John McDougall, MD reports family ownership of the McDougall program

Big Pharma & Big Medicine

Approximately 2.3 times more than what expenditures would be in the absence of diabetes.

Type-1 Diabetes
(Lack of Insulin Production)
“insulin dependent”

Type-2 Diabetes
(Full Pancreatic Sufficiency)
“non-insulin dependent”
Type-1.5 Diabetes
(Partial Pancreatic Insufficiency)
"non-insulin dependent"

A spectrum called “type-one and a half (1.5) diabetes.”
Enough insulin to stay well (avoid ketoacidosis and death)
Not enough to maintain a normal blood sugar.

Type-2 Diabetes Worldwide Epidemic

Research
Prevalence and Control of Diabetes in Chinese Adults

CONCLUSIONS AND RELEVANCE: The estimated prevalence of diabetes among a
representative sample of Chinese adults was 11.6% and the prevalence of prediabetes was
50.1%. Projections based on sample weighting suggest this may represent up to 113.9 million
Chinese adults with diabetes and 493.4 million with prediabetes. These findings indicate the
importance of diabetes as a public health problem in China.

$322 Billion annually with nearly 30 million Americans
diagnosed as diabetic and 86 million said to have prediabetes.

Obesity = Type-2 Diabetes

Risk ratios:
20.1 for overweight and obese
38.8 for morbid obese

Overweight and obese (30 and 35 kg/m²)
Morbid Obesity (> 35 kg/m²)
Compared with a BMI <23 kg/m²


Type-2 Diabetes – the Expected Adaptation
to Over-nutrition

February 2004 McDougall Newsletter
Insulin Resistance

**Definition:** A state of reduced responsiveness to normal circulating levels of insulin

**Lipotoxicity:** Abnormalities in fatty acid metabolism may result in inappropriate accumulation of lipids in muscle, liver, and beta-cells.

Treating Diabetes

<table>
<thead>
<tr>
<th>Class of Medication</th>
<th>Diabetic Drugs</th>
<th>Mechanism of Action</th>
<th>Some Side Effects from Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biguanides: metformin (Glucophage)</td>
<td>Cardiac death, weight gain, hip fractures</td>
<td>Decreases hepatic glucose production</td>
<td></td>
</tr>
<tr>
<td>Sulfonylureas: glibenclamide, glyburide, glimepiride</td>
<td>Diabetes, stroke, myocardial infarction, hypoglycemia</td>
<td>Increases secretion of insulin</td>
<td></td>
</tr>
<tr>
<td>GLP-1 receptor agonists: exenatide, liraglutide, exenatide, albiglutide, lixi!</td>
<td>Diabetes, stroke, myocardial infarction, hypoglycemia</td>
<td>Increases secretion of insulin</td>
<td></td>
</tr>
<tr>
<td>DPP-4 inhibitors: sitagliptin, saxagliptin, linagliptin,</td>
<td>Diabetes, stroke, myocardial infarction, hypoglycemia</td>
<td>Increases secretion of insulin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SGLT2 inhibitors: canagliflozin, empagliflozin,</td>
<td>Diabetes, stroke, myocardial infarction, hypoglycemia</td>
<td>Increases urinary loss of glucose</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Meglitinides: nateglinide, repaglinide</td>
<td>Diabetes, stroke, myocardial infarction, hypoglycemia</td>
<td>Increases secretion of insulin</td>
<td></td>
</tr>
<tr>
<td>Thiazolidinediones: pioglitazone, rosiglitazone</td>
<td>Diabetes, stroke, myocardial infarction, hypoglycemia</td>
<td>Increases secretion of insulin</td>
<td></td>
</tr>
<tr>
<td>Alpha-glucosidase inhibitors: acarbose, miglitol</td>
<td>Diabetes, stroke, myocardial infarction, hypoglycemia</td>
<td>Inhibits carbohydrate digestion</td>
<td></td>
</tr>
<tr>
<td>Insulin (various forms)</td>
<td>Diabetes, stroke, myocardial infarction, hypoglycemia</td>
<td>Inhibits pancreatic insulin</td>
<td></td>
</tr>
</tbody>
</table>

Criteria for FDA Approval

For a Diabetic Medication Approval, FDA Requirement from 2008 to Currently:

Glycemic control, as measured by changes in glycated hemoglobin levels (HgBA1c), remains an acceptable primary efficacy and point for approval of drugs to treat hyperglycemia.

