

**Type 2 Diabetes Prevention:
Lifestyle Change and Coverage
Considerations**

***Making the Case for Type 2 Diabetes
Prevention and Delay***

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Disclosures

- Consultant:
 - Heartland Food Products Group, manufacturer of SPLENDA® Sweeteners
 - Insulet Corporation
 - Johnson and Johnson Diabetes Institute (JDI)
 - WellDoc, developer of BlueStar mobile medical app
- Book royalties
 - American Diabetes Association

Outline

- Latest Stats
- Disease Onset, Continuum
- Diagnostic numbers, recommendations
- Research – clinical
- Research – translational
- Management – nutrition
- Management – glucose lowering medications

WHY T2 Diabetes Prevention Matters?

Da Qing Diabetes Prevention Study in China¹

- Longest (30 yrs) study
- 23 yrs follow up: development of T2D associated with a **73% higher risk of death**
 - 79% (428 of 542) developed T2D (174 died)
 - 70% higher death rate than age, sex matched with normal glucose tolerance



1. Gong Q, Zhang P, Wang J, et al. Changes in mortality in people with IGT before and after the onset of diabetes during the 23-year follow up of the Da Qing diabetes prevention study. *Diabetes Care*. 2016;39:1550-1555.

Meet M.W.



- Annual physical
 - 2016: FPG 113, Didn't get A1c
 - 2017: FPG 100, A1c 6.4%
- Wt: 230 (Ht: 5'10")
- Family hx: Father, grandmother
- Work: Non-profit Quaker org, Retired, consulting.
- Family: Married 37 yrs, two sons married, 1 grandson
- Hobbies: gardener, "old-fashioned foodie"
- 4/17 Enrolled NDPP within DSMES, Chester County Hospital

U.S. Diabetes Prevention Timeline (~20 years)

From Research at NIH/NIDDK:

DPP/DPPOS: 1998 start, Continuing 2026

To Translation of DPP:

Real-World Studies: Early 2000s – Present

CDC National DPP: 2002*, 2012 program inception

Work to scale, evaluate and improve NDPP continues

To Medicare Service:

CMS grants study NDPP in Ys Medicare. Results in improved care, cost savings for Medicare beneficiaries: 2011- 2016

MDPP 1st preventive service model studied by CMMI, certified for expansion in Medicare: 2017 – 2018, Implement 4/2018

*2002 Congress authorized CDC to establish and manage National DPP

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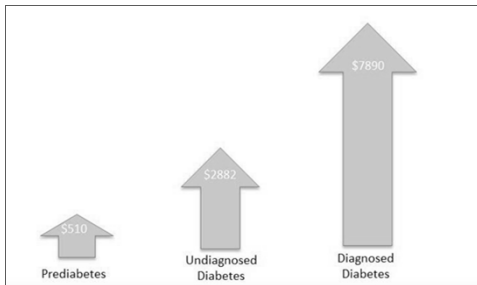
The Latest Stats - Prediabetes

- Estimated Population (U.S.)
 - 84 million, 1 in 3 people¹
 - 38% adults²
 - >50% over 65 yrs²
 - Majority overweight
- Awareness: 11%³ (↑ from 8%³)
 - 9 out of 10 people are unaware
- Progression from PreD to T2D
 - Yearly incidence of T2D is 5%–10% in people with prediabetes⁴
 - Overtime 74% estimated progress to T2D⁵
- Future:
 - By 2050, 25-28% in US estimated to have diabetes (T1D, T2D)⁵



1. CDC, National Diabetes Statistics Report – 2015 <https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf>. (Accessed 7-19-17)
 2. Morita A. Prevalence of and Trends in Diabetes Among Adults in the United States, 1988-2012. JAMA. 2015;314(10):1021-1029.
 3. Li Y, Geiss LS, Burrows NR, Rolka DB, Albright A. Awareness of Prediabetes: United States, 2005–2010. Morbidity and Mortality Weekly Report. <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6211a4.htm?cid=rr6211a4>.
 4. Lighthart S, et al. [http://www.thelancet.com/journals/landia/article/PIIS2213-8587\(15\)00362-9/abstract](http://www.thelancet.com/journals/landia/article/PIIS2213-8587(15)00362-9/abstract) (Accessed 7-19-17)
 5. Preventing Type 2 Diabetes in Communities Across the U.S. Am J Prev Med. 2013. 44(Suppl 4):S346-51.

Average Per Person Annual Costs of Care in U.S.

