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Uma Mudaliar Date

Do lifestyle interventions modeled after the Diabetes Prevention Program change weight, blood glucose and A1c? A meta-analysis

By

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Masters in Public Health

Global Health

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M.D., University at Texas Southwestern Medical Center, 2009

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An abstract of

A thesis submitted to the Faculty of the
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Abstract

Do lifestyle interventions modeled after the Diabetes Prevention Program change weight, blood glucose and A1c? A meta-analysis

By Uma Mudaliar

This manuscript is a systematic review and meta-analysis of studies in the US which implemented principles tested in the Diabetes Prevention Program's Lifestyle Intervention, which has shown to effectively help participants with prediabetes decrease their risk of progressing to diabetes by 58%. We included all US based studies published between January 2003 and April 2011 which evaluated a DPP based intervention in people 18 years and older at high risk of diabetes which reported pre- and post-intervention values in weight, fasting blood glucose, or hemoglobin A1c.

A total of thirty-two studies met eligibility for inclusion in this meta-analysis by reporting one or more outcomes of interest. All studies reported weight change, seventeen had pre- and post-intervention data on FBG (capillary or venous), and six had follow up measures on HbA1c. In total, there were 5,094 participants enrolled across all studies. On average, participants' mean age was 54.5 years, 73.1% were female, and BMI was 34.0 kg/m^2.

Mean absolute weight change was -4.18 kg (95% CI: -5.12; -3.24), mean change in A1c was -0.19%% (95% CI: -0.28; -0.11) and mean change in fasting blood glucose was -2.68 mg/dl (95% CI:-4.15; -1.11). Despite the modifications made to the original DPP intervention, the translation into real world settings still accomplished similar decreases in weight, FBG and HbA1c as the original DPP study.

Diabetes is fortunate to have an early, reliable predictor of future disease risk. The opportunity to intervene early in approximately 79 million in the US with prediabetes with timely referral to lifestyle intervention programs is currently missed. Although patients are often advised to lose weight and make dietary changes, the ability of standard advice alone is not effective. Many of these programs show great promise in decreasing the cost, incidence, morbidity and mortality of diabetes.

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Introduction

Diabetes currently affects approximately 12% of the US population.[1] Together with an ageing population and rising incidence, prevalence is estimated to increase to 25% by 2050.[2] An additional 35% of US adults (79 million adults) 20 years or older have prediabetes, which puts them at over 4 times the risk of progression to diabetes compared to those who are normoglycemic.[3,4] Adults with diabetes have 2 to 4 times higher rates of death from heart disease or stroke, and have medical expenses that are more than two times higher than for people without diabetes.[5] Diagnosed diabetes alone led to an economic burden of $245 billion in 2012, with $176 billion in direct medical expenditures secondary to higher use of healthcare services in this population. This translates to over $700 for every American regardless of disease status.[5-7]

There is however evidence that diabetes onset can be delayed, at least in people at high-risk of converting (i.e., those with prediabetes). Large studies, including the US Diabetes Prevention Program (DPP) Study, have shown that intensive and structure lifestyle interventions can lower the incidence of diabetes, relative to basic lifestyle advice, by 58%.[7-12] Although primary prevention of diabetes through lifestyle intervention is deemed cost-effective, the first year costs of the DPP study lifestyle intervention was prohibitively expensive ($1,399 per participant), which limits scalability for the nearly 79 million Americans with prediabetes who would be eligible for intervention.[13-15] To find lower-cost alternatives to the resource-intensive DPP intervention, a number of studies have modified the original DPP- lifestyle intervention for typical clinic and community settings in the US. Lifestyle and cultural patterns vary significantly, across and even within communities, necessitating tailoring of interventions to the populations depending on regional and ethnic differences. Across these studies in diverse U.S. settings which utilize the same DPP principles with the aim of reducing diabetes incidence, little is known about the effectiveness of the interventions on aggregate, and even less is known regarding the impacts of these interventions on actual glycemia levels.

Increased levels of glycemia in the prediabetes range can be a simple and accurate predictor not only of future type 2 diabetes risk but also increased risk of subsequent cardiovascular disease.[16] To update a prior meta-analysis which evaluated aggregate weight change across diabetes prevention translation studies, and to investigate the change in glycemic markers (fasting blood glucose [FBG] and glycated hemoglobin [HbA1c]),[17] we systematically compiled all existing and new data and performed a meta-analysis.

Methods

Study Selection

The search strategy used for the prior meta-analysis included studies published from January 2003 to April 2011.[17] To identify all additional studies, we systematically searched the same databases (MEDLINE, EMBASE, Cochrane Library, and Clinicaltrials.gov electronic databases) for translation (or effectiveness) studies based in the US that were published between April 1, 2011 to April 1, 2013 which assessed lifestyle interventions which adhered to the DPP trial principles in real world settings. The original trial emphasized calorie restriction together with a minimum of 150 minutes of moderate physical activity per week with the aim of achieving 5-7% weight reduction; thus, we excluded studies that solely tested the impacts of dietary advice. We used medical subject heading and free text terms related to diabetes and prevention (see Appendix for further details.)

