

Diets Decoded: Low Carb and Other Dietary Strategies in Diabetes Management

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Faculty/Presenter Disclosure

- **Faculty/Presenter: Lorraine Anderson**
- **Relationships with commercial interests:** *(grants/research support, consulting fees, etc.)*
- *Employee, Animas Canada, Johnson & Johnson (no relevance to topic being discussed)*

Disclosure of Financial Support

- **Potential for conflict(s) of interest:**

I am receiving an honorarium from Langs for my time. I am employed as a clinical educator with Animas Canada, but there is no relevance to the topic being discussed.

Mitigating Potential Bias

My presentation offers my expertise as a dietitian including evidence based information and is not influenced by the sponsoring organizations or my employer.

Today's Objectives

- Discuss the evidence for the use of low carbohydrate diets in the management of diabetes.
- Describe the potential roles of alternative eating patterns, intermittent energy restriction and nutrient sequencing as dietary strategies in diabetes management.

What defines a Low Carbohydrate Diet?

- 1. Less than 100g of carbohydrate per day.
- 2. At least 40% of total energy from fat.
- 3. No more than 50g of carbohydrate per day.
- 4. There is no definition. - X

Defining a Low Carbohydrate Diet

- In general: < 45% of total daily energy
- Systematic reviews and meta-analyses in people with T2DM:
 - Carbohydrate restricted diets were 4% - 45% of total energy
 - Less than or equal to 40% energy from carbohydrate
- Limited number of short term studies in people with T1DM target was less than 75 grams per day

There is no definition



Definitions – What is “Low Carb”?

- Ketogenic - < 20 - 50 g/day
- Very low carb - 20 - 70 g/day (ie. Atkins, South Beach)
- Low Carb - In general: < 40 - 45% of total daily energy or 50 – 130 g/day (ie. Paleo, Zone)
- Moderate Carb – 130 – 170 g/day or 40 – 45% of energy
 - (ie. Mediterranean, DASH)
- High Carb – 50 – 80% of energy (ie. Asian, vegetarian/vegan)

What does this mean?

Nomenclature*	Carbohydrate g/day			
	1–5 years	6–10 years	11–16 years	Adult
High-carbohydrate diet (>55% total energy)	>170 g	>230 g	>320 g	>280 g
Average dietary intake of carbohydrate (~45% total energy)	140 g	200 g	280 g	220 g
Low-carbohydrate diet (< 26% total energy)	<80 g	<110 g	<150 g	< 130 g
Very-low-carbohydrate diet (< 10% total energy)	<30 g	<40 g	<60 g	<50 g

*Based on definitions in the literature, mean estimated energy requirements for age and activity, and current population intakes.

CPG Guidelines 2018: Nutrition Therapy

Carbohydrate

- > 45% -60% (DRIs) of total daily energy
- No less than 130 g of available carbohydrate per day (RDA)
- Focus on low glycemic, high fibre foods
- Systematic reviews and meta-analyses of controlled trials of CHO-restricted diets for people with T2DM have not shown consistent improvements in A1C compared to control
- Low-CHO diets for people with T2DM have not shown significant short or long term advantages for weight loss
- **Very low-CHO diets that have ketogenic effects may be a concern for those at risk for DKA taking insulin or SGLT2 inhibitors**
- There may be benefit of substituting fat as MUFA for carbohydrate

Question

- Carbohydrate is an essential nutrient in the human diet.
 - 1. True
 - 2. False
 - 3. We don't know - X

Question

- Carbohydrate is an essential nutrient in the human diet.
 - 1. True
 - 2. False
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“The amount of carbohydrate intake required for optimal health in humans is unknown.”

What's New?

- Reviewed 8 alternative eating patterns: Mediterranean-style, vegetarian/vegan, low-fat, very low-fat, low-carb, very low-carb, DASH and paleo.
- Look favorably upon every one of these eating styles, particularly to the extent that they all share commonalities with current mainstream healthy eating advice: **more non-starchy vegetables, fewer refined sugars and grains, fewer processed foods.**
- For people with type 2 diabetes “...not meeting glycemic targets or where reducing anti-glycemic medications is a priority, reducing overall carbohydrate intake with a low- or very low-carbohydrate eating plan is a viable approach.”

The Controversy – Fad or Fiction?

Could a low-carb diet shorten your life?

10 Health Benefits of Low-Carb and Ketogenic Diets

Ignore the low-carb cult: eating lots of fat won't really make you slim



'No One Should Be Doing Keto Diet'
Says Leading Cardiologist

7 Reasons You NEED to Eat Carbs

Low-Carbohydrate, High-Fat: A Controversial Diet And The Start Of A Food War

What is the evidence?