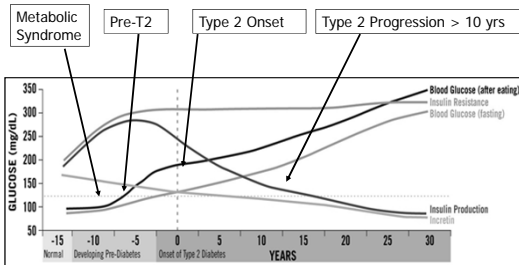


Dall TM, et al. The Economic Burden of Elevated Blood Glucose Levels in 2012: Diagnosed and Undiagnosed Diabetes, Gestational Diabetes Mellitus, and Prediabetes. Diabetes Care 2014;37:3172-79.

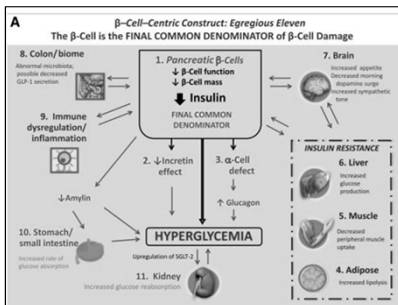
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Progression of Dysglycemia to T2 Diabetes

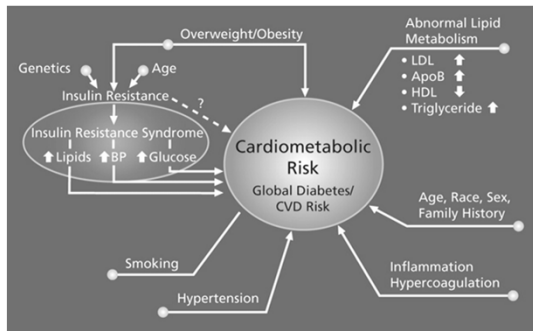


Egregious Eleven Explains Pathophysiology of Disease Progression



Schwartz S: The Time Is Right for a New Classification System for Diabetes: Rationale and Implications of the β-Cell-Centric Classification Schema. Diabetes Care. 2016;39:179–186. <http://care.diabetesjournals.org/content/39/2/179.full.pdf>

Prediabetes IS a Cardiometabolic Risk Factor



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Diagnostic Criteria^{1,2}

	Nondiabetes	Prediabetes	Diabetes (T1 or T2)
Fasting (FPG)	< 100	100 - 125	≥ 126
Random/casual (PPG)	< 140	140 - 199	≥ 200
A1c (added 2010)	5.7%	5.7 – 6.4%	≥ 6.5%

Notes:
 - Not for diagnosis of GDM
 - If results from one test are not convincingly indicative of the diagnosis, then a repeat test should be done on a different day
 - Risk is continuous and becomes disproportionately greater at the higher end of range

1. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 1997;20:1183-1197.
 2. ADA. 2. Classification and Diagnosis of Diabetes. Standards of Medical Care in Diabetes - 2018. Diabetes Care 2018; 41 (Suppl. 1): S13-S27

Testing for Diabetes or Prediabetes in Asymptomatic Adults

Table 2.3—Criteria for testing for diabetes or prediabetes in asymptomatic adults

1. Testing should be considered in overweight or obese (BMI ≥ 25 kg/m² or ≥ 23 kg/m² in Asian Americans) adults who have one or more of the following risk factors:
 - First-degree relative with diabetes
 - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
 - History of CVD
 - Hypertension ($\geq 140/90$ mmHg or on therapy for hypertension)
 - HDL cholesterol level < 35 mg/dL (0.90 mmol/L) and/or a triglyceride level > 250 mg/dL (2.82 mmol/L)
 - Women with polycystic ovary syndrome
 - Physical inactivity
 - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
2. Patients with prediabetes (A1C $\geq 5.7\%$ [39 mmol/mol], IGT, or IFG) should be tested yearly.
3. Women who were diagnosed with GDM should have lifelong testing at least every 3 years.
4. For all other patients, testing should begin at age 45 years.
5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.

Classification and Diagnosis of Diabetes:
Standards of Medical Care in Diabetes - 2018. Diabetes Care 2018; 41 (Suppl. 1): S13-S27



Prediabetes: Recommendations (2)

- If tests are normal, repeat testing carried out at a minimum of 3-year intervals is reasonable. C
- To test for prediabetes, fasting plasma glucose, 2-h plasma glucose during 75-g oral glucose tolerance test, and A1C are equally appropriate. B
- In patients with prediabetes, identify and, if appropriate, treat other cardiovascular disease risk factors. B

Classification and Diagnosis of Diabetes:
Standards of Medical Care in Diabetes - 2018. Diabetes Care 2018; 41 (Suppl. 1): S13-S27



Risk-Based Screening in Asymptomatic Children and Adolescents

Table 2.5—Risk-based screening for type 2 diabetes or prediabetes in asymptomatic children and adolescents in a clinical setting*

- Criteria
- Overweight (BMI > 85 th percentile for age and sex, weight for height > 85 th percentile, or weight $> 120\%$ of ideal for height) A
- Plus one or more additional risk factors based on the strength of their association with diabetes as indicated by evidence grades:
- Maternal history of diabetes or GDM during the child's gestation A
 - Family history of type 2 diabetes in first- or second-degree relative A
 - Race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander) A
 - Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight) B

*Persons aged < 18 years.