To be considered for inclusion, studies had to meet three inclusion criteria. First, the study needed to report on a DPP-based intervention in the US and describe both the exercise and dietary components of the intervention. Second, studies had to involve patients $\geq$ 18 years old who were at high risk of diabetes. "High risk" was defined as participants who met any definition of prediabetes – any abnormal screening glucose or oral glucose tolerance test (OGTT) measure indicating impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or a random blood glucose between 110-199 mg/dl. The multi-ethnic population of the US has higher rates of diabetes among Asian Americans, Hispanics, and non-Hispanic

blacks compared to non-Hispanic whites.[5] Therefore we chose to evaluate populations who qualified as high risk by criteria additional to the traditional classification by blood glucose testing. This other accepted definition of "high risk" is based on the American Diabetes Association's guidelines for diabetes screening and include participants who were overweight (body mass index [BMI] $\geq$ 25 kg/m^2) with one additional risk factor (such as race [African American, Latino, Native American, Asian American, or Pacific Islander], strong family history, or a personal history of abnormal blood pressure (BP), high density lipoprotein [HDL], triglycerides, cardiovascular disease [CVD], or gestational diabetes [GDM]). The final criterion was that studies must have also reported pre- and post-intervention data on at least one of the following measures: weight, HbA1c, or fasting blood glucose (venous or capillary).

We excluded studies that were based outside the US, involved children or adolescents, or if the lifestyle intervention did not conform to the principles tested in the DPP trial. Interventions that included medications (including metformin) were also excluded. Studies that involved patients with previously diagnosed diabetes (unless it was less than 50% of the study population), polycystic ovarian syndrome, current pregnancy, or participants who were recently post-partum patients were also excluded.

Abstracts were reviewed by two independent authors who used pre-specified search criteria to determine study eligibility. All discrepancies were resolved by consensus of the study team. When data was not fully reported, authors were contacted for further study details.

Quality Assessment

The DPP trial findings already established that standard lifestyle advice alone has very a low level of efficacy in terms of reducing diabetes incidence. Also, in the trial, adherence to lifestyle principles, and weight loss in particular, were correlated with reduction in diabetes incidence.[18] Additionally, most translation studies have small sample sizes and limited funding, and are most commonly designed with a single group, pre- and post- intervention design which makes allocation and blinding largely irrelevant.[9] Therefore, to assess the quality of the studies included and provide

meaningful data to aid readers' interpretation of the available literature, we applied a modified scoring system based on Jüni's criteria to evaluate each study on five criteria.[19]

First, the target population must have been defined as high risk using at least two of the following measures: self-reported risk factors (race, family history), blood glucose testing, or anthropometric measurements (e.g., BMI). The second criterion assessed whether studies used steps to minimize bias from attrition by using an intention to treat analysis, achieving low attrition rates ($\leq$ 20%), or comparing characteristics of completers and non-completers. The third criterion was focused on credibility of study findings based on whether studies had sample sizes $\geq$ 100 participants or provided estimates of precision (uncertainties or distribution of the estimates). The fourth criterion was that the study should have reported on four or more of the following aspects of translating their evidence: describing the process of designing the program, describing the enrollment process, documenting session attendance, reporting costs and/or resource inputs, documenting the training process or qualifications of personnel, or describing the qualitative feedback from participants or providers. Lastly, we noted the studies that had a control group (randomized, matched, or unmatched comparison). Further details are in the Appendix.

Data Analysis

Data on study populations, study design, characteristics of the intervention (number of core and follow up sessions, duration of intervention and follow up time period), and data on baseline and follow up values for each outcome (weight, FBG, and HbA1c) were systematically extracted and compiled into a database. Descriptive characteristics of the study populations were pooled and mean estimates were weighted according to sample size. Data for the change and standard errors for each of the three outcomes were analyzed with the statistical software Mix 2.0 to determine the absolute mean change in each outcome from baseline to the last reported time point. We used a random-effects meta-analysis model to account for heterogeneity between studies which was quantified with the I^2 and corresponding χ^2 p-value for heterogeneity. All data from each pre-post intervention were pooled, and each study was weighted

proportionally to the inverse of the variance, which account for sample size through the use of standard error.

Results

A total of thirty-two studies met eligibility for inclusion in this meta-analysis by reporting one or more outcomes of interest. Twenty four articles from the initial review were included, with eight new studies published from April 2011 to April 2013. All studies reported weight change, seventeen had pre- and post-intervention data on FBG (capillary or venous), and six had follow up measures on HbA1c. Eighteen studies were single group pre-post studies, four studies had two intervention arms with pre-post study design (each contributing two separate groups for analysis), and ten studies had separate control arms, resulting in thirty-six distinct single pre-post groups.

In total, there were 5,094 participants enrolled in the studies. On average, participants' mean age was 54.5 years, 73.1% were female, and BMI was 34.0 kg/m^2. Across all studies combined, non-Hispanic whites (NHW) accounted for 54.8% of study populations, though many community focused studies, for example, those based in African American churches and Latino communities, had single-race/ethnicity populations. Of the thirty-six groups, eleven used some type of glucose measure to classify participants' risk for diabetes, eighteen used BMI with an additional risk factor, and seven allowed either definition to classify risk status.

Programs most commonly made modifications to the original DPP intervention by changing the number or duration of core sessions (originally sixteen sessions offered over 24 weeks), offering group sessions (instead of individual one-on-one sessions), modifying the type of lifestyle coach (originally qualified dieticians), and by changing or removing the monthly maintenance where participants were seen face-to-face every 2 months for the remainder of the follow up period to promote continued adherence.

Regarding characteristics of different interventions, the number of core sessions offered ranged from one to twenty-four, with a mean of 13.1 core sessions offered and 10.8 sessions attended (range: 1.0 to 22.5). Twenty-one interventions offered a maintenance component, which varied from emails to intermittent group sessions. Average study duration was 8.94 +/- 4.07 months (range: 3 to 15 months.) Across all studies, overall attrition was 19.11% (range: 0.00 to 43.18%).

