratio} = \text{Insulin dose}

Are we setting up patients to fail with an approach that doesn’t work?
Limitations and Assumptions.....

Carbohydrate quantity \times \text{Insulin-to-Carb ratio} = \text{Insulin dose}

Is accuracy in carb counting a realistic goal for most patients?
Carbohydrate counting skills in adult pump patients at Joslin

Patient estimated quantity (grams)

HbA1c

30 grams
Carbohydrate counting skills in adult pump patients at Joslin

HbA1c

Patient estimated quantity (grams)

36 – 45 grams
Limitations and Assumptions…..

Carbohydrate quantity × Insulin-to-Carb ratio = Insulin dose

Is accuracy in carb counting a realistic goal for most patients?

Assumes that carbs are the only dietary ingredient that affects insulin requirements
Is there any scientific validity to carb-based insulin dosing?

Is getting the insulin dose correct all that matters?
To achieve optimal postprandial glucose control insulin action needs to match carb absorption
Insulin Pharmacodynamics

- Aspart
- Lispro

Cheerios Glycemic Index = 83
Oatmeal Glycemic Index = 49

Insulin Pharmacodynamics

- Aspart
- Lispro

Oatmeal Glycemic Index = 49
53 year old man with T1DM X 10 years, HbA1c 7.6%
I/CHO ratio 1/10, sensitivity factor 40
53 year old man with T1DM X 10 years, HbA1c 7.6%
I/CHO ratio 1/10, sensitivity factor 40

Plans to eat 120 gram pizza
What should he bolus?
What should he bolus?

I/CHO ratio 1/10, sensitivity factor 40, BG target 100 mg/dL
Premeal BG 140 mg/dL
Food: pizza 120 gram carbohydrate

1. 13 units: normal bolus
2. 13 units: 9 units initially & 4 units over 2 hrs
3. 13 units: 7 units initially & 6 units over 6 hrs
4. None of the above
53 year old man with T1DM X 10 years, HbA1c 7.6%
I/CHO ratio 1/10, sensitivity factor 40

What he did:
8 units initially &
4 units over 2 hrs
53 year old man with T1DM X 10 years, HbA1c 7.6%
I/CHO ratio 1/10, sensitivity factor 40, target 100

4 unit correction dose calculated by Bolus Wizard
53 year old man with T1DM X 10 years, HbA1c 7.6%
I/CHO ratio 1/10, sensitivity factor 40, target 100

6 unit correction dose calculated by Bolus Wizard
Free fatty acids induce insulin resistance

Plasma FFA (mmol/L)

Glucose infusion rate (μmol/[kg·min])

+ p < 0.01
† p < 0.001

Roden, 1996
Dietary fat delays gastric emptying and glucose absorption in T1D adolescents

Paracetamol/Acetaminophen absorbed in duodenum > Blood levels correlate with rate of gastric emptying

Lodefalk, 2008
Dietary fat delays gastric emptying and glucose absorption in T1D adolescents

Delayed gastric emptying from dietary fat > Delayed glucose absorption

Lodefalk, 2008
Low-fat diet improves insulin sensitivity in patients with T1D

Euglycemic insulin clamp at:
- Baseline
- After isocaloric low-fat (26%) diet X 3 mths
- After standard diet (30% fat) X 3 mths

Rosenfalck, 2005
Association of fat intake with glycemic control in the intensive treatment cohort in the DCCT