Classification and Diagnosis of Diabetes:
Standards of Medical Care in Diabetes - 2018. Diabetes Care 2018; 41 (Suppl. 1): S13-S27



Prevention or Delay of T2DM: Recommendations

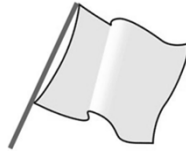
- At least annual monitoring for the development of diabetes in those with prediabetes is suggested. E
- Patients with prediabetes should be referred to an intensive behavioral lifestyle intervention program modeled on the Diabetes Prevention Program to achieve and maintain 7% loss of initial body weight and increase moderate-intensity physical activity (such as brisk walking) to at least 150 min/week. A
- Technology-assisted tools including Internet-based social networks, distance learning, and mobile applications that incorporate bidirectional communication may be useful elements of effective lifestyle modification to prevent diabetes.

Prevention or Delay of Type 2 Diabetes:
Standards of Medical Care in Diabetes - 2018. Diabetes Care 2018; 41 (Suppl. 1): S51-S54



Words We Use in Diabetes Prevention and Prediabetes

- Prediabetes is not a diagnosis, T2 Diabetes is a diagnosis
 - Different? Or a continuum?
 - Research-based "line in the sand"?
 - Pluses, minuses of diagnosis
- Do we "prevent" or delay?
 - For how long?
- Right word(s) to use?¹
 - Cure, reverse or remission
 - Metabolic surgery?



1. Buse J, et al: How Do We Define Cure of Diabetes? Diabetes Care. 2009 Nov; 32(11): 2133-2135

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Global Diabetes Prevention Research

Name/Area	Years	Study Basics	Results
Da Qing/China Intervention F/U	1986 - 1992 Ongoing	3 treatment groups: diet only, exercise only, or diet plus exercise to a control group 600 adults with IGT, 33 clinics F/U 2 yr intervals	At 6 yrs : 31-45% reduction in diet plus exercise group, lowest in exercise-only group At 20 yrs: 43% overall, 47% reduction in severe retinopathy At 23 yrs: CVD, death data (shared)
Finnish DPS (FIN-D2D) Intervention F/U			
DPP DPPPOS DPPPOS (Phase 3)			

1. Li G, Zhang P, Wang J, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. *Lancet* 2008; 371:1783-1789.

2. Lindstrom J. Improved lifestyle and decreased diabetes risk over 13 years: long-term follow-up of the randomized Finnish Diabetes Prevention Study (DPS). *Diabetologia*. 2013 Feb;56(2):284-93

3. DPPPOS (May 2016) <https://dppos.bsc.gwu.edu/documents/1124073/1127212/Version+4.2+May+1%2C+2016/14e782f2-2da9-47d1-a501-6004bcaee74e>

Global Diabetes Prevention Research

Name/Area	Years	Study Basics	Results
Da Qing/China Intervention F/U			
Finnish DPS (FIN-D2D) Intervention F/U	1993 – 2000 2013	ILI vs. usual care > 500 Finnish overweight adults with IGT 5 hospital districts Delivered as individual and group sessions	At 1 yr: 18% lost ≥ 5% body weight BG, lipid measures improved more in ILI group At 4 yrs: IGT to T2D reduced by 58% At 7 yrs f/u: 43% at 7 years At 13 yrs f/u: 38% reduction, ILI group lower absolute levels of BW, FPG, PPG, and eating healthier diet
DPP DPPPOS DPPPOS (Phase 3)			

1. Li G, Zhang P, Wang J, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. *Lancet* 2008; 371:1783-1789.

2. Lindstrom J. Improved lifestyle and decreased diabetes risk over 13 years: long-term follow-up of the randomized Finnish Diabetes Prevention Study (DPS). *Diabetologia*. 2013 Feb;56(2):284-93

3. DPPPOS (May 2016) <https://dppos.bsc.gwu.edu/documents/1124073/1127212/Version+4.2+May+1%2C+2016/14e782f2-2da9-47d1-a501-6004bcaee74e>

Global Diabetes Prevention Research

Name/Area	Years	Study Basics	Results
Da Qing/China Intervention F/U			
Finnish DPS (FIN-D2D) Intervention F/U			
DPP DPPPOS DPPPOS (Phase 3)	1998-2001 2002-2015 2015-2026	3000 participants with PreD or high risk (GDM, ethnic groups) 3 groups: ILI, metformin plus standard behavioral counseling and education (usual care) and placebo (usual care)	At 3 yrs: 3 yrs 58% reduction ILI, 31% metformin

