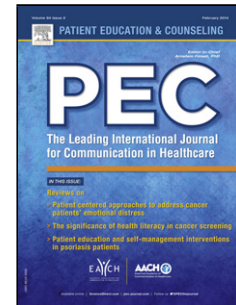


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Author: Sharon Brown A. Alexandra A. García Adama
Brown Betsy J. Becker Vicki S. Conn Gilbert Ramírez Mary
A. Winter Lisa L. Sumlin Theresa J. Garcia Heather E. Cuevas



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Biobehavioral Determinants of Glycemic Control in Type 2 Diabetes: A Systematic Review and Meta-analysis

Sharon A. Brown^a
Alexandra A. García^a
Adama Brown^a
Betsy J. Becker^b
Vicki S. Conn^c
Gilbert Ramírez^d
Mary A. Winter^a
Lisa L. Sumlin^a
Theresa J. Garcia^e
Heather E. Cuevas^a

^aThe University of Texas at Austin, School of Nursing, Austin, TX, USA

^bFlorida State University, College of Education, Tallahassee, FL, USA

^cUniversity of Missouri Health, Sinclair School of Nursing, Columbia, MO, USA

^dTexas A&M Health Science Center, School of Public Health, College Station, TX, USA

^eTexas A&M—Corpus Christi, School of Nursing, Corpus Christi, TX, USA

Corresponding Author:

Sharon A. Brown, PhD, RN, FAAN
The University of Texas at Austin
School of Nursing
1710 Red River Street
Austin TX 78701
Telephone: 512.232.4704
Email: sabrown@mail.utexas.edu

Highlights

- A model-driven meta-analysis was conducted of predictors of diabetes outcomes.
- Self-efficacy most consistently predicted all adherence behaviors.
- Dietary adherence was the most significant predictor of HbA1c.
- Physical activity was the most predictive factor of BMI.

ABSTRACT

Objectives: To conduct a model-driven meta-analysis of correlational research on psychological and motivational predictors of diabetes outcomes, with adherence factors as mediators.

Methods: A comprehensive literature search of published and unpublished studies located a sample of 775 individual correlational or predictive studies reported across 739 research reports.

Results: Results varied according to the outcome variable included in the regression models. Depression had a larger negative effect on adherence to physical activity than on dietary adherence. Coping and self-efficacy were strongly related to dietary adherence, which was strongly related to improved glycemic control. Medication adherence was related to glycosylated hemoglobin, whereas medications and self-monitoring were related to fasting blood glucose. Adding appointment keeping to the models did not significantly alter the results.

Conclusion: Self-efficacy was the most consistent predictor of all adherence behaviors and dietary adherence was the most significant predictor of HbA1c. Physical activity was the most predictive factor of BMI and glucose self-monitoring the most predictive of FBG.

Practice Implications: Metabolic control is a primary goal in T2DM, so the best pathway to attaining that goal appears to be an emphasis on self-efficacy and dietary adherence.

Keywords: type 2 diabetes; meta-analysis; depression; self-efficacy; explanatory models; HbA1c

1. Introduction

Type 2 diabetes (T2DM) affects more than 23.6 million Americans, or 8% of the U.S. population, and is a major health problem [1-6]. Tight glucose control achieved through

intensive medical treatment, coupled with diabetes self-management education (DSME), has been shown to reduce diabetes complications by 50% to 75%, save \$79,280 per individual, and result in 6 years of additional life [7-9]. However, fewer than 30% of individuals with T2DM achieve “good glucose control,” defined by the International Diabetes Federation as a glycosylated hemoglobin (HbA1c) level below 6.5% [10,11]. The large numbers of individuals who do not achieve glycemic control are labeled “noncompliant” and receive inadequate or inappropriate diabetes treatments, such as higher dosages and/or more frequent doses of insulin, in order to compensate for anticipated “indiscretions,” for example in dietary intake [12,13]. Plausible explanations for low rates of glycemic control are depression and the complexities of daily self-management regimens coupled with low self-efficacy, all of which may negatively impact one’s quality of life [14].

Individuals with diabetes must align dietary preferences with recommended guidelines, reverse sedentary habits, and accurately adhere to medications prescribed for diabetes as well as for its co-morbidities (e.g., hypertension). **For some individuals with T2DM, they also may be required to self-monitor glucose levels several times per day with home glucometers, particularly if they are newly diagnosed or have ongoing problems achieving metabolic control** [15]. Lifestyle changes are difficult, attested to by failure to achieve glycemic goals, low rates of physical activity, and rising obesity rates with high levels of recidivism after successful weight loss attempts. **Large clinical trials have shown that glycemic control improves health [7,9]; and the connections and comparisons between multiple predictors, such as stress or self-efficacy, and diabetes outcomes, such as BMI and metabolic control, have been studied extensively.** But this descriptive body of research has never been systematically reviewed in such a way that researchers could compare the relative effects of these predictors. Thus, few clinical guidelines are available to direct health care professionals in maximizing health and preventing or delaying diabetes complications. Variables that exert the greatest

influence in positively affecting metabolic control, e.g., self-efficacy or depression, could be targeted to enhance future diabetes care efforts.

We conducted an extensive model-driven meta-analysis to examine a set of testable models that included psychological (stress, depression, anxiety, coping) and motivational (self-efficacy) factors in predicting the primary diabetes outcomes of metabolic control (HbA1c and FBG) and BMI. Behavioral factors — adherence to diet, physical activity, medications, monitoring, appointment keeping — were examined as mediators and key targets for diabetes interventions.

The primary research questions that guided the analyses reported here were:

1. What are the *predictive relationships* among psychological factors and motivational factors on metabolic control and BMI?
2. What is the role of *behavioral factors* as possible mediators of the associations among the psychological and motivational factors and metabolic control and BMI outcomes?

