A Novel Medical Nutrition Therapy for the Management of Glucose Control

Clinical Results from a 16 week Intervention Study Using a Uniquely Formulated Medical Food

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Food Addiction by Simple Carbohydrates has led to Glucose Toxicity

World Health Organization guidelines recommend only 5% of total energy intake for adults of normal Body Mass Index (BMI)

- Not new to us but bigger than any of us thought
- Health consequences worse than ever imagined

Source: World Health Organization Draft Guideline: Sugars intake for adults and children

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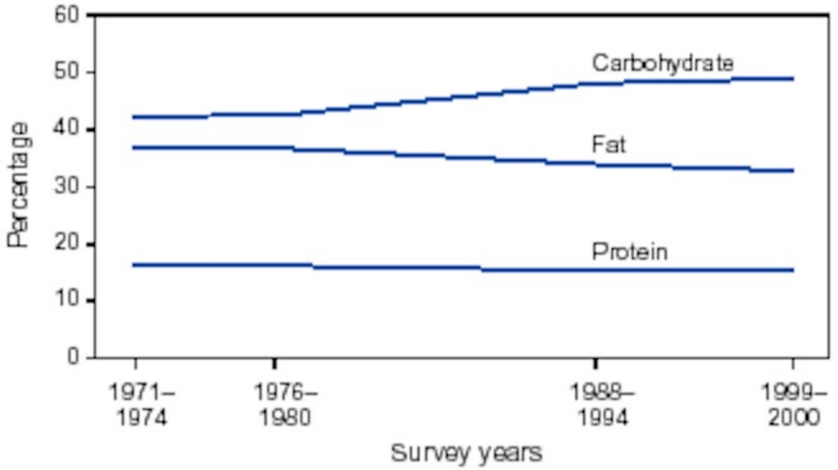
We see what you see…

- Nearly 60% of the population has a genetic predisposition for the development of diabetes and/or obesity.
- The predisposition is accelerated with poor diet and leads to chronic illnesses.
- 2 out 3 patients are overweight or obese.
- 1 out 3 adult patients have pre diabetes.
- 1 out 10 adult patients will have diabetes.

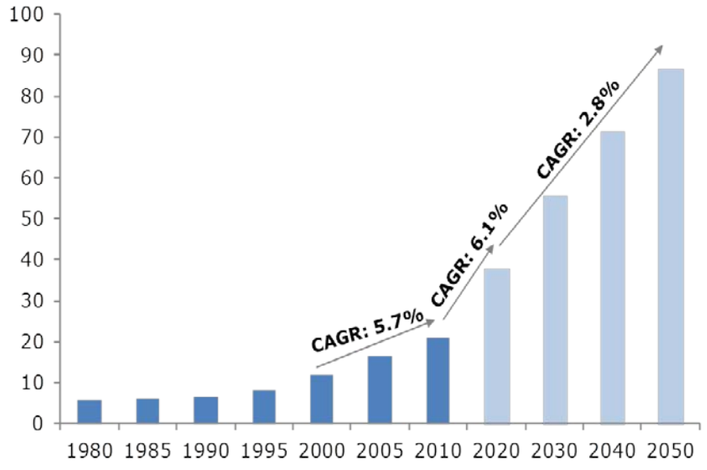
An Overlooked Trend Correlated to Disease

FIGURE 1. Percentage of kilocalories from macronutrient intake among men aged 20–74 years*, by survey years — National Health and Nutrition Examination Surveys (NHANES), United States, 1971–2000



*Age adjusted by direct standardization to the 2000 U.S. Census population by using age groups 20–39, 40–59, and 60–74 years.

Historical and Projected US Cases of Type II Diabetes
For the Years Ended and Ending December 31, 1980 - 2050P
 # in millions



Source: CDC; *Population Health Metrics*, Projection of the year 2050 burden of diabetes in the US population: dynamic modeling of incidence, mortality, and prediabetes prevalance

Source: CDC Population Health Metric Projection of the 2050 Burden of diabetes in the US population dynamic modeling of incidence, mortality and prediabetes prevalence

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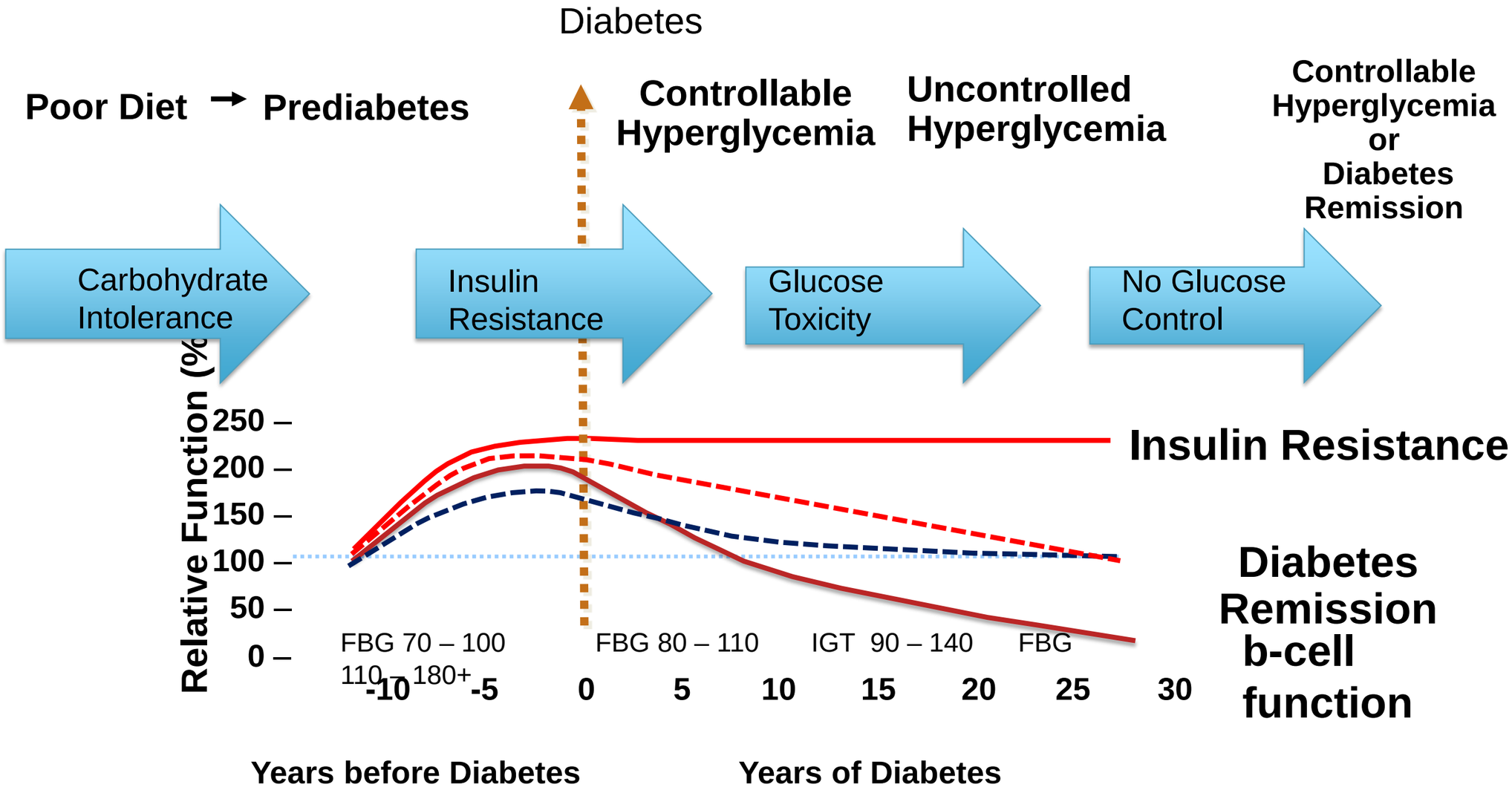
Progression Of Carbohydrate Intolerance Leads To Cascade Of Diabetes And Co-morbidities



