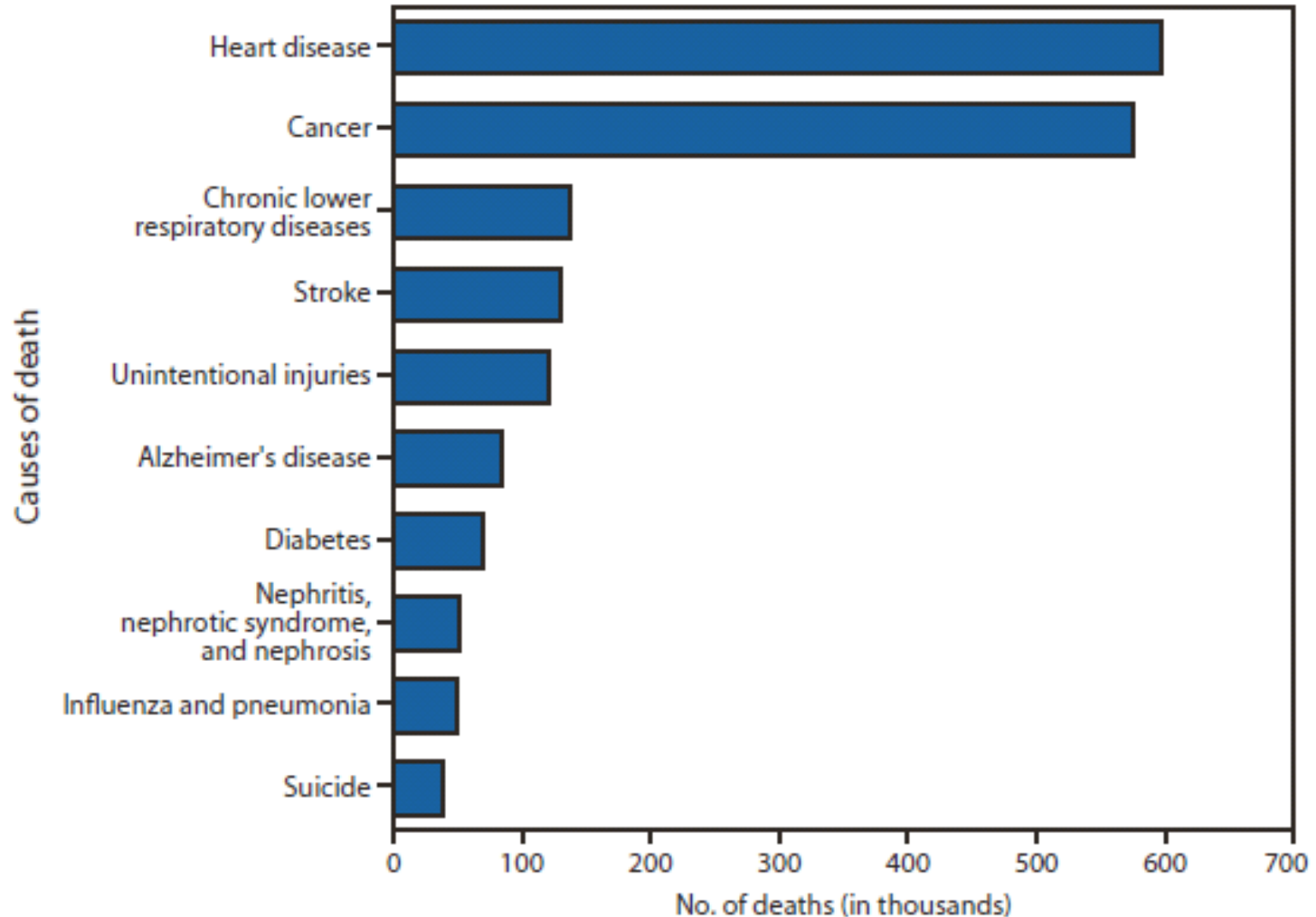# TREATING OBESITY TO REDUCE CARDIOVASCULAR RISKS IN TYPE2 DIABETES

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June 8, 2022

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Heart disease remains leading cause of death in US

Bar chart. X-axis: No. of deaths (in thousands), 0 to 700. Y-axis: Causes of death.