2. Methods

We employed a relatively novel research design that has not been used previously in diabetes research, a model-driven research synthesis to test the sufficiency of a set of testable diabetes models. Decisions regarding the variables included in the model were based on those commonly posited in the literature to affect diabetes outcomes.

2.1 Search Methodology

With the guidance of a reference librarian, a rigorous literature search located relevant published and unpublished data. We searched numerous literature databases (e.g., PubMed, Cochrane, PsychINFO, Dissertation Abstracts International), hand searched journals and reference lists of relevant research reports (ancestry searching), and searched diabetes registries and conference abstracts for unpublished studies (“grey literature”). Search terms were a combination of “type 2 diabetes” and two variables of interest, e.g., “type 2 diabetes AND stress AND HbA1c OR glycosylated hemoglobin.” We established a fully electronic process to organize references, code sheets, a decision log, and other study materials [16].

2.2 Study Selection and Eligibility Criteria

Each included primary study involved: a) a sample of participants diagnosed with T2DM; b) data reported between 1960 and 2013; c) a report written in English; d) HbA1c, FBG, and/or BMI measured as the criterion variable(s); e) a measure of at least one of the following predictors: psychological factors (stress, depression, anxiety, coping), motivational factors (self-efficacy), or behavioral factors (adherence to diet, physical activity, medications, glucose self-monitoring, or appointment keeping); and f) correlations between at least one predictor and a criterion variable OR associational data that could be converted into a correlation with online calculators. For example, if authors reported a *t*-test of the mean HbA1c based on levels of depression, we converted those data into a correlation between HbA1c and depression. We excluded studies that involved combined samples of T1DM and T2DM, unless the T2DM data were presented separately.

Each study that was potentially relevant to the meta-analysis was reviewed a minimum of three times. The first review involved examining the bibliography of each research report to locate additional potentially relevant studies. Then, two independent reviewers determined if each study on face value seemed relevant; i.e., was it a study of T2DM with data or, rather, was it a clinical review article or commentary? Specific inclusion criteria were then applied in the third review to the studies determined to contain data. Raters were trained extensively in applying inclusion criteria; members of the research team arbitrated disagreements at regularly scheduled team meetings [17].

2.3 Data Extraction

Information from studies that met inclusion criteria was extracted and coded onto code sheets. Coding variables included: 1) identifying information (author[s], title, journal, year of publication, source of reference, funding, country of origin); 2) characteristics of subjects (mean age, age range, mean diabetes duration in years, mean age of diabetes onset, sample size, percent female/male, race/ethnicity or percent of each racial/ethnic group, economic status,

educational level, diabetes treatment regimen); 3) methodological characteristics (measurement instruments and reliabilities); and 4) quantitative data (descriptive data [means, SD] and correlations between each predictor [e.g., stress] and outcome variable [e.g., HbA1c]). Research quality measures were integrated into the study coding form [18-21]. Based on the Cochrane recommendations to focus quality assessment on the risk of bias, we developed four criteria: 1) rate of attrition; 2) selection and specification of the study sample; 3) whether the diabetes diagnosis was verified by the author/researcher; and 4) overall instrument reliabilities reported in the primary study.

A panel of diabetes experts, including two master's-prepared nurses, one of whom was a certified diabetes educator, assessed the content validity of the code sheet and codebook. For the first six months of the meta-analytic study, the research team coded studies together during group meetings as part of the training and consensus process. Then, two trained project staff coded each primary study that met inclusion criteria. Interrater agreement for extracting data from the primary studies was determined by comparing the coding by the 2 coders on a randomly selected subsample of 10 studies, achieving 87% agreement. The research team met weekly during the first six months, and then biweekly thereafter, to discuss disagreements in coding between the coders until consensus was reached. Thus, a minimum of two people coded all studies and we achieved 100% coding agreement.

2.4 Data Analyses

The data analysis approaches used in this study have been reported previously [22]. The general model-testing process is listed below. We:

1. Established priority testable models from an overall comprehensive model, considering which variables had a sufficient number of primary studies that contributed data;
2. Computed raw correlations for each variable combination in a testable model;

3. Conducted homogeneity analyses of correlations across studies for each variable combination in a testable model and developed histograms to determine skewness and identify outliers;
4. Computed univariate mean correlations across studies, weighted for sample size and variance, for each variable combination in each testable model; and
5. Conducted a standardized regression analysis of predictors for each outcome within a testable model.

Extracted data from primary studies were entered into an Excel data file and ultimately imported into a SPSS or SAS data file. Data were screened for accuracy by checking original data on the data forms against the computerized database. A further check involved the use of univariate descriptive statistics to determine if all the values were within expected ranges and whether means and standard deviations were plausible.

Basic information on the characteristics of the subjects and research methods of each primary study, including the reliability of each instrument, was coded and then summarized with descriptive statistics. Correlational data were summarized by computing an overall average correlation across studies for each set of correlations and a test of homogeneity [23], a very strong test of stability [24-26], was conducted for each correlational set across studies. Multivariate analyses estimated not only the variation of each correlation parameter across studies, but also the covariation of each pair of parameters (the between-study covariance components). The covariance components were then used in the multivariate random-effects procedure for combining the correlations across studies. The result of this analysis is a combined correlation matrix (Table 2). These results were used, in turn, to estimate path coefficients for the predictive model and their standard errors, which were used in the significance tests [25].