The potential benefits of low carbohydrate diets in diabetes management may include:

- 1. Weight loss
- 2. Lower blood pressure, improvements in HbA1C, HDL-C and TG's
- 3. Reductions in use of diabetes medications
- 4. All of the above - X

Benefits of Low-Carbohydrate Diet in Diabetes

1. Lower glucose and A1C reduction often with less medication
2. Weight Loss (short-term)
3. Lowered blood pressure
4. Increased HDL-C and lowered triglycerides
5. Reduced inflammation

Dietary carbohydrate intake and mortality: a prospective cohort study and meta-analysis

- 15 428 adults aged 45–64 years, in four US communities, who completed a dietary questionnaire at enrolment in the Atherosclerosis Risk in Communities (ARIC) study (between 1987 and 1989).
- 25 year follow up

Dietary carbohydrate intake and mortality: a prospective cohort study and meta-analysis

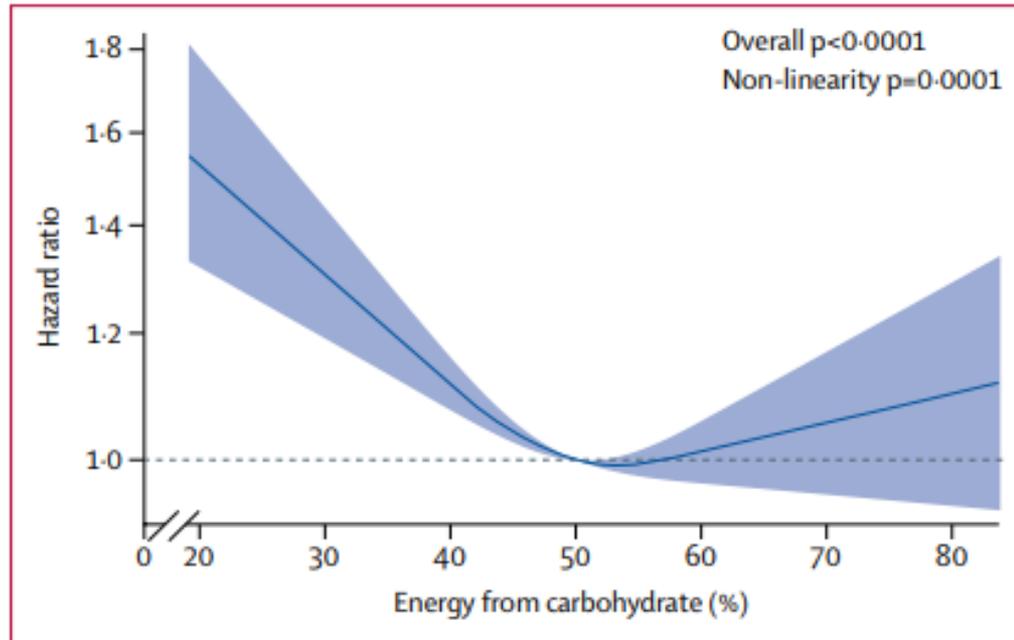


Figure 1: U-shaped association between percentage of energy from carbohydrate and all-cause mortality in the ARIC cohort

The reference level is 50% energy from carbohydrate. Results are adjusted for age, sex, race, ARIC test centre, total energy consumption, diabetes, cigarette smoking, physical activity, income level, and education. ARIC=Atherosclerosis Risk in Communities.

