HHS Public Access

Author manuscript

Int J Yoga Therap. Author manuscript; available in PMC 2018 November 15.

Published in final edited form as:

Int J Yoga Therap. 2018 November ; 28(1): 123–132. doi:10.17761/2018-00026.

Yoga as a complementary therapy for patients with type 2 diabetes: Design and rationale of the HA1C study

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Abstract

Diabetes is the seventh leading cause of death in the United States. For most patients, medication alone is not sufficient to achieve glycemic control; it requires attention to multiple healthy behaviors including a diet plan, regular physical activity, and stress management. Yoga, a mindfulness practice, with emphasis on relaxation, meditation, and deep breathing, may have special relevance to people with T2DM. Yoga practice may positively impact stress, and other self-care tasks that will contribute to improved glycemic control.

The *Healthy Active and in Control* (HA1C) study is designed to examine the feasibility and acceptability of yoga among adult patients with type 2 diabetes. In this pilot randomized controlled trial, adult diabetics are randomly assigned to either; (1) a 12-week Iyengar yoga

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Conflict of Interest

The authors declare no conflict of interest.

intervention given twice weekly, or (2) a twice-weekly 12-week program of traditional exercise (e.g., walking, stationary cycling). Assessments are conducted at end of treatment (12-week), and at 3- and 6-months post-intervention. In the HA1C study, we will assess feasibility and acceptability (e.g., attendance/retention rates, satisfaction with program), glycemic outcomes (e.g., HbA1c, fasting blood glucose, post-prandial blood glucose), and changes in physiological (e.g., salivary cortisol) and behavioral factors (e.g., physical activity, diet) relevant to the management of T2DM. Focus groups will be conducted at end of intervention to explore participants' experience with the program and their perception of the potential utility of yoga for diabetes management.

Keywords

Yoga; type 2 diabetes; randomized controlled trial

Introduction

Diabetes affects more than 29 million adults and is the seventh leading cause of death in the United States (Center for Disease Control and Prevention, 2016). Type 2 diabetes (T2DM) accounts for 90–95% of all diabetes cases in adults. Controlling blood glucose level is fundamental to the management of T2DM (American Diabetes Association, 2013), and improved glycemic control is associated with a significant decrease in long-term complications (Skyler et al., 2009; Stettler et al., 2006; Stratton et al., 2000; UKPDS, 1998). In general, every 1% reduction in Hemoglobin A1c (HbA1c) decreases the risk of developing eye, renal and nerve disease by 40% (Center for Disease Control and Prevention, 2012; Stratton et al., 2000).

Yoga, an ancient Indian practice, has shown promising results in glycemic control among patients with T2DM (Cui et al., 2016; Innes & Selfe, 2016; Kumar et al., 2016). Yoga practice involves a physical activity component (postures/*asana*), and a relaxation component (meditation, *shavasana*). Yoga, with its focus on controlling breath, holding postures, and meditation, increases the practitioners' attention to body sensations and present moment experiences. This state of being nonjudgmental and attentive to one's moment-to-moment experiences contributes to yoga as a mindfulness-based activity (K. W. Brown & Ryan, 2003; Kabat-Zinn, 2003). This may help with diabetes management since mindfulness training has been shown to increase one's ability to recognize and skillfully respond to emotional stress, leading to effective coping responses (Shapiro, Carlson, Astin, & Freedman, 2006; Vago & Silbersweig, 2012).

Yoga may also reduce activation of the sympatho-adrenal system and hypothalamic-pituitary-adrenal axis, and may enhance parasympathetic activity, thereby alleviating stress (R. P. Brown & Gerbarg, 2005; Streeter, Gerbarg, Saper, Ciraulo, & Brown, 2012). Clinical trials with both healthy and ill participants have shown the benefit of yoga on stress reduction (Chong, Tsunaka, Tsang, Chan, & Cheung, 2011; Kohn, Persson Lundholm, Bryngelsson, Anderzen-Carlsson, & Westerdahl, 2013; Li & Goldsmith, 2012). By supporting stress resilience, yoga may prevent stress-induced rises in cortisol, thus controlling rise in blood glucose levels (Bjorntorp, Holm, & Rosmond, 1999; Else, Hammer,

