HOW TO GET THE RIGHT MEAL TIME INSULIN DOSE WITH TYPE 1 DIABETES

Diabetic™
MUSCLE & FITNESS

CRITIQUE OF AVAILABLE INSULIN DOSING STRATEGIES

JOHN PEMBERTON | TYPE 1 DIABETES | REGISTERED DIETITIAN

WWW.DIABETICMUSCLEANDFITNESS.COM

ABBREVIATIONS

AA = Amino Acid
ADP = Adenosine Di Phosphate
ATP = Adenosine Tri Phosphate
AUC = Area Under the Curve
BCAA = Branches Chain Amino Acids
Ca = Calcium
CGM = Continuous Glucose Monitoring
FFA = Free Fatty Acid
FPU - Fat and Protein Units
GDH = Glutamate Dehydrogenase
GI = Glycaemic Index
GL = Glycaemic Load
GLP-1 = Glucagon-like peptide-1
GIP = Gastric Inhibitory Polypeptide
GPCR = G-Protein Coupled Receptor
I:G = Insulin to Glucagon ratio
ICR = Insulin to carbohydrate ratio
MDI = Multiple Daily Injections
MUFA = Monounsaturated Fatty Acids
KATP = ATP-regulated potassium channel
mTOR = mammalian target of rapamycin
SFA = Saturated Fatty Acid
TCA = Tri-Carboxyl-Acid cycle

CURRENT AVAILABLE INSULIN DOSING STRATEGIES

We have developed a good understanding of the hormonal interplay required to maintain a stable blood glucose level after eating. We have also highlighted the unique challenges a person with Type 1 Diabetes faces. We are now in a fantastic position to evaluate the most popular insulin dosing strategies.

Let's have a look at the current insulin dosing strategies to;

- Appreciate their benefits and draw backs
- Know when they will work and when they will not
- See what diet types they fit best
- See if we can swap and change strategies depending on meal composition

CARBOHYDRATE COUNTING

This method is based on counting the carbohydrate content of a meal, then applying an ICR to determine the insulin dose. For example if you have a ratio of 1unit for 10g carbs and eat 30g, that's 3 units, simple!

Carbohydrate counting is the gold standard method for determining meal timeinsulin dose recommended by the main regulatory bodies (ADA 76, ISPAD 77, NICE 78) .Therefore you would assume there is a solid evidence base on carbohydrate counting's effectiveness.

Carbohydrate counting became the gold standard approach following the DCCT results. The DCCT (45) found intensiveinsulin treatment by MDI or pump therapy, combined with regular follow-up, aiming to get HbA1c to 6% (42mmol/mol), significantly reducedHbA1c compared to two injections per day. On average the intensive group had 6.5 years of improved HbA1c control, where their Hba1c was on average 2% lower. This lead to a huge relative risk reductions in microvascular complications at 6.5 years:

- 76% reduction in eye disease
- 50% reduction is kidney disease
- 60% reduction is nerve disease

It was too soon to determine the effect on cardiovascular health, after only 6.5 years. Therefore the research group followed up 90% of the DCCT trial patients for the EDIC study. The intensive groups HbA1c drifted back up to the two injections per day group almost as soon as the 6.5 years were up. The EDIC study found what is to be known as "metabolic memory". This is where the period of 6.5 years improved control by 2% lead to persistent microvascular benefits, but not just that, massive macrovascular health relative risk reductions also:

- 42% reduced risk of a cardiovascular event
- 57% reduced risk of non-fatal heart attack, stroke, or death from cardiovascular causes

This landmark trial was the clear evidence that certified HbA1c as the crucial marker for monitoring diabetes control. Also that intensive management of Type 1 Diabetes is necessary to achieve a lower Hba1c that is sustained.

Most people assume the intensive group in the DCCT used carb counting to determine meal time insulin dosing. However, when you look into the DCCT trial, the insulin dosing strategies used at mealtimes was different at each of the 29 American Centres participating. The strategies used can be grouped into three main categories:

- Food exchanges, where the person can exchange, starchy, dairy, protein, and fruit and veg portions. In some centres the insulin was adjusted based on the amount of different foods groups at the meal time. In other centres the participants were given fixed meal insulin dose, then they could exchange the food groups to meet the dose.