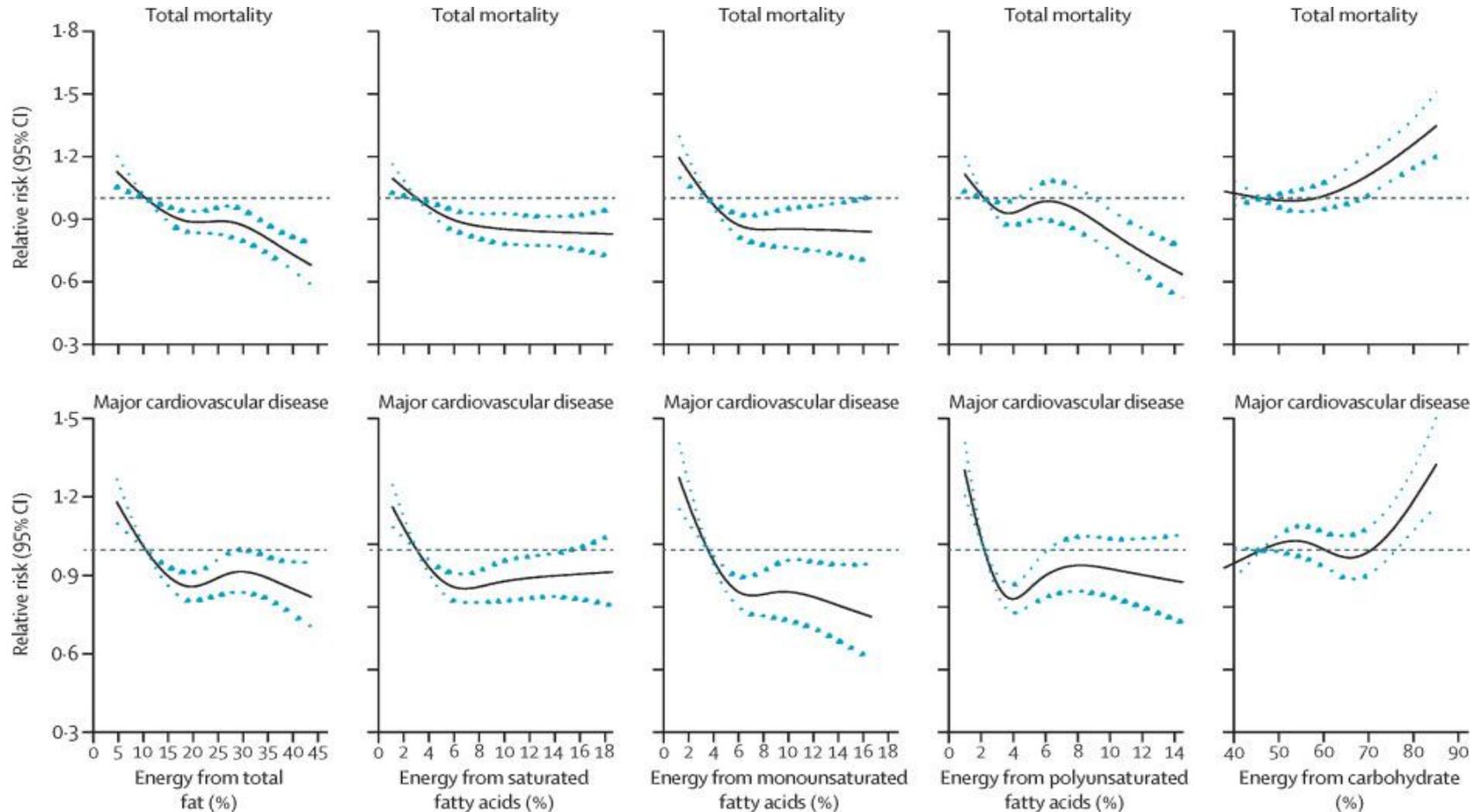
PURE Study

- **Prospective Urban Rural Epidemiology Study**
 - Epidemiological cohort study of 135,355 with no CV hx
 - 18 countries, enrolled between 2003-2013, median follow-up 7.4 years
 - Food frequency questionnaires to compare carbohydrates, proteins and type of fats
 - Primary outcomes: total mortality and major cardiovascular event

Results:

- Saturated and unsaturated fatty acids (MUFA and PUFA) were associated with lower risk of total mortality and stroke
- High carbohydrate was associated with an adverse impact on total mortality

PURE Study: Association between estimated percentage energy from nutrients and total mortality and major cardiovascular disease



Dietary Carbohydrate Restriction

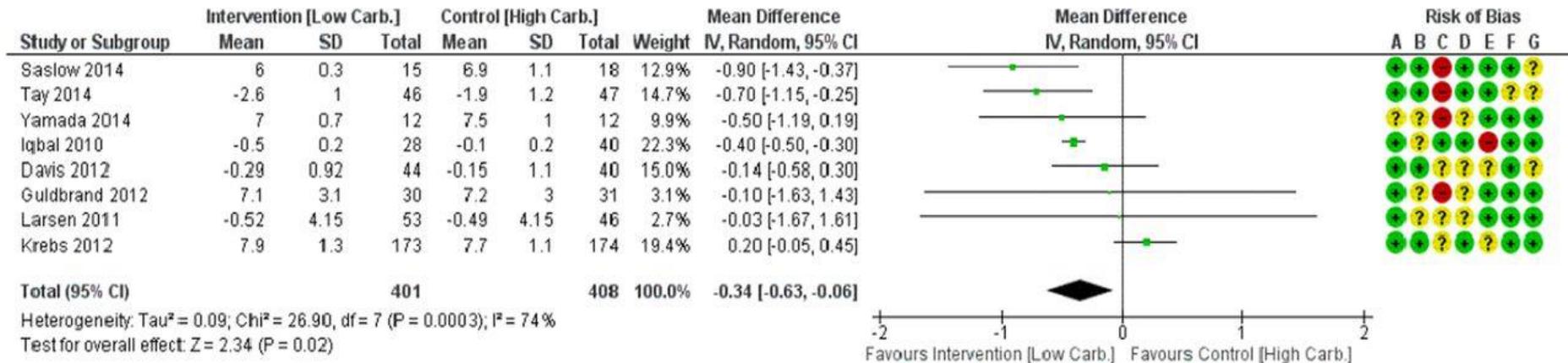
- Diabetes is a defect in the response to food, particularly to carbohydrates¹
- Feinman et al. proposed that dietary carbohydrate restriction should be the first approach in diabetes management:
 - Favourable effects such as weight loss and improvements in insulin sensitivity
- More recent meta-analyses include well-controlled studies and did not see beneficial changes on many parameters in the longer term.

