Relations between Inflammation and Access to care, Treatment, and Diabetes in Older Mexico

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Author Note

List of group members ordered by alphabet.

Abstract

Background. Background goes here. *Methods.* Methods go here. *Results.* Results here.

Conclusions. Conclusions here.

Keywords: Diabetes, access to care, inflammation, health, Mexico, China

Word count: X (this cannot easily be done automatically, we can also just leave it out)

Relations between Inflammation and Access to care, Treatment, and Diabetes in Older Mexico

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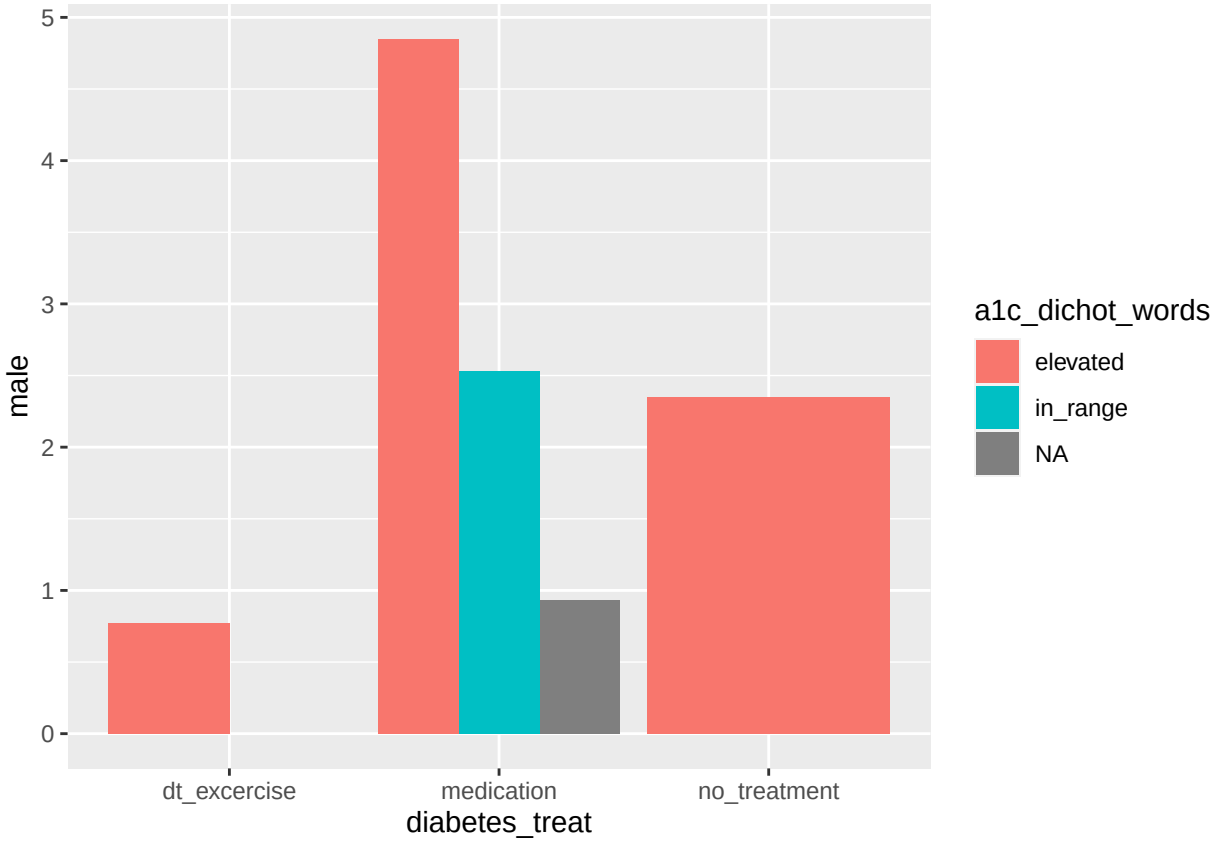