Findings Stratified by Outcome

Across all studies, mean baseline weight was 100.00 ± 8.58kg and mean absolute weight change was -4.18 kg (95% CI [-5.12; -3.24], I^2 99.28%, p for heterogeneity of 0.00) (As seen in Figure 1). When only studies with a control arm were analyzed, the incremental weight loss was 2.84 kg higher for intervention versus control groups.

The six studies which evaluated HbA1c showed a mean baseline HbA1c of 5.78 ± 0.33% and an average change of -0.19% (95% CI [-0.28; -0.11], I^2 84.74%, p for heterogeneity of 0.00.) (As seen in Figure 2) The analysis of the seventeen studies reporting FBG showed a baseline of 105.00 ± 5.06mg/dl and mean change over the course of all studies was -2.68 mg/dl(95% CI [-4.15; -1.11] I^2 91.33 %, p for heterogeneity of 0.00.) (As seen in Figure 3).

Table 1

Value	Number of studies	Mean baseline	Mean follow up	Mean change (95% CI)
Weight (kg)	32	100.00 +/ 8.58	95.80	-4.20(-5.12; -3.24)
A1c (%)	6	5.78 +/- 0.33	5.59	-0.19 (-0.28; -0.11)
FBG (mg/dl)	17	105.00 +/- 5.06	102.32	-2.63(-4.15; -1.11)

Figure 1: Mean weight change of study participants

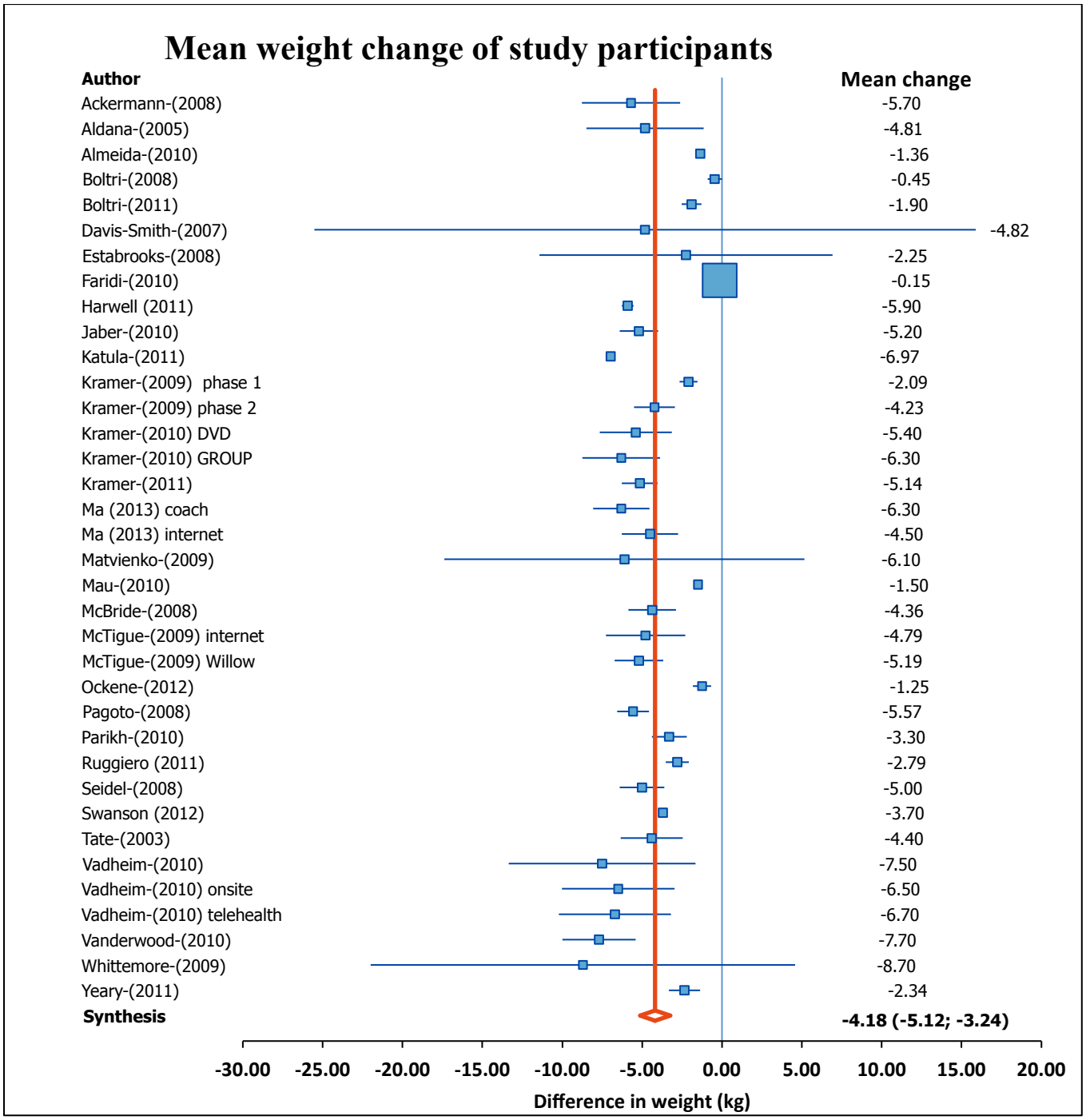


Figure 1: Analysis of all thirty-six study groups which reported weight change from baseline to end of follow up period. Data was analyzed with Mix 2.0 using random effects method with the weighting of each study proportional to the inverse of the variance. Study weight is indicated by the size of the box, and horizontal lines indicate the 95% confidence interval. The red line indicates the overall percentage weight change, and summary diamond indicates pooled estimate with reported mean (95% CI).