“Unparalleled opportunity to study the clinical course of type 2 diabetes”
“Focus on the effects of metformin therapy on CVD and cancer”

1. Li G, Zhang P, Wang J, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. *Lancet* 2008; 371:1783-1789.

2. Lindstrom J. Improved lifestyle and decreased diabetes risk over 13 years: long-term follow-up of the randomized Finnish Diabetes Prevention Study (DPS). *Diabetologia*. 2013 Feb;56(2):284-93

3. DPPPOS (May 2016) <https://dppos.bsc.gwu.edu/documents/1124073/1127212/Version+4.2+May+1%2C+2016/14e782f2-2da9-47d1-a501-6004bcaee74e>

Diabetes Prevention Program (DPP): Trial Details¹



- DPP initiated: 1998, stopped early 2001
- RCT, multi-site in U.S.
 - ~3000 subjects
- 3 arms:
 - Intensive Lifestyle Intervention (ILI)
 - Metformin w/ standard care
 - Placebo w/ standard care

1. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393-403.

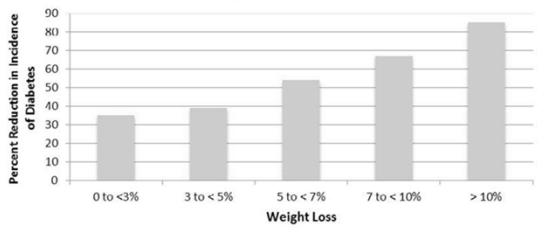
Core Goals of DPP ILI¹



- Attain weight loss of at least 5-7%
 - Maintain maximal weight loss long term
- Promote/consume healthy eating pattern (similar to the U.S. Dietary Guidelines for Americans)
- Engage in regular physical activity (at least 150 minutes of aerobic activity/week)
- Frequent individual counseling with behaviorist
 - Weekly 1st 16 wks, less frequency over time

1. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393-403.

Reduction in Risk for Diabetes by Percent Weight Loss in the Intensive Lifestyle Intervention Arm of DPP



1. From Maruthur N, et al: Early response to preventive strategies in the Diabetes Prevention Program. J Gen Int Med. 2013;28(12):1629-1636.

DPP: Weight Loss or Physical Activity?

- Wt loss = dominant predictor of reduced T2D incidence and return to normoglycemia¹
 - For each kg weight loss = 16% reduction in risk for T2²
 - Subjects who lost > 5 – 7% reduced T2 risk > 90%²
- Physical activity helps sustains weight loss
 - It plays a “supporting role” doesn’t get “best actor/actress”

1. Perreault et al. Regression from pre-diabetes to normal glucose regulation in the DPP. Diabetes Care. 2009;32(9):1583-1588.
 2. Hamman R, Wing R, Edelstein SL, et al. Effect of Weight Loss With Lifestyle Intervention on Risk of Diabetes. Diabetes Care. 2006;29(9): 2102-2107.
 3. Delahanty L, Nathan D: Implications of the DPP and Look AHEAD clinical trials for lifestyle interventions. J Am Diet Assoc. 2008;108 (4 Suppl 1): S66-72.

Transition: DPP to DPP Outcomes Study (1)

- Study Q: Does further reduction (delay) in development of T2D and development and/or progression of complications?
 - Measured annually by ADA criteria, confirmed by repeat testing
- Timeline:
 - DPP ends July 2001
 - DPPPOS began Sept 2002
- Weight status by group: b/w end DPP, start DPPPOS (~1 yr)
 - ILI: gained ~1 kg on average (had lost most in DPP)
 - Metformin: lost ~1.5 kg (then weight regain began)
 - Placebo: lost ~2 kg (had lost least in DPP)

1. Hamman R, et al: Factors Affecting the Decline in Incidence of Diabetes in the Diabetes Prevention Program Outcomes Study (DPPPOS). Diabetes. 2015 Mar; 64(3): 989-998.

Transition: DPP to DPP Outcomes Study (1)

- All participants offered quarterly ILI, modified for groups
 - Additional group classes offered to ILI
 - 57% placebo, 58% metformin, and 40% ILI attended some sessions
 - Metformin participants given unmasked drug (850 mg twice a day, as tolerated)
- At DPPPOS start: 72% not diagnosed with T2D
 - Higher proportion of ILI entered DPPPOS:
 - Without T2D (81.2%)
 - Lower fasting insulin levels, better insulin secretion
 - Lower BMI, waist circumference, fewer daily calories
 - Higher physical activity (minutes)
 - Met more DPP goals than other groups
- Participants observed continually thru DPPPOS or until T2D developed (then withdrawn)

1. Hamman R, et al: Factors Affecting the Decline in Incidence of Diabetes in the Diabetes Prevention Program Outcomes Study (DPPPOS). Diabetes. 2015 Mar; 64(3): 989-998.