Figure 1

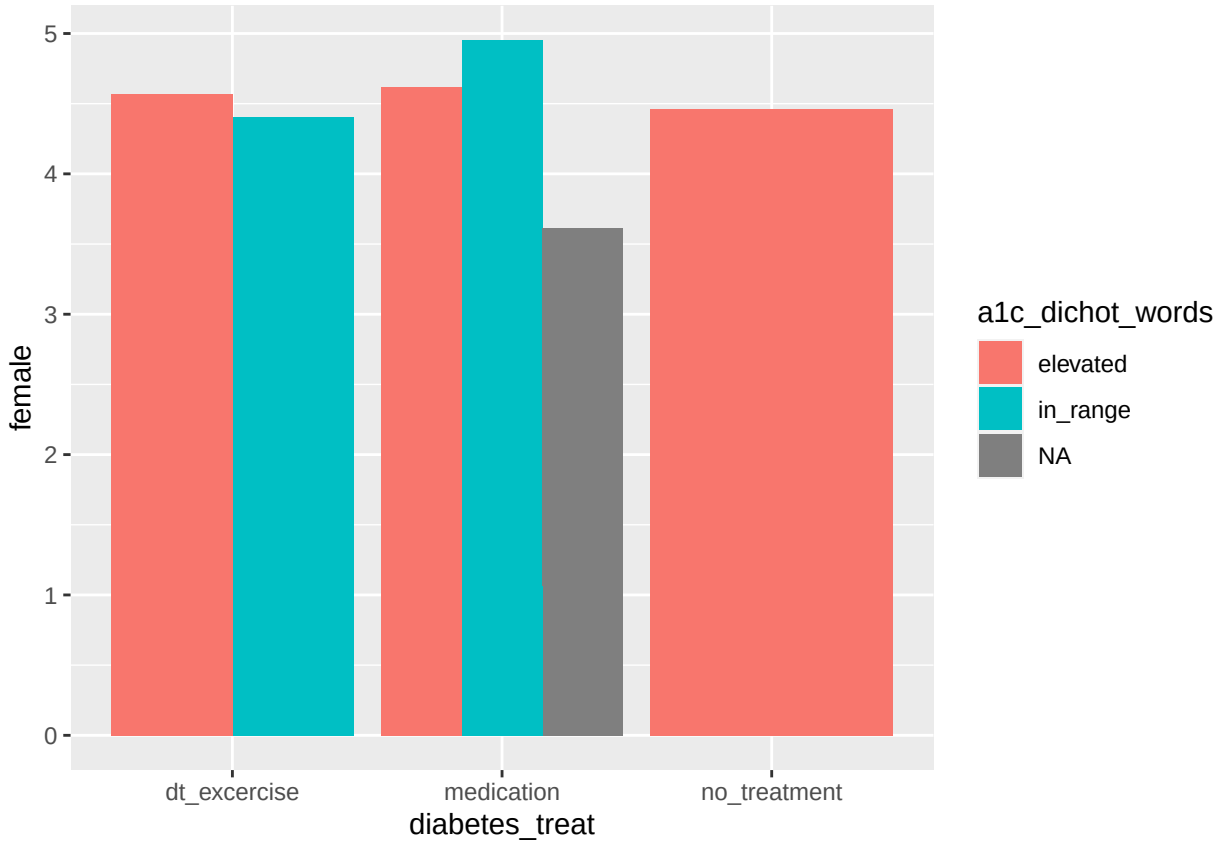

Figure 2

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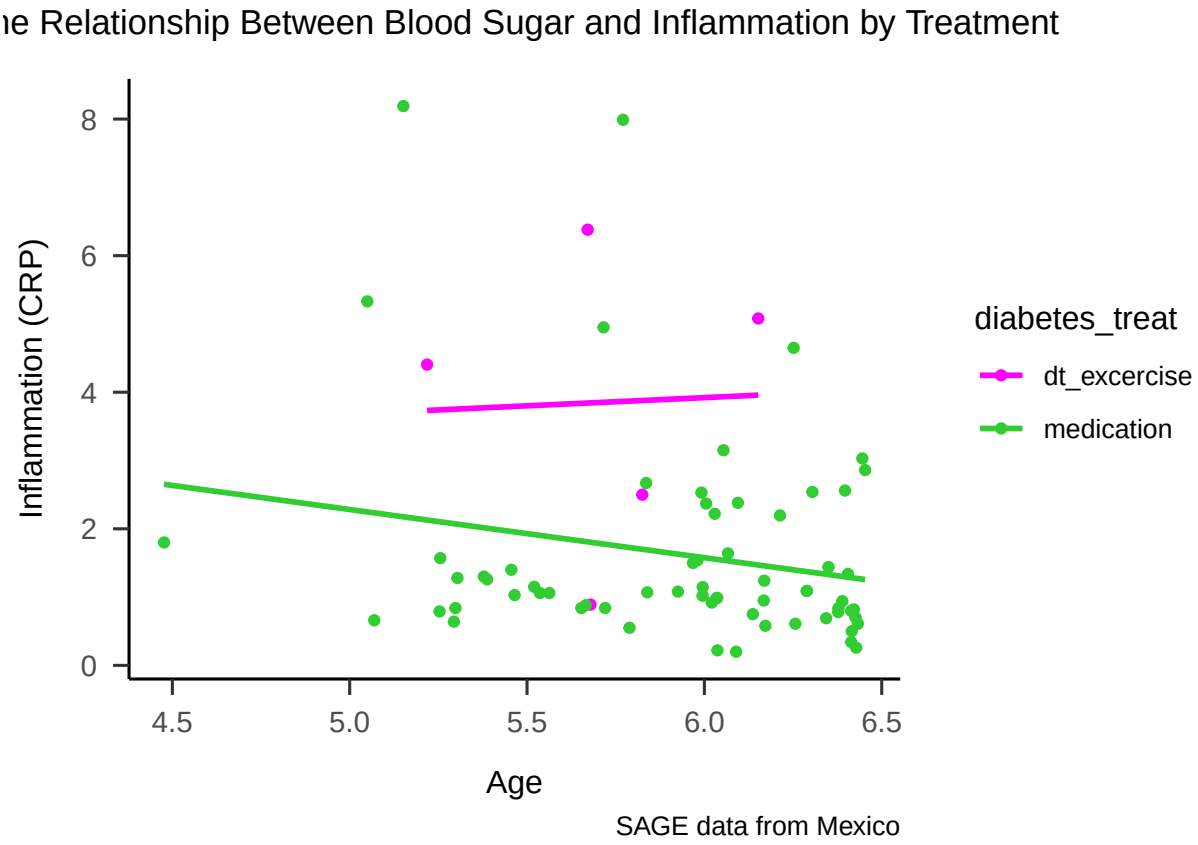