Figure 2: Mean change in fasting blood glucose in study participants

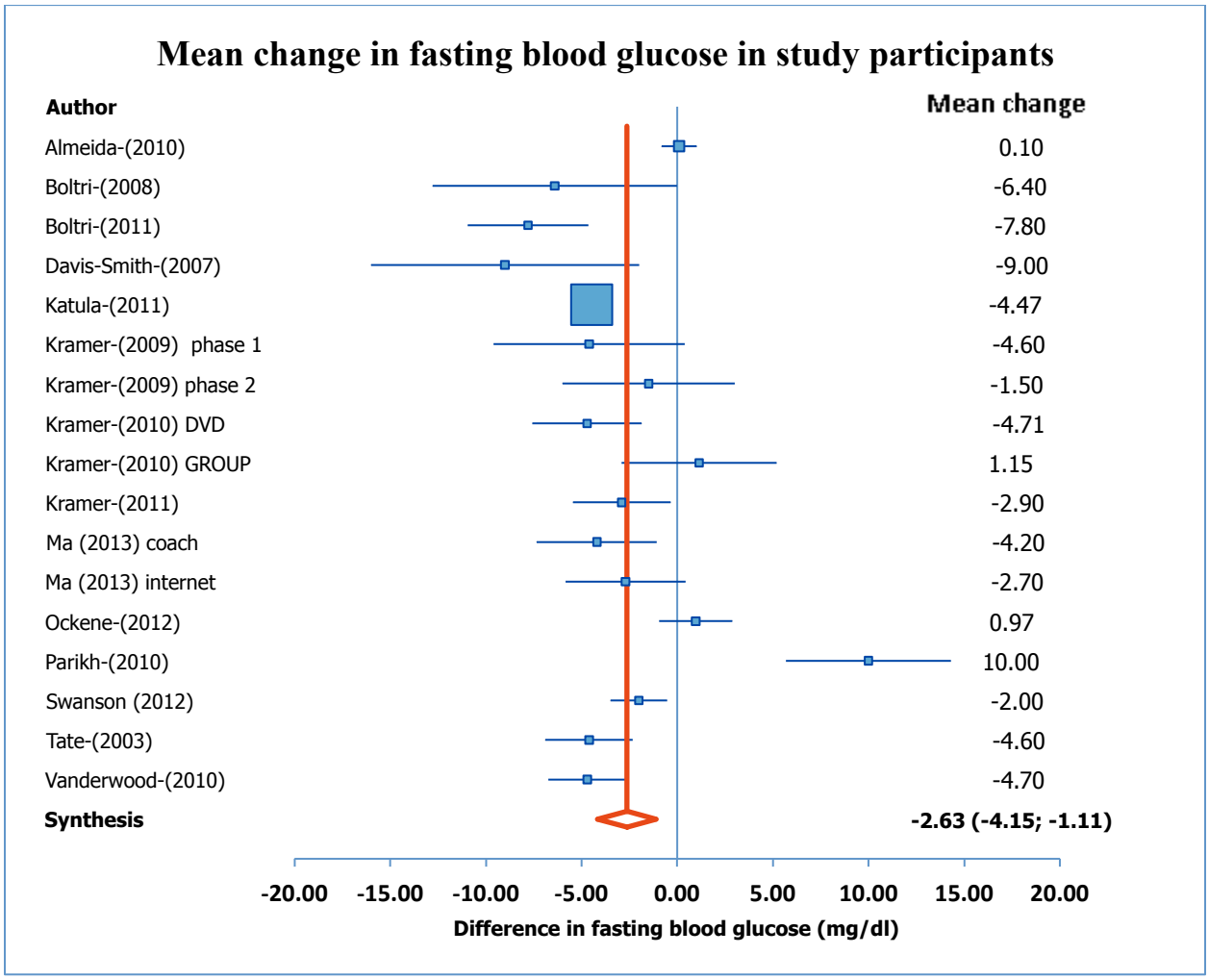


Figure 2: Analysis of all seventeen study groups which reported fasting blood glucose values from baseline to the end of follow up period. Data was analyzed with Mix 2.0 using random effects method with the weighting of each study proportional to the inverse of the variance. Study weight is indicated by the size of the box, and horizontal lines indicate 95% confidence interval. The red line indicates the overall percentage weight change, and summary diamond indicates pooled estimate with reported mean (95% CI).