Diabetic Management

“...it is important to remember that ‘diabetic control’ means a lot more than ‘blood sugar control.’” T.D.R. Hockaday, 1987

Medications (oral and insulin) effectively lower blood sugar levels and the patients die sooner with better looking numbers!


“2nd line Therapy:” Sulfonylureas

About 30% of sales of diabetic medications

**Glipizide**

Extended-Release Tablets (anti-diabetic agent)

5 mg

Sulfonylureas also used as herbicides:
Interfering with biosynthesis of the amino acids valine, isoleucine, and leucine.

Generic names: acetohexamide, carbutamide, chlorpropamide, glyceclamide (tolbutamide), metahexamide, tolazamid and tolbutamide, glipizamide (glyburide), glibenamide, glimepiride, glipizide, gliclazide, glimepiride, glimepiride and glyclopyramide, glimepiride

Sulfonylureas have been studied since the 1960s

UGDP reported that patients treated for 5 to 8 years with diet plus a fixed dose of tolbutamide (1.5 grams per day) had a rate of cardiovascular mortality approximately 2-1/2 times that of patients treated with diet alone


Avandia (rosiglitazone)
Avandia (rosiglitazone)

Reduced hemoglobin A1c by 1.5%

Had 66 percent more heart attacks
39 percent more strokes
20 percent more deaths from cardiovascular-related problems
100,000 heart-related problems among seniors

The manufacturer, GlaxoSmithKline, recently paid $3 billion to the FDA for its mischievous behavior; More than 50,000 Avandia lawsuits have been filed in state and federal courts across the US.

Almost taken off US market after 2007. Banned in New Zealand. The European Medicines Agency recommended on 23 September 2010 that Avandia be suspended from the European market, etc.

Avandia (rosiglitazone)

Special Warnings from Physician’s Desk Reference (PDR)

WARNING: CONGESTIVE HEART FAILURE AND PHYSIOLOGICAL IMPAIRMENT

Due to the possibility of concurrent bariatric surgery, patients with a BMI greater than 35 kg/m^2 are at increased risk for cardiovascular events, including death, cardiovascular disease, and myocardial infarction. Patients with a BMI greater than 40 kg/m^2 are at increased risk for adverse cardiovascular events, including death, cardiovascular disease, and myocardial infarction.

Avandia is contraindicated in patients with severe renal impairment (creatinine clearance < 30 mL/min) or end-stage renal disease.

Metformin (Glucophage)

“first-line medication”

More than half of the 58 million Medicare claims for non-insulin-dependent diabetes
Metformin (Glucophage)

Reappraisal of Metformin Efficacy in the Treatment of Type 2 Diabetes: A Meta-Analysis of Randomised Controlled Trials

“Although metformin is considered the gold standard, its benefit/risk ratio remains uncertain. We cannot exclude a 25% reduction or a 31% increase in all-cause mortality. We cannot exclude a 33% reduction or a 64% increase in cardiovascular mortality.”


Lack of Cardiovascular Benefits from Metformin - Review

Impact of metformin on cardiovascular disease: a meta-analysis of randomised trials among people with type 2 diabetes

Simon J. Griffin1, James K. Lawrenson2, Greg J. Irving3

Conclusions/interpretation: There remains uncertainty about whether metformin reduces risk of cardiovascular disease among patients with type 2 diabetes, for whom it is the recommended first-line drug.

Funded by a National Institute of Health Research (NIHR) Clinical Lectureship

Diabetologia (2017) 60:1623–1629

Noninferior to a Bad Drug?