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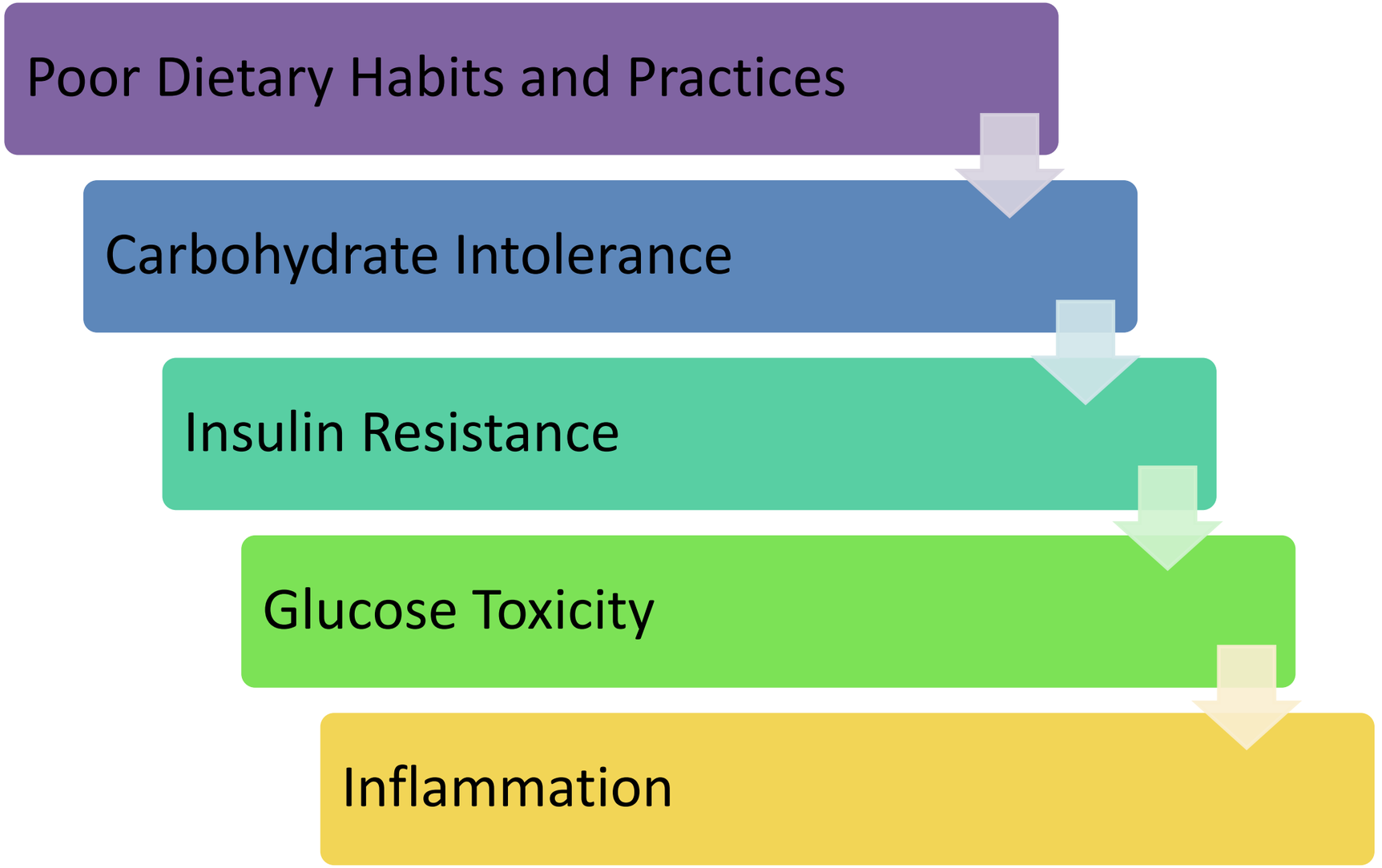
Managing a Sequence of Events is Key



This sequence of events culminates in Diabetes and associated comorbid health conditions

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So what if we caught it upstream?

Genetics

Insulin resistance

Acquired:
- Obesity
- Sedentary lifes
- Aging

Hyperinsulinemia

Compensated insulin resistance
Normal glucose tolerance

Impaired glucose tolerance

Genetics

β-cell "failure"

Acquired:
- Glucotoxicity
- ↑ FFA levels
- Other

Type 2 diabetes
- ↑ Insulin resistance
- ↑ Hepatic glucose outp
- ↓ Insulin secretion

FFA = free fatty acid.

Source: Kruszynska Y, Olefsky JM. *J Invest Med.* 1996;44:413-428.

Medical Nutrition Therapy with a Novel Medical Food Affords Three Levels of Prevention

Prevention	Application
Primary	To prevent diabetes in at-risk populations
Secondary	To improve glycemic control and prevent or delay worsening of early diabetes
Tertiary	To prevent or delay complications and death in long-standing diabetes

Position Paper of the ADA. *Diabetes Care.* 2002;25:148 –198.

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Carbohydrate Intolerance starts early and can be defined by patient segmentations

At Risk

69% of Americans

BMI: ≥25 kg/m²

- Over 45
- Central Obesity
- Family History
- Inactivity
- High BP
- Standard American Diet

Pre Diabetes

79 million Americans

- **Fasting Plasma glucose:** ≥100 -125 mg/dL
- **Oral Glucose Tolerance Test:** ≥140-199 mg/dl
- **A1C:** ≥5.5 – 6.4%

Diabetes Type 2

26 million Americans

- **Fasting Plasma glucose:** ≥126 mg/dL
- **Oral Glucose Tolerance Test:** ≥200 mg/dl
- **A1C:** ≥ 6.5%

Source: Diabetes Care January 2014 vol. 37 no. Supplement 1 S14-S80
Cowie CC, Rust KF, Ford ES, et al.. *Diabetes Care*. 2011; 32(2): 287-294.

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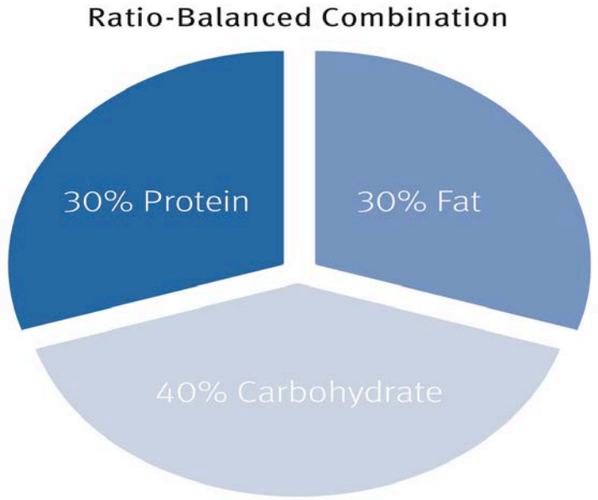
Ratio Balanced Macro Nutrient Effect on Glucose

Ratio Balanced Nutrients

% Calorie Distribution	Clinical Glucose Metabolism Center Guidelines
Carbohydrates	40
Protein	30
Fat	30

A Novel Nutrition Approach delivers a 40:30:30 [3] balanced ratio of macronutrients, consistent with guidelines of Joslin Center & Brandeis University[1]



1. Joslin Diabetes Center and Brandeis University
2. Data taken from competitive product nutritional labels
3. Average % calories. Actuals may vary.

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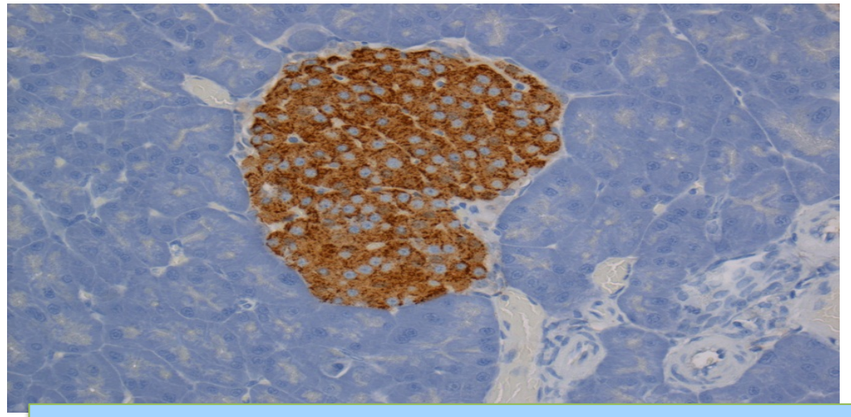
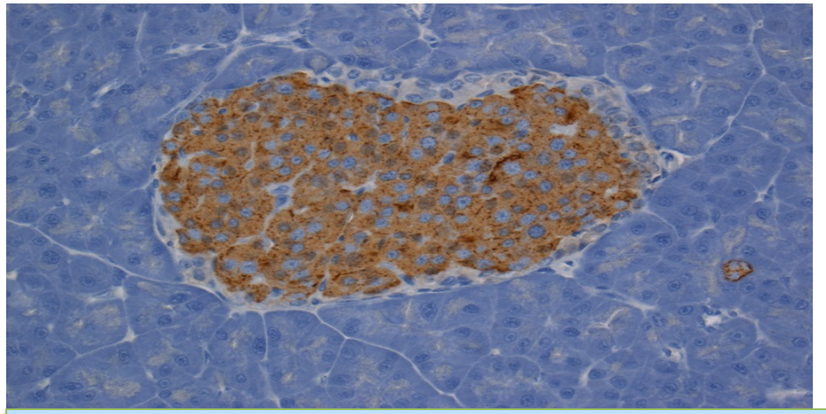
Macro-Nutrient Ratio

Nutrient Ratios Help Preserve Healthy Beta Cell Function in animal model

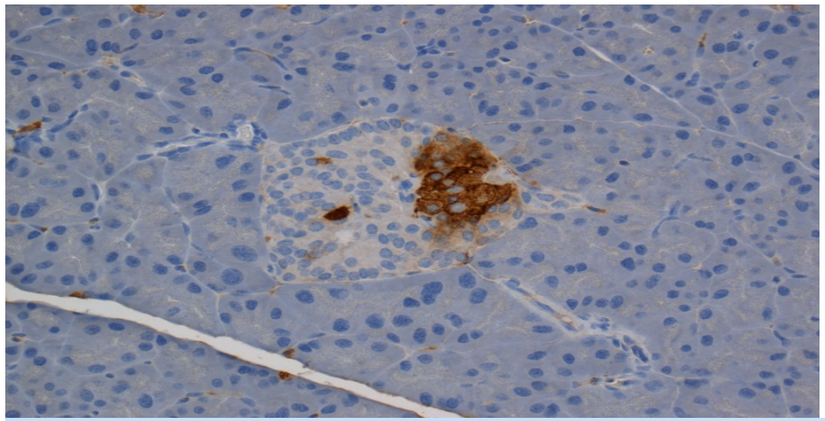


Normal Healthy Pancreatic Cells



Four weeks of balanced macronutrients

* beta cells fail



High Carb/No Balanced Macronutrients

Animal pancreatic islets
stained for insulin

Source: Hayes et al., unpublished 2014
* Research done in Nile River Rats

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Macro-Nutrient Ratio

Nutrient Ratios Help Preserve Healthy Liver Size in animal model

Source: Hayes et al., unpublished 2014
* Research done in Nile River Rats

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Clinical Studies

Clinical Research Findings Supporting Advanced Clinical Outcomes

- Two clinical studies conducted with The Joslin Diabetes Center in Boston, MA over 2015 and 2016 in selected diabetic patients,
- Study 1 included a randomized control trial of an acute Oral Glucose Tolerance Test (OGTT) following consumption of a single serving of the medical food, novel medical food. This included measurements of post-prandial glucose, insulin and the hormone GLP1. Comparison to a control diet of an ‘American Breakfast’ or another medical food, ‘Commercial Product’ was carried out in diabetic patients.
- Study 2 included a randomized control trial of16 week intervention comparing outcomes of three treatments including American Diabetes Association Recommendations, use of specially formulated medical food, novel medical food and use of medical food along with formal nutritional counseling
- The results show a superior glucose control and balanced response with a significant improvement in HbA1c over 16 weeks of use as part of a medical nutrition therapy program

Study 1: Objective

- The 1st aim of this study is to compare the post prandial glycemic response to a single serving of 2 diabetes-specific formulas, versus oatmeal breakfast of equal calories in patients with type 2 diabetes.