Figure 3: Mean change in A1c in study participants

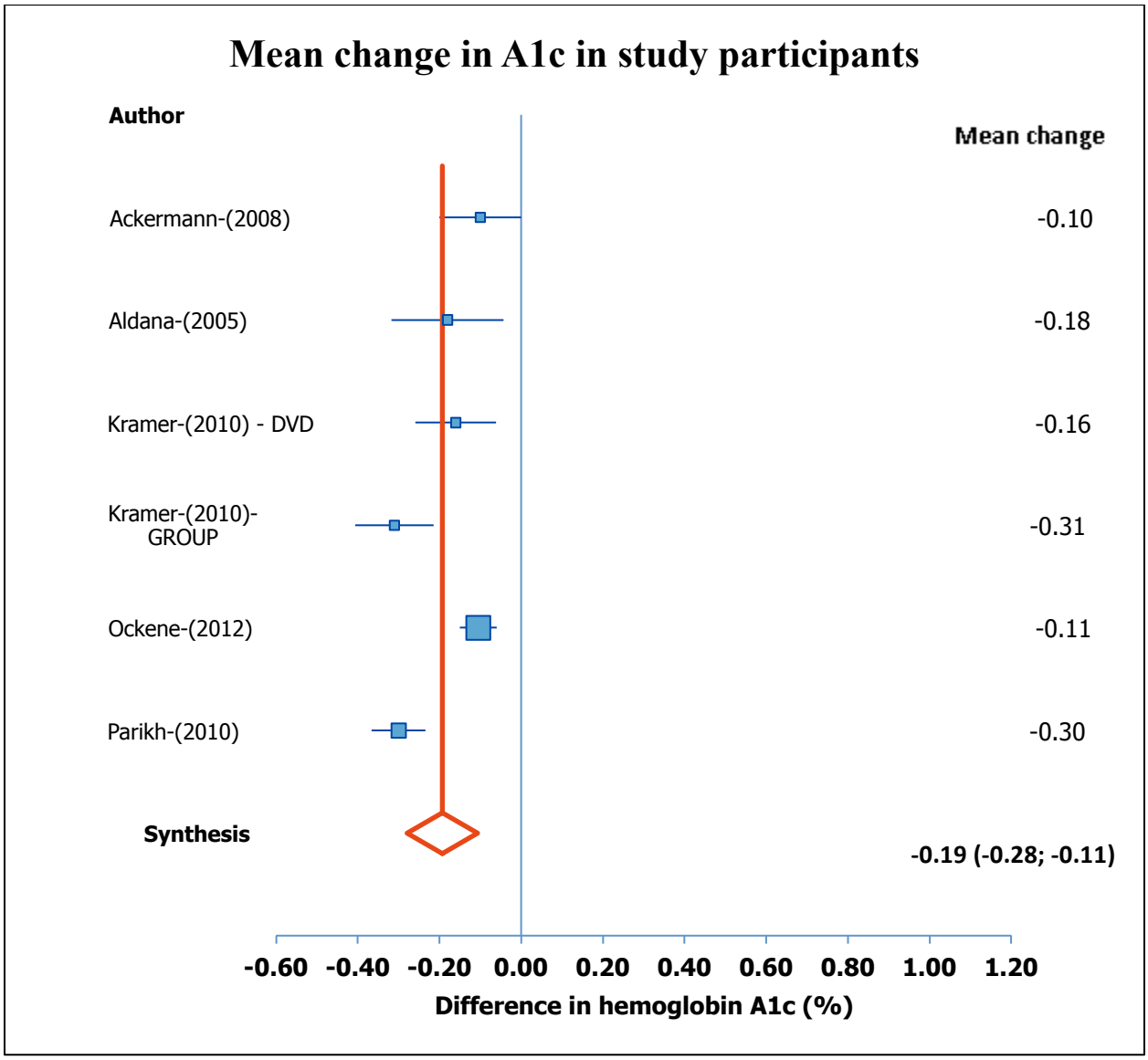


Figure 3: Analysis of all six study groups which reported change in hemoglobin A1c from baseline to end of follow up period. Data was analyzed with Mix 2.0 using random effects method with the weighting of each study proportional to the inverse of the variance. Study weight is indicated by the size of the box, and horizontal lines indicate 95% confidence interval. The red line indicates the overall percentage weight change, and summary diamond indicates pooled estimate with reported mean (95% CI).

Discussion

This is the first meta-analysis to estimate the aggregate impact of intensive diabetes prevention lifestyle interventions on weight *and* glycemic measures. Most translation studies of the DPP have limited their evaluations to the effect of an intensive lifestyle intervention on weight. A mean decrease in HbA1c of 0.2% is known to correlate with approximately a 2.8 mg/dl decrease in the estimated average serum glucose levels, which is concordant with our findings.

The baseline characteristics of those who enrolled had similar age, BMI, fasting glucose, and A1c when compared to those of the original DPP, but a slightly higher starting weight (100.0 vs. 94.1 kg) and higher percentage of females (72.3 vs. 68.0%).[9] The original DPP participants had a greater mean weight loss than the participants in our study (5.6 kg vs. 4.2 kg), which was likely due to the more resource intensive intervention with more sessions, individualized support, tailoring of the intervention to an ethnically diverse population, possibly higher motivated enrollees, and longer duration of follow-up to promote adherence.[9] However, this weight loss correlates well with the Finnish Diabetes Prevention Study (DPS) participants who had a similar weight loss of 4.2 kg.[7] When we compared all intervention studies with their respective control groups, the incremental change in weight was approximately 2.9 kg greater weight loss.

These differences are likely secondary to modifications made to the DPP, often in an attempt to decrease cost. Over 80% of the study populations had group interventions, fewer mean core sessions were offered (13.1 sessions compared to sixteen), and only 58% offered a maintenance component. Additionally, the method of delivery of the intervention was variable, as some interventions were clinic based, others community based, and some self-directed using virtual media support (video conference or internet-based intervention delivery).

In the studies that reported glycemic measures, participants also had similar baseline values of glycemia as in the DPP, with a mean baseline FBG of 105.0 mg/dl (vs. 106.3 mg/dl) and HbA1c of 5.8% (vs. 5.9%). In the DPP, mean FBG decreased by approximately 5.0 mg/dl and mean A1c decreased by 0.10%. In the DPS, mean FBG decreased by 4.0 mg/dl. The participants in the translation studies had a

less significant decrease in glucose (2.7 mg/dl) however had a greater decrease in HbA1c (0.2%). However, the results for HbA1c and glucose likely do not correlate with each other as different studies reported on these measures, and many which reported on FBG did not report on HbA1c. For people with diabetes, every percentage point drop in HbA1c can reduce the risk of microvascular complications (eye, kidney and nerve) by 40% but it is still unclear how reductions in HbA1c affect those who do not yet meet criteria for the diagnosis of diabetes, such as in our study population[5].