Results Reduction of Incidence of T2D

	ILI*	Metformin/Std Care*
DPP1**	58%**	31%
DPPOS at 10 yrs ²	34%	18%
DPPOS at 15 yrs ^{3***}	27%	17%

*Compared to placebo/std care. All DPP participants offered lifestyle intervention post DPP, leading to reduction in differences over time.
 **71% reduction in 60 yo and older
 ***DPPOS remains an ongoing NIH/NIDDK study to 2026.

1. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 302:342-350-353.
 2. Diabetes Prevention Program Research Group 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *The Lancet*. 2009;374(9702):1677-1686.
 3. Diabetes Prevention Program Research Group Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. *Lancet Diabetes Endocrinol*. 2015;3: 866-875.

DPPOS – 15 yr F/U¹

- Conclusions¹:
 - Can prevent/delay T2D with ILI or metformin over long term
 - Regardless of DPP treatment type, participants w/ out T2D at 15 yrs had 28% lower occurrence of microvascular disease
 - Minimal incidence of CVD (HA, stroke) (still relatively young, healthy population)
 - Metformin: DPPOS largest, longest trial using drug, safe and well-tolerated; small increase in B-12 deficiency
- Summary: Weight loss key factor in preventing progression of prediabetes to type 2 and in restoring normoglycemia to some.²

1. American Diabetes Assoc. 2014 Scientific Sessions. Long-term follow-up of DPP show continued reduction in diabetes development. <http://www.diabetes.org/newsroom/press-releases/2014/long-term-follow-up-of-diabetes-prevention-program-shows-reduction-in-diabetes-development.html>
 2. Diabetes Prevention Program Research Group 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *The Lancet*. 2009;374(9702):1677-1686.

DPPOS – Predictors of Achieving Normoglycemia¹

- Diagnosis of T2 diabetes:
 - 56% lower for participants who had achieved normoglycemia sometime during DPP vs. consistent hyperglycemia (unaffected by DPP group assignment)
- Factors predicting normoglycemia:
 - Previous achievement of normoglycemia (even if transient)
 - “legacy or memory” effect?
 - Increased β-cell function and insulin sensitivity
 - Diagnosis at younger age
 - Maximum pounds lost

1. Perreault L, et al: Effect of regression from prediabetes to normal glucose regulation on long-term reduction in diabetes risk: results from the Diabetes Prevention Program Outcomes Study. *Lancet*. 2012;16:379(9833):2243-2251

Risk Stratification for Type 2 Diabetes Prevention Interventions^{1,2}

Risk Level	Adult Prevalence (%)	10 Years diabetes Risk (%)	Risk Indicators	Intervention
Very High	~15%	>30%	A1c >5.7% FPG >110	Structured Lifestyle Intervention in Community Setting (NDPP)
High	20%	20 to 30	FPG >100 Many risk factors	
Moderate	30%	10 to 20	2+ risk factors	Risk Counseling
Low	35%	0 to 10	0-1 risk factors	Build Healthy Communities

1. Gregg EW, et al. Implications of Risk Stratification for Diabetes Prevention, Am J Prev Med. April 2013 Volume 44, Issue 4, Supplement 4, Pages S375-S380.
2. Albright A: Making diabetes prevention a reality: The National DPP. 6/16/16

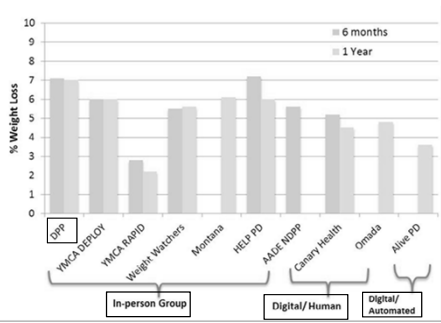
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Translating DPP to Real-World Settings to Test Models, Scale Delivery

- Timeline: Began ~early 2000s
- > 50 studies
- Variety of:
 - Models
 - Settings
 - Providers
 - In-person, virtual delivery

Comparison Weight Loss in Several Translational Studies to DPP: 6, 12 Months¹



1. Adapted from Institute for Clinical and Economic Review (ICER) (Final Report) Diabetes Prevention Programs. July 2016. <https://icer-review.org/material/final-report-dpp/>

ICER Report Conclusions Focus: Cost Effectiveness¹

- In-person DPP delivered in a group was most cost effective
- In-person DPP delivered individually is cost effective
- DPP adapted to a digital platform with a human coach is cost effective but conclusion based on fewer studies
- Unable to calculate cost effectiveness of fully digital programs due to insufficient research at this point