- Total available glucose (TAG). This method counted every gram of each macronutrient and then used a proportion of each gram to determine the insulin load grams. They would then apply an insulin load ratio, which works on the same principle as an ICR. The breakdown of the maths is below.
    - Every gram of carbohydrate as 1g
    - Every gram of protein as 0.5g
    - Every gram of fat as 0.1g

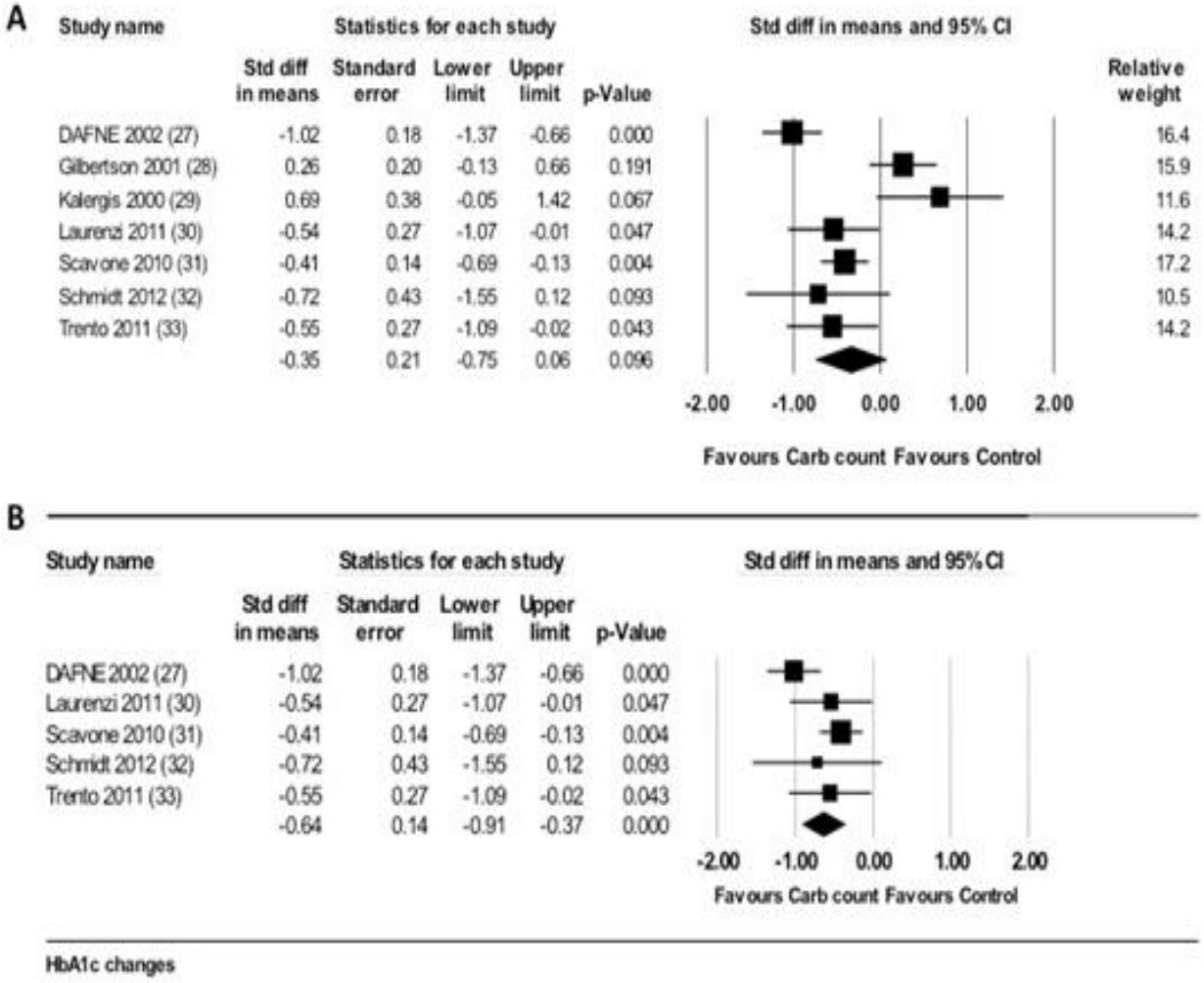
- Carbohydrate counting and applying an ICR.