- Heart disease: ~600
- Cancer: ~580
- Chronic lower respiratory diseases: ~140
- Stroke: ~130
- Unintentional injuries: ~120
- Alzheimer's disease: ~85
- Diabetes: ~70
- Nephritis, nephrotic syndrome, and nephrosis: ~50
- Influenza and pneumonia: ~50
- Suicide: ~40

(CDC Quick Stats: Number of deaths from 10 leading causes; cdc.gov)

Cardiovascular Risks in Type 2 Diabetes

- Cardiovascular disease is the principal cause of death and morbidity among people with diabetes especially type 2

- 2-4 times increased cardiovascular risk compared with adults without diabetes.

Diabetes-related macrovascular and microvascular complications including CAD, CV disease, HF, PVD, CKD, diabetic retinopathy and CV autonomic neuropathy are responsible for the impaired quality of life, disability and premature death associated with diabetes, not to mention the higher medical expenses.

OBESITY LEADS TO

insulin resistance ➡

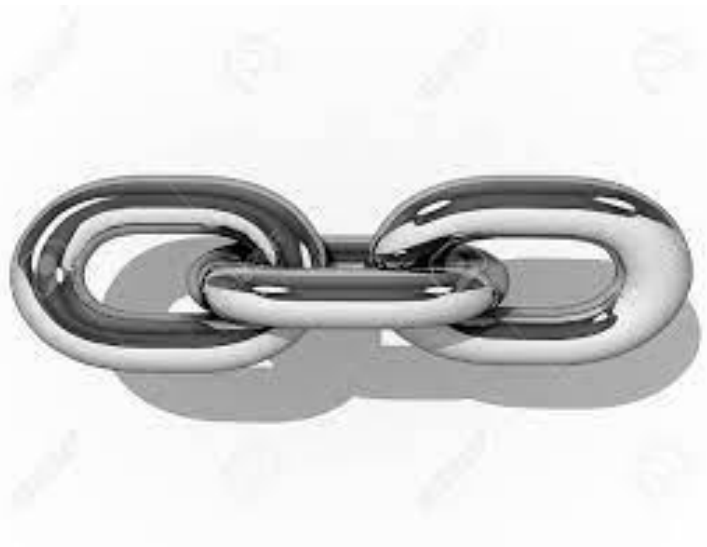Leads to perivascular adipose tissue

Which promotes local inflammation

Which leads to endothelial dysfunction.

Endothelial dysfunction is associated with cardiovascular conditions like atherosclerosis, hypertension, hyperlipidemia.
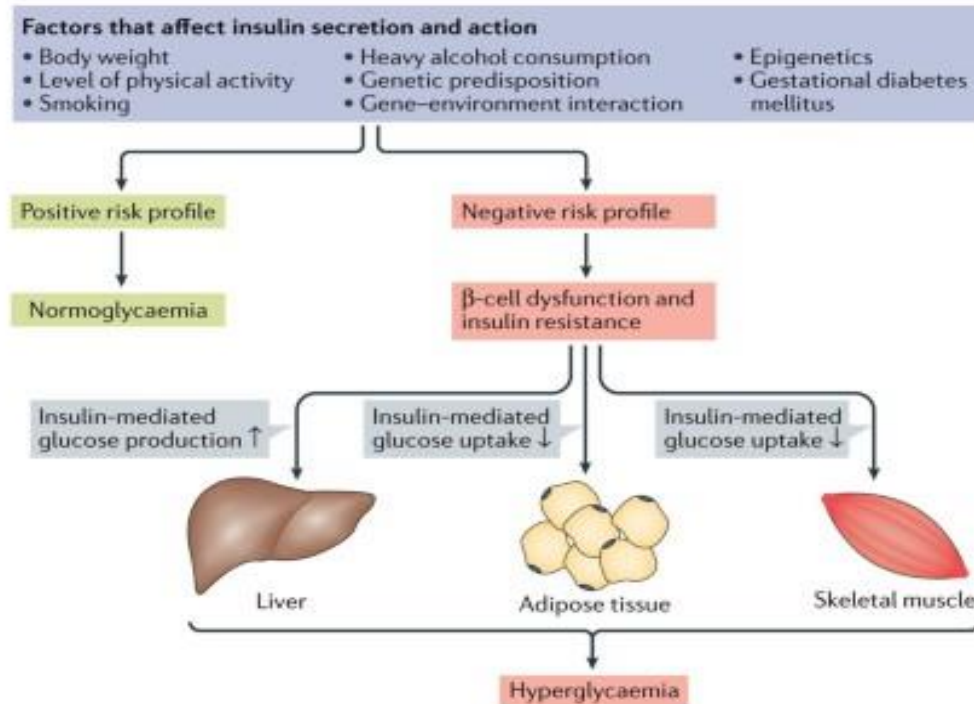
Mechanism that links diabetes and obesity

- Type 2 diabetes has a different pathophysiology and etiology as compared to type 1 diabetes.