The general statistical theory required for combining correlations across studies to estimate a common correlation matrix under both fixed- and random-effects models is known [27]. SAS

Interactive Matrix Language (IML) uses a programming language that incorporates complex matrix operations, such as the ones we used here. We used SAS to implement fixed-effects estimation of the common correlation matrix from several studies, a test for heterogeneity of the correlation matrices from several studies, estimation of the between-studies covariance components matrix via the EM-algorithm, and random-effects estimation of the common correlation matrix, along with either fixed- or random-effects estimation of the path coefficients of the predictive model, and the associated standard errors and significance tests. Modifications to the computing algorithms described by Becker and Schram were made to permit estimation using the EM-algorithm when some studies did not provide estimates of every correlation of interest, so that random-effects analyses could be performed when some studies provided incomplete data.

3.0 Results

3.1 Search Results

The extensive literature search resulted in a total of 32,922 non-duplicate citations across multiple search variables that were screened by a minimum of 2 coders, according to established screening criteria. The final sample included 775 individual studies reported across 739 research reports that met inclusion criteria (Figure 1).

3.2 Characteristics of the Sample of Studies

Studies included in this meta-analysis represented a cumulative sample of 533,445 participants. Authors of 707 studies (91%) reported mean ages of their study participants; ages ranged from 32 to 84 years with a mean age across studies of 58.9 (SD=6.2) years (Table 1). The majority (>50%) of the studies lacked data on the socio-economic and/or educational levels of study participants, or the level could not be determined from the information that was provided. The sample sizes across studies varied widely with a few studies involving large national samples. The *median* sample size was 147 participants. Approximately 31% of the individual samples reported across primary studies was treated with insulin, either singly or in

combination with oral hypoglycemic agents. This level of insulin treatment is consistent with CDC estimates of insulin rates in the general population of persons with T2DM [27].

Primary studies in the meta-analysis sample were conducted between 1980 and 2013, with a marked increase in the number of studies reported over each decade. Of the total sample of studies, 400 (52%) were conducted in the U.S., either solely by U.S. authors or in collaboration with researchers from other countries. The remaining studies were conducted across 66 other countries, e.g., Japan ($n=31$), Canada ($n=25$), UK ($n=23$), China ($n=20$), and Australia ($n=14$). Of the total, 569 (73%) were published articles; 206 (27%) were unpublished research reports or dissertations. The majority of primary studies (~60%) were conducted in hospital or clinic settings and most authors employed descriptive or predictive/regression study designs.

Sample attrition rate was approximately 11% across studies, determined by comparing the initial sample size to the final sample size of each study. While this rate of attrition may not seem sufficiently excessive to confound the results of an individual study, these studies were not longitudinal in nature and thus would be expected to have very little attrition. Given that the majority of the study sample sizes were <150 , an 11% attrition rate could be considered significant, at least for those studies with a small sample size. A research quality score was computed, with possible scores ranging from 0 to 10. The mean quality score across primary studies was low (mean=2.8, SD=1.6, $n=775$). Ninety-four percent of the sample of studies was rated ≤ 5 ; 69% ≤ 3 . Only 4% to 10% of the primary studies met the top level for each quality indicator.

3.3 Mean Weighted Bivariate Correlations

First, we examined the associations among the psychological factors, the major motivational factor of self-efficacy, behavioral mediating factors (adherence to diet, physical activity, medications, and self-monitoring), and clinical outcome variables of interest (HbA1c, FBG, and BMI). (Table 2) Members of the research team computed 31% of the correlations included in this meta-analysis by using established online calculators that allowed conversion of other types

of association data to correlations. Mean bivariate correlations were weighted by the inverse of the variance and sample size, so that primary studies with smaller sample sizes contribute less to the overall mean correlations and variability of the weighted mean would be minimized. For this step, we report the mean effects (weighted correlations) without considering statistical significance; for our purposes, we were interested in the size of the effects to inform selection of variables for the model-testing analyses reported below.

The weighted correlations ranged from -0.34 for the association between stress and self-efficacy to the largest correlation, $r = 0.53$, for the association between depression and anxiety. Psychological/motivational factors most commonly associated with behavioral factors were self-efficacy and coping, with correlations ranging from $r = 0.15$ for the relationship between coping and physical-activity adherence, to $r = 0.34$ for the relationship between self-efficacy and dietary adherence. The strongest relationships were for coping and self-efficacy with dietary adherence. In particular, higher coping and self-efficacy scores were associated with higher rates of dietary adherence. Similarly, both coping and self-efficacy were associated with physical activity adherence but these relationships were not as strong as for dietary adherence. The strongest relationship with the variable depression was a negative association with physical activity adherence, $r = -0.16$.

In terms of the primary metabolic control outcome, HbA1c, relationships were seen with coping ($r = -0.18$), stress ($r = 0.17$), dietary adherence ($r = -0.17$), and self-efficacy ($r = -0.13$). Stress was associated with an increase in HbA1c; but coping, dietary adherence, and self-efficacy were associated with decreases in HbA1c, or improved metabolic control. The strongest relationship involving BMI was with self-efficacy ($r = -0.17$); higher rates of self-efficacy were associated with lower BMI. Self-efficacy was negatively related to depression ($r = -0.23$), stress ($r = -0.34$), and anxiety ($r = -0.27$); and positively related to coping ($r = 0.31$).

3.4 Model-Testing Results

3.4.1 Depression as Predictor of Adherence Factors and Health Outcomes: For this first set of models, we analyzed predictive relationships among a major psychological factor (*depression*); two behavioral factors in T2DM, adherence to diet and/or physical activity/exercise; and HbA1c and FBG as outcomes. We focused these first analyses on depression because of the recent and ongoing emphasis on depression and its influence on diabetes glycemic control, or possibly the effects of glycemic control on depression. The full data set including these variables involved 238 studies with up to 5 variables. There were 10 possible correlations for a total of 2,380 possible correlations across studies; however, the number of observed correlations was 400. The minimum number of correlations from any one study was 1; the maximum number of correlations from a study was 6; and the mean number of correlations per study was 1.7.