WHAT DOES THE RESEARCH SAY ABOUT CARBOHYDRATE COUNTING?

The only high quality meta-analysis performed on the effectiveness of carbohydrate counting was performed by Bell in 2014 (41). Only seven (5 adult and 2 paediatric) out of 311 studies passed the inclusion criteria, highlighting the poor quality of research studies on carbohydrate counting,

WHAT DID THEY FIND?

Figure A below shows a HbA1c reduction of only 0.35% in three months or longer, which was not statistically significant. Figure B shows sub-group analysis of those studies running parallel design, where a 0.64% reduction was found, which was both statistically and clinically significant. Carbohydrate counting was only found to be beneficial for adults (-0.4%), but not for children.



Copied from Bell (41)

The results do not find resounded support for carbohydrate counting, especially for children where there was no benefit found.

Why is that?

Accuracy is one issue. It has been shown those families in the top 25% of counting accuracy have a 0.8% lower HbA1c than those in the bottom 25% (42).

So if accurate then all good right, but how accurate do you need to be?

A set of innovative meal experiments have shown that counting accuracy only needs to be within 10-15g of the actual amount of carbohydrate on the plate, to calculate an effective insulin dose (79).

Can people actually count carbohydrate within a 10-15g accuracy?

Carb counting accuracy within 10-15g can be achieved by 50-80% of motivated parents, under experimental conditions in the lab. For adolescents, only 23% achieve the necessary level of accuracy (48).For adults, the research consistently shows 50% achieve

an accuracy within 10-15g (44).

So if you are within 10-15g accuracy, all is good right?

No quite. we have discussed carbohydrate counting only works when protein and fat content are within usual amounts for the individual. When a person has a low fat and protein meal and applies their ICR, they go on average 2.9mmol/l lower from where they started at five hours. Conversely when they add a large amount of fat and protein to a meal and apply their ICR, the blood glucose is on average 2.3mmol/l higher at five hours (28).

When a person has meals way outside their norms, there are blood glucose consequences. Bell (40) showed on average 65% extra insulin was needed for a heavily cheesed pizza, compared to when just ate the pizza base. Both meals contained 50g of carbohydrate.