Hamdy O. et al. Specific Nutrition Product Focus on Glucose Metabolism. Abstract and poster presented at ADA in Boston, MA

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Study 1: Methods

- This is an open-label 3 way randomized comparative study conducted at The Joslin Diabetes Center.
- Subjects enrolled in this study came for three visits on three separate days. All 3 visits had to be completed in a 3 week period with at least 2 days between each visit.
- On each visit, subjects were fasting overnight and then served a breakfast with a caloric value of 200 kilocalories.
- The breakfast consumed was either the Metagenics Ultra-Glucose Control formula, another formula or regular oatmeal.
- The order by which subjects received the breakfast was randomized.

Hamdy O. et al. Specific Nutrition Product Focus on Glucose Metabolism. Abstract and poster presented at ADA in Boston, MA

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Study 1: Subjects

- 25 subjects were recruited for the study.
- 22 subjects completed the 3 visits of the study.
- 2 subjects dropped out after completing 1 visit.
- 1 subject's participation was terminated due to failure to attend the first visit.
- No adverse events were reported.

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Study 1:Demographics

Variables	N (%)
Male	12 (54.6%)
Female	10 (45.5%)
Diabetes	N (%)
Type II	22 (100%)
	Mean ± SD
Age (yrs)	62.3 ± 6.8
Height (cm)	171.1 ± 8.9
Weight (kg)	97.4 ± 21.3
BMI (kg/m^2)	33.2 ± 5.9
Diabetes Duration (yrs)	9.5 ± 9.8
A1C (%)	6.8 ± 6.0

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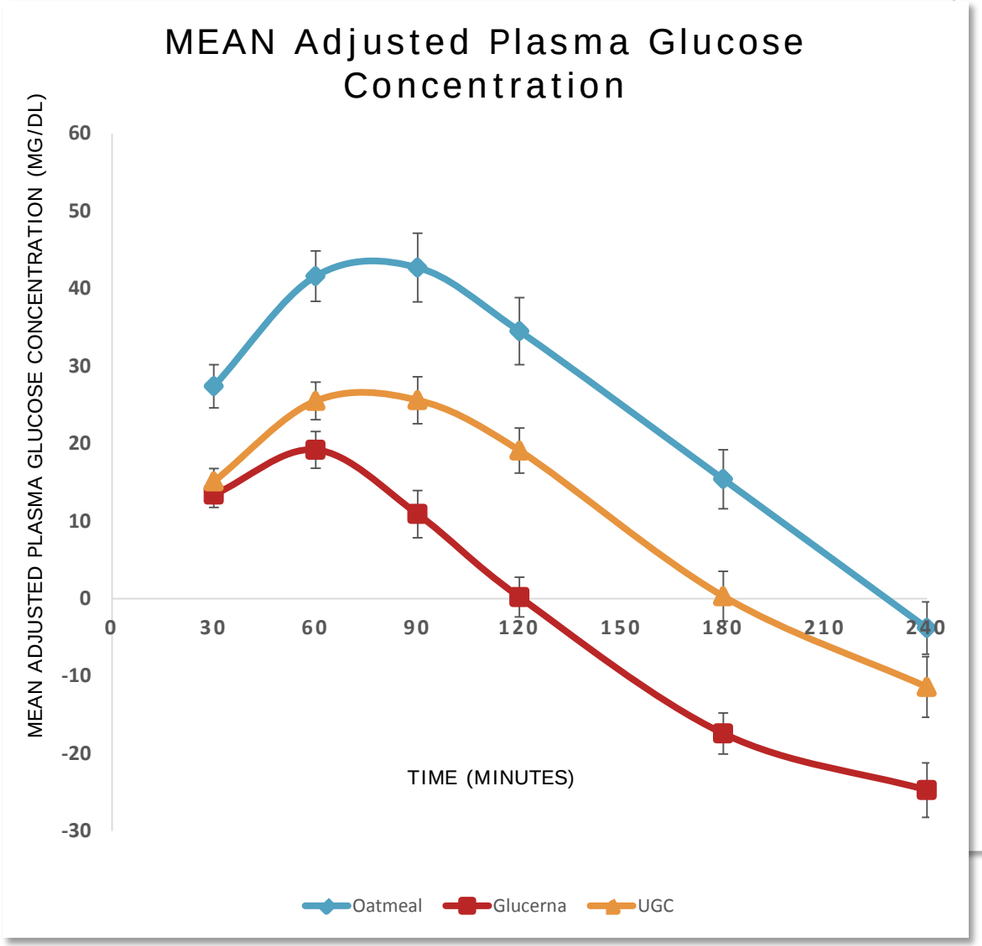
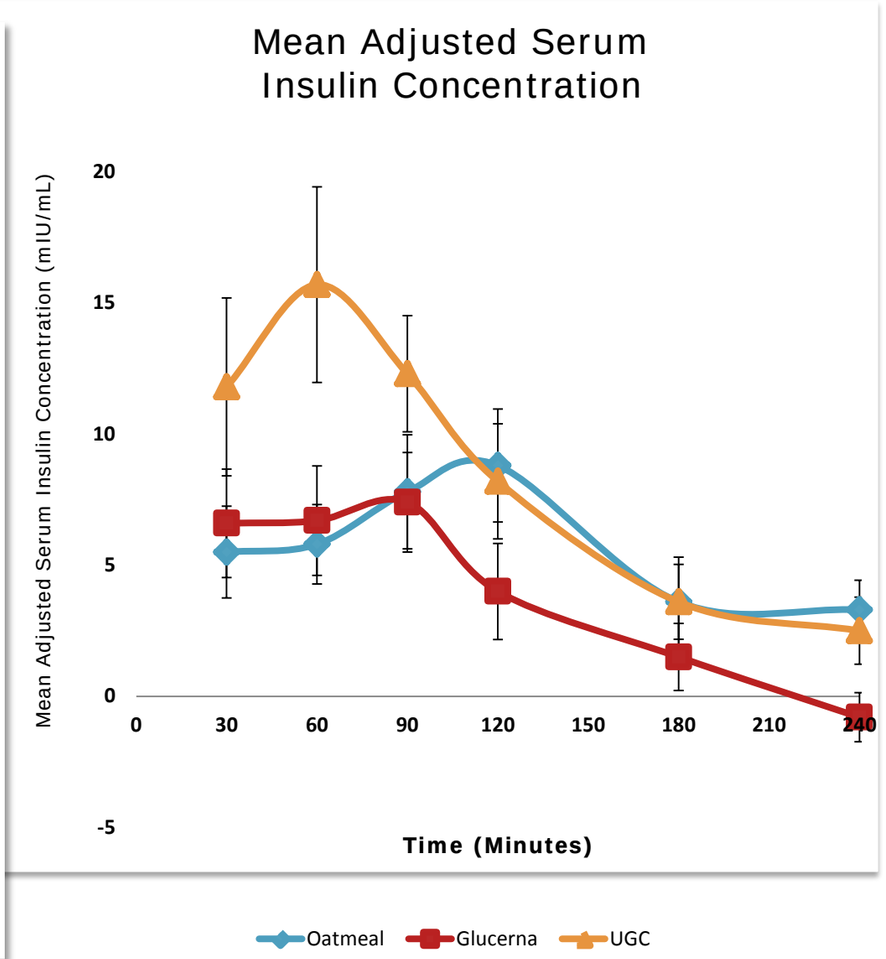
Study 1:Study Visits

- No diabetes medications were taken by the subjects on the morning of the study and DPP-IV inhibitors were stopped 2 days prior to each visit to ensure that no medications are going to alter our results.
- Blood samples were withdrawn at 7 time points (Baseline-30-60-90-120-180-240 minutes after start of meal).
- The baseline measurement was drawn immediately before the start of the meal.
- Subjects were given 3-5 minutes to consume the meal.