T2 Diabetes and Low Carbohydrate Diet

Snorgaard et al. 2017 Systematic review and meta-analysis of dietary carbohydrate restriction in patients with type 2 diabetes

- Years: 2004-2014 using GRADE
- Duration of studies: 3mth-24 mths
- N = 1376 taken from 10 randomized trials
- Low carb (below 45% daily kcal from carb) vs. high carb diet >45%

Forest plot of change in HbA1c (%-point) after 3 or 6 months of low to moderate carbohydrate diet compared with high-carbohydrate diet in type 2 diabetes.

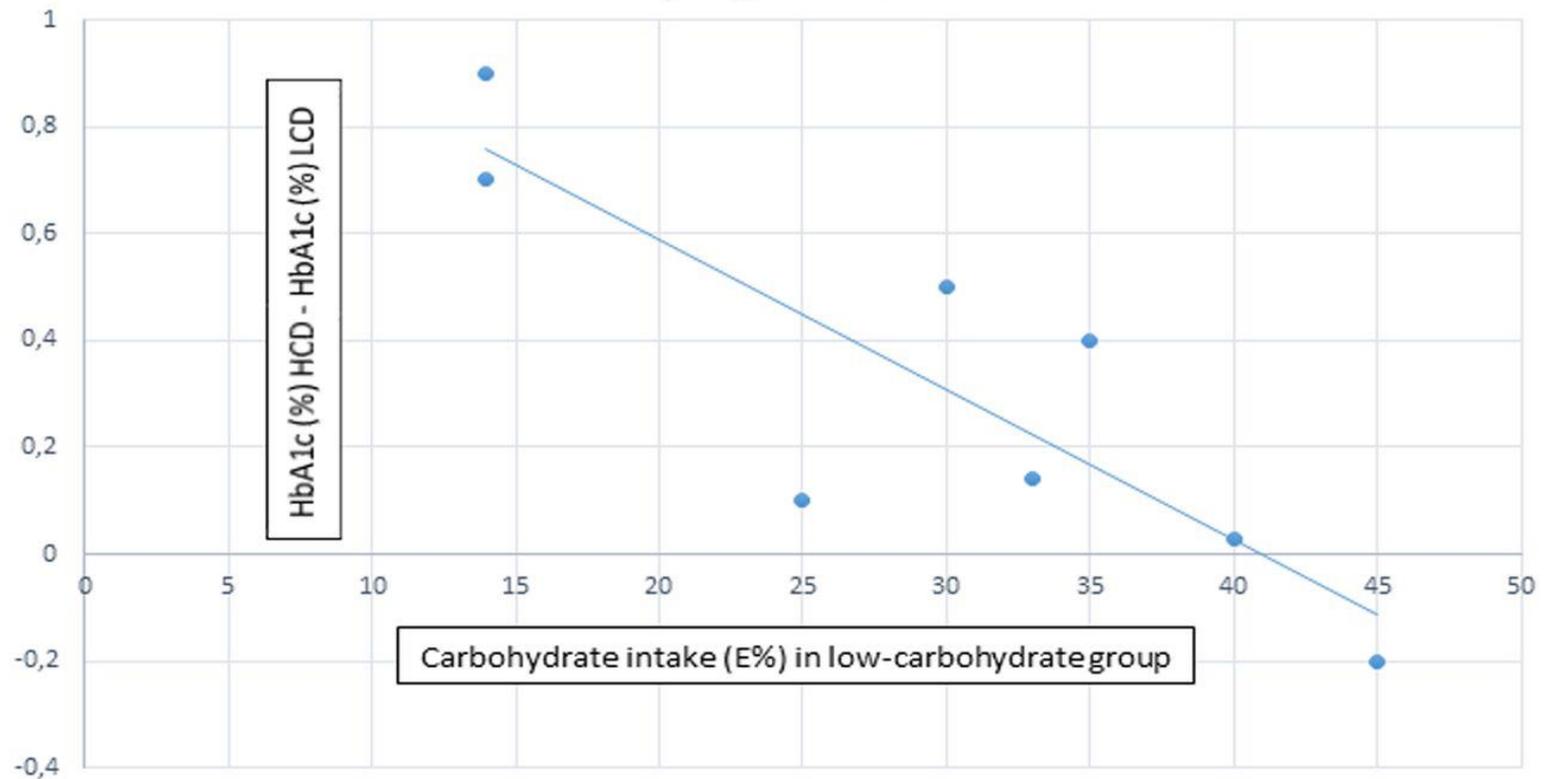


Risk of bias legend

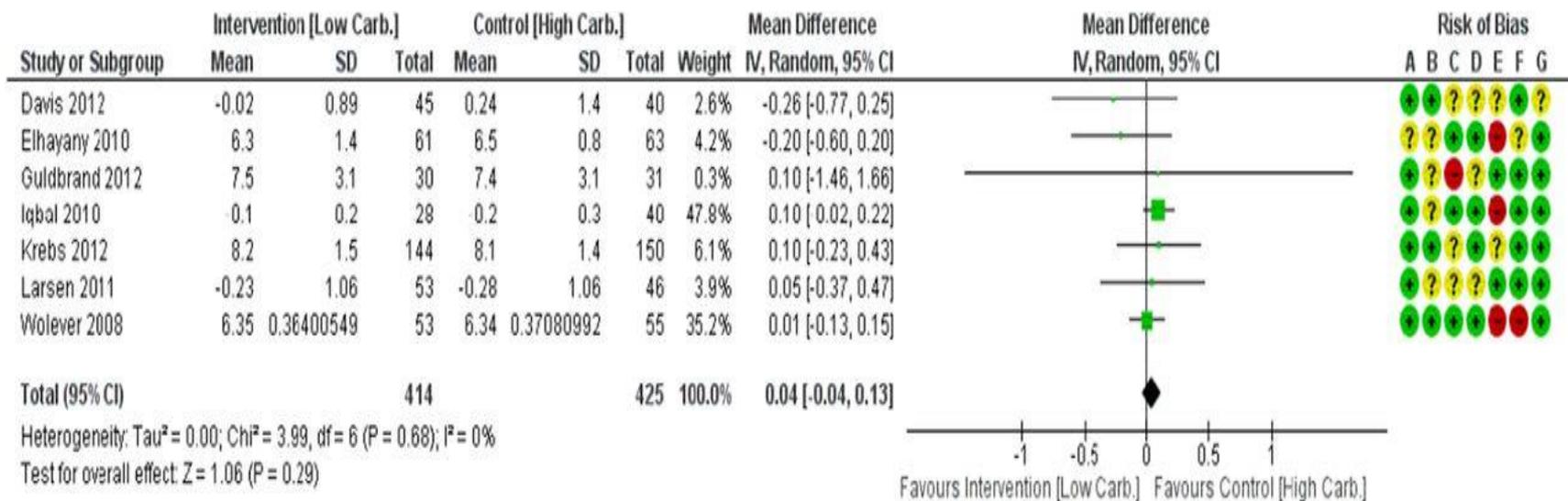
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Low/mod vs high carb 3-6 months on HbA1C – 8 RCT's

Excess reduction in HbA1c (%) versus carbohydrate intake (E%), 8 RCTs



Forest plot of change in HbA1c (%-point) after 12 months of low to moderate carbohydrate diet compared with high-carbohydrate diet in type 2 diabetes.



Risk of bias legend

- (A) Random sequence generation (selection bias)
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T2 Diabetes and Low Carbohydrate Diet

Snorgaard et al. 2017 Systematic review and meta-analysis of dietary carbohydrate restriction in patients with type 2 diabetes

Outcomes: (A1C, BMI, weight, LDL)

- Low to mod carb greater reduction in A1C < 1 year
- Great carb restriction = greater reduction in glucose
- LCD had no superiority in glucose control, wt or LDL cholesterol beyond 1 year

Evidence – Diabetes Management

- As CHO is primary nutrient affecting glycemic control in PWD, by reducing CHO we should see improvements in glycemia.
 - Is this the case?
- Recent meta-analyses on LCD's have further added to the confusion regarding their efficacy.
 - Naude et al reported that LCD's offered similar reductions in BW and glycemia as HCD's
 - Bueno et al reported that LCD's offered greater improvements in both these parameters.