& McPhee, 2010; Walker, 2006). Pilot studies conducted mainly in India have shown decreased stress levels among diabetics after a yoga intervention (Beena & Sreekumaran, 2013; Singh et al., 2001; Vizcaino, 2013). Evidence also suggests that stress leads to poor food choices, including increased consumption of foods high in fat, sugar and salt (Oliver, Wardle, & Gibson, 2000; Schiffman, Graham, Sattely-Miller, & Peterson-Dancy, 2000).

By reducing stress and improving mindfulness, yoga practice may lead to improved self-care behaviors including improved diet and physical activity. Randomized trials with adults at risk for cardiovascular disease and binge eaters have shown improved dietary outcomes after yoga intervention (Alexander, Innes, Selfe, & Brown, 2013; Carei, Fyfe-Johnson, Breuner, & Brown, 2010; McIver, McGartland, & O'Halloran, 2009; McIver, O'Halloran, & McGartland, 2009). Thus, yoga may positively impact stress, diet and other self-care tasks that contribute to improved glycemic control; however, this has not yet been tested among individuals with T2DM.

Methods

Study design

The *Healthy Active and in Control* (HA1C) study is designed to examine the feasibility and acceptability of yoga among adult patients with type 2 diabetes (T2DM). In this pilot randomized controlled trial, adult diabetics are randomly assigned to either; (1) a 12-week Iyengar yoga intervention given twice weekly, or (2) a twice-weekly 12-week program of traditional exercise (e.g., walking, stationary cycling). Both interventions are delivered in group format in two consecutive cohorts. Assessments are conducted at end of treatment (12-week), and at 3- and 6-months post-intervention. In the HA1C study, we will assess feasibility and acceptability (e.g., attendance/retention rates, satisfaction with program), glycemic outcomes (e.g., HbA1c, fasting blood glucose, post-prandial blood glucose), and changes in psychological (e.g., stress, self-efficacy) and behavioral factors (e.g., physical activity, diet) relevant to the management of T2DM. Qualitative data will be collected in focus group discussions to understand participants' experience with the program activities.

Aims and hypotheses

The primary aim of this study is to determine the feasibility and acceptability of a 12-week Yoga intervention for adults with T2DM. We will record participant recruitment, attendance and retention rates, compliance with study protocols and general satisfaction with the program. Focus groups will be conducted at the end of intervention (week 12) to identify facilitators and barriers to yoga practice and examine participant perceptions and beliefs about yoga and its relationship to any changes in their health behaviors and/or diabetes management.

A secondary aim of the study is to conduct preliminary tests of the effect of yoga on glycemic control among adults with T2DM. We will measure HbA1c levels at baseline, end of treatment (12-weeks), and at 3- and 6-months post-intervention. We hypothesize that those randomized to Yoga will have better glycemic control (i.e., greater reductions in

HbA1c) compared to those randomized to the Exercise control group at follow-ups. We will also assess fasting and postprandial blood glucose (FBG and PPBG).

We will also examine data on potential mediators (mechanism of action) of yoga as it may impact glycemic control. We will examine the effect of yoga on perceived stress and will measure salivary cortisol (a biomarker of stress) at baseline and end of treatment. We will also explore changes in other potential mediators including anxiety, mindfulness and self-efficacy between the yoga and exercise groups. We will explore the effect of yoga on secondary outcomes including changes in diabetes medication, diet, exercise, and body composition (body mass index and waist circumference).

Sample size and power calculations

A primary focus of this pilot research project is to accumulate evidence about feasibility and acceptability of the yoga intervention for this population of adults with T2DM. We did not conduct a formal power analysis on traditional T2DM outcome variables, such as change in HbA1c levels, but rather, based the initial sample size (N=60; i.e. two cohorts with 30 individuals in each) on a number sufficient to measure feasibility and to allow us to obtain initial estimates of efficacy for our outcome variables. In this study, we will calculate the effect size estimates, along with its 95% confidence interval, for the yoga intervention to aid in the calculation of an accurate power analysis for a larger future efficacy trial.