Sustained & Balanced Glucose Control Delivering Superior Results





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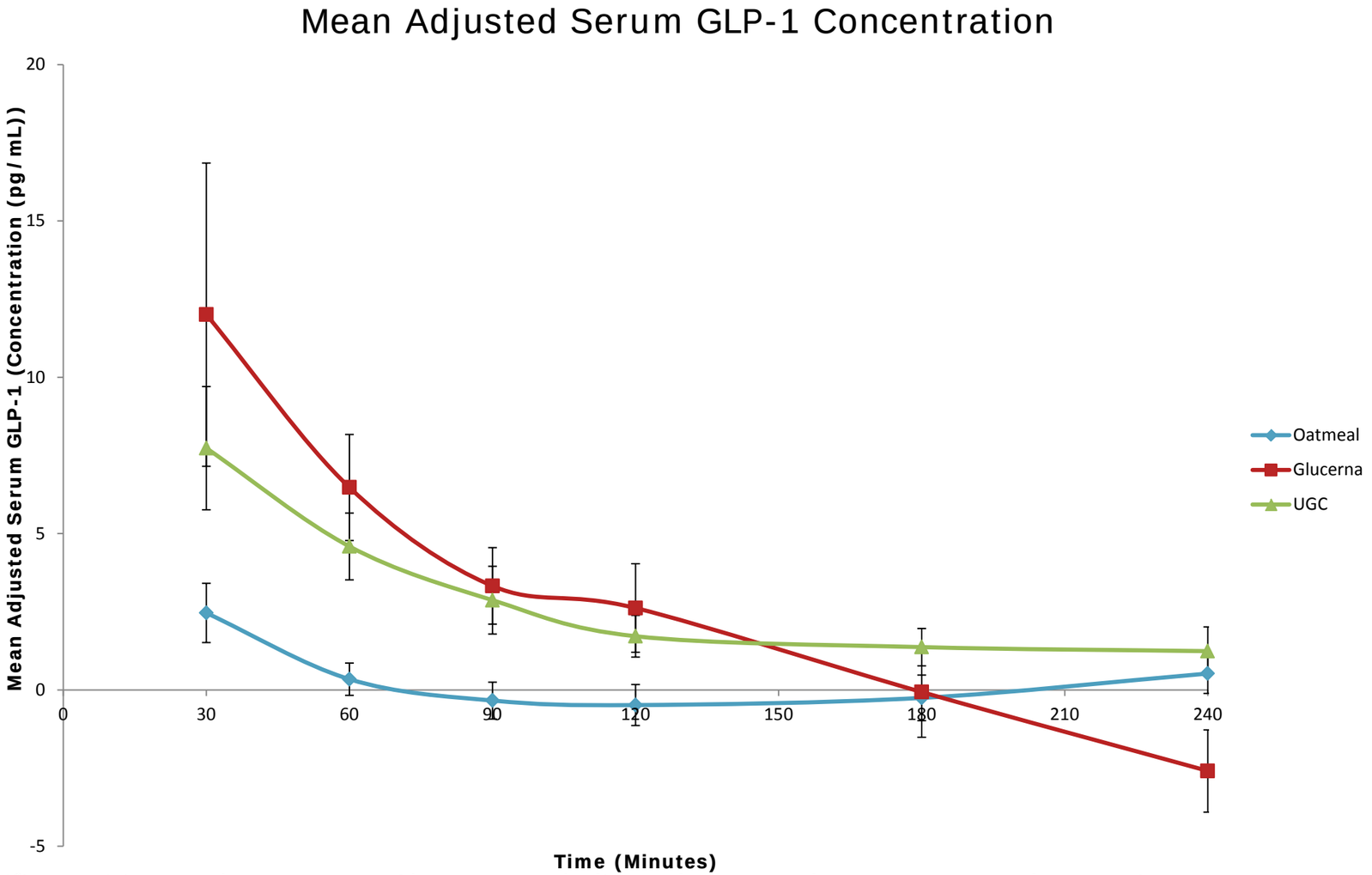
Glucagon Like Peptide -1



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Novel Mechanism for Glucose Control

- Two mechanisms to stimulate insulin for greater glucose control – GLP1 and DIAAS protein stimulation
- Superior sustained and balanced glucose response
- Early phase insulin response patterns with elevated insulin levels to control glucose
- Similar to response and effect of leading Rx category of drug management (DPP-IV inhibitors)

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Study 1: Summary Results

1. novel medical food provides a unique management approach to the control of glucose response

2. Stimulation of both GLP1 and insulin stimulation results in a more sustained and balanced glucose response curve
3. Magnitude of response not different than Rx use of DPP IV Inhibitors

4. Avoidance of hypoglycemic response and spiking of response helps manage the risk for development of long term complications

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16 week Intervention Trial

Introducing the 16 week outcome study–
The new ‘HMS-5’ Program Results

Superior to Diet Alone
Significant Improvement in HbA1c
Significant Weight Loss
Significant Healthcare Cost Savings

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16 week Intervention: Subject Demographics

Baseline Characteristics

	Group A	Group B	Group C
Age (years)	57 ± 10	61 ± 10	61 ± 9
Sex (M%)	36	44	47
Diabetes Duration (years)	11 ± 10	11 ± 6	11 ± 6
Number of DM Medications	1.6 ± 0.8	1.9 ± 0.9	2.0 ± 1.1
BMI (kg/m^2)	35.4 ± 7.1	36.4 ± 9.4	33.9 ± 6.1
Body weight (kg)	101.2 ± 20.7	105.4 ± 25.3	97.5 ± 16.3
A1C (%)	8.15 ± 1.02	8.16 ± 1.20	7.99 ± 0.90
Fasting Glucose (mg/dL)	182 ± 69	176 ± 59	157 ± 33
Total cholesterol (mg/dL)	170 ± 42	172 ± 49	158 ± 47
HDL-cholesterol (mg/dL)	46 ± 11	44 ± 9	47 ± 13
LDL-cholesterol (mg/dL)	94 ± 37	95 ± 41	75 ± 36
Triglycerides (mg/dL)	152.4 ± 66.9	166.8 ± 97.5	158.3 ± 88.3

There were no significant differences between groups at baseline

Hamdy O. et al. Randomized Clinical Study Shows Superiority of Structured Medical Nutrition Therapy that includes novel medical food® in Reducing A1C and Body Weight in Overweight and Obese Patients with Type 2 Diabetes. Presented as an abstract and a poster at ADA in New Orleans, LA.

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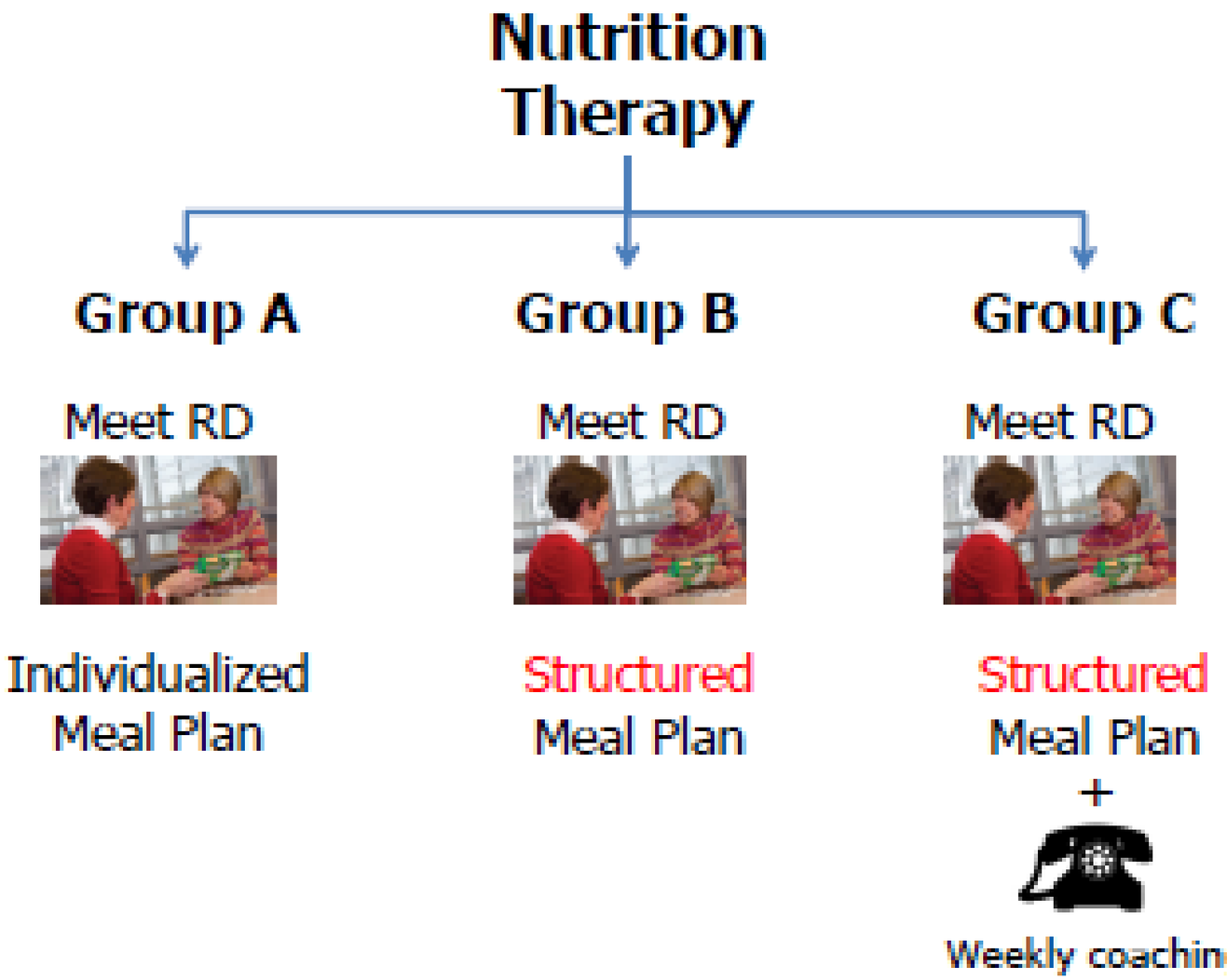
16 week Intervention Trial :Design