Figure 3. This is the caption of figure 3.

```
## <ggproto object: Class ScaleDiscrete, Scale, gg>
##     aesthetics: colour
##     axis_order: function
##     break_info: function
##     break_positions: function
##     breaks: waiver
##     call: call
##     clone: function
##     dimension: function
##     drop: TRUE
##     expand: waiver
##     get_breaks: function
```

```
##     get_breaks_minor: function
##     get_labels: function
##     get_limits: function
##     guide: legend
##     is_discrete: function
##     is_empty: function
##     labels: Diet & Exercise Medication
##     limits: NULL
##     make_sec_title: function
##     make_title: function
##     map: function
##     map_df: function
##     n.breaks.cache: NULL
##     na.translate: TRUE
##     na.value: NA
##     name: Diabetes Treatment
##     palette: function
##     palette.cache: NULL
##     position: left
##     range: <ggproto object: Class RangeDiscrete, Range, gg>
##         range: NULL
##         reset: function
##         train: function
##         super:  <ggproto object: Class RangeDiscrete, Range, gg>
##     rescale: function
##     reset: function
##     scale_name: brewer
```

Table 1

Effect of Medication on CRP, controlling for Age.

Predictor	*b*	95% CI	*t*	*df*	*p*	predictor
Intercept	2.00	[1.06, 2.94]	4.18	354	$< .001$	Intercept
Age	-0.01	[-0.02, 0.01]	-0.91	354	.362	Age
Medication2	0.20	[-0.17, 0.56]	1.07	354	.284	Medication

Note. Model fit: $F(2, 354) = 1.06$, $p = 0.35$, $R^2 = 0.01$.

```
##     train: function
##     train_df: function
##     transform: function
##     transform_df: function
##     super:  <ggproto object: Class ScaleDiscrete, Scale, gg>
```

Here, I want to point the reader to Figure 3.

Demo of inline code usage. We found that this regression model (Table 1) using 357 participants was not significant $F(2, 354) = 1.06$, $p = 0.35$ with $R^2 = 0.01$. The regression coefficient for age was b_{age} = -0.01 ($SE = 0.01$, $p = 0.36$), and for use of medication $b_{medication} = 0.20$ ($SE = 0.18$, $p = 0.28$).

Table 2

Effect of Diet and Exercise on CRP, controlling for Age.

Predictor	*b*	95% CI	*t*	*df*	*p*	predictor
Intercept	2.10	[1.17, 3.04]	4.43	354	< .001	Intercept
Age	-0.01	[-0.02, 0.01]	-0.83	354	.408	Age
Dt exrcse2	-0.25	[-0.47, -0.02]	-2.11	354	.036	Diet and Exercise

Note. Model fit: $F(2, 354) = 2.71$, $p = 0.07$, $R^2 = 0.02$.