1. Adapted from Institute for Clinical and Economic Review (ICER) (Final Report) Diabetes Prevention Programs. July 2016. <https://icer-review.org/material/final-report-dpp/>

Conclusion of Community Preventive Services Task Force¹

- U.S.-based Community Preventive Services Task Force (CPSTF) conducted systematic review of 53 studies and 66 ILI programs published through 2015
- Results showed:
 - Healthier eating patterns and regular physical activity reduced T2D incidence by 41% vs. usual care
 - Average reduction in BW: 2.2%
 - Average reduction in FPG: 2.2 mg/dL
- More intensive programs with higher frequency of visits, individual sessions and use of additional personnel resulted in
 - Greater weight loss
 - Less likelihood of developing T2D

1. Pronk NP, Remington PL et al. Combined Diet and Physical Activity Promotion Programs for Prevention of Diabetes: Community Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2015;163:465-468

Conclusion of Community Preventive Services Task Force¹

Strong evidence of effectiveness for participation in combined diet and PA promotion programs, such as NDPP, to reduce new-onset T2D in those at risk.

1. Prank NP, Remington PL et al. Combined Diet and Physical Activity Promotion Programs for Prevention of Diabetes: Community Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2015;163:465-468

NDPP at 4 Years: At-a-Glance¹

- From 2/12 – 1/16 (data from 435 CDC-recognized programs)
- Populations studied:
 - 13K attended 4 or > sessions (threshold) 87% completed \geq 4
 - 87% completed (1st 6 months)
 - 43% completed 16 or > sessions
 - 2K participants did not meet, both populations studied.
 - Median sessions attended: 14, most in first 6 months
- Demographics:
 - 80% women
 - 56% 45 - 64 yo
 - 45% non-Hispanic white
 - 75% obese, 23% overweight



Ely EK, et al. National effort to prevent T2D: Participant-level evaluation of CDC's NDPP. Diabetes Care. 2017;40:1331-1341.

NDPP at 4 Years: At-a-Glance¹

- Average weight loss: 4.2%, 36% achieving \geq 5% (goal)
 - Greater weight loss > with number of sessions attended (5% generally achieved by people who attended \geq 17 sessions)
 - Per session attended 0.31% wt loss
 - Every 30 min more PA resulted in 0.3% wt loss
- Physical Activity 88% reported
 - Average 152 weekly minutes
 - 42% achieved goal of 150 min/week
 - PA increased with increased number of sessions attended

Conclusion: Engagement, Attendance
=
Weight loss, Prevent/delay PD

1. Ely EK, et al. National effort to prevent T2D: Participant-level evaluation of CDC's NDPP. Diabetes Care. 2017;40:1331-1341.

NDPP at 4 Years: At-a-Glance¹

- 46 and DC offer NDPP in various venues
- Virtual: since 2/15
- Coverage increasing:
 - Commercial insurance: > 70
 - Millions state employees (15 state plans)
 - Medicaid (few states including PA, PA start 1/1/18², demo projects)
- Current study in > 100 sites:
 - Why attrition?
 - Program implementation strategies
 - Enrollment drivers
 - Engagement activities
 - Program retention (early, late in program)

How to:
Hook 'em &
Hold 'em!

1. Ely EK, et al. National effort to prevent T2D: Participant-level evaluation of CDC's NDPP Diabetes Care. 2017;40:1331-1341
 2. NACDD. Working together to prevent T2D: The NDPP state engagement outcomes summit outcomes brief. <http://online.flipbuilder.com/dvos/xbz/mobile/index.html#p=1> (page 72-73)

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Nutrition Management¹

- DPP ILI focus: initial low-fat, calorie counting, person ID/set behavior change goals²
 - ADA: Recent evidence suggests that the quality of fats consumed in the diet is more important than the total quantity of dietary fat and may help reduce T2D (Ex: Mediterranean diet)
- Promote/consume healthy eating pattern (similar to the U.S. Dietary Guidelines for Americans)
 - Eating pattern one can adopt, manage and implement over time (not a "diet")
 - Least disturbance to a person's current dietary pattern
 - Consideration and respect for food and cultural preferences
- NDPP curriculum³

1. ADA. Prevention or Delay of Type 2 Diabetes. *Standards of Medical Care in Diabetes - 2018*. *Diabetes Care* 2018; 41 (Suppl. 1): S51-S54
 2. DPP Research Group. The Diabetes Prevention Program (DPP) Description of lifestyle intervention. *Diabetes Care*. 2002 Dec; 25(12): 2165-2171.
 3. Prevent Type 2D curriculum: <https://www.cdc.gov/diabetes/prevention/lifestyle-program/curriculum.html>