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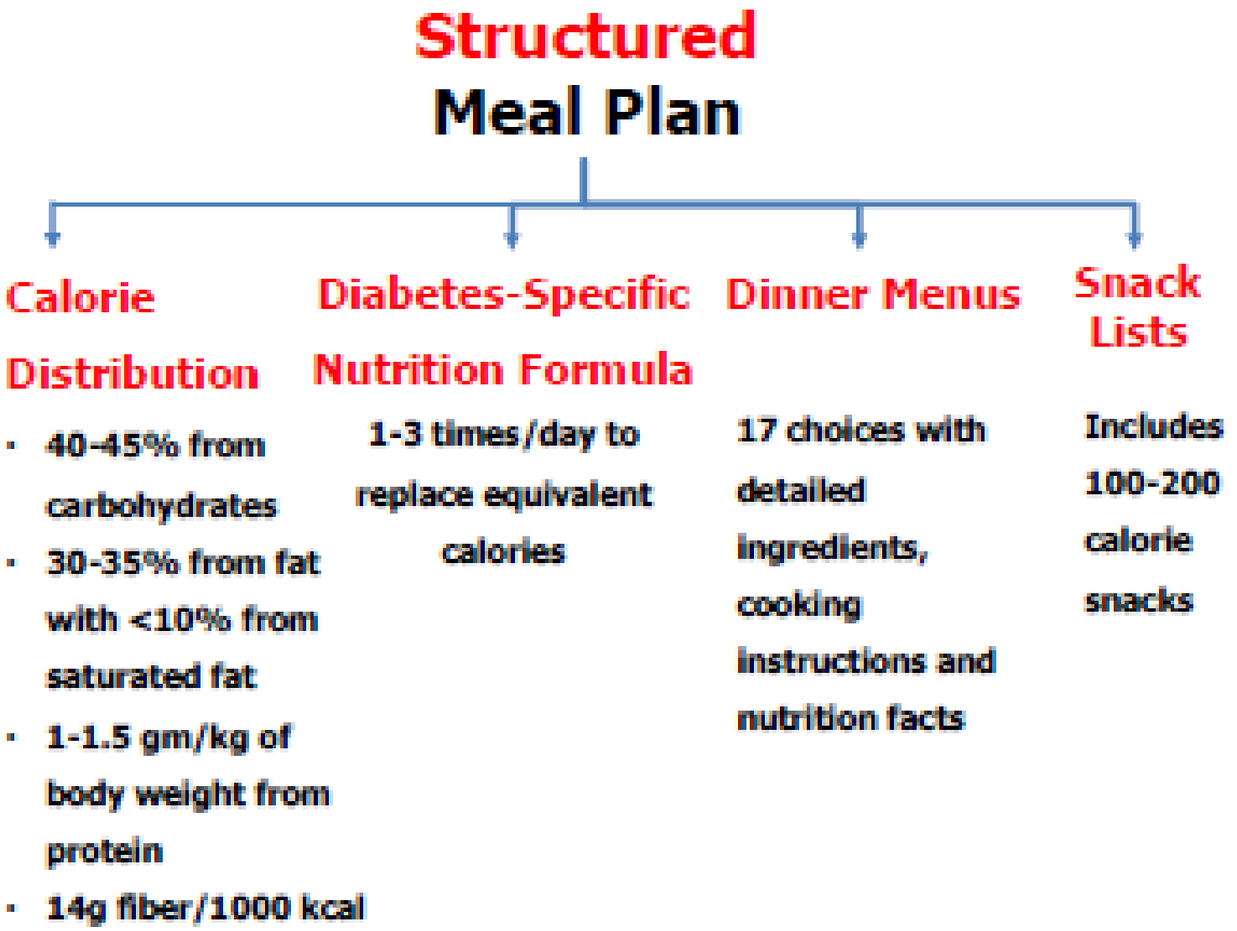
16 week Intervention Trial: Structured Meal Plan



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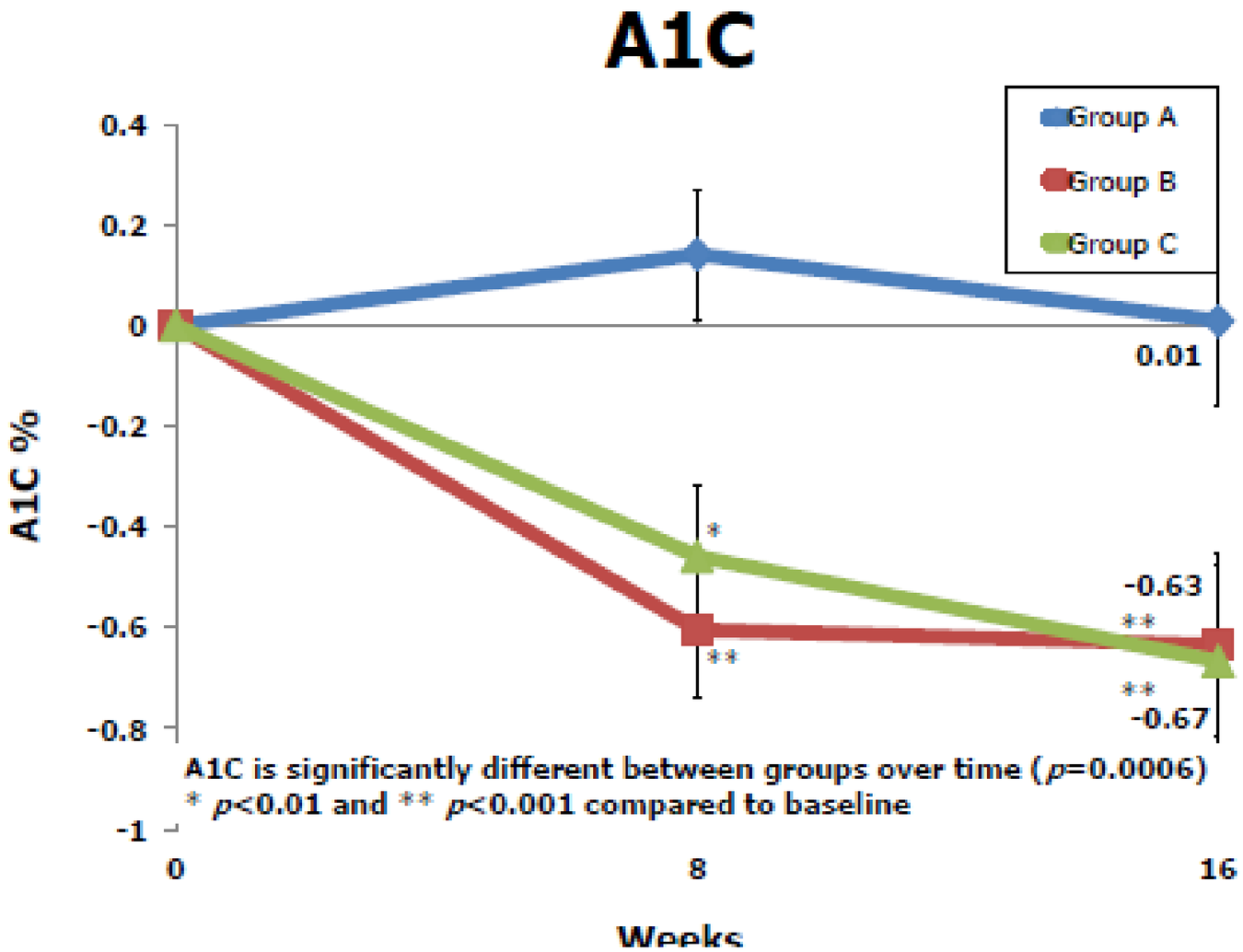
16 week Intervention Trial: Hemoglobin A1c – Significant Improvement and Better than Diet Alone



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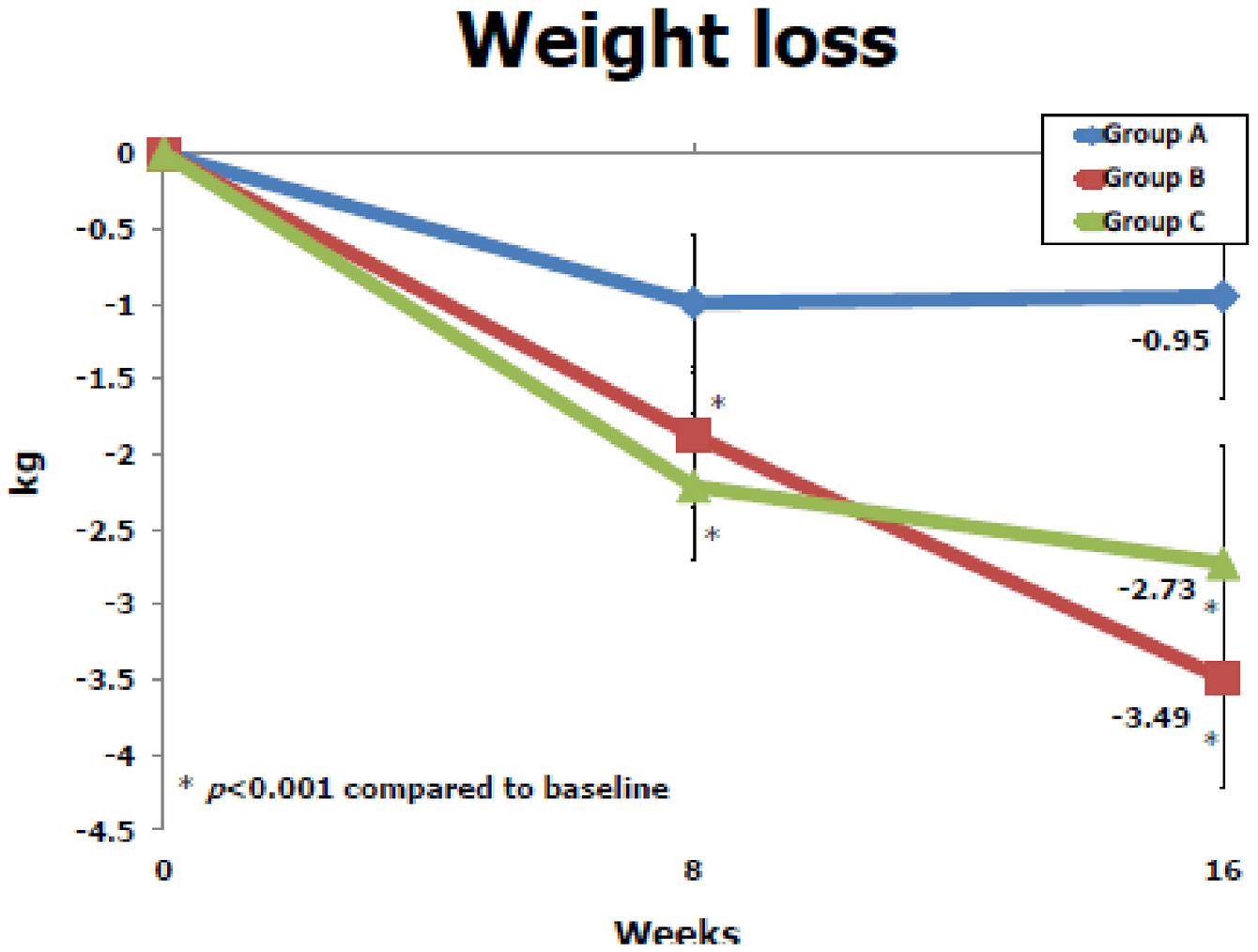
16 week Intervention Trial: Weight Loss Did not Differ Between Groups