<table>
<thead>
<tr>
<th>Variable</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Q5</th>
<th>P value²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal/kg)³</td>
<td>18.0 (0.4)</td>
<td>23.3 (0.4)</td>
<td>27.1 (0.4)</td>
<td>32.3 (0.4)</td>
<td>43.3 (0.4)</td>
<td>—</td>
</tr>
<tr>
<td>Mean total energy intake (kcal)</td>
<td>1574 (33–35)</td>
<td>1831 (33–35)</td>
<td>2051 (33–35)</td>
<td>2298 (33–35)</td>
<td>2969</td>
<td>—</td>
</tr>
<tr>
<td>Hb A₁c (kcal/kg)</td>
<td>7.31 (0.11)</td>
<td>7.45 (0.11)</td>
<td>7.28 (0.11)</td>
<td>7.11 (0.11)</td>
<td>7.23 (0.11)</td>
<td>0.64</td>
</tr>
<tr>
<td>Daily dietary intake³</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean carbohydrate (g)</td>
<td>201 (6)</td>
<td>236 (6)</td>
<td>239 (6)</td>
<td>260 (6)</td>
<td>269 (6)</td>
<td>—</td>
</tr>
<tr>
<td>Total carbohydrate (% of energy)</td>
<td>37 (0.2)</td>
<td>42 (0.2)</td>
<td>45 (0.2)</td>
<td>49 (0.2)</td>
<td>56 (0.2)</td>
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<tr>
<td>Hb A₁c by carbohydrate intake quintile</td>
<td>7.47 (0.11)</td>
<td>7.29 (0.11)</td>
<td>7.42 (0.11)</td>
<td>7.12 (0.11)</td>
<td>7.08 (0.11)</td>
<td>0.01</td>
</tr>
<tr>
<td>Mean available carbohydrate (g)</td>
<td>181 (5)</td>
<td>215 (5)</td>
<td>216 (5)</td>
<td>236 (5)</td>
<td>246 (5)</td>
<td>—</td>
</tr>
<tr>
<td>Total available carbohydrate (% of energy)</td>
<td>34 (0.2)</td>
<td>38 (0.2)</td>
<td>41 (0.2)</td>
<td>44 (0.2)</td>
<td>49 (0.2)</td>
<td>—</td>
</tr>
<tr>
<td>Hb A₁c by available carbohydrate quintile</td>
<td>7.45 (0.11)</td>
<td>7.29 (0.11)</td>
<td>7.42 (0.11)</td>
<td>7.16 (0.11)</td>
<td>7.07 (0.11)</td>
<td>0.01</td>
</tr>
<tr>
<td>Mean protein (g)</td>
<td>89 (2)</td>
<td>96 (2)</td>
<td>95 (2)</td>
<td>98 (2)</td>
<td>102 (2)</td>
<td>—</td>
</tr>
<tr>
<td>Total protein (% of energy)</td>
<td>15 (0.1)</td>
<td>17 (0.1)</td>
<td>18 (0.1)</td>
<td>19 (0.1)</td>
<td>22 (0.1)</td>
<td>—</td>
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<tr>
<td>Hb A₁c by protein quintile</td>
<td>7.34 (0.11)</td>
<td>7.35 (0.11)</td>
<td>7.29 (0.11)</td>
<td>7.3 (0.11)</td>
<td>7.12 (0.11)</td>
<td>0.2</td>
</tr>
<tr>
<td>Mean total fat (g)</td>
<td>62 (2)</td>
<td>79 (2)</td>
<td>84 (2)</td>
<td>99 (2)</td>
<td>120 (2)</td>
<td>—</td>
</tr>
<tr>
<td>Total fat (% of energy)</td>
<td>28 (0.2)</td>
<td>34 (0.2)</td>
<td>37 (0.2)</td>
<td>40 (0.2)</td>
<td>45 (0.2)</td>
<td>—</td>
</tr>
<tr>
<td>Hb A₁c by total fat quintile</td>
<td>7.14 (0.11)</td>
<td>7.12 (0.11)</td>
<td>7.32 (0.11)</td>
<td>7.35 (0.11)</td>
<td>7.47 (0.11)</td>
<td>0.004</td>
</tr>
<tr>
<td>Mean saturated fat (g)</td>
<td>20.0 (1)</td>
<td>26 (1)</td>
<td>30 (1)</td>
<td>36 (1)</td>
<td>43 (1)</td>
<td>—</td>
</tr>
<tr>
<td>Total saturated fat (% of energy)</td>
<td>10 (0.01)</td>
<td>11 (0.01)</td>
<td>13 (0.01)</td>
<td>14 (0.01)</td>
<td>17 (0.01)</td>
<td>—</td>
</tr>
<tr>
<td>Hb A₁c by saturated fat quintile</td>
<td>7.05 (0.11)</td>
<td>7.23 (0.11)</td>
<td>7.40 (0.11)</td>
<td>7.30 (0.11)</td>
<td>7.41 (0.11)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Delahanty, 2009
To test the hypothesis that high fat meals would require more insulin coverage than low fat meals with identical carbohydrate content → Regulated the macronutrient intake of adults with T1D undergoing closed loop glucose control
Clinical Research Center Protocol

Day 1  Day 2  Day 3

Admit
Open Loop

Closed Loop
Mild activity

12  6p  11p  8a  12  6p  11p  8a  12
Lunch  Dinner

High Fat
or
Low Fat
<table>
<thead>
<tr>
<th></th>
<th>Low Fat Dinner</th>
<th>High Fat Dinner</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fat</strong></td>
<td>10g</td>
<td>60g</td>
</tr>
<tr>
<td><strong>Carbohydrate</strong></td>
<td>Same (75-112.5g depending on caloric intake)</td>
<td></td>
</tr>
<tr>
<td><strong>Protein</strong></td>
<td>Same (40-60g depending on caloric intake)</td>
<td></td>
</tr>
</tbody>
</table>

**Low Fat Dinner**
- Chicken breast, rice, broccoli, carrots, green salad, grapes

**High Fat Dinner**
- Grilled cheese sandwich, green salad with cheese, croutons & grilled chicken, orange slices
Clinical Research Center Protocol

Day 1
- Open Loop
- Mild activity
- Breakfast
- High Fat or Low Fat
- Dinner

Day 2
- Closed Loop
- Breakfast
- High Fat or Low Fat
- Lunch

Day 3
- Open Loop
- Mild activity
- Closed Loop
- Breakfast
- High Fat or Low Fat
- Dinner