Effect of Linagliptin vs Glimepiride on Major Adverse Cardiovascular Outcomes in Patients With Type 2 Diabetes: The CAROLINA Randomized Clinical Trial

CONCLUSIONS AND RELEVANCE Among adults with relatively early type 2 diabetes and elevated cardiovascular risk, the use of linagliptin compared with glimepiride over a median 6.3 years resulted in a noninferior risk of a composite cardiovascular outcome.

Sponsored by Boehringer Ingelheim and Eli Lilly and Company

JAMA. 2019;322(12):1355-1366

Blood Glucose & HgBA1c

Glucose meter (sugar meter device): Momentary blood sugar levels. Normal fasting blood sugar is below 100 mg/dL (5.6 IU).

Hemoglobin A1c (HgBA1c) is a long-term, laboratory-performed test. Measures average sugars over a previous two to three month period. Normal HgBA1c is considered less than 6%. Levels can rise as high as 14%.
McDougall’s Medicine 1985

Aggressive Treatment Harms!

Aggressive Treatment (HgBA1c) = 6%
Standard Treatment (HgBA1c) = 8%

Only 7 Major Studies Performed

Intensive Therapy Increases Problems

United Kingdom Prospective Diabetes Study (UKPDS)
HgBA1c: 7.0% vs. 7.9%. 10 years.

Absolute reductions:
- Any diabetes related end point: 5.1 per 1000
- Diabetes related death: 0.9 per 1000
- All cause mortality: 1 per 1000
- Myocardial Infarction: 3 per 1000
- More weight gain
- More hypoglycemia

Lancet. 1998 Sep 12;352(9131):837-53

Intensive Therapy Increases Problems

"...may increase the risk of coronary artery disease in this subset of subjects with time.”

More weight gain, higher blood pressure, and higher levels of triglyceride, total cholesterol, low-density lipoprotein cholesterol (LDL-C), and apolipoprotein B.

JAMA. 1998 July 8;280(2):140–146
Intensive Therapy Increases Problems

CARDIOVASCULAR EVENTS AND CORRELATES
in the Veterans Affairs Diabetes Feasibility Trial
Veterans Affairs Cooperative Study on Glucose Control and Complications in Type II Diabetes

"...found a strong tendency toward worsening of CV outcomes in patients with intensive control."


Intensive Therapy Increases Problems

LON-TERM PROGNOSIS OF DIABETIC PATIENTS WITH MYOCARDIAL INFARCTION: RELATION TO ANTIDIABETIC TREATMENT REGIMEN

Diabetic patients treated with oral hypoglycaemic agents or insulin, but not those treated with diet alone, have a significantly increased mortality following acute myocardial infarction compared with non-diabetic patients.

Trandolapril Cardiac Evaluation (TRACE) study

Intensive Therapy Increases Problems

Effects of Intensive Glucose Lowering in Type 2 Diabetes

Intensive therapy was stopped before study end because of higher mortality in that group


Intensive Therapy Increases Problems

"There were no significant effects of the type of glucose control on major macrovascular events, death from cardiovascular causes, or death from any cause..."

Intensive Therapy Increases Problems

Glucose Control and Vascular Complications in Veterans with Type 2 Diabetes

"Intensive glucose control...no significant effect on the rates of major cardiovascular events, death, or microvascular complications with the exception of progression of albuminuria."


Drug Managements

Lower blood sugars, but...

Higher mortality
More heart disease
Increased risk of sudden death
Much more hypoglycemia
Twice the weight gain

So, What’s the Sales Pitch?