Table 3 depicts the results of standardized regression analyses using multivariate fixed effects modeling. Fixed effects modeling was used, rather than random effects modeling. Subsequent analyses incorporated between-studies variation to account for heterogeneity of the effects across studies. Several models were examined for each outcome to assess whether predictors were interacting and their slopes changing due to collinearity. Results indicated little change as additional predictors entered the equation.

Results for the models involving depression demonstrated consistencies across both metabolic control outcomes for T2DM — HbA1c and FBG. Both are indicators of glycemic control; HbA1c for long-term glycemia and FBG for short-term glycemia. The largest effect in the model ($\beta=0.18$, $p<0.001$) was seen between two individual adherence factors — adherence to diet and adherence to physical activity. Individuals who tended to follow dietary guidelines for T2DM are also likely to follow physical activity recommendations as well. Depression had a slightly larger negative effect on adherence to physical activity ($\beta=-0.15$, $p<0.001$) than on dietary adherence ($\beta=-0.10$, $p<0.001$). Adherence to diet had a larger effect on HbA1c ($\beta=-0.16$, $p<0.001$) than did adherence to physical activity ($\beta=-0.06$, $p<0.001$). Better

adherence to diet was associated with lower HbA1c levels, or better metabolic control. Effects on FBG were comparable to those on HbA1c for all predictors, except for the relationship between adherence to diet and FBG. The effect of adherence to diet on FBG ($\beta = -0.06$, $p < 0.001$) was less than on HbA1c ($\beta = -0.16$, $p < 0.001$), perhaps indicating high within-patient variability on FBG [28]. The direct relationship between depression and each metabolic control outcome was consistent and small, although statistically significant.

3.4.2 Psychological Variables as Predictors of Adherence Factors and Health Outcomes:

Next, we examined relationships among psychological variables (stress, depression anxiety, and coping); behavioral factors including a behavioral composite variable that combined all five of the adherence factors — adherence to diet, physical activity, self-monitoring, medications, and appointment keeping; and the health outcomes of HbA1c, FBG, and BMI (Table 4). The full data set contained 535 studies with up to 14 variables. Thus, we had 91 possible relationships; or a total of 48,685 possible correlations. The exact number of relationships that have been studied is 86 and the number of observed correlations was 1,525. The minimum number of correlations from a single study was 1 for body weight; thus, we did not include the body weight variable in any of the analyses. The maximum number of correlations from a single study was 24; and the mean number of correlations per study was 2.85.

Starting with the *composite behavioral variable* as the criterion variable, depression with a negative relationship and coping with a positive relationship showed strong relationships. Deleting anxiety from the model did not change the patterns.

The next analyses involved psychological predictors of *individual adherence components*. For dietary adherence, coping predicted adherence strongly and stress replaced depression as a statistically significant predictor. Removing anxiety from the model did not change the strong relationship between coping and dietary adherence. For predicting physical activity, if stress was removed from the model, anxiety as a predictor was statistically significant ($p = .05$) and exhibited a negative relationship (i.e., more anxiety was associated with lower physical

activity/exercise adherence). In this model, depression and coping were the strongest predictors of physical activity, with depression showing the strongest relationship; higher levels of depression predicted lower physical activity levels. Medication adherence was predicted by stress and anxiety, with high stress levels leading to less adherence and high anxiety leading to higher levels of adherence.

We then examined how psychological factors predicted BMI and metabolic control, measured in two ways: HbA1c for long-term control and FBG for short-term control. All but anxiety appeared to predict HbA1c levels. Higher stress predicted higher HbA1c levels and higher coping skills predicted lower levels of HbA1c. For FBG, the results for stress held; but depression was replaced by anxiety as a significant predictor, albeit with a relatively small effect. High levels of anxiety led to lower FBG levels ($p = .04$). The relationship between coping and FBG was marginally significant ($p = .07$). For BMI, stress and coping were statistically significant positive and negative predictors, respectively.

3.4.3 Behavioral Factors and Health Outcomes: The next analyses involved *adherence components* as predictors of health outcomes (HbA1c, FBG, and BMI). (See Table 5.) For HbA1c, all adherence variables except physical activity, that is, adherence to diet, monitoring, and medications, were significant predictors, with adherence to diet being the most significant. For FBG, adherence to diet and monitoring were statistically significant predictors. Monitoring was the strongest predictor, with higher levels of monitoring associated with higher FBG levels. For BMI, patterns in the data remain similar, with diet and monitoring being significant predictors; however, physical activity also was a significant predictor of BMI ($p = 0.005$).

3.4.4 Appointment-Keeping Adherence: In the next set of models (Table 6), we added a motivational factor, self-efficacy, to the psychological factors as predictors of health outcomes, with and without the appointment-keeping adherence variable in the model. Appointment keeping did not appear in any primary studies with several of the other variables we examined (anxiety, coping, etc.); thus we ran models that included appointment keeping along with

different subsets of variables because it was not possible to estimate a model if we didn't have correlations among all pairs of the variables involved. Self-efficacy is a consistently strong variable in predicting health outcomes across the models but some interesting differences appear in comparing the models with or without appointment-keeping adherence. For the models without appointment keeping, five variables — stress, depression, coping, diet adherence, and medication adherence — were significant predictors of HbA1c. For FBG, additional variables — anxiety, self-efficacy, physical activity, and monitoring — entered the model, replacing medication adherence. For BMI, the strongest predictive relationship was seen with self-efficacy. With regard to the major behavioral adherence factors, diet and medication adherence were related to HbA1c, whereas diet, physical activity, and self-monitoring were related to FBG. Adding appointment keeping to the models generally did not alter significantly the results; appointment keeping was more related to FBG than to HbA1c. Stress had the largest direct effects on both HbA1c and FBG in models without appointment keeping; but stress did not enter the models when appointment-keeping adherence was included. Self-efficacy was a significant predictor across most of the models and was a strong predictor of FBG and BMI, regardless of whether appointment keeping was in the models.