Nutrition Management

- Within overall healthy low-calorie eating pattern(s)¹
 - Evidence for reduced T2D:
 - Nuts
 - Berries
 - Yogurt
 - Coffee and Tea
 - Evidence for increased T2D:
 - Red meats
 - Sugar-sweetened beverages
- Studies in T2D prevention span from vegan to ketogenic
 - Consumer and clinician confusion ensues
 - Media headlines, over promises
- **BIG Q: What can people reasonably follow long term?**

1. ADA. Prevention or Delay of Type 2 Diabetes. *Standards of Medical Care in Diabetes - 2018*. *Diabetes Care* 2018; 41 (Suppl. 1): S51-S54

Recent “Diet” Weight Loss Study

- 2/18 JAMA: DIETFITS RCT¹
- Q: What is the effect of a healthy low-fat (HLF) diet vs a healthy low-carbohydrate (HLC) diet on weight change at 12 months and are these effects related to genotype pattern or insulin secretion?
- Subjects: 609 adults, 18 to 50 yo without T2D, BMI: 28 and 40
- Intervention:
 - “RD/health educators” delivered the behavior modification intervention in 22 diet-specific small group sessions over 12 months
 - Sessions focused on achieving the lowest fat or carbohydrate intake that could be maintained long-term and emphasized diet quality
- Mean 12-month macronutrient distributions (end): 48% vs 30% for carbohydrates, 29% vs 45% for fat, and 21% vs 23% for protein
- Conclusions:
 - Weight change (12 mos) not significantly different for HLF vs. HLC diet group
 - No significant diet-genotype interaction
 - No significant diet-insulin interaction

1. Gardner C, et al. Effect of Low-Fat vs Low-Carbohydrate Diet on 12-Month Weight Loss in Overweight Adults and the Association With Genotype Pattern or Insulin Secretion The DIETFITS Randomized Clinical Trial. *JAMA*. 2018;319(7):667-679

Services for NDPP and MNT

- Strongest evidence for diabetes prevention comes from DPP delivered as NDPP¹
 - Year-long lifestyle change, structured program (wt loss /maintenance, healthy food choices, healthy eating behaviors, physical activity)
 - Cost-effective, scaleable
 - Increasingly covered by Medicare (4/18), Medicaid, private-payers, state employers, others
- Individualized MNT is effective in lowering A1c in those with prediabetes¹

1. American Diabetes Association. *Standards of Medical Care in Diabetes - 2018*. 5. Prevention or delay of T2 Diabetes. *Diabetes Care*. 2018;41(Suppl. 1):S53-S54.

Providers for NDPP and MNT

- NDPP/MDPP: Lifestyle Coaches must have attended CDC-Recognized Lifestyle Change Program. Maybe HCP, but credentials not required.¹
 - The use of community health workers to support DPP efforts has been shown to be effective with cost savings
 - Lifestyle Coaches: “facilitate don’t educate”
- MNT provided by RDN effectively improves outcomes, QOL and is cost-effective²
- Service vs. program?

1. CDC: DPP Standards and Operating Procedures. <https://www.cdc.gov/diabetes/prevention/pdf/dpp-standards.pdf> (1/1/2015) [New 3/1/18]; List of CDC-recognized LSC Programs: <https://www.cdc.gov/diabetes/prevention/lifestyle-program/staffing-training.html>.
 2. AND: Role of MNT and RDN in prevention and treatment of prediabetes and type 2 diabetes. *J Acad Nutr Diet*. 2018;118(2):343-352.

Outline

- Latest Stats
- Disease Onset, Continuum
- Diagnostic numbers, recommendations
- Research – clinical
- Research – translational
- Management – nutrition
- Management – glucose lowering medications

U.S. FDA: Approval GL Meds for Prediabetes

- None approved for prediabetes
- No clear FDA pathway
 - 2008 draft industry guidance never finalized
 - States: “FDA’s expectation for safety of prevention-related products likely to be higher than for T2D.”
- Manufacturer interest, potential ROI?
- Prediabetes is not a disease state (line in the sand?)
- Prescribing any of these meds is “off-label”
- Yes, prescribed, metformin mainly, but barely



1. Cefalu WT, Buse JB, Tuomilehto J, et al. Update and Next Steps for Real World Translation of Interventions for Type 2 Diabetes Prevention: Reflections from a Diabetes Care Editors’ Expert Forum. *Diabetes Care* 2016;39:1186-1201

Pharmacologic Interventions for Prevention: Recommendations

- Metformin therapy for prevention of type 2 diabetes should be considered in those with prediabetes, especially for those with BMI ≥ 35 kg/m², those aged <60 years, and women with prior GDM. A
- Long-term use of metformin may be associated with biochemical vitamin B12 deficiency, and periodic measurement of vitamin B12 levels should be considered in metformin-treated patients, especially in those with anemia or peripheral neuropathy. B