Microvascular Disease

Retinopathy (eye)
Nephropathy (kidney)
Neuropathy (nerves)

Medication and Micro-vascular Disease

Summary of Results for Microvascular Complications

<table>
<thead>
<tr>
<th>Study</th>
<th># of Participants</th>
<th>Benefit Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Control and Complications Trial</td>
<td>1441</td>
<td>Yes – type 1</td>
</tr>
<tr>
<td>Stockholm Diabetes Intervention Study</td>
<td>91</td>
<td>Yes – type 1</td>
</tr>
<tr>
<td>UK Prospective Diabetes Study (UKPDS) Group</td>
<td>753</td>
<td>Yes – type 2</td>
</tr>
<tr>
<td>Insulin Study</td>
<td>118</td>
<td>Yes – type 2*</td>
</tr>
<tr>
<td>ADVANCE*</td>
<td>11,140</td>
<td>Yes – type 2*</td>
</tr>
<tr>
<td>ACCORD Study</td>
<td>10,251</td>
<td>No – type 2</td>
</tr>
<tr>
<td>Veterans (VAUDT) study</td>
<td>1,791</td>
<td>No – type 2</td>
</tr>
</tbody>
</table>

*albuminuria

July 2011 McDougall Newsletter
ACCORD: No Microvascular Benefits

Effect of intensive treatment of hyperglycaemia on microvascular outcomes in type 2 diabetes: an analysis of the ACCORD randomised trial

"Intensive therapy did not reduce the risk of advanced measures of microvascular outcomes..."


ACCORD: Summary

“Microvascular benefits of intensive therapy should be weighed against the increase in total and cardiovascular disease-related mortality, increased weight gain, and high risk for severe hypoglycaemia.”


Meta-analysis: No Microvascular Benefits

Effect of intensive glucose lowering treatment on all cause mortality, cardiovascular death, and microvascular events in type 2 diabetes: meta-analysis of randomised controlled trials

“The harm associated with severe hypoglycaemia might counterbalance the potential benefit of intensive glucose lowering treatment... Intensive treatment was associated with a significant reduction in only one end point—the rate of microalbuminuria.”

BMJ. 2011 Jul 26;343:d4119.

Metformin and Microvascular Benefits

In the case of metformin, claims for microvascular benefits rest solely on the difference in one highly subjective measurement of eye damage—retinal photocoagulation.

Lancet. 1998 Sep 12;352(9131):837-53
Latest In Diabetes Drugs

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

7020 patients were treated (median observation time, 3.1 years)
No significant differences in the rates of myocardial infarction or stroke
2.2% lower death from cardiovascular causes (3.7% vs. 5.9%)
1.4% fewer hospitalizations for heart failure (2.7% and 4.1%)
2.6% lower death from any cause (5.7% and 8.3%)

An increased rate of genital infections
Increased risk of leg and foot amputations

Funded by: Boehringer Ingelheim and Eli Lilly

*N Engl J Med. 2015 Nov 26;373(22):2117-28*

Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes

9340 patients with a median follow-up was 3.8 years
1.3% fewer patients died from cardiovascular causes (4.7% vs. 6.0%)
1.4% lower rate of death from any cause (8.2% vs. 9.6%)
The rates of nonfatal myocardial infarction, nonfatal stroke, and hospitalization for heart failure were nonsignificantly lower

Adverse events were primarily gastrointestinal
Pancreatitis, hypoglycemia, kidney damage, thyroid cancers

Funded by: Novo Nordisk


Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes

3297 patients, treated once-weekly for 104 weeks
2.3% reduction composite outcome - cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke (6.0% vs. 8.9%)
1% reduction nonfatal myocardial infarction (2.0% vs. 3.0%)
1.1% nonfatal stroke occurred (1.6% and 2.7%)

Adverse events were primarily gastrointestinal
Retinopathy (eye) complications (vitreous hemorrhage, blindness, and/or treatment)

Funded by: Novo Nordisk (weekly injectable)

**Meters & Pumps**

Continuous Glucose Monitoring (CGM)
readings as often as every five minutes:
$1,000 to $1,400.
The sensors good for three to seven days:
$35 to $100 apiece.
Fingertip blood checks two to four times a
day to keep the monitor calibrated.
Insulin pump costing more than $5,000.
No health benefits.
CGM over standard (glucose-finger-stick)
monitoring
0.04% HgB1A1c