4. Discussion, Conclusion, and Practice Implications

4.1 Discussion

Multiple testable models were examined in this model-testing meta-analysis. Variables were added or removed from the models to determine possible collinearity among the concepts. The best predictor(s) of specific diabetes-related variables varied depending on the criterion variable included in the model. With regard to adherence factors, coping was the strongest predictor of dietary adherence, with higher coping levels predicting more dietary adherence. Depression was the strongest predictor of adherence to physical activity, with higher levels of depression predictive of lower physical activity levels, consistent with fatigue as a component of depression. Both stress and anxiety were predictors of adherence to medications, beta weights reflecting

both negative and positive relationships, respectively. The best predictors of HbA1c were coping, stress, and dietary adherence. The best predictor of FBG was adherence to glucose self-monitoring, with higher levels of FBG associated with higher levels of self-monitoring. One plausible explanation for this finding is that in T2DM, there are no clinical standards for glucose self-monitoring except for individuals with a new diabetes diagnosis or whose glycemic levels are not stable or close to normal range. Interestingly, appointment keeping had a larger effect on FBG than on HbA1c, perhaps due to the fact that FBG can be affected by short-term lifestyle changes and thus is known for high within-patient variability. For BMI, the best predictor was adherence to physical activity. With appointment keeping added to the models, the main change was seen in FBG with appointment keeping, monitoring, and self-efficacy entering the model as the best predictors. Consistently across all of the models tested to date, self-efficacy was a strong predictor of behavioral factors, and adherence to diet was most consistently predictive of improved metabolic control.

One of the main strengths of this review was that it involved a thorough quantitative synthesis of the literature relative to one of the most pressing problems facing society today, diabetes associated with growing rates of obesity. This body of literature is extensive and has never been systematically reviewed and synthesized. Findings are useful for informing the design of future evidenced-based interventions by identifying the relative strength of the relationships among predictor variables and diabetes outcomes. Meta-analysis allows us to examine research questions and interrelationships that could not be done in a single primary study. The data base of 775 coded studies that was generated during the course of this meta-analytic study provides numerous ongoing opportunities for additional secondary and moderator analyses, based on methodologies employed in the primary studies (e.g., effect of specific instruments that were used), characteristics of the subjects included in the primary studies (e.g., gender, age), and diabetes-related issues (e.g., insulin versus non-insulin treatment modalities).

Publication bias is a potential threat to any systematic review and relates to the fact that statistically significant research findings are more likely to be published than are non-significant results. The published data that are most easily accessed may reflect this bias and result in meta-analytic results that tend to be larger than data from unpublished sources [29]. Thus, published research may not be representative of the entire body of literature on a given topic [30,31]. The solution is to conduct a comprehensive search of published AND unpublished data, which we have done. More than 26% of the sample of studies came from unpublished sources, e.g., dissertations, likely due to the descriptive nature of most dissertation studies. This mix of data sources provided us with a diverse sample upon which findings are based.

One of the complexities of conducting studies in diabetes, whether they are descriptive, experimental, or meta-analytic, is the determination of the impact of medical management versus health behavior change or other explanations of diabetes outcomes. It is difficult to separate the effects of medical management, such as medications, from behavioral adherence to recommended lifestyle behaviors, which includes adherence to diabetes medications as well. However, we tested models with and without appointment keeping and interesting differences were seen, particularly for FBG versus HbA1c outcomes. Adding appointment keeping to the models did not significantly alter the results.

Clear quality (or risk of bias) criteria have been established for RCTs but the criteria recommended to assess the “quality” of descriptive research studies are less clear. The four criteria here were designed by the research team, based on the nature of the targeted studies for this meta-analysis and the factors that could potentially bias the results of each primary study. The initial sets of model-testing analyses reported here involved the entire sample of studies, irrespective of each individual study’s quality score. Ultimately, additional sub-analyses will be conducted based on these quality scores and other study characteristics, e.g., whether correlations were derived directly from author-provided data or were calculated by members of

the research team using online calculators. In these additional analyses, we will be able to determine if these quality criteria relate to study findings.

A positive aspect of the diabetes focus of this study was that clinical indicators of diabetes outcomes, e.g., HbA1c, are well established [32]. The DCCT and UKPDS trials documented the importance of tight glycemic control in reducing diabetes-related morbidity and mortality [7,9]. In this model-testing meta-analysis, we identified those factors that predict the best diabetes outcomes. "...meta-analysis results (...properly derived) have a certain robustness that makes them especially attractive as a basis for policy, practice guidelines, and the like" [29]. The *median* sample size of the studies included in this meta-analysis was 147 participants, most likely a sample size representing insufficient power for most analyses that were conducted in the primary studies. A sample with 147 participants has .80 power to detect a correlation of .23; the power to detect a rho of .15 is only .45. This finding alone justifies the need for a meta-analysis such as the one reported here; meta-analyses have increased statistical power due to the combining of multiple primary studies [33]. **Note, however, that all of the primary studies included in this meta-analysis were cross-sectional studies, which is a limitation of this review.**

4.2 Conclusion

Contrary to common clinical and research practice in which individual predictors, e.g., stress, are used to frame DSME interventions and studies, the results of this meta-analysis indicated that the best predictor(s) of diabetes-related outcomes varied depending upon the specific outcome included in the model. In general, self-efficacy was the most consistent predictive factor of adherence behaviors and dietary adherence was the most predictive factor of HbA1c, the long-term measure of glycemic control, with physical activity the most predictive of BMI and glucose self-monitoring the most predictive of FBG, the short-term measure of glycemic control.