Evidence – Diabetes Management

- As CHO is primary nutrient affecting glycemic control in PWD, by reducing CHO we should see improvements in glycemia.
 - Is this the case?
- **Short-term, yes.**
- **Long-term, needs further study.**

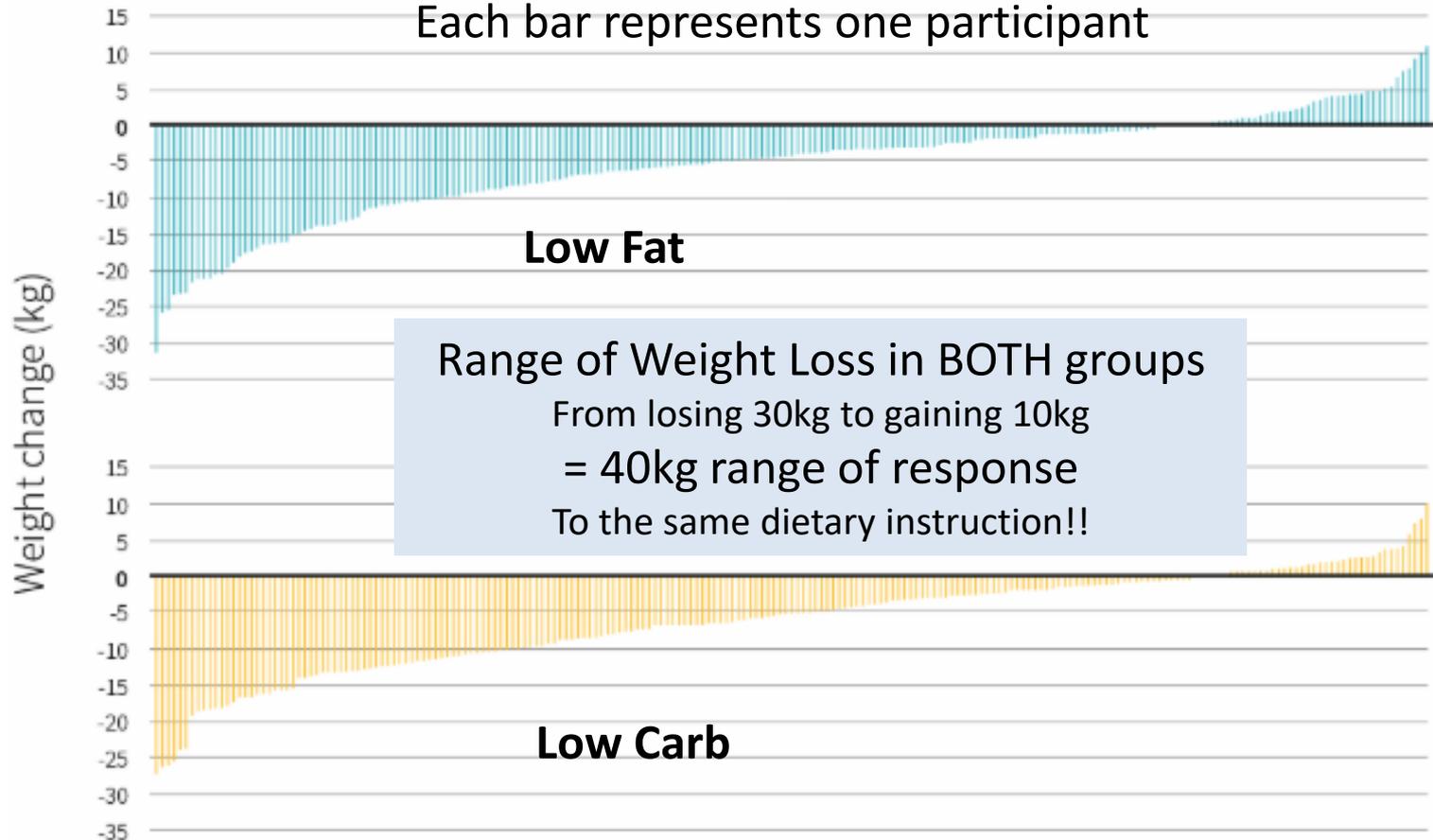
Evidence - Weight Loss

- Evidence is MIXED....why?
- The CHO-insulin model of obesity theorizes that diets high in CHO drive insulin secretion resulting in fat storage.
 - Hall states that this hypothesis (cited by many in support of LCHF diets) cannot be verified by controlled studies.
 - Mechanisms are far more complex than previously thought
- Low carb vs low fat – both diets have merit.
- Weight loss still dependent upon energy restriction

DIETFITS – Low Fat vs Low Carb

12 Month Weight Change (kg)

Each bar represents one participant



LCD and Weight Loss in T1 Diabetes

- Recent 12 week crossover comparing $< 100\text{g/d}$ vs $> 250\text{g/d}$
- LC group lost 2.0 kg while HC group gained 2.6 kg.
- Treatment satisfaction dropped significantly in **both groups**

Importance of Individualization

- Multitude of variables impacting response to dietary consideration (macronutrient composition, energy intake to achieve wt mgmt goals)
 - Baseline insulin dynamics?
 - Genotype patterns?
 - Metabolic goals (glycemia, lipid profile)
 - Physical activity
 - Food preferences/availability
 - Other factors affecting response or not to LCD
 - “Personalized Nutrition”

Which of the following foods are typically included on a low carbohydrate diet:

1



3



2



4



Future: Long-term clinical outcomes

- “What is needed is an appropriately powered and designed clinical trial demonstrating that a low carbohydrate diet improves measurable clinically relevant outcomes in diabetes.”