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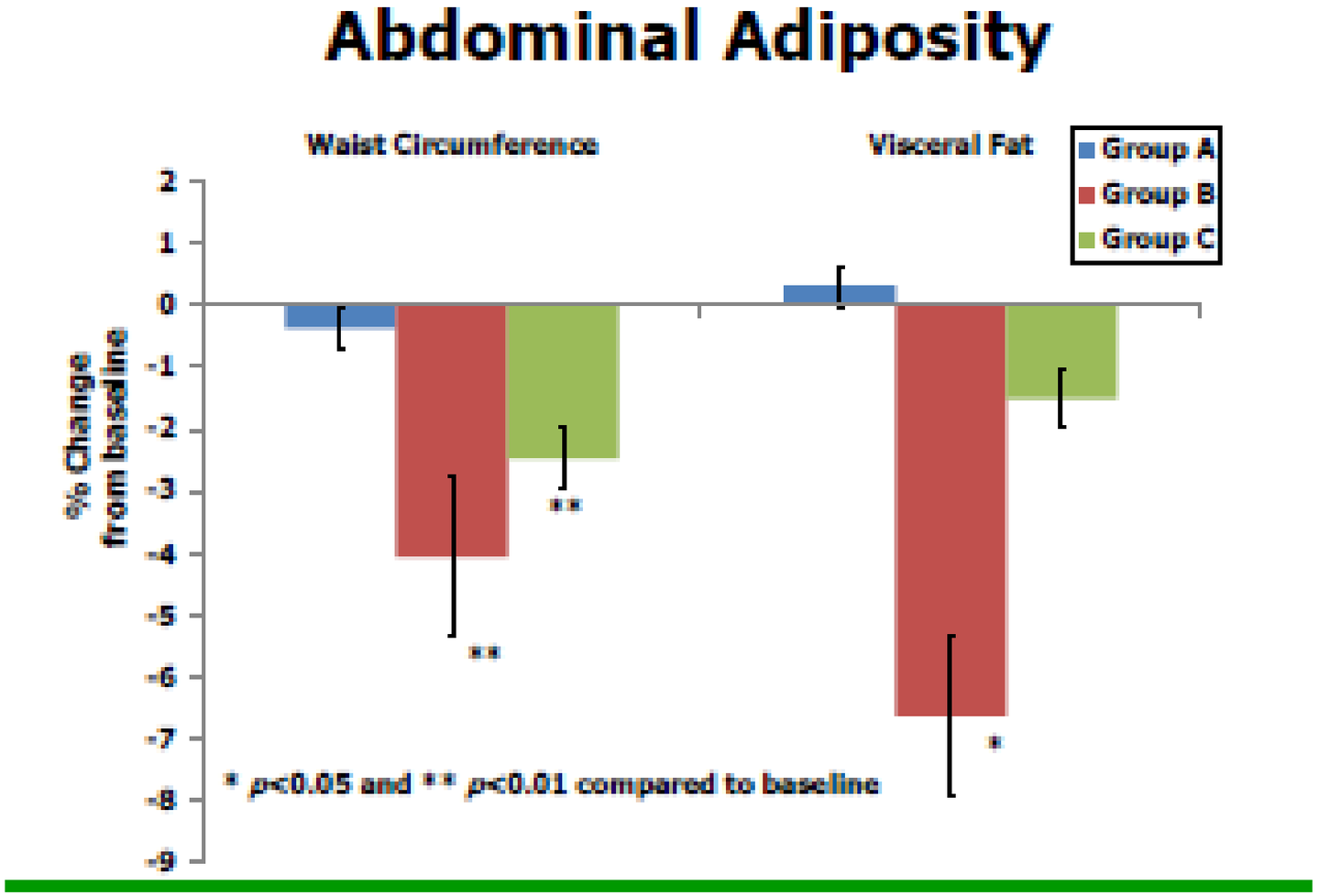
16 Weeks Intervention Trial : Showed Significant Improvement and Shift in Fat Stores



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16 Weeks Intervention Trial: Summary Results

1. 16 weeks of intervention with a specialty formulated medical food resulted in significant improvement in HbA1c

2. These results demonstrate that an organized structured medical nutrition therapy program with a specific medical food formula provides improved outcomes vs food or the ADA recommended approach to glucose management,

3. The magnitude of improvement with this medical food is within the observed range seen with selected prescription medications,

4. The lack of difference across groups in weight suggest that the medical food delivers specific metabolic improvements beyond weight management

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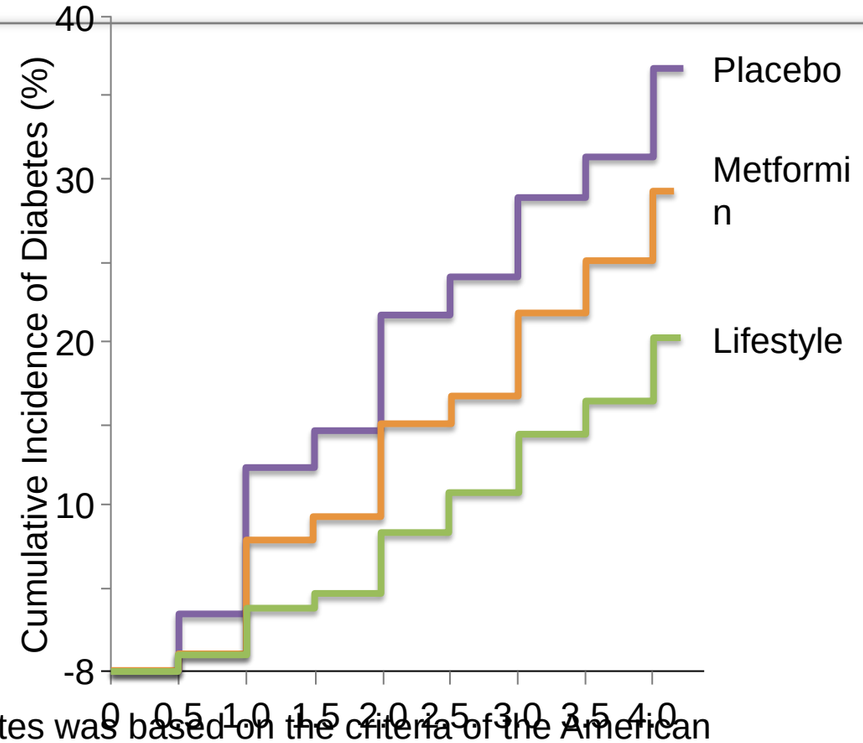
Lifestyle medicine programs that include use of medical foods like novel medical food have been shown to decrease the onset of diabetes

Subjects
N=3234

Placebo
n=1082
Metformin
n=1073
Lifestyle
n=1079



The diagnosis of diabetes was based on the criteria of the American Diabetes Association.
The incidence of diabetes differed significantly among the three groups (P<0.01 for each comparison).

Knowler WC, et al. Diabetes Prevention Program Research Group. *N Engl J Med*. 2002;346:393-403.