- Type 2 diabetes is described as a combination of low amount of insulin production from pancreatic b cells and peripheral insulin resistance.

Hyperglycemia

Pathophysiology of hyperglycemia in type 2 diabetes mellitus

Factors that affect insulin secretion and action
- Body weight
- Level of physical activity
- Smoking
- Heavy alcohol consumption
- Genetic predisposition
- Gene–environment interaction
- Epigenetics
- Gestational diabetes mellitus

Positive risk profile → Normoglycaemia

Negative risk profile → β-cell dysfunction and insulin resistance

Insulin-mediated glucose production ↑ — Liver

Insulin-mediated glucose uptake ↓ — Adipose tissue

Insulin-mediated glucose uptake ↓ — Skeletal muscle

→ Hyperglycaemia

What can we do?

In clinical studies, weight loss of around 5-10% can result in a reduced risk of T2D and cardiovascular disease.
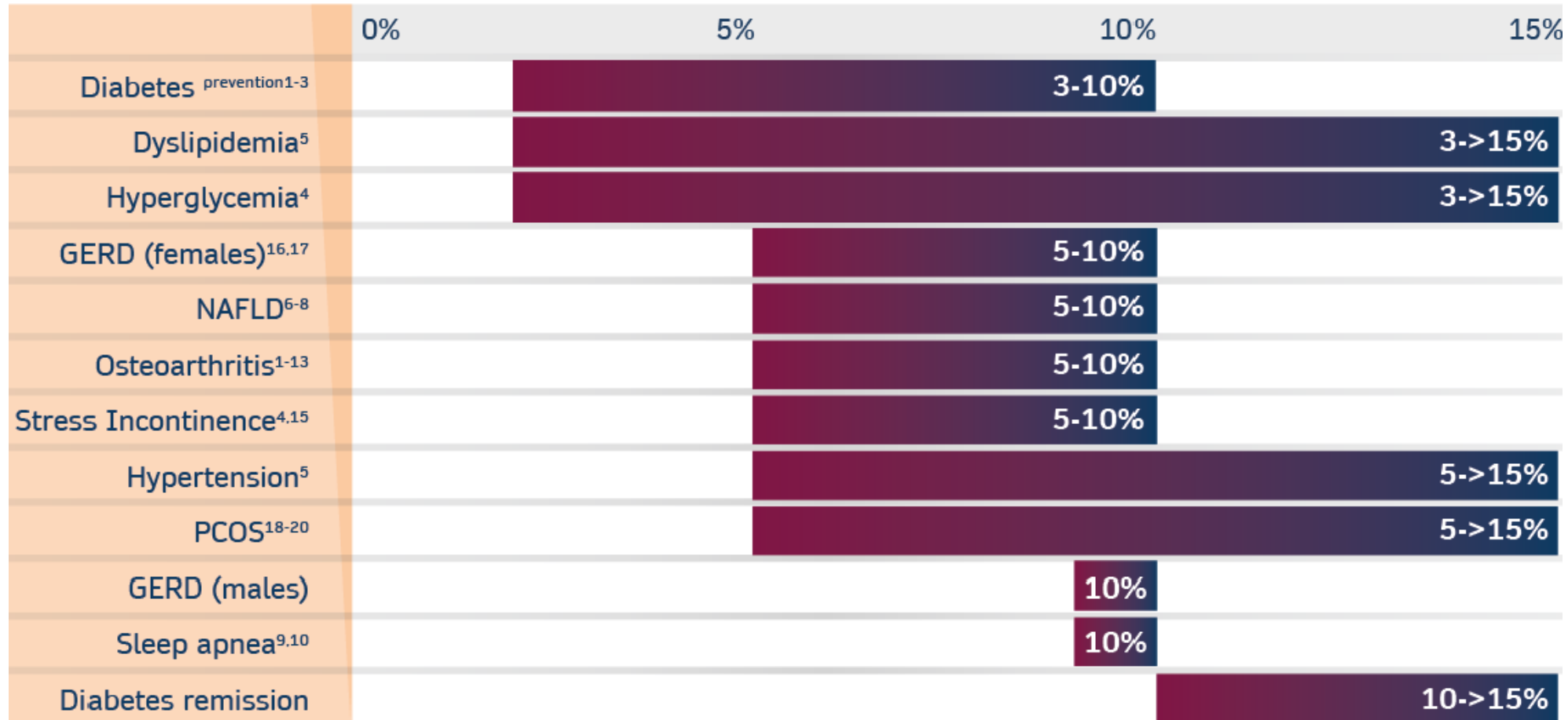
Anti-obesity medications/bariatric procedures and surgeries increase the likelihood of achieving clinically meaningful weight loss.