- Editor-in-chief of the *New England Journal of Medicine*, Jeffrey M. Drazen, M.D.

Is Low Carbohydrate Right for Everyone?

- Long term LCD wt loss inconclusive, short term - yes
- LCD diet may result in reducing hunger/increasing satiety
- Sustainability: Carbohydrates creep back into diet
- Plant based diets/vegans
- Caution in pregnancy, eating disorders, other co-morbidities
- Affordability
- Overall food plan must be individualized
- Take advantage of the expertise and support of your local diabetes education team



- yes
- no
- maybe

The Bottom Line on Carbohydrates

- We all agree that restriction of poor quality, refined carbs high in sugar, low in fibre, high in saturated fat is beneficial for health
- ADA consensus emphasizes more non-starchy vegetables, fewer refined sugars and grains, fewer processed foods.
- Low – moderate carb intake 100 – 150 g/d
 - Choose lower GI, high quality carbs



Healthy carbs

Less healthy carbs

Other Considerations

- Intermittent Fasting
- Food order

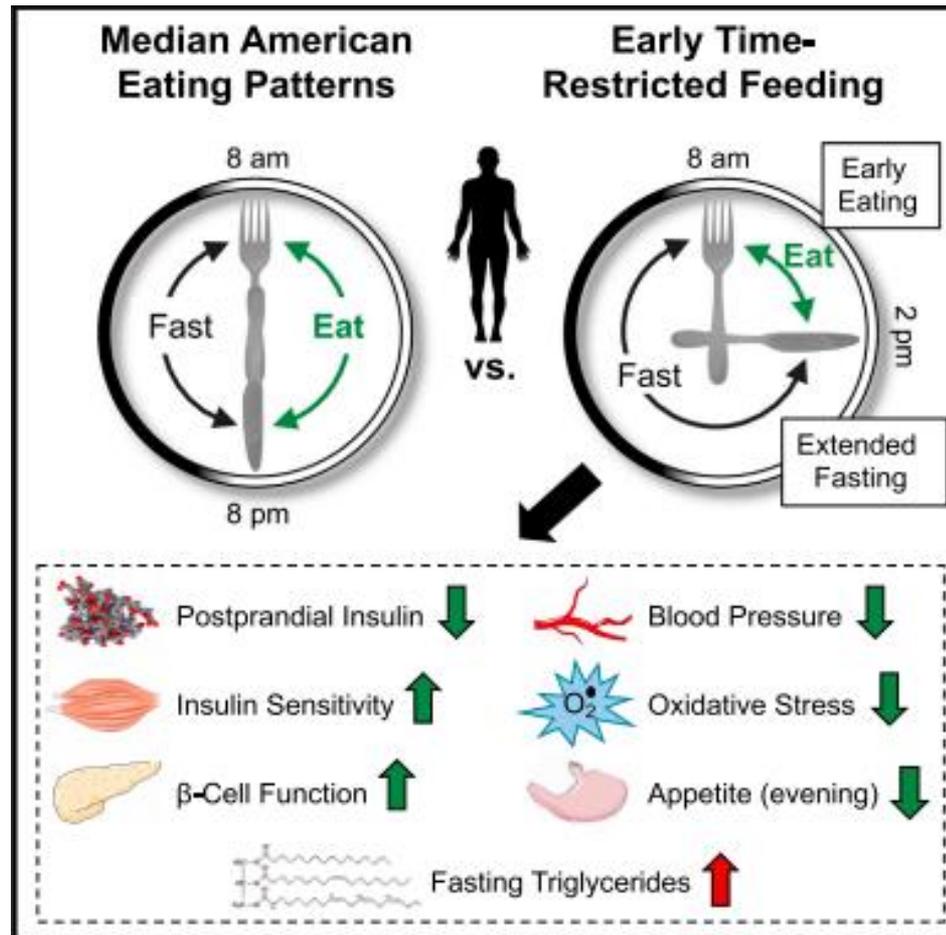
What is Intermittent Fasting?