Study Procedures

Eligibility criteria

Inclusion criteria include adults age ≥ 18 years with T2DM for more than 6 months, HbA1c levels of >6.5. Individuals with serious co-morbid condition (e.g. uncontrolled hypertension, heart failure, heart transplant, angina in past 12 months, implanted heart device, uncontrolled asthma, stroke or seizure in past 12 months), serious psychiatric disorder (e.g. panic attacks, suicidality, Alzheimer's, Schizophrenia), bone or joint problem limiting ability to exercise, BMI <42 kg/m2, pregnancy or planned pregnancy are excluded. Individuals are also excluded who have engaged in any mindfulness-based (i.e. yoga, Tai Chi) or stress management therapy in the past month or attended more than 3 such classes in past six months. Individuals unable to read or write English are also excluded.

Recruitment and screening

We are using active as well as passive recruitment strategies. Potential participants are identified through medical records of the collaborating diabetes center, and initial contact is made by sending letters to potential candidates through the diabetes center. In addition, the research nurse at the diabetes center informs patients about the study during routine clinic visits. We also advertise the study using announcements on local radio stations, internet (i.e. craigslist, Study center's website), local newspaper inserts, and flyers at public locations. Interested individuals calling the study phone are screened by trained research assistants for eligibility based on the above mentioned criteria. We are using a revised Physical Activity Readiness Questionnaire (PAR-Q +) (S. Thomas, Reading, & Shephard, 1992) to screen for

diabetes-specific complications (i.e. gangrene, foot ulcer, amputations, etc.). If one or more items are endorsed on PAR-Q+, physician consent is required for participation in the study.

Informed consent, enrollment and randomization

Individuals who screen eligible are scheduled for an in-person orientation visit where a study research assistant describes the protocol in detail. Height and weight are measured to determine body mass index (BMI) before obtaining the written informed consent. Participants are given the baseline survey to complete and are scheduled for laboratory assessments. Baseline HbA1c levels are verified, and if individuals remain eligible (i.e. HbA1c >6.5), they are scheduled for a second visit to complete randomization. At the second visit, participants complete the interviewer administered 7-day Physical Activity Recall (Blair et al., 1985; Sallis et al., 1985), provide saliva samples to assess cortisol levels, and are then randomized to the yoga or control condition. We are using a permuted-block randomization procedure with randomly selected block sizes conducted within each of four strata: a) Females with low HbA1c levels; b) Females with high HbA1c levels; c) Males with low HbA1c levels; d) Males with high HbA1c levels. Specific group assignments are delivered by the study statistician in sealed envelopes to a blinded research assistant. The research assistant meets with each newly recruited participant and based on the appropriate stratum, opens the next consecutively numbered envelope for that stratum in the presence of the participant to reveal the group assignment. This procedure ensures a blinded randomized group assignment process, and provides that both treatment groups have an approximately equal proportion of participants within gender and HbA1c levels (≤ 9 vs. >9). All participants are provided with handouts on diabetes management (i.e. basics of diabetes, symptoms and management of hypoglycemia, hydration, foot care). Participants then receive schedule of their respective group assignment (i.e. yoga or exercise sessions) and are advised to follow the medication plan as prescribed by their physician.

Interventions

Yoga intervention—Participants in the yoga group attend two 60-minute yoga sessions weekly for 12 weeks. We selected this duration because past studies of yoga have shown significant effects in 3 months (Amita, Prabhakar, Manoj, Harminder, & Pavan, 2009; Hegde et al., 2011; Yang et al., 2011). Classes are conducted in a group format by certified Iyengar yoga instructors with over 15 years of experience. The intervention consists of beginner's level Iyengar yoga, designed to be practiced by someone with no previous experience of yoga. We chose Iyengar yoga because it involves use of props such as wooden blocks, blankets, etc. that help the practitioner to achieve and maintain postures with relative ease while reducing the risk of injury. Iyengar yoga emphasizes postural alignment and involves precise use of language, demonstration, and observation. Alignment and breath awareness are used as tools to keep the mind in focus and cultivate awareness. As students develop awareness of their physical body, they are also directed to observe the effect of their practice on their state of mind. Each class consist of: Guided meditation and breath-work, active and passive asanas including standing, sitting, twists, backbends, inversions, and restorative postures, as well as Savasana, guided relaxation. Prior to the start of study enrollment, the specific sequences were finalized by the yoga instructor based on review of literature and input from investigators and other yoga experts (Table 1). These yoga sessions are designed