Clinical Research Center Protocol
Closed Loop Control

Glucose (mg/dL)

High Fat Dinner
Low Fat Dinner

**** p < 0.0001
### Carbohydrate-to-Insulin Ratio: Low Fat Dinner (LFD) vs High Fat Dinner (HFD)

Carbohydrate-to-Insulin Ratio for Dinner:
Carbohydrates consumed 6pm -11pm, divided by total insulin delivered

<table>
<thead>
<tr>
<th>Subject</th>
<th>LFD</th>
<th>HFD</th>
<th>% increase for HFD</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1</td>
<td>14.9</td>
<td>10.4</td>
<td>43%</td>
</tr>
<tr>
<td>#2</td>
<td>9.6</td>
<td>7.2</td>
<td>34%</td>
</tr>
<tr>
<td>#3</td>
<td>17.8</td>
<td>11</td>
<td>62%</td>
</tr>
<tr>
<td>#4</td>
<td>13.2</td>
<td>10.3</td>
<td>28%</td>
</tr>
<tr>
<td>#5</td>
<td>9.9</td>
<td>4.8</td>
<td>108%</td>
</tr>
<tr>
<td>#6</td>
<td>9.3</td>
<td>11.2</td>
<td>---</td>
</tr>
<tr>
<td>#7</td>
<td>12.8</td>
<td>9.4</td>
<td>36%</td>
</tr>
</tbody>
</table>

P = 0.01
These studies highlight the limitations of the carbohydrate counting-based method for calculating meal-time insulin dosage. Higher fat meals require alternative dosing algorithms with an altered insulin delivery pattern and dose.

However:

- Marked inter-individual differences, so fixed dosing increase for higher fat meals will not be safe/effective.
- Different fat types have different effect on insulin sensitivity: Saturated vs monounsaturated, palmito-oleic acid.
- Dose response vs threshold effect?
Four test breakfasts with identical carbohydrate content, but varying protein and fat quantities
Influence of Pure Protein on Postprandial Blood Glucose in Individuals with Type 1 Diabetes Mellitus

MEGAN A. PATERSON, CARMEL SMART, PATRICK MCELUFF, PRUDENCE LOPEZ, CLAIRE MORBEY. JOHN ATTIA, BRUCE KING, Newcastle, Australia

T1DM, aged 7-40 years, fed several test meals:
- Varying amounts pure protein - 12.5g, 25g, 50g, 75g and 100g
- Two pure glucose powder test meals (10g and 20g) for comparison
- No insulin was given for test meals
- Postprandial glycemia assessed for 5 hours

- Protein amounts of **0-50g > NO effect** on glucose
- Protein amounts of **75 & 100 g > increase in glucose starting at 100 minutes**, equaling rise with the 20g glucose test meal
- Equivalent to consuming an 8oz steak

55-OR, ADA Sci Sessions, 2014
Pizza meal in children with T1D

**Dose:** Carb-based

**Bolus:** Normal

**Dose:** $n$ CU (10g Carb) X ICR + $n$ fat-protein X ICR

**Bolus:** Dual, extended to 6 hr

Hypoglycemia (< 50 mg/dL):
2 of 12 subjects who received fat-protein bolus
Practical Implications – Insulin dosing

Current Studies

1. Investigate glycemic effect of different fats:
   Saturated vs Poly- & Mono- unsaturated
2. Develop and validate “fat bolus” (alternative insulin delivery pattern and dose)
   Identify individual characteristics that are predictors of “fat-sensitivity”
Practical Implications – Nutrition

Restriction of dietary fat intake is an important nutritional consideration in individuals striving for tight glycemic control.

Carbohydrate counting is a foundation for calculating meal-time insulin doses. However, to achieve optimal glycemic control carbohydrate counting needs to be combined with:

1) Specific focus directed at identifying whether higher fat (or high glycemic index) meals are contributing to glycemic fluctuations, in conjunction with

2) Individualized guidance about changing to alternative meal/food choices with less glycemic impact

i.e. Some form of meal-planning should be an explicit focus of nutrition counseling in patients with T1D
On any given day, roughly 13 percent of the U.S. population, or more than 1 in 8 Americans, consumes pizza.

In pizza-eaters:
- Pizza accounts for 25% (among kids) and 29% (among adults) of daily food energy intake.
- Pizza accounts for 33% (among kids) and 39% (among adults) of daily saturated fat intake.
Increased Cheese consumption in the US
Case Example: Variable overnight glucoses due to high fat supper meals in a CGM user

What would you do?
1. Suggest use of dual/combo bolus for higher fat meals
2. Advise against eating out
HI alarm threshold set at 280 mg/dL
HI alarm threshold set at 220 mg/dL

Recommendation:
Reduce HI alarm threshold to 220 mg/dL
Acknowledgements

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Study subjects