- An “eating pattern” that cycles between periods of fasting and eating.
 - Doesn't specify WHAT you should eat just WHEN
 - Various forms (ie. 5:2, 16/8, 24h fast)
- Time Restricted Eating (TRE)
 - 16h fast : 8h ‘feeding window’
 - Circadian rhythm fasting – Early TRE

Intermittent Fasting

- Observational studies suggest:
 - Decreased hunger or food intake
 - Weight loss though non-superior
 - Reduced glucose and insulin levels and improved insulin sensitivity
 - Lowered blood pressure
 - Increased fat oxidation (i.e., fat burning)
 - No clinical trials on CVD, observational studies have shown risk reductions

Early Time Restricted Feeding (TRF) – Benefits Independent of Weight Loss



Intermittent Fasting Key Take Aways

- Safe and effective if sustainable
- Consider a simple form of intermittent fasting. Limit the hours of the day when you eat, and for best effect, make it earlier in the day (between 7 am to 3 pm, or even 10 am to 6 pm).
- Avoid snacking especially at night-time.

Meal Timing

- “Eating Breakfast Like a King” improves glycemic control in T2
 - One week feeding study in 18 adults with T2¹
- In addition, late TRF may worsen cardiometabolic health
 - Eating only between 5 – 9pm worsened glucose, insulin, blood pressure and lipid levels^{2,3}

1. Jakubowicz et al. Diabetologia. 2015. 58(5):912-9.

2. Stote et al. Am J Clin Nutr.2007.

3. Carlson et al. Metabolism. 2007 Dec;56(12):1729-34.

Medication Adjustment for IF

Class of Medication	Drugs	Risk of Hypoglycemia	Dose Adjustment	Comments
Biguanides	metformin	low	None	
Thiazolidinediones	pioglitazone, rosiglitazone	low	None	
Sulfonylureas	glyburide, glipizide, glimepiride	high	Skip that day for a 24-h fast; as utilized in one study [6], take half the dose for a partial day fast (i.e., when a meal is consumed at some point part way through the fasting day)	A caution for the half dose is that substantial education and monitoring may be required to avoid hypoglycemia [6]. Another study skipped the whole dose on any even partial fasting day, which is more conservative and cautious [8].
Meglitinides	nateglinide, repaglinide	moderate	Skip prior to a meal containing no carbohydrates	
DPP4 Inhibitors	saxagliptin, sitagliptin, alogliptin, linagliptin	low	None (or can skip on the day of fasting)	The dose can be skipped because there is no benefit to taking it and this would reduce healthcare costs to the patient.
SGLT2 Inhibitors	dapagliflozin, empagliflozin, canagliflozin, ertugliflozin	low	Can skip on the day of a 24 h fast OR should skip if concern for dehydration exists	The dose can be skipped because there is no benefit to taking it and this would reduce healthcare costs to the patient.
GLP-1 Receptor Analogues, weekly	dulaglutide, albiglutide, semaglutide, exenatide-XR	low	None	
GLP-1 Receptor Analogues, daily	liraglutide, lixisenatide	low	None	For lixisenatide only, with a 24-h fast, can skip the dose
Alpha glucosidase inhibitors	acarbose, miglitol	low	Skip if patient not eating carbohydrates that meal	
Bile Acid Sequestrants	colesevelam	low	Skip	If the primary indication is for lowering cholesterol, dose should be taken
Dopamine Agonists	bromocriptine	low	None	

Intermittent Fasting?

- Risks → Hypoglycemia if on meds, protein/vit/min malnutrition, risk of dehydration, insufficient energy (nausea, dizziness, headache, weakness, hunger)
- Caution with any chronic disease esp diabetes
- Contraindicated for pregnancy, young children, older adults, immunodeficiencies, eating disorders, dementia

Other Considerations

- Intermittent Fasting
- Food order/nutrient sequencing

Food Order has a Significant Impact on PPG and insulin levels in T2 Diabetes

- 11 subjects, T2, metformin only
- After 12h fast: food order was carbohydrate (bread and orange juice) followed 15 minutes later by protein (skinless chicken breast) and vegetables (lettuce/tomato salad w low fat dressing and steamed broccoli with butter)
 - Carb – 68g
 - Protein – 55g
 - Fat – 16g

Shukla, AP et al. Diabetes Care
2015.;38(7)e98-e99.

Food Order has a Significant Impact on PPG and insulin levels in T2 Diabetes

- 1 week later, same meal, reverse order
- Postmeal BG response was significantly reduced when the protein/vegetables were consumed first (-28.6%, -36.7% and -16.8% at 30, 60 and 120 min)
- Another factor to consider...

Food Sequence in T2 under Free-living Conditions

- After 8 weeks, similar reduction in BW (1.9, 2.0 kg)
- Experimental diet: ↓HbA1C (0.3%),
↓FBG (-1.0mmol/L)
↓ PPG excursions
- Conclusion: Manipulating the sequence of nutrient ingestion might reveal a rapid, feasible, economic and safe strategy for optimizing glucose control in T2D.

Thank you! Questions?

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