Association between Weight Loss and Prediabetes Progression to Diabetes at Cheyenne

UW Family Medicine:

A Retrospective Cohort Study

Sidney Y. Ren

University of Wyoming School of Pharmacy
Abstract

Introduction: In 2015, one in three U.S. adults had prediabetes. Substantial evidence supports the use of lifestyle interventions in patients with prediabetes to prevent or delay the incidence of diabetes progression, with the primary benefit derived from interventions targeting weight loss. However, limited evidence elucidates the association between weight loss and progression from prediabetes to diabetes outside of structured interventional programs such as the Diabetes Prevention Program. In this retrospective cohort analysis, we evaluate the association between weight loss on reducing the risk of progression to diabetes over one year in prediabetic patients seen in a family practice clinic.

Methods: This retrospective cohort study evaluated patient data collected from the University of Wyoming Family Medicine in Cheyenne, Wyoming under institutional review board approval. Patients were included in the study if the following two criteria were met: an initial HbA1c of 5.7 to 6.4 percent from June 2014 to June 2017; a follow-up HbA1c between 6 to 18 months after the initial HbA1c. Patients were then stratified into two groups: patients who did not lose 5 percent of their body mass by the second HbA1c (control group) and those who did (weight loss group). The body weights in this study were those associated with the HbA1c visit (primarily on the same day). Patients who did not have a corresponding weight recorded within 2 weeks were excluded. The primary outcome measured was a mean difference of the proportion of patients who progressed to diabetes (HbA1c greater than or equal to 6.5 percent). The secondary outcome measured the difference of mean HbA1cs between the two groups. Statistical comparison of the control group and weight loss group was performed using Fisher’s exact test. Statistical significance was achieved at p less than 0.05. All statistical analyses were performed using R Studio and R 3.5.1.
Results: Between June 2014 and June 2017, 142 patients matched the inclusion criteria for this study. 22 patients lost greater than or equal to 5 percent weight loss over the study period and were stratified into the weight loss group, while 120 patients were included in the control group. Mean follow-up time between HbA1c was 343 days for the combined groups, with no significant differences between groups. Other baseline characteristics were also similar between groups. In total, 30 patients (21 percent) progressed to diabetic status upon follow-up (HbA1c greater than or equal to 6.5). Three patients (14 percent) and 27 patients (22.5 percent) progressed to diabetes in the weight loss and control groups respectively. There was no significant difference in the primary outcome between the weight loss group and control group, odds ratio 0.55 (95 percent confidence interval, 0.1 to 2.1, P equals 0.57). There was no significant difference between the follow-up HbA1Cs between the two groups (P equals 0.52).

Conclusion: This retrospective cohort study found no significant difference between prediabetic patients who achieved 5 percent loss of their starting body weight to those who did not, suggesting the benefit of weight loss may be limited to interventional programs. One significant limitation of the study, however, was the small sample size. There were only 22 patients who achieved 5 percent weight loss in the year of follow-up. Larger scale studies are necessary to elucidate the role of weight loss in prevention of diabetes in prediabetic patients, especially outside of prevention programs such as the Diabetes Prevention Program.
Background

Diabetes mellitus is a complex, chronic disease associated with significant microvascular and macrovascular complications, which lead to increased morbidity and mortality\(^1\). In 2015, one in every ten people in the United States met the criteria for diabetes, with up to one-fourth of diabetics unaware of their status. Unfortunately, the economic and social impact of diabetes continues to grow annually; in 2015, there were 1.5 million new diagnoses of the chronic disease\(^2\). Consequentially, diabetes is now the costliest chronic illness in the U.S, with diabetes-associated health care expenses incurring $327 billion in 2017. For perspective, a quarter of every health care dollar spent is on behalf of individuals diagnosed with diabetes\(^3\). To combat both the economic and health impact of diabetes, management of the disease is vital. Strategies to treat diabetes traditionally focus on the management of hyperglycemia, with the goal of preventing the long-term manifestations of elevated blood sugar. Despite major advances in medical treatment, even those with well-controlled diabetes remain at increased risk of complications. Given these circumstances, the prevention or delay of the development of diabetes is the key factor to reduce the negative impact of the disease.