Additionally, the DPP enrolled patients with both impaired glucose tolerance (IGT) and impaired fasting glucose, who are at approximately 3 times higher risk of diabetes compared to those with impaired fasting glucose alone[3]. The Finnish DPS used patients classified only by OGTT, who are only at slightly higher risk (1.2 times) compared to those with IFG alone[3]. No translation studies in the US solely used the oral glucose tolerance test (OGTT) to determine high risk status, which suggests the participants in the DPP-translation studies are at slightly lower risk. Assuming the participants are at a lower baseline risk, it would be more difficult to find significant decreases in glucose measures. Previous evaluation of people without diabetes at baseline showed a hazard ratio for death from any cause of 1.10 (95% CI 1.09-1.11). for each 18 mg/dl (or 1 mmol/dl) increase above 100 mg/dl (assuming a log linear relationship above the 100 mg/dl.)[20]

Within the participants in the DPP translation studies, rates of enrollment were approximately the same (72%) when we compare the individual vs. group interventions with no significant difference in rates of attrition. The programs that reported their findings were most often by practitioners who reported their work in this field, leading to geographic clustering of studies found in Georgia, Montana, and Pennsylvania. With the recent CDC rollout of the national DPP, six multi-state organizations were recently granted the funding to expand the availability and geographic reach of these programs. There is also a growing number of centers across the US who are becoming recognized by the CDC's National Diabetes Prevention Program as recognized providers of diabetes prevention lifestyle interventions if they utilize the curriculum that was initially developed and evaluated by the DPP.[21]

The participants who agreed to participate in the DPP are likely more motivated and interested in losing weight than that of the general population; our study, therefore, is a better representation of the typical real-life high-risk populations in the US. Among the studies we examined, there were three main definitions of target communities—geographic, ethnic, and workplace. In groups with higher levels of social cohesion, such as one intervention in an African American church, participants continued to meet for a year after the conclusion of the program. The three studies with the lowest rates of attrition were based in churches and workplaces. These settings are more convenient as participants do not have to find additional time to travel to participate in these interventions. Qualitative feedback from participants showed the importance of tailoring the intervention to be more culturally appropriate, especially in immigrant populations where language and cultural/religious norms may differ.

The original DPP showed the superiority of lifestyle changes to metformin-- these programs are more efficacious in decreasing the incidence of diabetes, more sustainable given the changes in exercise which persisted after 4 years, have less side effects than metformin, and have collateral benefits for blood pressure and lipid levels. However, currently, the availability, accessibility, and likelihood of insurance reimbursement for a lifestyle program is much lower than that for metformin, which is likely the largest barrier to real-world translation. The high rates of enrollment (72%) illustrate the demand among patients, especially once they are aware of their risk status.

Limitations

The main limitation of our analysis was the heterogeneity of the studies included, which is inherent given our desire to include all currently available data. As of now, there are still limited data on real-life implementation of lifestyle modification programs to prevent diabetes and few that have well-designed, large sample-size studies. To contend with the variability between the studies, as reflected by the high I^2 values, we used a random effects model to account for heterogeneity between studies. These sources of heterogeneity were most likely secondary to differences in the designs of intervention studies, such as different durations of follow-up (from 3 to 15 months), location of delivery, and modifications to

the original DPP program. Other sources of heterogeneity include differences in the populations under evaluation (racially, geographically and by level of risk). Variability in reporting methods likely contributed to discrepancies in the data as well. And lastly, even if these differences were equalized, multiple small studies are not likely to generate the same results as one large study.

However this is the first meta-analysis to evaluate the intermediate cardiovascular risk factor changes in DPP based interventions. To minimize missing or incomplete data, all attempts to contact authors were made. Overall, the population of interest had similar baseline characteristics, and despite heterogeneity, our findings correlate fairly well with those of the DPP and DPS. Additionally, this analysis is the first to aggregate the limited available data.

Conclusion

Despite the modifications made to the original DPP intervention, the translation into real world settings still accomplished similar decreases in weight, FBG and HbA1c as the original DPP study. However, it is still unclear how and if these changes truly translate into reductions in diabetes incidence. Although this meta-analysis represents the aggregate of available translation studies, it is still unclear how to scale up lifestyle interventions while maintaining effective delivery to culturally and socially diverse populations. No clear predictors of enrollment, weight loss, or attrition emerged and given the relatively short durations of these interventions, the long term sustainability and clinical significance will need to be assessed further.