Therapeutic Benefit of Weight Loss

Percent Initial Body Weight Lost for Therapeutic Benefit

Condition	Percent Initial Body Weight Lost
Diabetes prevention[1-3]	3-10%
Dyslipidemia[5]	3->15%
Hyperglycemia[4]	3->15%
GERD (females)[16,17]	5-10%
NAFLD[6-8]	5-10%
Osteoarthritis[1-13]	5-10%
Stress Incontinence[4,15]	5-10%
Hypertension[5]	5->15%
PCOS[18-20]	5->15%
GERD (males)	10%
Sleep apnea[9,10]	10%
Diabetes remission	10->15%

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The 5 Pillars in a Staged Approach to Treating Obesity

	BMI 25-26.9	BMI 27-29.9	BMI 30-34.9	BMI 35-39.9	BMI ≥ 40
Nutrition	✓	✓	✓	✓	✓
Physical Activity	✓	✓	✓	✓	✓
Behavioral	✓	✓	✓	✓	✓
Pharmacotherapy		✓ with co-morbidity	✓	✓	✓
Bariatric Surgery				✓ with co-morbidity	✓

Pre-diabetes is a common problem and strongly associated with obesity
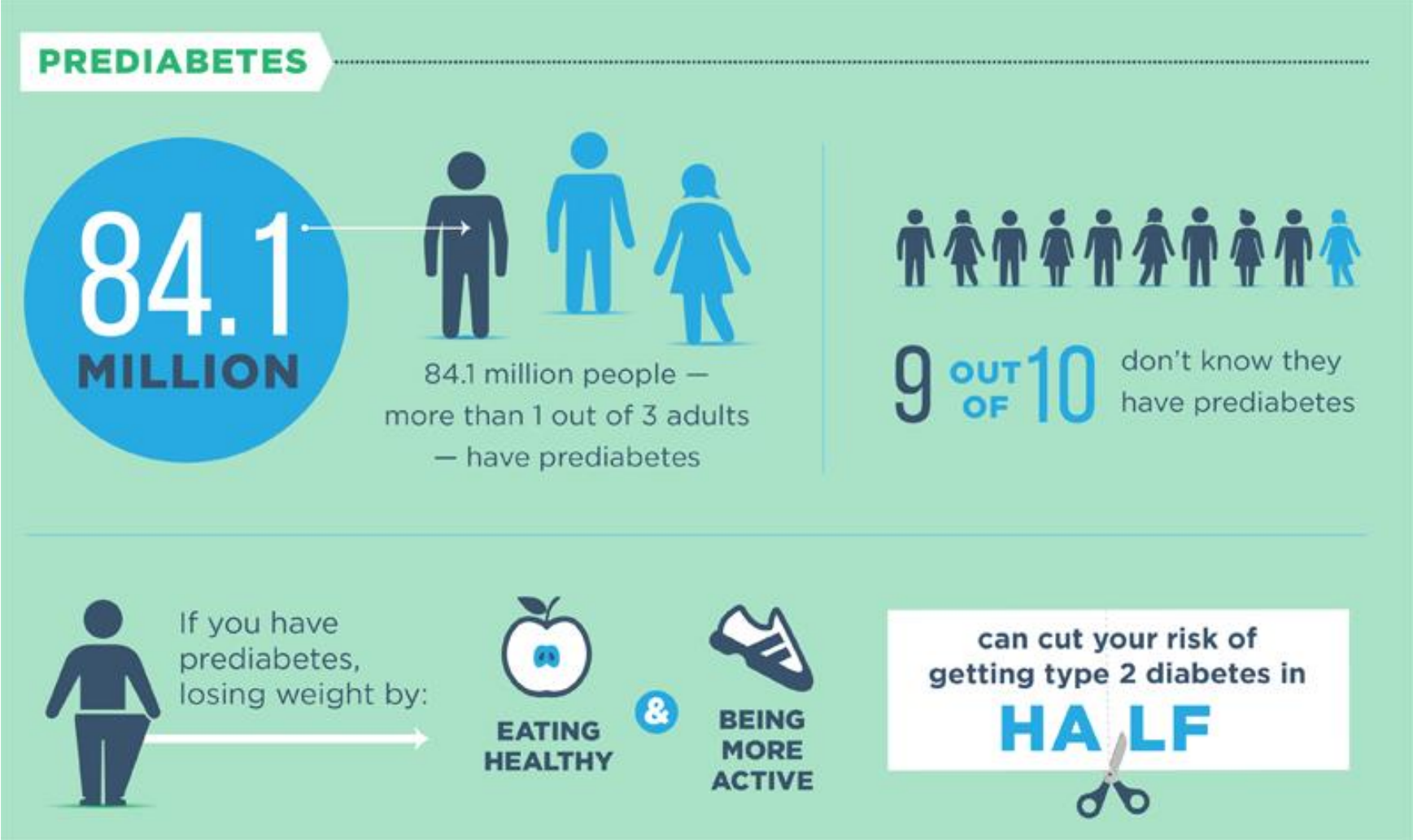
Many patients with pre-diabetes convert to diabetes