to emphasize mindfulness (i.e., staying focused on the present moment), meditative state (i.e., calming and stilling the mind), creating more ease, safety and well being in one's body and with one's self. A manual was developed with instruction for each week. Participants are encouraged to practice yoga at home. Printed workbooks with photos of the yoga postures and sequences are provided to participants along with props and a DVD to aid home practice. The goal is to train participants in the basic yoga poses and gradually move them to independent home practice after week 12. At end of intervention, participants are provided with eight vouchers to a local Iyengar yoga studio to promote maintenance of yoga practice.

Exercise control intervention—The exercise control condition consists of a 60-minute session twice weekly for 12 weeks and matches the dose and duration of the yoga condition. The sessions are held in a gym-type facility on a hospital campus. Sessions are conducted on the same days and times as the yoga intervention, but at a different venue to avoid treatment diffusion. The facility has an indoor walking track, treadmill, elliptical machines, stationary bicycles and rowing machine. Only research participants and study staff are present in the facility during study sessions. Each session includes a 5- minute warm-up (i.e. stretches), followed by 50 minutes of moderate-intensity exercise and then a 5-minute cool-down. Each session is supervised by two study staff with training in exercise physiology to ensure participants' safety. At the start of each session, participants are instructed to exercise in a perceived exertion range of fairly light to somewhat hard (11–13 on the Borg perceived exertion scale) (Borg, 1982). Participants are instructed to wear comfortable shoes.

Data collection and blinding

Data are collected from participants at screening, enrollment (baseline), end of intervention (12-week), and two follow-ups (3-month and 6-month post intervention). One week before the scheduled assessment date, participants are provided with survey questionnaire, laboratory slips to complete blood tests, and tubes for saliva collection. Participants are instructed to bring the completed survey along with the saliva tubes to each follow-up visit. Assessments are conducted by research staff blinded to the randomization condition.

Measures

Diabetes and related outcome measures—The primary clinical outcome for the study is HbA1c. In addition, we assess both fasting and post prandial glucose. We also ask participants to answer questions related to their diabetic history (e.g. years since diagnosis) and medicines being used. Diabetes medicine type and dosage is assessed using a detailed questionnaire at baseline and each follow-up visit. Participants will be categorized as either increased, decreased, or no change in diabetes medications based on baseline and follow-up dosages. When diabetes medication is changed, the study physician will be consulted to categorize the change. Adherence to diabetes management is assessed using the Morisky 8-Item Medication Adherence Questionnaire (Morisky, Green, & Levine, 1986), and Summary of Diabetes Self-care Activities Measure (Toobert, Hampson, & Glasgow, 2000). Quality of life is assessed using the Diabetes-39 instrument (Boyer & Earp, 1997).