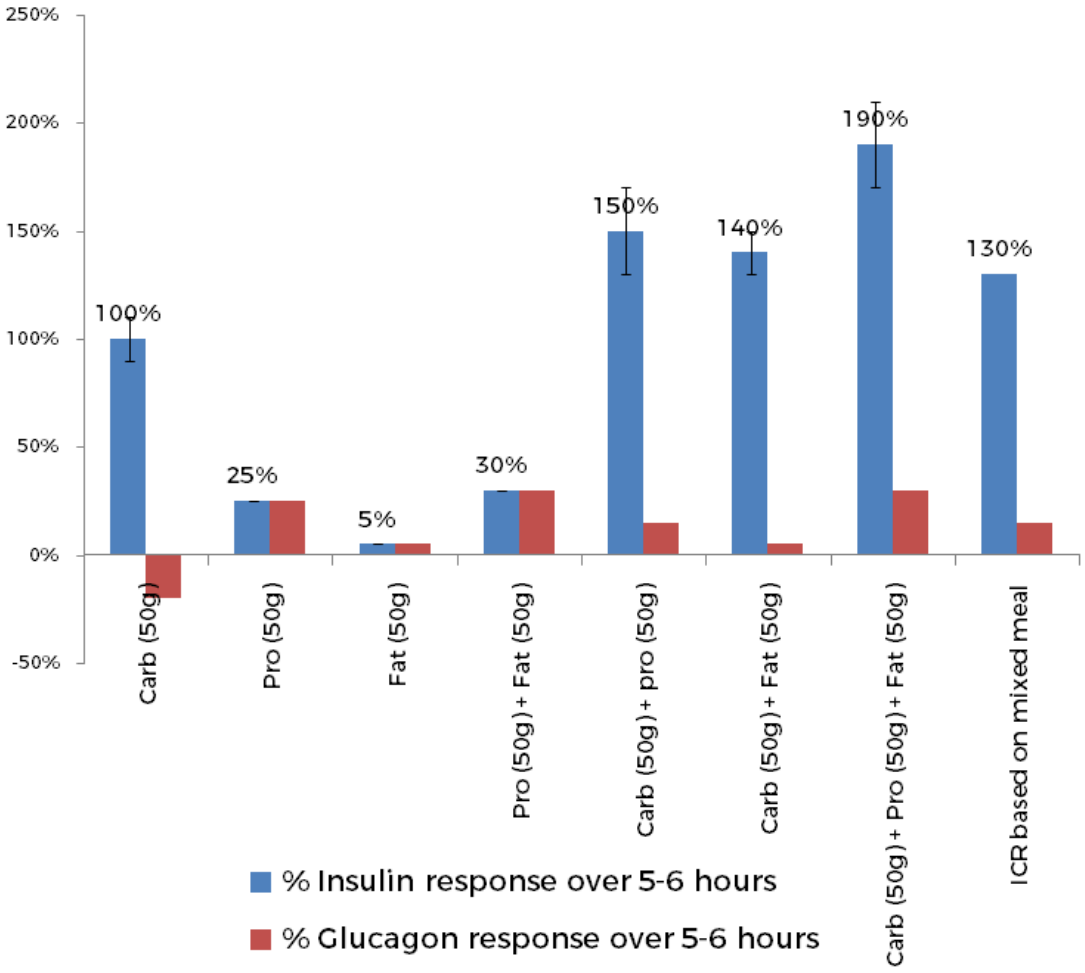
Taken together this research shows:

> **If you keep fat and protein consistent then carbohydrate counting accuracy only needs to be within 10-15g.**
>
> **For example if breakfast is usually cereal with milk (60g carb, 10g protein, 5g fat), then the carb count only needs an accuracy of 50-70g. If the same 60g carbohydrate is eaten as toast, but this time with scrambled egg (4 eggs, 28g protein, 16g fat), the ratio will not work despite a carb accuracy of 50-70g.**

This is of massive practical significance because most people who carbohydrate count believe as long as there accuracy is within 10-15g, all will be good. However, if they change their usual fat and protein amounts, all good will not be good!

As discussed earlier, ICR's are tried and tested eating usual mixed meals, therefore they already take into account the glucose raising effect of your usual protein and fat intake. So really it's not an ICR, it's a usual mixed meal ratio using carbohydrate as the main determinant.

This point is shown schematically in the graph we have built throughout this document. When people work out their ICR it's based on their usual mixed meal, and that is actually covers about 130% of the insulin response needed for the 100% carbohydrate. The other 30% is the insulin required for the protein and fat content of that meal. Therefore as long as the fat and protein amounts at meal time stay similar, the ICR will work because the carbohydrate is the main determinant of the insulin response needed.



If no fat and protein are eaten with the carbs, for example three pieces of fruit, and then ICR is applied, a hypo is likely, as there will be 30% too much insulin. On the reverse, if a high fat and high protein is eaten the 30% covered by the ICR will not be enough, another 60% would be needed, and some portion of the extra insulin delayed.

Carbohydrate counting can lead to a reliance on packaged food and a disregard for a healthy balanced nutritional intake (49).

FAT AND PROTEIN UNITS (FPU) - WARSAW METHOD

The Warsaw FPU (5) method acknowledges fat and protein have an effect on post-prandial blood glucose level, and require insulin to mitigate. The FPU methods assumes that 100kcal of either fat (11g) or protein (25g) has the same insulin requirement as 10g carbohydrate. So if the person has a 1u:10g ICR, then 100kcal of fat and protein requires 1 unit of insulin, called 1 FPU. If ICR is 1u:20g, then 100kcal of fat and protein needs 0.5 units insulin, 0.5FPU.