In 2015, one in every three U.S. adults were at high risk for developing diabetes, a condition defined as prediabetes. In large patient surveys, of those with the diagnostic criteria for prediabetes, only 11% reported that a health professional had addressed their condition\(^2\). This is despite the problem that prediabetes is characterized by abnormal, elevated glycemic parameters that have not yet met the diagnostic criteria for diabetes; up to 10% of prediabetic patients will progress to diabetes annually\(^4\). With now over 84 million U.S. adults affected by prediabetes, the prevention or delay of the progression of prediabetes into diabetes offers a potent strategy to improve populational health outcomes and reduce a significant economic burden.
Substantial evidence supports the use of interventions in patients with prediabetes to prevent or delay the incidence of diabetes progression, with the primary benefit derived from nonpharmacological lifestyle interventions such as increasing exercise and targeting weight loss. Large clinical studies, such as the Finnish Diabetes Prevention Study and the Da Qing study, have shown lifestyle interventions sustaining a reduction of the incidence of diabetes by nearly 50% at 7 and 20 years respectively in non-U.S. populations\(^5,6\). Within the U.S, the U.S. Diabetes Prevention Program (DPP) demonstrated that intensive lifestyle interventions reduced the incidence of diabetes by 58% over 3 years compared to the control group\(^7\). Similarly to the other clinical trials, follow-up studies showed sustained reductions of the incidence of diabetes by 34% at 10 years and 27% at 15 years among the intensive lifestyle intervention group\(^8,9\). These intensive lifestyle interventions included a structured 24-week curriculum of group sessions and educational classes paired with the goals of targeting at least 150 minutes of moderate-intensity physical activity per week and achieving at least 7% weight loss within the first 6 months. Subsequent analyses show weight loss as the primary driver of the reduction in diabetes progression seen in the DPP, with a 16% relative risk reduction for each kilogram of weight loss. By the end of the first year, the DPP intensive lifestyle intervention arm achieved an average weight loss of 6.8 kg (7.2%)\(^10\).

Limited evidence elucidates the association between progression from prediabetes to diabetes and weight loss in practice settings outside of lifestyle interventions modeled after the DPP. In practice, common approaches to prediabetes management include recommending diet and exercise changes to promote weight loss. In this study, we evaluate retrospectively the effect of prediabetic patients achieving at least a 5% weight loss on the risk of progression to diabetes in a community setting.
Methods

Study Design

This study was a retrospective cohort study based on patient data that was collected from the University of Wyoming Family Medicine (UWFM) Residency Program in Cheyenne, Wyoming. UWFM is a Federally Qualified Health Center that offers comprehensive medical clinic that provides comprehensive medical care from physicians, medical residents, midlevel practitioners, nurses, and social workers. Our study was granted IRB exemption from the University of Wyoming (see Appendix). All patients with an initial A1C of 5.7 to 6.4 percent (the American Diabetes Association [ADA] criteria for prediabetes) between June 2014 and June 2017 were included in this retrospective cohort study. Additionally, a repeat A1C was required to assess the primary outcome, therefore patients whom did not have a follow-up A1C between 6 to 18 months after the initial A1C were excluded from this study. Patients with pre-existing diabetes or on metformin therapy were excluded from the trial.

As weight loss is commonly recommended in the prevention of diabetes, to assess the role of weight loss on the progression of prediabetes to diabetes, patients included in this study were stratified according to whether they achieved greater than or equal to 5% loss of their body weight by the follow-up A1C. Body weight measurements corresponding to the in-house A1C laboratory measurements were used as comparators. The method of losing weight was not evaluated during this study, nor was the analysis adjusted based on provider. Those who achieved 5% weight loss were stratified into the intervention group and those who did not reach 5% weight loss were stratified into the control group.
Outcomes

The primary outcome was the incidence of progression from prediabetes to diabetes, defined as an A1C of greater than or equal to 6.5% upon follow-up between 6 to 18 months. The only defined secondary outcome evaluated whether there was a difference between the HbA1Cs of the control and weight loss groups.

Statistical Analysis

An analysis for power was not calculated. 95% confidence intervals were calculated using binomial distributions. Statistical comparison of the control group and weight loss group was performed using Fisher’s exact test. Statistical significance was achieved at $p < 0.05$. All statistical analyses were performed using R Studio and R 3.5.1\textsuperscript{11, 12}.

Results

Between June 2014 and June 2017, 643 patients at UWF were screened for eligibility, with 501 patients not meeting the criteria for inclusion into the study. 142 patients that met inclusion criteria were randomly selected to be included in the study and undergo statistical analysis. Of those selected, 22 patients met the criteria for greater than or equal to 5% weight loss over the study period and were assigned to the intervention group. 120 patients did not meet the criteria for weight loss over the study period and were assigned to the control group. The median age of the patients was 60. Follow-up A1Cs were measured at a median follow-up close to one year. Baseline characteristics were similar between groups.
Figure 1. Patient Selection

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Control (n=120)</th>
<th>Intervention (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>59 (54 to 64)</td>
<td>60 (49 to 71)</td>
</tr>
<tr>
<td>Male (%)</td>
<td>45 (36 to 55)</td>
<td>37 (15 to 59)</td>
</tr>
<tr>
<td>White (%)</td>
<td>69 (60 to 78)</td>
<td>74 (49 to 91)</td>
</tr>
<tr>
<td>Initial A1C (%)</td>
<td>6 (5.9 to 6.1)</td>
<td>6.2 (6.0 to 6.4)</td>
</tr>
<tr>
<td>Initial Weight (lbs)</td>
<td>204 (183 to 225)</td>
<td>237 (190 to 284)</td>
</tr>
<tr>
<td>Follow-Up Time (days)</td>
<td>336 (301 to 371)</td>
<td>378 (278 to 478)</td>
</tr>
</tbody>
</table>

*95% confidence intervals are additionally shown*
Upon the one-year follow-up, a total of 30 patients (21%) within the study cohort progressed to diabetic status defined as an A1C greater than or equal to 6.5%. Three patients (14%) and twenty-two patients (23%) met the primary outcome in the intervention and control groups respectively. There was no significant difference in the primary outcome between the weight loss group and control group, \( \text{OR} \ 0.55 \ (95\% \ CI, \ 0.1 \ to \ 2.1, \ p = 0.57) \). There was also no significant difference between the follow-up HbA1Cs, the secondary outcome, between the two groups \( (p = 0.52) \).