Potential mediators—Salivary cortisol assays provide a reliable, non-invasive estimate of free cortisol, appropriate for assessing circadian variability in cortisol levels (Kudielka, Gierens, Hellhammer, Wust, & Schlotz, 2012). Participants are asked to provide saliva samples for two consecutive days at baseline and 12-weeks. Participants collect samples three times daily based on MacArthur recommendations (Stewart & Seeman, 2000): (1) awakening, (2) wake + 30 minutes, and (3) bedtime, allowing us to assess cortisol output over the day. To increase compliance participants receive: (1) detailed written and oral instructions, and (2) a reminder call on night before saliva sampling is due. All retrieved samples are frozen at −80 degrees at our center's facilities until shipping for analysis by expanded range high-sensitive enzyme immunoassay (ER-HS-EIA; r=.91). Participants also complete two self-report measures of stress (Problem Areas in Diabetes: PAID; Perceived Stress Scale: PSS) at each assessment visit. The PAID is a valid and reliable measure of diabetes-related emotional distress that correlates strongly with self-care behaviors and glycemic control (Polonsky et al., 1995; G. Welch, Weinger, Anderson, & Polonsky, 2003; G. W. Welch, Jacobson, & Polonsky, 1997). The Perceived Stress Scale is the most widely used instrument to assess the degree to which situations in one's life are perceived as stressful (S. Cohen, Kamarck, & Mermelstein, 1983).

Other covariates—Demographic information including age, gender, marital status, race, ethnicity, income and education are collected at baseline. Physical activity measures include the interviewer administered 7-day Physical Activity Recall (PAR) (Blair et al., 1985; Sallis et al., 1985). Self-efficacy for physical activity is measured using a 5-item scale (Marcus, Selby, Niaura, & Rossi, 1992), and readiness to engage in physical activity is assessed using Stages of Change questionnaire (Marcus, Rossi, Selby, Niaura, & Abrams, 1992). The Pittsburgh Sleep Quality Index is used to assess the duration and quality of sleep (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Alcohol consumption and cigarettes smoked are also assessed at each data collection time point. Symptoms associated with depression are assessed using the Center for Epidemiological Studies-Depression Scale (CESD-10 item), and the Five Facet Mindfulness Questionnaire (FFMQ) is used to measure mindfulness (Baer et al., 2008).

To calculate BMI (weight [kilograms]/ height [meters^2]), height is measured without shoes at baseline and body weight is measured with light clothing at all assessment points using a calibrated balance beam scale. Waist circumference, a surrogate measure of intra-abdominal fat, is measured at the point immediately above the iliac crest on the mid-axillary line in standing position at the end of normal expiration (Chumlea & Kuczmarski, 1995). Waist circumference measures are obtained twice from each participant by trained research staff and then averaged.

Process measures—All study procedures and contacts with the participants are documented by the research staff. A tracking database is used to record screened, consented, and randomized individuals. Attendance at each session (yoga and exercise) and follow-up visits is logged throughout the study. Acceptability of each intervention is assessed by an anonymous program satisfaction survey with which participants can provide feedback on the

program content, structure, and instructions (including evaluation of yoga and exercise instructors) at week 12.

Qualitative research

Focus groups are conducted at the end of the intervention (week 12) with the Yoga and Exercise groups separately. A qualitative data collection guide is used to delineate topics and concepts to be addressed during the focus group discussions. Focus groups will examine the feasibility and acceptability of the study protocol and intervention components. In particular, we will identify facilitators and barriers to yoga and examine participants' perceptions about the intervention and its relationship to any changes in stress or diabetes management. Participants are also asked for feedback on intervention content, study design (timing and length of classes), and materials. Focus groups are designed to take about 90–120 minutes, are audiotaped and transcribed for analysis. Transcripts will be independently coded by two researchers and master codes (i.e., codes agreed upon by both coders) will be entered in NVivo qualitative software for thematic analysis. Both a priori themes and those that emergent from patient narratives will be analyzed.

Subject payment

Participants do not receive any incentive to attend weekly yoga or exercise sessions. But compensation ($50 each) is provided for time and effort related to completing follow-up assessment visits (12-week, 3- and 6-month post intervention). Individuals receive $5 for each tube of saliva sample returned (i.e. total $30 at baseline and $30 at week 12). In addition, participants receive $50 for participation in the focus group discussion.

Ethical and safety oversight

All study procedures and materials have been approved by the Institutional Review Board of The Miriam Hospital (IRB registration #TMH IRB - 00000482). In addition, the Data Safety Monitoring Board (DSMB), comprised of three individuals (researcher, physician, biostatistician) not affiliated with the study, annually reviews the study procedures and reports. Report from the DSMB meetings are sent by the DSMB chair to the funding agency (NIHNCCIH).