How that FPU insulin is delivered is unique. The insulin for the carbohydrate is always

given before eating. Then the insulin required for the FPU is then spread out using and extended bolus over a number of hours via a pump. The length of extension for the FPU is determined by the total FPUs:

- 1 FPU = 3 hours
- 2FPU = 4h hours
- 3FPU = 5 hours
- >3FPIU = 8 hours

Potential issues:

- This method assumes fat and protein have similar effect on insulin requirement, regardless if they are consumed on their own or in combination. Our discussion has shown that fat and protein alone require less insulin than when they are combined carbohydrate. Also that protein has a greater insulin requirement than fat on a gram by gram basis.

- The FPUs are delivered over a extended bolus, regardless of if the FPUs are due to protein or fat. The research discussed shows the protein portion needs to be delivered before eating, and the fat portion later (28). There is a big chance of mis-matching the insulin dose to the food.

- The extension times suggest 3-8hours depending on the FPU. This leaves lots of active insulin working when people do physical activity many hours after eating, leading to hypos.

WHAT DOES THE RESEARCH SAY ABOUT THE WARSAW FPU METHOD?

Research has shown following the FPU system caused a lot of hypoglycaemia when compared to carbohydrate counting(50). This potentially could have been reduced if the ICR was made less aggressive before the group started the FPU system. There did not appear to be an understanding that the current ICR takes into account 30% of the response of usual fat and protein. If they reduced the FPU ICR by 60% before starting, they may have had better results.

We must consider the maths involved. We already discussed the most motivated groups only count carbohydrate with 50-80% accuracy, adults 50%, and adolescents at 23%. What would happen if they also needed to count fat and protein grams and apply formulas?

Personal and clinical experience has taught me it does not work for the vast majority! Obviously APP's and new technology may make this easier to use in practice.

Food Insulin Index (FII) and Food Insulin Demand(FID):

The FII was developed by measuring the incremental area under the plasma insulin curve observed by a 1000 kJ portion of a test food, expressed as a percentage of the response to a 1000 kJ portion of the reference food (glucose) within a lean, healthy subject.

The final FII of a food is calculated as the average FII in 10 subjects.

Food Insulin Index (FII) =

(120min AUC Insulin for 1000 kJ test food / 120min AUC Insulin for 1000 kJ reference food) x 100

Therefore instead of measuring the glucose response, like the GI, it measures the insulin requirement, which is much more useful for people with Type 1D.

The FII database has been added to over 20 years and has 147 foods, some singular foods, other mixed meal foods. The FII is a percentage insulin response over two hours compared to 100% of Glucose, a summary is presented below in the table.