*JAMA. 2017;317(4):363-364*

---

**Medication = Weight Gain = Diabetes**

**Downward Cycle**

---

**Bariatric Surgery**

A meta-analysis included 3188 patients with type-2 diabetes:

78.1% = complete resolution

86.6% = improved or resolved

Surgically-induced malabsorption, malnutrition,
and sickness

*Am J Med. 2009 Mar;122(3):248-256.e5*

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**Healthy Medical Students**

2-days on carbohydrate-diet*

---

*Arch Intern Med.1927;40:818-830.*
Healthy Medical Students
2-days on high-protein diet*

*lean meat, whites of eggs

Arch Intern Med 1927;40:818-830.

Healthy Medical Students
2-days on high-fat diet*

*olive oil, butter, mayonnaise (egg yolk, 20% cream)

Arch Intern Med 1927;40:818-830.

Sir Harold Percival (Harry) Himsworth
(1905–1993)

CAL JOURNAL
AY MAY 4 1940

INSULIN INEFFICIENCY *

H, M.D., F.R.C.P.
late Director of the Medical Unit, University
Ost, London


Sugar Makes Diabetes Better

45% vs. 85% Carbohydrate: FBS fell, OGT improved, fasting insulin lower
(Over 10 days of feeding of formula feeding – dextrose and maltose)

“These data suggest that the high carbohydrate diet
increased the sensitivity of peripheral tissues to insulin.”

Fat Paralyzes Insulin Type-1 Diabetes

Dietary Fat Acutely Increases Glucose Concentrations and Insulin Requirements in Patients With Type 1 Diabetes

Implications for carbohydrate-based bolus dose calculation and intensive diabetes management.

CONCLUSIONS — This evidence that dietary fat increases glucose levels and insulin requirements highlights the limitations of the current carbohydrate-based approach to bolus dose calculation. These findings point to the need for alternative insulin dosing algorithms for higher-fat meals and suggest that dietary fat intake is an important consideration for glycemic control in individuals with type 1 diabetes.

Diabetes Care 36:810–816, 2013

Pritikin Longevity Center


James Anderson, MD
University of Kentucky, College of Medicine

Metabolic Ward Study
Weight Maintaining Diet

Insulin Usage
Average reduction: 26 to 11 units daily

11 of 20 lean patients discontinued insulin
CHO initially ~ 43%
7 days average
CHO intervention: ~ 70%
16 days average


Neal Barnard, MD
Randomized Clinical Trial in Individuals With Type 2 Diabetes

<table>
<thead>
<tr>
<th></th>
<th>Vegan</th>
<th>ADA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced Medication</td>
<td>21/49</td>
<td>13/50</td>
</tr>
<tr>
<td>Hgb A1c*</td>
<td>-1.23</td>
<td>0.38</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>6.5</td>
<td>3.1</td>
</tr>
<tr>
<td>LDL (% change)*</td>
<td>21.2</td>
<td>10.7</td>
</tr>
<tr>
<td>Urate protein</td>
<td>15.9</td>
<td>10.9</td>
</tr>
</tbody>
</table>

Vegan diet = (10% of energy from fat, 15% protein, and 75% carbohydrate)
ADA diet = (40% fat, 20% protein, 40% carbohydrate, < 200 mg cholesterol)

*No medication changes

Important Medical Findings from 7 Days of Enjoying the McDougall Diet: 1615 Patients

- Average weight loss was 3.1 pounds while eating unrestricted amounts of food
- Average cholesterol reduction was 22 mg/dL
- An average decrease of 18/11 mmHg in blood pressure in patients with hypertension (140/90 or greater)
- Nearly 90% of patients were able to reduce or stop blood pressure and diabetic medications

Low-fat, plant-based diet in multiple sclerosis: A randomized controlled trial

Any issues here could improve with a better scan or clearer text.