All participants are actively monitored by the study research assistants and program staff with whom participants interact during the active phase of the study. At each study visit participants are enquired about any illness, injuries, changes in health status experienced since our last interaction. In addition, participants are asked to call the study staff to report any side effects that are distressing to them. In case of a missed visit, the study staff calls the participant to enquire about any illness or injury. Sessions are facilitated by trained and experienced personnel. The study staff has been trained to monitor blood glucose; glucometers and glucose tablets are available on-site for all sessions if need arise. All adverse events (AEs) are recorded by staff and reviewed in weekly study meetings. We define an AE as any sign or symptom experienced by the participants during the course of the study. All AEs are reviewed by the principal investigator and categorized regarding its severity (mild, moderate, severe) and likely relatedness to the study (not related, unlikely, possibly, likely related, definitely related). Serious adverse events will be reported to IRB

and DSMB immediately. All other adverse events are reported and reviewed during annual meetings of the DSMB.

Planned Analysis

While randomization should equalize group characteristics, particularly in larger studies, this is less certain in smaller trials. Thus, initial analyses will be conducted to examine the groups for comparability at baseline on demographic, psychosocial and behavioral characteristics using Chi-Square tests for categorical variables and analysis of variance (ANOVA) for continuous variables. We will also examine the distributional properties of continuously-scaled variables to determine if normalizing transformations should be applied before conducting any ANOVA procedure. If group differences are found for any specific variable, we will evaluate those differences and, if necessary, we will statistically control for them in outcome analyses.

Feasibility will initially be assessed using descriptive analyses to measure the participant recruitment rate, the retention rate, and session attendance. We will then use ANOVA to compare group differences on the retention rate and session attendance. We will also use ANOVA to compare group differences on scores from the Program Satisfaction Measure to determine acceptability. Additionally, we will use Cohen's d to quantify the effect sizes for any ANOVA comparisons.

To accomplish the secondary aim of the study of examining the effect of yoga on glycemic control, we will conduct a longitudinal linear mixed effects model analysis to assess group differences in mean HbA1c at each follow-up, controlling for baseline values and any conceptually important baseline differences identified in the preliminary baseline group analyses. We will conduct similar longitudinal linear mixed effects model analyses to assess the effects of yoga on fasting and postprandial blood glucose (FBG and PPBG). We will also monitor the change in participants' diabetes medications over the course of the study, and conduct exploratory analyses to determine how it is related to HbA1c change during that period, and if it appears warranted we will enter that information into our primary analyses as a time-varying covariate. These analyses also accommodate missing values under the assumption of missing at random (Little & Rubin, 1987) and will allow maximum use of the existing data to detect treatment effects.

Our initial analyses to examine potential mediating effects on change in glycemic control will first examine for any effects of the Yoga intervention on stress (i.e. via the biomarker of salivary cortisol) using analysis of covariance to examine for change at 12-weeks and covarying on baseline cortisol value. We will next examine whether change in cortisol is related to change in glycemic control (HbA1c) through a series of cross-sectional and time-ordered regressions predicting change in glycemic control (HbA1c). If there are treatment differences for stress, and relationships between stress and changes in glycemic control (HbA1C), we will then conduct an initial mediation analysis using path analysis with a structural equation modeling framework. For the mediation analysis, we will use a bias-corrected percentile-based bootstrap approach (Hayes, 2009) with 5,000 draws and provide a 95% confidence interval for the potential mediation effect to assess its statistical

significance. For several other potential behavioral mediators (anxiety, mindfulness, and self-efficacy), we will first conduct longitudinal linear mixed effects model analyses using all follow-up data in the analyses and using baseline values as covariates. We will next examine whether change in potential behavioral mediators is related to change in glycemic control (HbA1c) through a series of cross-sectional and time-ordered regressions predicting change in glycemic control (HbA1c). If there are treatment differences for any of the behavioral mediators, and relationships between any of the behavioral mediators and changes in glycemic control, we will next explore a similar path analytic mediation modeling strategy, as will be implemented above with salivary cortisol.