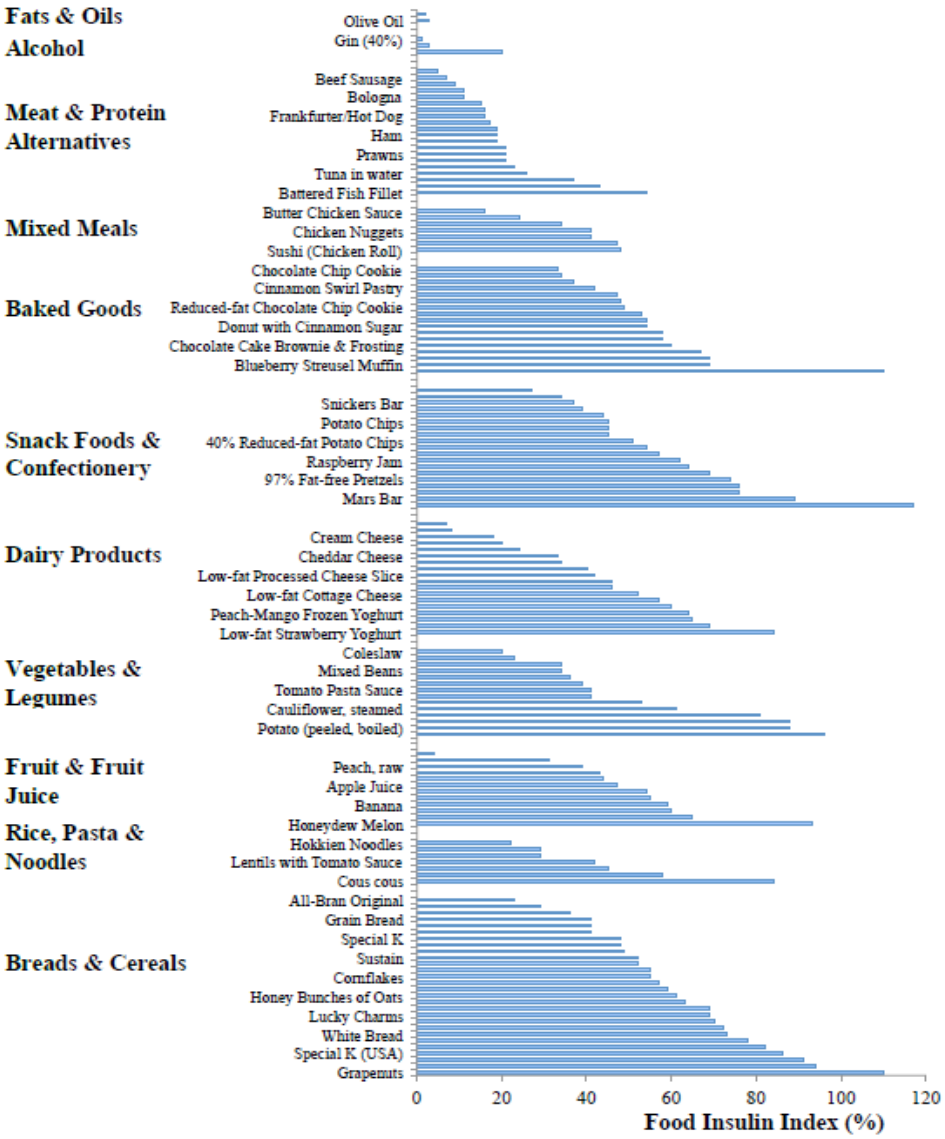


Figure 3.3: Observed insulin responses of 147 single foods, relative to an isoenergetic reference food (FII) arranged by food group.

Copied from Bell (70)

The researchers (67) completed a lot of statistical analysis to determine the strongest predictors of insulin response. From their analysis they found the best fit formula could predict 78% of the variance in insulin response:

FII = - 4.2 + (0.9 x Glucose Score) + (0.3 x Sugar (g)) + (0.5 Protein(g)) + (0.4 Fat (g))

Glucose score can only be determined by assessing the food individually using the FII protocol, therefore it cannot be applied to commercially available nutritional information. The best fit for commercially available information was using carbohydrate and protein. This below formula explained 50% of the insulin variance over two hours.

FII = 10.4 + (1.0 x Carbohydrate (g)) + (0.4 x Protein (g)

Using this FII for each of the 147 foods, the researchers developed a Food Insulin Demand (FID) score, with the below formula.

FID = FII x kJ per serving /1000

This allows an FID score to be generated for the 147 foods, accounting for portion size. A FID ratio can then be given to an individual to be used in the same way as the ICR. Obviously this somewhat restricts people to only 147 foods, but it is based on the insulin response over two hours.

WHAT DOES THE RESEARCH SAY ABOUT THE FOOD INSULIN INDEX (FII) METHOD?

The researchers assessed the FID vs. carbohydrate counting in a one meal study. They found the FID insulin dose improved time in glucose target range over 5hrs by 31%. This improvement was not at the cost of any increased risk of hypoglycaemia (67).

The big question is could this one meal study translate into real life. To answer this the researchers conducted a three month RCT of FID vs. carbohydrate counting.

The FOODII (80) study tested the FID vs. carbohydrate counting in 26 patients with T1D over three months. The team developed resources, a SMART phone APP, and other educational materials equivalent to those available for the carb counting. If you want to take a look, you can find them in part 2 of Bells Thesis (67):

> If you are going to try this method, please note you will need to relax your carb ratio by 60% to prevent hypos. So for example if your ICR is 1u:10g, you will need to change it to 1u:16g. all you need to do is apply the formula, ICR x 1.6.