**Figures 2 & 3.** Progression from Prediabetes to Diabetes in Control and Weight Loss Groups
Discussion

This retrospective cohort study aimed to evaluate the effect of weight loss on the progression of prediabetes to diabetes in a real-world community setting. Notably, the study did not detect a significant difference in the progression of diabetes between prediabetic patients who lost 5% of their starting body weight compared to those who did not undergo 5% weight loss after one year of follow-up. The results from this cohort study contrast with the various clinical trials performed showing the beneficial effect of weight loss on preventing diabetes progression. However, there are several important differences and limitations to this study in comparison to larger clinical trials.

First, this study was performed using existing patient data to identify subjects for inclusion using real-world data from a single clinic in Wyoming. Unlike a randomized, blinded, placebo-controlled trial, the methods used to achieve weight loss or individual dietary recommendations made to the patients by their providers were unknown to the primary researcher. Secondly, based on the small sample size, this trial was likely underpowered to detect a significant difference if one existed. A power calculation prior to the initiation of this trial would have likely been useful to evaluating outcomes. Although dietary and lifestyle modifications to achieve weight loss are commonly recommended to prediabetic patients, great interindividual variability exists between health care providers in their recommendations to achieve such lifestyle changes. Notably, a minority of patients achieved significant weight loss after meeting prediabetic status. This variability could not be controlled nor measured in this study. Larger scale cohort studies are needed to evaluate the role of weight loss on the progression of diabetes, especially outside of interventional programs such as the DPP. These
studies could further elucidate the role of body weight and the development of the chronic disease.

**Conclusion**

In conclusion, this retrospective cohort study found no significant difference between prediabetic patients who lost 5% of their starting body weight to those who did not lose 5% of their body weight. Notably, the study was underpowered, as there were only 22 patients who achieved 5% weight loss in the year of follow-up. Larger scale studies are necessary to elucidate the role of weight loss in prevention of diabetes in prediabetic patients, especially outside of prevention programs such as the DPP.

**References**


Supplementary Appendix

Supplement 1. IRB Approval Copy

UNIVERSITY OF WYOMING

Vice President for Research & Economic Development
1000 E. University Avenue, Department 3355 • Room 305/308, Old Main • Laramie, WY 82071
(307) 766-5353 • (307) 766-5320 • fax (307) 766-2608 • www.uwyo.edu/research

September 17, 2018

Sidney Ren
Graduate Student
Pharmacy
University of Wyoming

Thanh-Nga Nguyen
Clinical Assistant Professor
Pharmacy
University of Wyoming

Protocol #20180917SR02110

Re: IRB Proposal “Association between weight loss and prediabetes progression to diabetes at Cheyenne UW Family Medicine: a retrospective cohort study”

Dear Sidney and Thanh-Nga:

The proposal referenced above qualifies as exempt and is approved as one that would not involve more than minimal risk to participants. Our exempt review and approval will be reported to the IRB at their next convened meeting on October 18, 2018.

Any significant change(s) in the research/project protocol(s) from what was approved should be submitted to the IRB (Protocol Update Form) for review and approval prior to initiating any change. Further information and the forms referenced above may be accessed at the “Human Subjects” link on the Office of Research and Economic Development website: http://www.uwyo.edu/research/human-subjects/index.html

You may proceed with the project/research and we wish you luck in the endeavor. Please feel free to call me if you have any questions.

Sincerely,

Nichole Person
Staff Assistant, Research Office
On behalf of the Chairman,
Institutional Review Board
Supplement 2. CITI Certification for Human Research

This is to certify that:

Sidney Ren

Has completed the following CITI Program course:

Basic/Refresher Course - Human Subjects Research (Curriculum Group)
Biomedical Research (Course Learner Group)
1 - Basic Course (Stage)

Under requirements set by:

University of Wyoming

Verify at www.citiprogram.org/verify?w492274ac-b612-40ab-9fee-da64a0e17020-27278621
Acknowledgements

I would like to thank David from UWFM for his assistance in retrieving and formatting the patient data in a meaningful manner. Importantly, I would like to thank Dr. Thanh-Nga Nguyen for her role in developing this research project and for the incredible assistance, guidance, and mentorship she provided during a critical part of the end of my time as a pharmacy student. Dr. Nguyen, alongside all the faculty and staff at the School of Pharmacy, have been instrumental in my path for the future. Lastly, I would also like to thank the University of Wyoming Honors College for providing an incredible opportunity to not only support the sciences, but also cultivate well-rounded individuals through studies of the humanities.