In our other analyses, we will also examine for any treatment group differences on secondary outcomes including changes in diabetes medication, diet, exercise, and body composition. If a secondary outcome variable is continuous, we will use a longitudinal linear mixed effects model approach, but if the secondary outcome variable is categorical (e.g., change in medication), we will employ a generalized estimating equation approach, and within both approaches we will use a baseline value as a covariate.

Qualitative analyses will explore participant perceptions of yoga and its relation to diabetes management. This includes adoption of yoga practice both in the intervention groups and in home practice, as well as participant anticipations of continued practice post-intervention. We will explore any differences in feasibility and acceptability by gender, weight status and HbA1c. Feedback provided by the yoga participants will be compared to the exercise group to examine any experiential differences. In addition, because the yoga and exercise programs inherently differ with respect to group dynamics as well as logistical constraints, we will be able to review these findings and consider alterations in both content and structure for future interventions.

Discussion

To our knowledge this is the first randomized controlled trial being conducted in the United States to examine the feasibility of yoga in comparison to an exercise group among adults with type 2 diabetes. Adherence to exercise is currently poor among adults with T2DM. Comorbid conditions such as obesity, perceived difficulty of exercising, and fatigue are some barriers to exercise participation reported among diabetics (Korkiakangas, Alahuhta, & Laitinen, 2009; N. Thomas, Alder, & Leese, 2004). Yoga, which can be a less strenuous activity, might be a good alternative for this population. Yoga is widely available in the community, simple to learn, and can be practiced by the elderly and people with no prior experience (Khalsa, 2004). Studies on yoga across diverse populations found no major adverse effects (Okonta, 2012; Ross & Thomas, 2010). Moreover, compliance with yoga interventions is usually high (B. E. Cohen, Chang, Grady, & Kanaya, 2008; B. E. Cohen et al., 2007; Flegal, Kishiyama, Zajdel, Haas, & Oken, 2007), and it is well accepted by majority of people (Khalsa, 2004; Li & Goldsmith, 2012). Yoga also requires little equipment and therefore is relatively inexpensive to maintain. Once trained, people can practice at home, leading to long-term adherence. Thus, yoga is a relatively low cost scalable intervention for reducing stress and improving outcomes among adults with T2DM. Though its benefits have been researched for other disease conditions (Cramer, Lange, Klose, Paul,

& Dobos, 2012; Cramer, Lauche, Haller, & Dobos, 2013; Cramer, Lauche, Langhorst, & Dobos, 2013), it has not been tested as a complementary therapy for diabetes in the United States. The HA1C trial is designed to establish intervention feasibility and acceptability in the target population. It will test recruitment and retention procedures and identify barriers to participation. In addition to examining the effect of yoga on glycemic outcomes, behavioral and psychological changes will be examined as this may provide valuable information regarding possible mechanisms of action (mediators) and/or secondary benefits to this population. We are also collecting a non-invasive biomarker (i.e. salivary cortisol); elucidating a mediating influence of circadian cortisol will give a window into biological mechanisms underlying alterations in glucose metabolism. Considering the burden on participants to complete laboratory, home and in-person assessments, this pilot study is crucial to establish feasibility of testing procedures before initiating the larger efficacy clinical trial.

Although the HA1C pilot study is designed to be a rigorous clinical trial, as with all research there are some limitations that need to be considered. We are using an exercise control group with equal contact time. This provides us with a contrast between yoga and an ideal situation: supervised standard exercise. However, this is far more intensive than usual care for patients with T2DM. It is expected that the control group participants will also benefit from the study and thus potential effect size for yoga relative to the control may be reduced. However, we selected this approach to avoid any bias resulting from unequal subject burden and attention, a limitation of treatment-as-usual or wait-list control study design. We are also using qualitative approach to capture any experiential differences from the yoga and control group participants, which may help to explain any similarities or differences in the quantitative outcomes in the two groups. Another protocol decision that can affect study outcomes is that participants may change their medication or insulin dose during the course of this study, if suggested by their physician. However, we are using this approach to mimic the real world situation where diabetes prescription is often changed based on patients' glucose levels, and also it would be unethical to withhold necessary medical treatment from the study participants. Instead we are collecting information about their medications, and will control for it in the analyses.