Implications and future directions

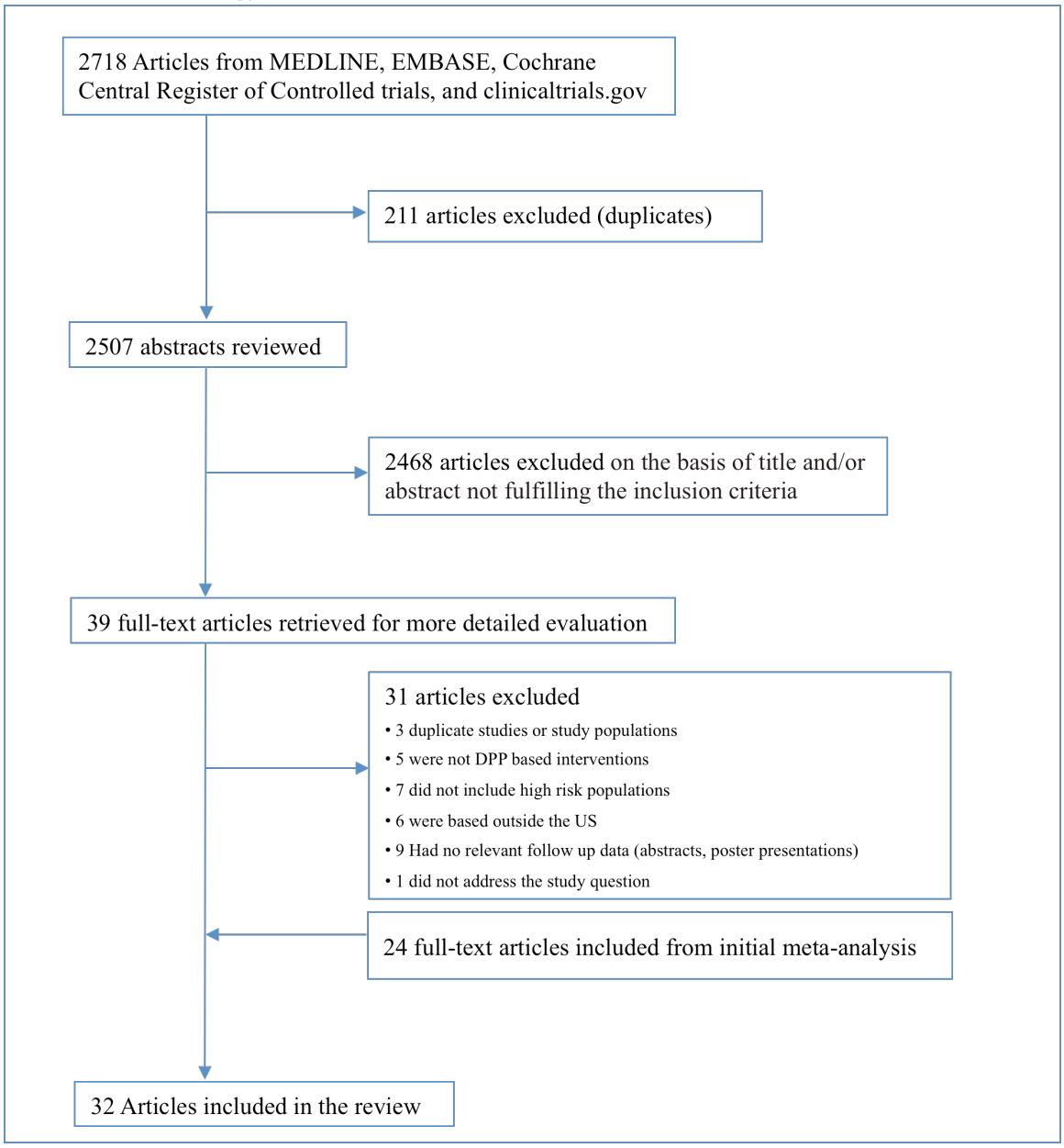
Diabetes is fortunate to have an early, reliable predictor of the development of disease. This is currently a missed opportunity to intervene, as most often patients are told to lose weight and make dietary changes. However, the ability of standard advice alone was shown ineffective in the DPP and confirmed by our findings.

At the level of the healthcare provider, this clearly indicates the need for both appropriate diagnosis and referral of patients with prediabetes to structured lifestyle modification intervention programs, which are rapidly increasingly in availability.[21] Additionally, both patients and communities need to work together in the development of these programs to encourage lifestyle changes and education on dietary changes with a focus on increased exercise in their own communities to help implement change in an evidence based manner.[22] Although convenience and social cohesion, likely play a role in compliance, other factors that influence patient participation and attrition remain unclear. Finally, the support of insurance companies is needed to cover the costs of enrollment, which have decreased significantly with the provision of group interventions with lay community or media delivery. These changes have started to develop as America's Health Insurance Plans (AHIP) has started to offer lifestyle programs in four states at this time (including Florida, New Mexico, New York, and Texas.)[21]

Many of these programs show great promise in decreasing the cost, incidence, morbidity and mortality of diabetes, however sustainability of the intervention has not yet been established. It is still unclear if ongoing maintenance is needed to keep the participants from progressing to diabetes, and to date there have been no large scale studies of longer duration to provide evidence on the differences in incidence of diabetes, especially when participants of different risk levels (i.e. lower than the combined IFG-IGT participants in the DPP). Lastly, the most critical piece, which is still missing, is a clear understanding of methods to both increase uptake and decrease attrition to enable long lasting, sustainable lifestyle changes, especially in patients with the highest risk of progression to diabetes and all associated complications.

Appendix

Exhibit A: Search strategy.



This flow chart describes the number of studies that were involved in each step of the process of study selection, from the initial study search. After the application of inclusion and exclusion criteria, 32 studies met criteria and were included in the final analysis.

Exhibit B: List of search terms

Cochrane Database (from April 2011 to April 2013) **78 studies**	**ClinicalTrials.gov (from April 2011 to April 2013)** **92 studies**
#1 "Overweight/prevention & control"[Mesh] #2 "Obesity/prevention & control"[Mesh] #3 "Glucose Intolerance"[Mesh] #4 "Prediabetic State"[Mesh] #5 "Diabetes Mellitus/prevention & control" [Mesh] #6 "Diabetes Mellitus, Type 2/prevention & control"[Mesh] #7 "Prediabetic State/prevention & control"[Mesh] #8 "Metabolic Syndrome X/prevention & control"[Mesh] #9 "Prediabetic State/therapy"[Mesh] #10 "Diabetes Prevention" #11 "Diabetes risk reduction" #12 OR / 1 -11 #13 Weight Loss #14 Lifestyle #15 OR/ 13-14 #18 12 AND 15 Limits: English, Humans, Publication Date from 2011 to 2013, product type: trials	#1 overweight prevention #2 obesity prevention #3 glucose intolerance #4 impaired glucose tolerance #5 impaired fasting glucose #6 impaired fasting glycemia #7 metabolic syndrome prevention #8 diabetes prevention #9 diabetes risk reduction Limits: Studies with results, Interventional Studies, English, adults/seniors