Annual conversion rate 12.2%[1]

Lifetime conversion rate up to 70%[2]

Blood Test Levels for Diagnosis of Diabetes and Prediabetes

	A1C (percent)	Fasting Plasma Glucose (mg/dL)	Oral Glucose Tolerance Test (mg/dL)
Diabetes	6.5 or above	126 or above	200 or above
Prediabetes	5.7 to 6.4	100 to 125	140 to 199
Normal	About 5	99 or below	139 or below

Definitions: mg = milligram, dL = deciliter
For all three tests, within the prediabetes range, the higher the test result, the greater the risk of diabetes.

1. Santaguida PL et al. AHRQ Study 128:1–12, 2006
2. Nathan DM et al. Diabetes Care 2007 Mar; 30(3): 753-759

Patients who convert to diabetes are at 2-4 fold higher risk for CV disease[1] and incur 230% higher healthcare expenditures *(Additional $9600/year)*[2]

1. Hudspeth B. The burden of cardiovascular disease in patients with diabetes. *Am J Manag Care.* 2018;24(13 Suppl):S268-S272
2. American Diabetes Association. Economic Costs of Diabetes in the U.S. in 2017. *Diabetes Care.* 2018;41(5):917-928. doi:10.2337/dci18-0007

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DPP Value Based Outcomes

Treating 100 high risk adults (age 50) for 3 years...

- Prevents 15 new cases of Type 2 Diabetes[1]

- Prevents 162 missed work days[2]

- Avoids the need for BP/Chol pills in 11 people[3]

- Avoids $91,400 in other healthcare costs[4]

- Adds the equivalent of 20 perfect years of health[5]

1 DPP Research Group. N Engl J Med. 2002 Feb 7;346(6):393-403
2 DPP Research Group. Diabetes Care. 2003 Sep;26(9):2693-4
3 Ratner, et al. 2005 Diabetes Care 28 (4), pp. 888-894
4 Ackermann, et al. Diabetes Care. 2006 Jun;29(6):1237-41; estimates scaled to 2008 $US
5 Herman, et al. 2005 Ann Intern Med 142 (5), pp. 323-32

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Value Proposition

231,315 patients with prediabetes x 12.2% annual conversion rate = 28,220 predictable new cases of diabetes

28,220 new patients with diabetes x $9,600* in excess medical expenditures/year attributed to diabetes =

$270,912,000 expected excess medical expenditures w/ out intervention

250 patients treated w/ 15 cases of DM2 avoided per 100 treated with DPP → 38 cases of DM2 avoided * $9,600 excess medical expenditures avoided per patient on average =

<u>$364,000 expected avoided excess medical expenditures from pilot</u>

Assuming scaled up to 10% of AAH pre-diabetic population: 231,315*0.10 → 23,132 * (15 cases avoided per 100 treated) → 3,470 avoided cases of diabetes * $9,600/case =

<u>$33,312,000 expected avoided medical expenditures from scale up</u>

SUMMARY

There is an epidemic of people who have the disease of obesity.

90-95% of patients with Type 2 Diabetes have this disease.

Diabetes and Obesity are the driver of cardiovascular diseases.

By treating obesity, we can reverse type 2 diabetes, lower cardiovascular disease and in many cases even prevent diabetes in those that were headed in that direction.