4.3 Clinical Implications

Rather than using a shotgun approach to setting and achieving clinical diabetes goals, which tends to overwhelm patients, clinicians must assist persons with T2DM in identifying an individualized priority goal (or goals). The results of this meta-analysis indicate that different outcomes, e.g., weight loss or enhancing physical activity, require different strategies or a different “pathway.” Both the patient and his/her clinician need to focus together on the best predictor or predictors of achieving each individual goal, starting with the highest priority. Metabolic control, typically measured as HbA1c or fasting blood glucose, is the primary goal in T2DM. From the results reported here, the best pathway to attaining metabolic control as a goal appears to be an emphasis on self-efficacy and dietary adherence, with attention given to reducing excessive stress when present. From a clinical perspective, it seems logical to posit that patient success in achieving clinical goals is more likely to be attained when patients are not overwhelmed with a long list of clinical goals and related behavioral changes.

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Author Contributions

Design concept of the overall study: SA Brown

Acquisition of data: SA Brown, Winter, A García, A Brown, Ramírez, Conn, T Garcia, Cuevas, Sumlin

Data analysis and interpretation: SA Brown, A Brown, A García, Becker, Ramírez, Conn, T García, Cuevas, Sumlin, Winter

Manuscript draft: SA Brown, Becker, A García, A Brown, Ramírez, Conn, Winter, T García, Cuevas, Sumlin

Statistical expertise: SA Brown, Becker, A Brown, A García, Ramírez

Acquisition of funding: SA Brown

Administrative: SA Brown, Winter

Supervision: SA Brown

Conflicts of Interest: All authors declare that they do not have any actual or potential conflicts of interest.

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Figure 1. Literature Search Flowchart

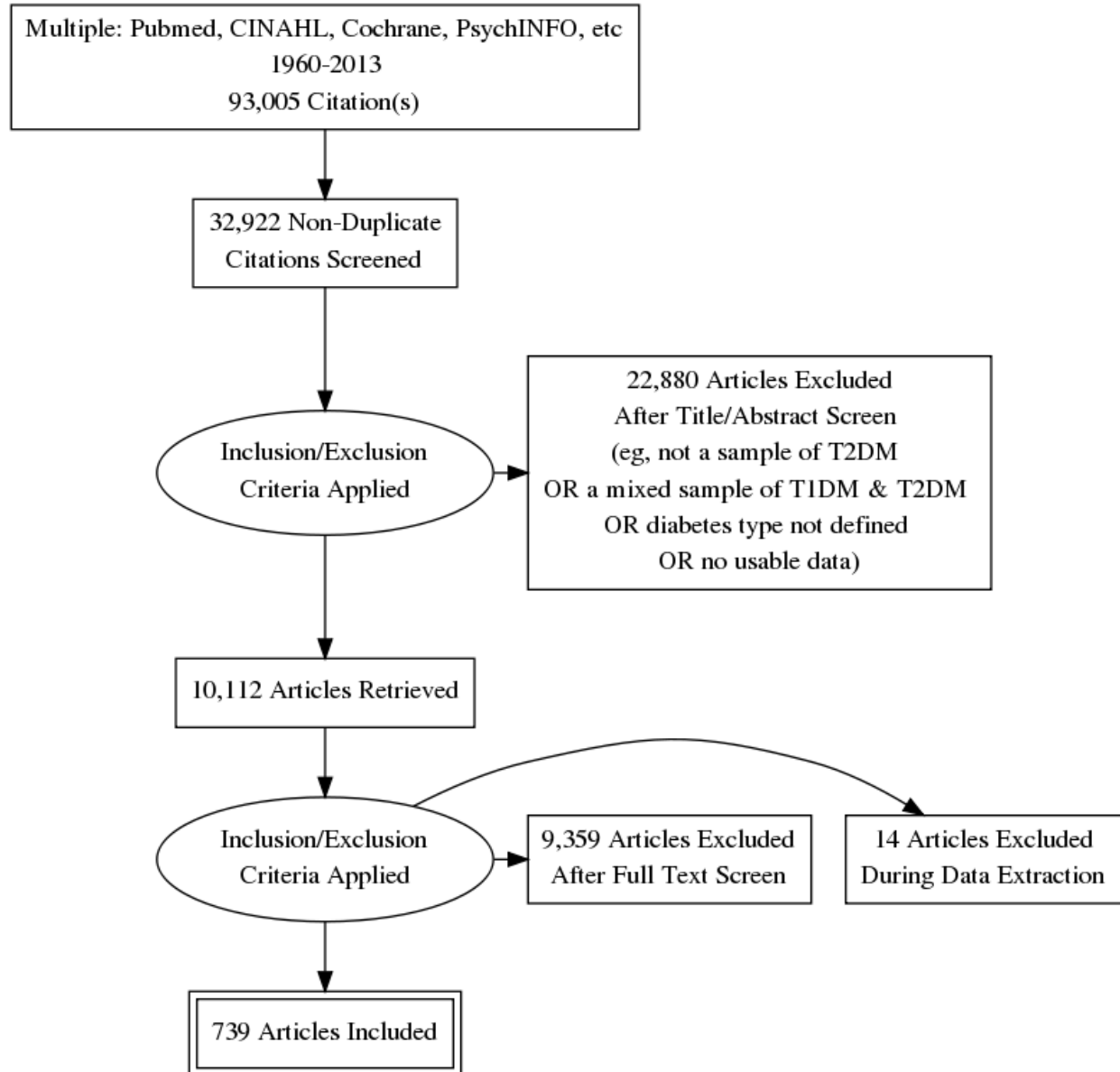


Table 1. Characteristics of the Participants in Primary Studies ($n = 775$)