Exhibit B (continued)

Medline via PubMed (from April 2011 to April 2013) **1426 studies**	**EMBASE (from April 2011 to April 2013)** **1291 studies**
#1 "Overweight/prevention & control"[Mesh] #2 "Obesity/prevention & control"[Mesh] #3 "Glucose Intolerance"[Mesh] #4 "Prediabetic State"[Mesh] #5 "Diabetes Mellitus/prevention & control" [Mesh] #6 "Diabetes Mellitus, Type 2/prevention & control"[Mesh] #7 "Prediabetic State/prevention & control"[Mesh] #8 "Metabolic Syndrome X/prevention & control"[Mesh] #9 "Prediabetic State/therapy"[Mesh] #10 "Diabetes Prevention" #11 "Diabetes risk reduction" #12 OR / 1 -11 #13 Weight Loss #14 Lifestyle #15 Preventive Health Services #16 Program evaluation #17 OR/ 13-10 #18 12 AND 18 Limits: English, Humans, Publication Date from 2011/04/01 to 2013/04/01	#1 overweight prevention #2 obesity prevention #3 glucose intolerance #4 impaired glucose tolerance #5 impaired fasting glucose #6 impaired fasting glycemia #7 metabolic syndrome prevention #8 diabetes prevention #9 diabetes risk reduction # 10 OR/ 1-9 #11 weight loss #12 lifestyle # 13 OR/ 10-11 #14 10 AND 13 Limits: English, Publication Date from 2011/04/01 to 2013/04/01

Exhibit C: List of Articles

		Patient characteristics					Intervention characteristics		
Study number	**Study name (year) group name**	**Age (years)**	**n**	**Male %**	**NHW %**	**Baseline BMI**	**Core Sessions**	**Months of follow up**	**Sessions (individual (i) or group (g))**
1	Ackermann-(2008)[23]	56.5	46	50.0	93.0	32.00	16	12	g
2	Aldana-(2005)[24]	46.0	37	34.3	48.6	32.01	16	12	g
3	Almeida-(2010)[25]	62.4	820	48.0	70.0	29.80	1	12	g
4	Boltri-(2008)[26]	52.0	8	42.0	0.0	31.60	16	12	g
5	Boltri-(2011)[27]	57.2	37	30.0	0.0	33.20	12	12	g
6	Davis-Smith-(2007)[28]	55.9	10	30.0	0.0	35.70	6	12	g
7	Estabrooks-(2008)[29]	57.8	39	28.2	69.0	-	12	3	I
8	Faridi-(2010)[30]	49.0	121	15.0	0.0	33.80	variable	12	i
9	Harwell (2011)[31]	-	989	19.0	-	-	16	10	g
10	Jaber-(2010)[32]	47.0	71	27.0	0.0	34.30	12	6	g
11	Katula-(2011)[33]	57.3	151	43.0	73.5	32.81	24	12	g
12	Kramer-(2009) phase 1[34]	52.9	51	18.0	73.0	36.60	12	3	g
-	Kramer-(2009) phase 2[34]	57.2	42	21.0	100.0	34.60	12	12	g
13	Kramer-(2010)- DVD[35]	57.3	22	29.0	83.0	32.85	12	3	I
-	Kramer-(2010)-GROUP[35]	61.0	26	29.0	83.0	35.09	12	3	g
14	Kramer-(2011)[36]	53.0	81	12.3	96.0	37.10	12	3	g
15	Ma (2013) coach[37]	54.6	79	51.9	77.2	31.80	12	15	g
-	Ma (2013) internet[37]	51.8	81	44.3	79.0	31.70	24	15	i
16	Matvienko-(2009)[38]	55.7	31	39.0	94.0	36.10	16	12	i
17	Mau-(2010)[39]	49.0	239	17.0	0.0	39.10	8	3	g
18	McBride-(2008)[40]	51.9	40	41.0	100.0	37.40	12	12	g
19	McTigue-(2009) internet[41]	51.9	50	24.0	86.0	36.40	16	12	g
20	McTigue-(2009) Willow[42]	53.0	81	17.0	86.0	38.89	12	12	g
21	Ockene-(2012)[43]	52.0	162	28.0	0.0	33.57	16	12	Both
22	Pagoto-(2008)[44]	48.7	118	28.0	90.7	43.30	16	4	g
23	Parikh-(2010)[45]	46.0	50	14.0	2.0	32.00	8	12	g
24	Ruggiero (2011)[46]	37.9	69	7.2	0.0	31.19	16	12	g
25	Seidel-(2008)[47]	54.0	88	15.9	72.7	36.20	12	6	g
26	Swanson (2012)[48]	62.0	221	33.0	88.0	31.20	4	6	g
27	Tate-(2003)[49]	49.8	46	9.0	89.0	32.50	5	12	I
28	Vadheim-(2010)[50]	50.5	101	12.0	92.5	36.20	16	10	g
29	Vadheim-(2010) onsite[51]	53.0	13	31.0	-	34.00	16	4	g
-	Vadheim-(2010) telehealth[51]	50.0	14	7.0	-	38.70	16	4	g

30	Vanderwood-(2010)[47]	52.3	1003	20.0	92.5	35.10	16	10	g
31	Whittemore-(2009)[52]	48.2	31	10.0	48.0	40.00	11	6	I
32	Yeary-(2011)[53]	50.8	26	15.0	0.0	35.00	16	4	g

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