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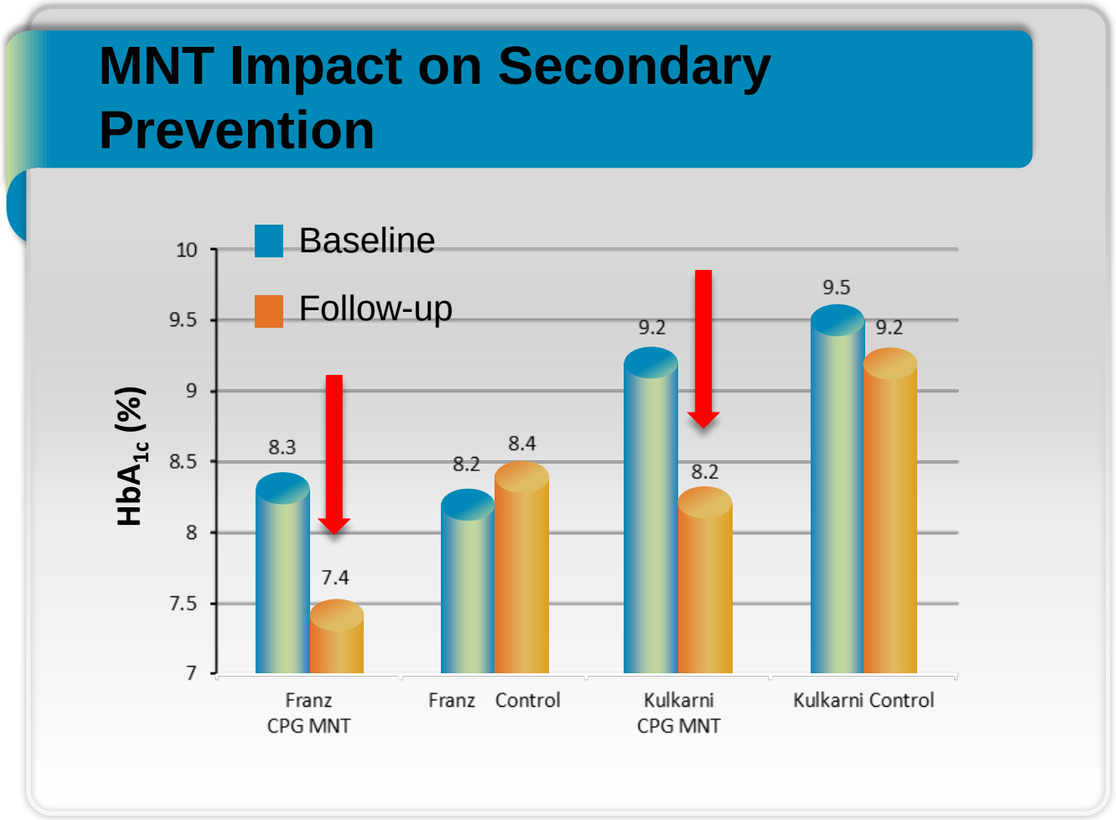
Medical Nutrition Therapy Has Been Shown to Reduce A1C by 1% to 2% in Patients With T2D



HbA1c, glycated hemoglobin; CPG MNT, medical nutrition therapy by clinical practice guidelines recommendations

Pastors, et al. *Diabetes Care*. 2002;25(3):608-613.
Morris SF, Wylie-Rosett J. *Clin Diabetes*. 2010;28:12-18.

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The use of medical foods as part of a medical nutrition therapy program reduces the need for Diabetes Medications

Diabetes Medication	Before # Patients (dose/day)	After # Patients (dose/day)	% Change # Patients (dose)
Sulfonylureas			
Glyburide	6 (9.5 mg/d)	2 (6.2 mg/d)	-67% (-35%)
Glipizide	8 (11.25 mg/d)	3 (6.6 mg/d)	-63% (-41%)
Thiazolidinediones			
Pioglitazone	8 (28.1 mg/d)	1 (15 mg/d)	-88% (-47%)
Rosiglitazone	7 (7.4 mg/d)	2 (5 mg/d)	-71% (-33%)
Metformin	46 (1664.1 mg/d)	47 (1862 mg/d)	2% (12%)
Exenatide	8 (15 mcg/d)	25 (17.6 mcg/d)	213% (17)
Insulin			
NPH	6 (47.5 unit/d)	3 (41.7 unit/d)	-50% (-12%)
Long-acting Analog	10 (60.9 unit/d)	13 (27.2 unit/d)	30% (-55%)
Short-acting Analog	14 (52.1 unit/d)	11 (24.1 unit/d)	-21% (-54%)
Pramlintide	2 (45 unit/d)	11 (47.3 unit/d)	450% (5%)

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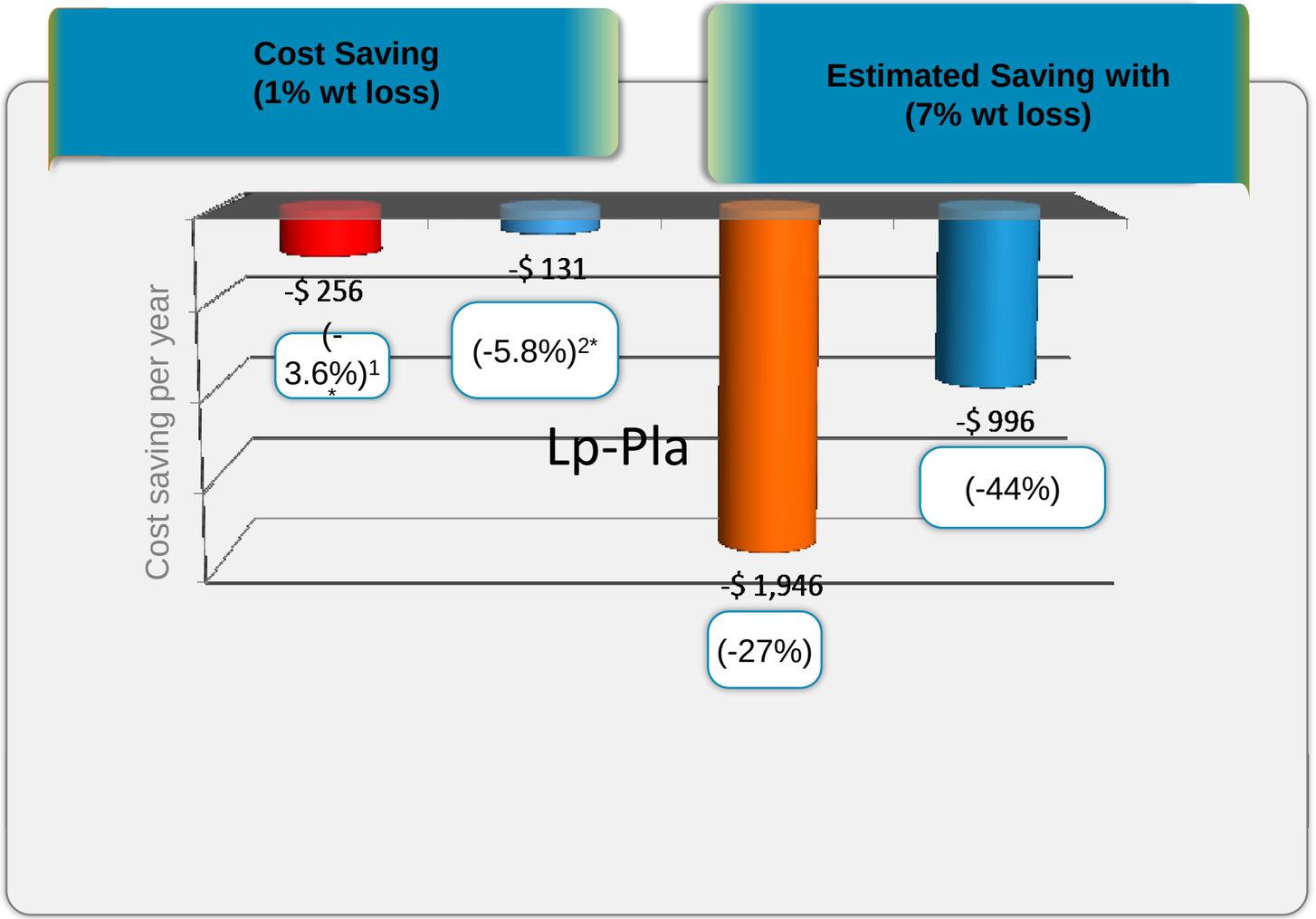
Economic Impact: A year of medical nutrition therapy with diabetic patients results in healthcare system savings of up to $1,946 per patient and $996 of savings in diabetes specific care costs.



YU AP, et al. *Curr Med Res Opin*. 2007;23(9):2157-69.

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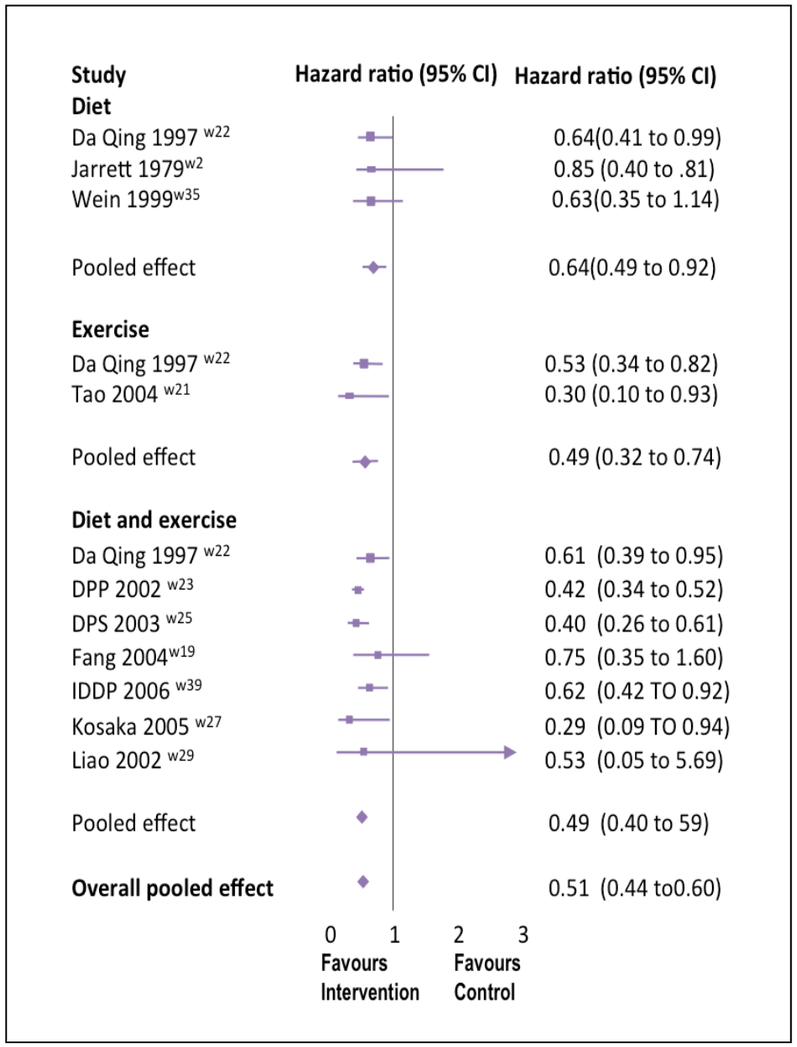
Use of Medical Nutrition Therapy with exercise results in a 49% reduction in the risk of developing diabetes as shown by a Meta-analysis on the Effect of Lifestyle Interventions on diabetes

The pooled effect for all forms of lifestyle interventions gave a hazard ratio of 0.51, indicating a relative 49% reduction in the risk of developing diabetes



Reproduced from BMJ, Gillies CL, et al. *BMJ Publishing Group Ltd*. 2007;Vol 334:299.