After three months they found no difference in HbA1c between the FID and carb counting groups. They did find a trend towards a reduction in hypoglycaemia in favour of the FID. The FID counters reported after the first couple of weeks learning it was easy to follow, certainly not more difficult than carb counting.

The FID in principle sounds like it should have improved HbA1c, why did it not show clear benefit in glycaemic control?

- When combining FID scores of individual foods, the insulin requirement for high fat foods will very likely be underestimated. For example, the FID for individual components such as Olive oil (FII 3) and butter (FII 2) will be very low, suggesting little insulin required. This is correct if they are had on their own. But when you combine them with bread, the synergy of carbohydrate and fat increases the insulin demand more than just adding the individual components together.

- The FID score only accounts for two hours insulin demand. To measure true insulin requirement, a period of 5-8 hours is needed. Again this likely means the insulin demand for mixed meals is massively underrepresented.

- It's a new system with limited food choices that would take some time to get used to. Whereas the carb counters are used to this approach and the carbohydrate info is everywhere, for every food!

To assess if the FII (70) could be useful for people with Type 2 Diabetes, the research team brought 10 people with Type 2 diabetes into the lab on two separate days. On day one they consumed a diet of high FID, and on the send visit a diet low in FID. It is Important to note that both diets were equal in macronutrient profile and kcal. The results showed clearly the low FID diet resulted in much lower blood insulin levels, 41% lower,

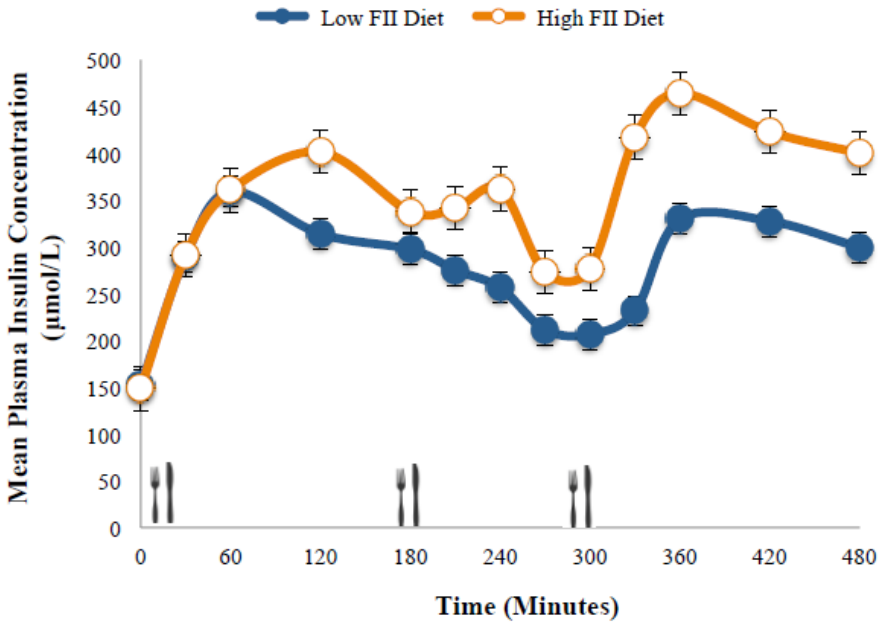


Figure 6.1: High FII vs Low FII Diet over 8 hours on the Mean Plasma Insulin Profile in Adults with Type 2 Diabetes (n=10)

Copied from (70)

As expected the blood glucose level was not different on the two occasions, essentially showing the pancreas has to work much harder to secrete enough insulin to keep up with a high FID diet. This may have some application for the insulin resistant person with Type 1 Diabetes.

SUMMARY

If you are thinking none of the current insulin dosing systems are full proof, you are correct. But at least you now understand the pro's and con's of each approach, and how different macronutrients require a different insulin response depending if they are eaten singularly or combined.

Rather than choosing an insulin dosing strategy and trying to make you diet fit around it. Why not choose the type of nutritional intake that best suits your lifestyle, food preferences, and goals in life. Then choose an insulin dosing strategy that best suits that nutritional intake.


Diabetic.
MUSCLE & FITNESS