CHARACTERISTICS	FREQUENCY (%)	MEAN (n , SD)	RANGE
PARTICIPANT CHARACTERISTICS			
Ages of study participants		58.9 (707, 6.2)	32.3 – 83.6
Diabetes duration (in years)		9.1 (476, 3.2)	<1.0 – 23.0
Sample size per individual primary study		690.1 (773, 3234.8)	11 – 56,181
Socio-economic status:			
• Predominantly low income	138 (17.8)		
• Predominantly middle income or above	50 (6.5)		
• Unable to determine	114 (14.7)		
• Not stated	454 (58.6)		
Educational level:			
• Less than high school (HS)	109 (14.1)		
• Some HS	59 (7.6)		
• HS graduate	116 (15.0)		
• Some college	64 (8.3)		
• College grad and/or post-grad	15 (1.9)		
• Unable to determine	110 (14.2)		
• Not stated	297 (38.3)		
% of sample on insulin		31.4 (440, 25.1)	0 – 100
METHODOLOGICAL CHARACTERISTICS			
Year of study:			
• 1980's	32 (4.1)		
• 1990's	111 (14.3)		
• 2000's	406 (52.4)		
• 2010 — 2013	226 (29.2)		
Countries where study was conducted:			
• USA (either singly or in collaboration)	400 (52%)		
• Other country	375 (48%)		
Setting:			
• Hospital(s)	41 (5.3)		
• Clinic(s)	419 (54.1)		
• Nursing home(s)	0		
• School(s)	0		
• Other community setting(s)	57 (7.4)		
• Mixed sites	134 (17.3)		
• Other	109 (14.1)		
• Not stated	15 (1.9)		
Study design:			
• Descriptive	212 (27.4)		
• Predictive/regression	482 (62.2)		
• Quasi-experimental	28 (3.6)		
• Experimental	53 (6.8)		
Data source:			
• Correlations provided by the author(s)	532 (68.6)		
• Correlations converted by the research team from data provided by the author(s)	243 (31.4)		
Publication status:			
• Published	569 (73.4)		
• Unpublished	206 (26.6)		

Table 2. Psychological and Motivational Factors with Behavioral Factors & Health Outcomes: Mean Correlations Across Studies, r (SE, n), Weighted by the Inverse of the Sample Size and Variance

Variable	Stress	Anxiety	Coping	Self-Efficacy	ADHERENCE				HbA1c	FBG	BMI
					Diet	Physical Activity	Medications	Monitoring			
Depression	0.45 (.006,48)	0.53 (.006,24)	-0.30 (.012,16)	-0.23 (.009,31)	-0.10 (.013,24)	-0.16 (.005,43)	-0.02 (.004, 21)	-0.06 (.010, 22)	0.07 (.004,116)	0.06 (.013,19)	0.09 (.004,76)
Stress		0.49 (.012,10)	-0.16 (.017,21)	-0.34 (.017,10)	-0.08 (.011,21)	-0.07 (.009,21)	-0.07 (.054, 4)	0.08 (.013, 11)	0.17 (.007, 66)	0.17 (.024,15)	0.08 (.007,32)
Anxiety			-0.09 (.031, 6)	-0.27 (.045, 3)	-0.02 (.033, 5)	-0.09 (.010, 9)	0.10 (.05, 3)	0.20 (.015, 5)	0.02 (.008, 35)	0.03 (.028, 4)	0.03 (.008,25)
Coping				0.31 (.013, 9)	0.33 (.019,13)	0.15 (.015,13)	0.00 (.045, 2)	0.13 (.031, 6)	-0.18 (.012, 21)	0.05 (.088, 2)	-0.11 (.015,10)
Self-efficacy					0.34 (.012,31)	0.27 (.009,39)	0.06 (.015, 15)	0.22 (.018, 16)	-0.13 (.007, 56)	-0.13 (.022, 1)	-0.17 (.012,12)
Adherence: Diet						0.19 (.005,51)	0.00 (.038,10)	0.10 (.006, 27)	-0.17 (.006, 66)	-0.06 (.021, 8)	-0.07 (.005,28)
Adherence: Physical Activity							0.03 (.023,10)	0.00 (.006, 22)	-0.08 (.006, 62)	-0.06 (.023, 9)	-0.11 (.005,44)
Adherence: Medications								0.04 (.007, 7)	-0.06 (.003, 42)	-0.10 (.020, 4)	-0.03 (.007,10)
Adherence: Monitoring									-0.06 (.005, 44)	0.13 (.015, 2)	0.03 (.005,11)

* $p \leq 0.01$

** $p \leq 0.001$

Table 3. Results of Standardized Regression Analyses: Depression, Behavioral Factors, and HbA1c and FBG as Health Outcomes