Prevention or Delay of Type 2 Diabetes: Standards of Medical Care in Diabetes - 2018. Diabetes Care 2018; 41 (Suppl. 1): S51-S54



Successful Use of Metformin in DPP/DPPOS

- Though lifestyle change most successful across all participants metformin was as effective in:
 - Participants with BMI ≥ 35 kg/m²
 - Women with history GDM, remained highly effective during 10-yr follow up
- Adherence to metformin:
 - DPP: 72%
 - DPPOS: 57%
- Metformin may be cost-saving over a 10 yr period (relative low cost of prescribing a low cost med)

1. Prevention or Delay of Type 2 Diabetes: Standards of Medical Care in Diabetes - 2018. Diabetes Care 2018; 41 (Suppl. 1): S51-S54
 2. Cefalu WT, Buse JB, Tuomilehto J, et al. Update and Next Steps for Real World Translation of Interventions for Type 2 Diabetes Prevention: Reflections from a Diabetes Care Editors' Expert Forum. Diabetes Care 2016;39:1186-1201

Metformin Use for Prediabetes: Remains Low

- Nationwide sample > 17K, 19-58 yo with prediabetes in U.S. from 2010-2012
 - 3.7% prescribed overall
 - 7.8% meet ADA guideline > BMI, GDM history
- Reasons:
 - Lack knowledge of DPP study
 - Reluctance providers, people to "medicalize" prediabetes
 - Lack of FDA approval is hurdle (prescribers? insurance?)

1. Cefalu WT, Buse JB, Tuomilehto J, et al. Update and Next Steps for Real World Translation of Interventions for Type 2 Diabetes Prevention: Reflections from a Diabetes Care Editors' Expert Forum. Diabetes Care 2016;39:1186-1201

Research on GL Meds in Prediabetes

- Research studies using these FDA approved meds have shown decrease in incident T2D (varying degrees)
 - Metformin
 - α-glucosidase inhibitors
 - Orlistat (weight loss med)
 - GLP-1 receptor agonists
 - Thiazolidinediones
- Metformin:
 - Strongest, longest evidence base (DPP/OS)
 - Long term safety
 - Low cost
 - Minimal side effects

Prediabetes to T2 Diabetes IS Progressive, Not Static

- Goal:
 - Achieve, maintain A1c & glucose targets to prevent, delay, and minimize chronic complications
- EARLY, AGGRESSIVE action can prevent/delay transition from prediabetes to T2D¹
- Can a GL lowering medication assist?
 - Age, years of prediabetes?
 - Risk for T2D development?
 - Ability, success at weight control, healthy eating, physical activity?
- HCP must: Regularly & objectively explain progressive nature T2D²

1. Cefalu WT, Buse JB, Tuomilehto J, et al. Update and Next Steps for Real World Translation of Interventions for Type 2 Diabetes Prevention: Reflections from a Diabetes Care Editors' Expert Forum. *Diabetes Care* 2016;39:1186-1201.
 2. American Diabetes Association. Standards of Medical Care in Diabetes - 2017. Pharmacologic Approaches to Glycemic Treatment. *Diabetes Care* 2017; 40 (Suppl. 3): S64-S74.

Weight Effects of Common GL Meds

Medication Category	Impact on Weight
GLP-1 Receptor Agonists	↓
SGLT-2 Inhibitors	↓
Metformin	neutral or ↓
DPP-4 Inhibitor	neutral
Insulins (all)	neutral or ↑
Sulfonylureas	↑

Repurposing Diabetes Drugs for Prevention “Evidence-Free Zone”

- **SGLT-2 inhibitors:**
 - A1c and BW reduction, CV benefits (empag, canag) (in T2D pop) no trials in preD yet
 - “Unlikely to happen in the foreseeable future” (cost large trial, cost med)
- **GLP-1 agonists:**
 - A1c and BW reduction, β -cell function improves
 - Semaglutide (Ozempic) injectable upcoming study in obesity, high-dose liraglutide (Saxenda for obesity) has shown T2D delay over 3 yrs
- **DPP-4 inhibitors:**
 - β -cell protection (?), more adherence-friendly, lower cost agent (generic closer to reality than others) (weight neutral, no CV benefit)
- **α -glucosidase inhibitors:**
 - Recent study showed 18% delay new-onset T2D
- Lack of clear regulatory pathway for prediabetes remains an obstacle for manufacturers

1. Close Concerns: Controversies to Consensus in Diabetes, Obesity and Hypertension (CODHy). Tel Aviv, 2/21-2/22.

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