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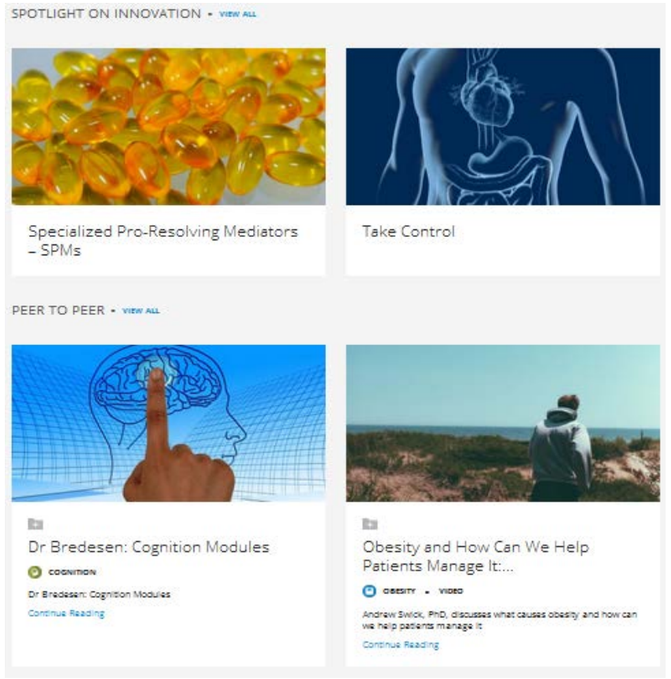
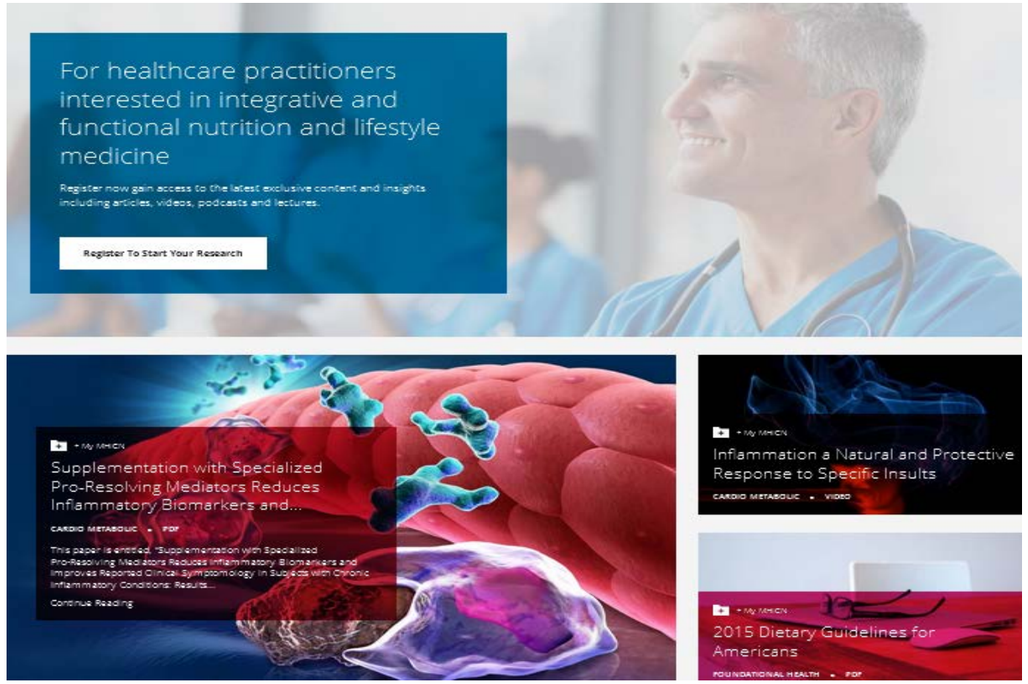
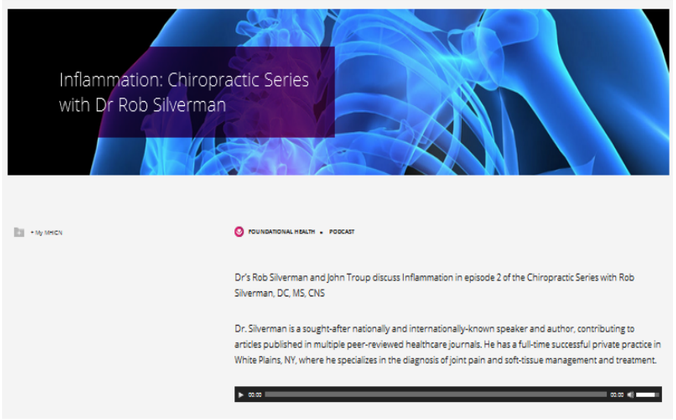
Key Take Home Messages

- Utilizing a Medical Food for Glucose Control in conjunction with a diet (40:30:30 plan) can have a significant effect on HbA1c
- Use 2 serving of the medical food with diet for 12-16 weeks for Type 2 diabetics and prediabetes
- Use 1 serving per day

Additional Educational Resources on MHICN.com







Register and login for full access at www.mhicn.com

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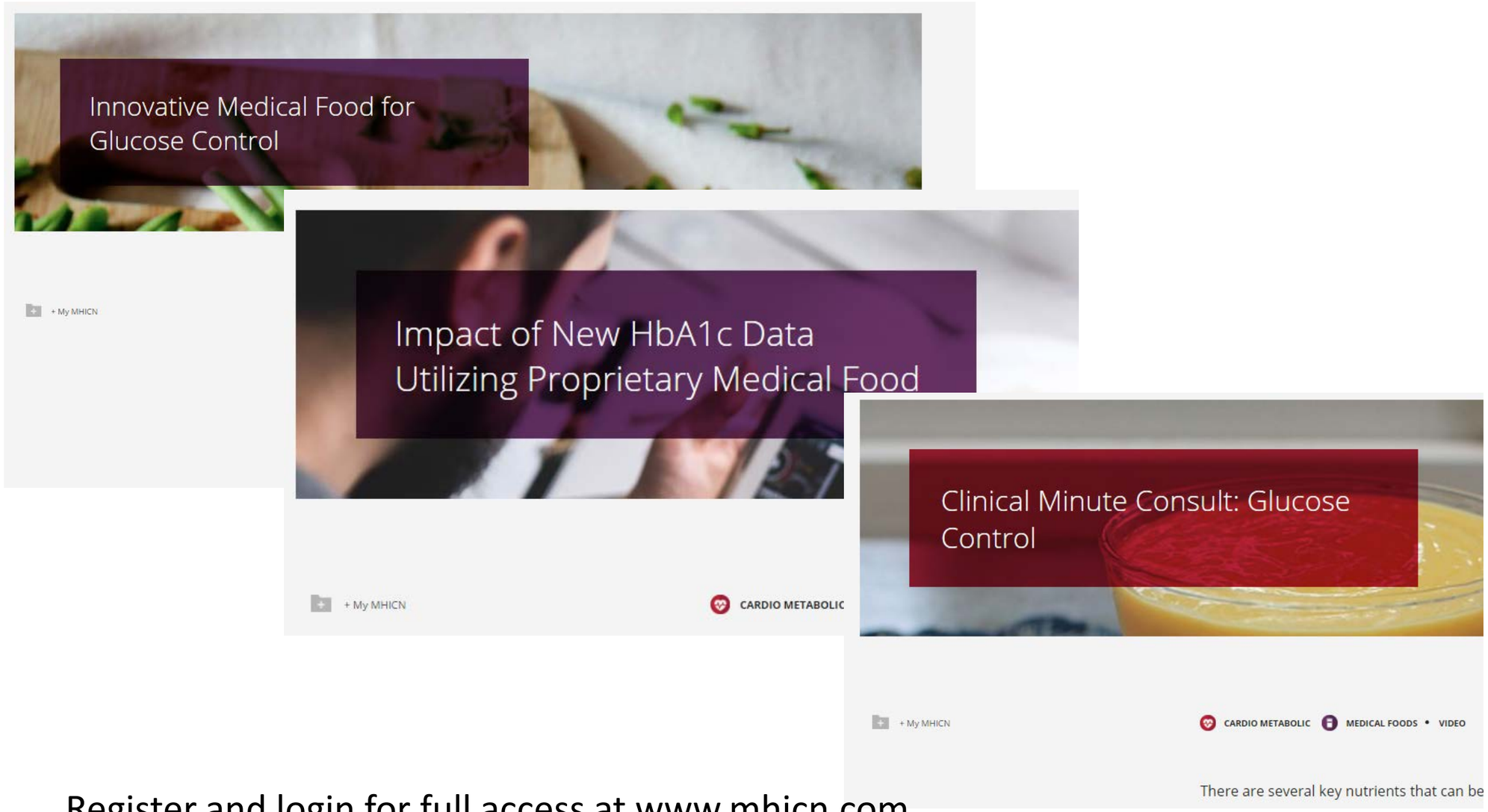
Specific resources on Medical Foods and Glucose Control Study results are on MHICN.com



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