Predictor Variable(s)	Outcome Variable	Beta	SE(Beta)	P value
Depression	Adherence: Diet	-0.10	0.013	<0.001
Depression	Adherence: Physical Activity	-0.15	0.012	<0.001
Adherence: Diet	Adherence: Physical Activity	0.18	0.005	<0.001
Depression	HbA1c	0.05	0.012	<0.001
Adherence: Diet	HbA1c	-0.16	0.004	<0.001
Depression	HbA1c	0.06	0.005	<0.001
Adherence: Physical Activity	HbA1c	-0.06	0.004	<0.001
Depression	HbA1c	0.05	0.012	0.001
Adherence: Diet	HbA1c	-0.15	0.006	<0.001
Adherence: Physical Activity	HbA1c	-0.04	0.004	<0.001
Depression	FBG	0.06	0.012	<0.001
Adherence: Diet	FBG	-0.06	0.012	<0.001
Depression	FBG	0.06	0.006	<0.001
Adherence: Physical Activity	FBG	-0.06	0.013	<0.001
Depression	FBG	0.05	0.013	<0.001
Adherence: Diet	FBG	-0.05	0.006	<0.001
Adherence: Physical Activity	FBG	-0.05	0.013	<0.001

Table 4. Results of Standardized Regression Analyses: Psychological, Behavioral, and Metabolic and BMI Outcome Variables

Predictor Variable(s)	Outcome Variable	Beta	SE(Beta)	P value
Stress	Adherence: Behavioral Composite	0.02	0.012	0.21
Depression		-0.19	0.028	<0.001
Anxiety		0.01	0.033	0.722
Coping		0.37	0.021	<0.001
Stress	Adherence: Behavioral Composite	0.02	0.015	0.127
Depression		-0.18	0.027	<0.001
Coping		0.37	0.021	<0.001
Stress	Adherence: Diet	-0.04	0.014	0.001
Depression		0.01	0.026	0.692
Anxiety		0.00	0.028	0.885
Coping		0.30	0.013	<0.001
Stress	Adherence: Diet	-0.04	0.013	0.001
Depression		-0.03	0.012	0.616
Coping		0.27	0.297	<0.001
Stress	Adherence: Physical Activity	0.01	0.012	<0.001
Depression		-0.12	0.021	<0.001
Anxiety		-0.04	0.027	<0.001
Coping		0.09	0.011	<0.001
Depression	Adherence: Physical Activity	-0.12	0.014	<0.001
Anxiety		-0.04	0.019	0.050
Coping		0.09	0.006	<0.001
Stress	Adherence: Medications	-0.15	0.013	<0.001
Depression		0.00	0.029	0.883
Anxiety		0.14	0.027	<0.001
Coping		-0.01	0.060	0.844
Stress	HbA1c	0.17	0.012	<0.001
Depression		-0.04	0.021	0.050
Anxiety		-0.04	0.026	0.160
Coping		-0.16	0.009	<0.001
Stress	FBG	0.19	0.012	<0.001
Depression		0.02	0.022	0.429
Anxiety		-0.05	0.026	0.040
Coping		0.05	0.025	0.072
Stress	BMI	0.07	0.012	<0.001
Depression		0.03	0.021	0.120
Anxiety		-0.01	0.026	0.622
Coping		-0.09	0.009	<0.001

Table 5. Results of Standardized Regression Analyses: Behavioral Factors and Metabolic and BMI Outcome Variables

Predictor Variable(s)	Outcome Variable	Beta	SE(Beta)	P value
Adherence: Diet	HbA1c	-0.15	0.009	<0.001
Adherence: Physical Activity		-0.04	0.039	0.281
Adherence: Medications		-0.05	0.006	<0.001
Adherence: Monitoring		-0.04	0.006	<0.001
Adherence: Diet	FBG	-0.06	0.011	<0.001
Adherence: Physical Activity		-0.08	0.039	0.469
Adherence: Medications		-0.01	0.010	0.309
Adherence: Monitoring		0.19	0.033	<0.001
Adherence: Diet	BMI	-0.05	0.009	<0.001
Adherence: Physical Activity		-0.11	0.039	0.005
Adherence: Medications		-0.01	0.006	0.159
Adherence: Monitoring		0.05	0.007	<0.001

Table 6. Results of Standardized Regression Analyses: Psychological Factors, Self-Efficacy, and Metabolic Control and BMI as Outcome Variables, Without and With Appointment Keeping Adherence

Predictor Variable(s)	Outcome Variable	Beta	SE(Beta)	P value
Model without Appointment Keeping Adherence				
Stress	HbA1c	0.15	0.013	<0.001
Depression		-0.05	0.023	0.024
Coping		-0.13	0.022	<0.001
Adherence: Diet		-0.12	0.058	0.044
Adherence: Medications		-0.05	0.007	<0.001
Stress	FBG	0.17	0.022	<0.001
Anxiety		-0.08	0.029	0.006
Coping		0.06	0.021	0.003
Self-efficacy		-0.11	0.019	<0.001
Adherence: Diet		-0.04	0.012	<0.001
Adherence: Physical Activity		-0.03	0.014	0.020
Adherence: Monitoring		0.15	0.026	<0.001
Stress	BMI	0.04	0.018	0.028
Coping		-0.06	0.018	0.002
Self efficacy		-0.11	0.015	<0.001
Adherence: Physical Activity		-0.07	0.013	<0.001
Adherence: Monitoring		0.06	0.008	<0.001
Model with Appointment Keeping Adherence				
Depression	HbA1c	0.04	0.013	0.002
Self-efficacy		-0.07	0.018	<0.001
Adherence: Diet		-0.14	0.033	<0.001
Adherence: Appt. Keeping		-0.06	0.004	<0.001
Self-efficacy	FBG	-0.13	0.022	<0.001
Adherence: Diet		-0.03	0.013	0.039
Adherence: Physical Activity		-0.05	0.020	0.016
Adherence: Monitoring		0.22	0.076	0.004
Adherence: Appt. Keeping		-0.26	0.040	<0.001
Depression	BMI	0.05	0.010	<0.001
Self-efficacy		-0.12	0.011	<0.001
Adherence: Physical Activity		-0.08	0.032	0.017
Adherence: Appt. Keeping		-0.05	0.005	<0.001