Despite these limitations, HA1C is a rigorous randomized controlled trial designed to establish feasibility and acceptability of yoga in comparison to an active exercise intervention. Findings from this study will be used to develop the protocol for a future larger clinical trial to test the efficacy of yoga for diabetes management.

Acknowledgments

Funding Source:

This study is funded by the National Center for Complementary and Integrative Health of the National Institutes of Health under award number R21AT008830 to Dr. Beth Bock (PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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Table 1:

Weekly Yoga Practice

Session	Practice
Week 1	1. Upward extended arms and bound knuckle pose 2. Sideways angle pose 3. Half wall stretch 4. Chair twist 5. Relaxation Poses: Legs up the wall and/or Corpse pose with breath awareness and Body Scan.
Week 2	1. Sideways angle pose 2. Flank stretch on wall 3. Standing chair twist at wall 4. Downward facing dog 5. Relaxation Poses: Legs up the wall and/or Corpse pose with breath awareness and Body scan.
Week 3	1. Bound knuckle, Cow face pose 2. Extended leg stretch 3. Hero pose 4. Four footed pose 5. Relaxation Poses: Legs up the wall and/or Corpse pose with breath awareness and Body Scan
Week 4	1. Reclining bound angle pose 2. Child's pose to Downward facing dog (back and forth- 3 poses) 3. Wall hang 4. Marichyasana 1 twist 5. Relaxation Poses: Supported corpse Pose. Practice Body Scan and breath awareness
Week 5	1. Triangle 2. Flank stretch 3. Hero pose with arm clasped 4. Seated twist 5. One or two of the relaxation poses* with breath awareness and Body Scan.
Week 6	1. Triangle 2. Revolved triangle pose 3. Supported bridge pose 4. Plow pose 5. Legs on chair pose 6. Corpse pose 7. One or two of the relaxation poses* with breath awareness and Body Scan.
Week 7	1. Extended leg stretch 2.3.4. Child's pose to Downward facing dog (back and forth – 3 poses) 5. Seated twist 2 6. Plow pose 7. One or two of the relaxation poses* with breath awareness and Body Scan.
Week 8	1. Downward facing dog 2. Hero Pose with Bound knuckle (hands clasped overhead) 3. Supported bridge pose 4. Supported shoulder stand 5. *Legs up the wall 6. *Corpse Pose 7. One or two of the relaxation poses* with breath awareness and Body Scan.
Week 9	1. Standing chair twist at wall 2. Revolved triangle pose 3. Downward facing dog 4. Plough pose 5. *Reclining bound angle pose 6. *Corpse Pose 7. One or two of the relaxation poses* with breath awareness and Body Scan.
Week 10	1. Upward extended arms 2. Seated twist 3. Plow pose 4. Supported shoulder stand 5. * Supported corpse pose 6. *Corpse Pose 7. One or two of the relaxation poses* with breath awareness and Body Scan.
Week 11	1. Sideways angle pose 2. Flank stretch pose

Session	Practice
	3. Boat pose 4. Seated twist 5. *Legs up the wall pose 6. *Corpse pose 7. One or two of the relaxation poses* with breath awareness and Body Scan.
Week 12	1. Upward extended arms 2. Downward facing dog 3. Locust pose 4. Standing twist 5. *Supported bridge on block 6. *Corpse Pose 7. One or two of the relaxation poses* with breath awareness and Body Scan.
	Relaxation Pose Index* 1. Legs up the wall 2. Legs on chair 3. Corpse pose 1 (with blankets supporting back) 4. Corpse pose 2 5. Reclining bound angle pose 6.,7. Reclining hero's pose (2 variations-one resting back on chair, one resting back on bolster) 8., 9.,. Supported bridge pose (2 variations- pelvis on block, blankets along spine and legs)