Demo of inline code usage. We found that this regression model (Table 2) using 354 participants was not significant $F(2, 354) = 2.70$, $p = 0.07$ with $R^2 = 0.02$. The regression coefficient for age was b_{age} = -0.01 ($SE = 0.01$, $p = 0.41$), and for diet and exercise b_{Diet} = -0.24 ($SE = 0.12$, $p < 0.05$).

```
## # A tibble: 171 x 2
##    `RQ4df$access` `RQ4df$crp2`
##    <fct>          <fct>
##  1 No             high
##  2 No             low
##  3 Yes            low
##  4 No             low
##  5 No             low
##  6 No             low
##  7 Yes            low
##  8 Yes            low
##  9 No             low
## 10 No             high
## # ... with 161 more rows
```

```
##
##  Pearson's Chi-squared test with Yates' continuity correction
##
## data:  RQ4df$access and RQ4df$crp2
## X-squared = 0.51779, df = 1, p-value = 0.4718
```

```
##             RQ4df$crp2
## RQ4df$access      low     high
##          Yes 67.26316 13.73684
##          No  74.73684 15.26316
```

```
##             RQ4df$crp2
## RQ4df$access low high
##          Yes  65   16
##          No   77   13
```

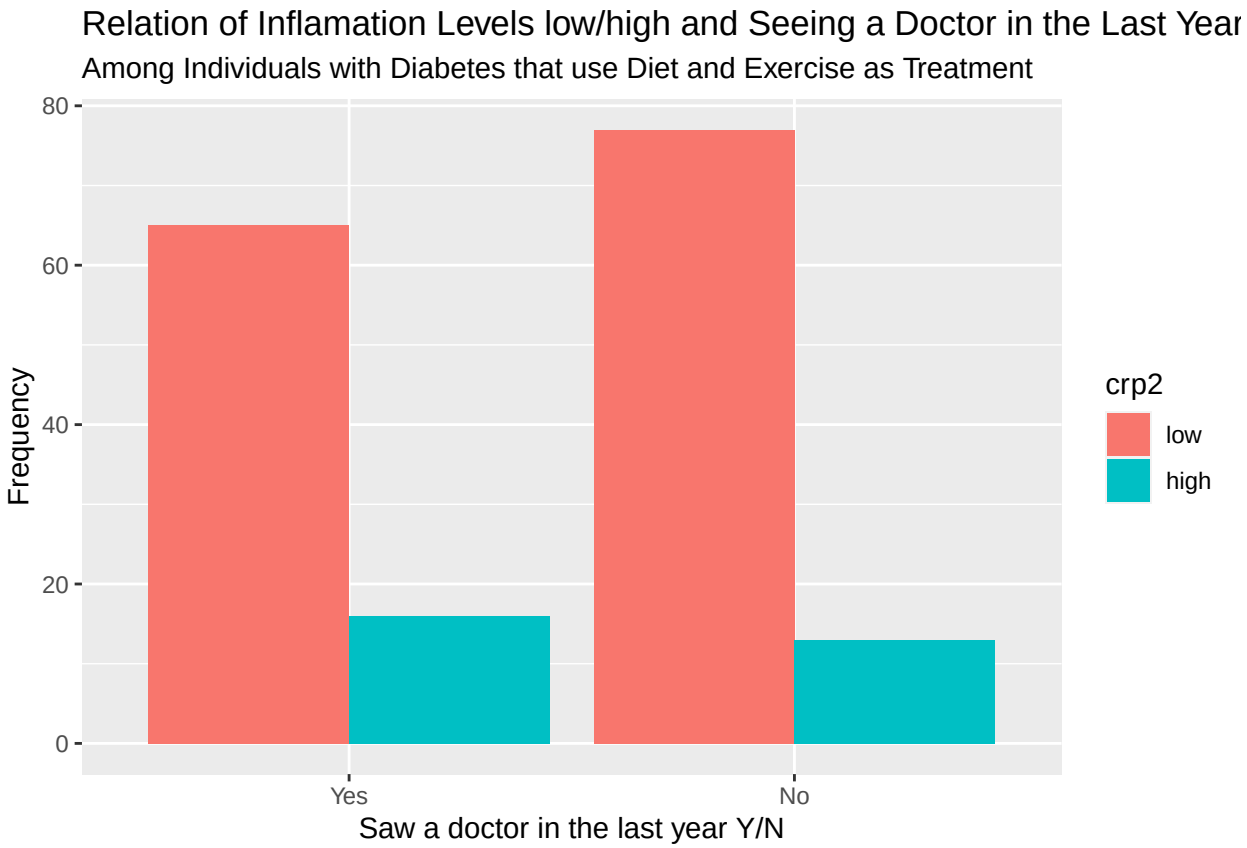

Figure 4

```
##
##  Chi-squared test for given probabilities
##
## data:  table(data$sex)
## X-squared = 44.596, df = 1, p-value = 2.422e-11
```

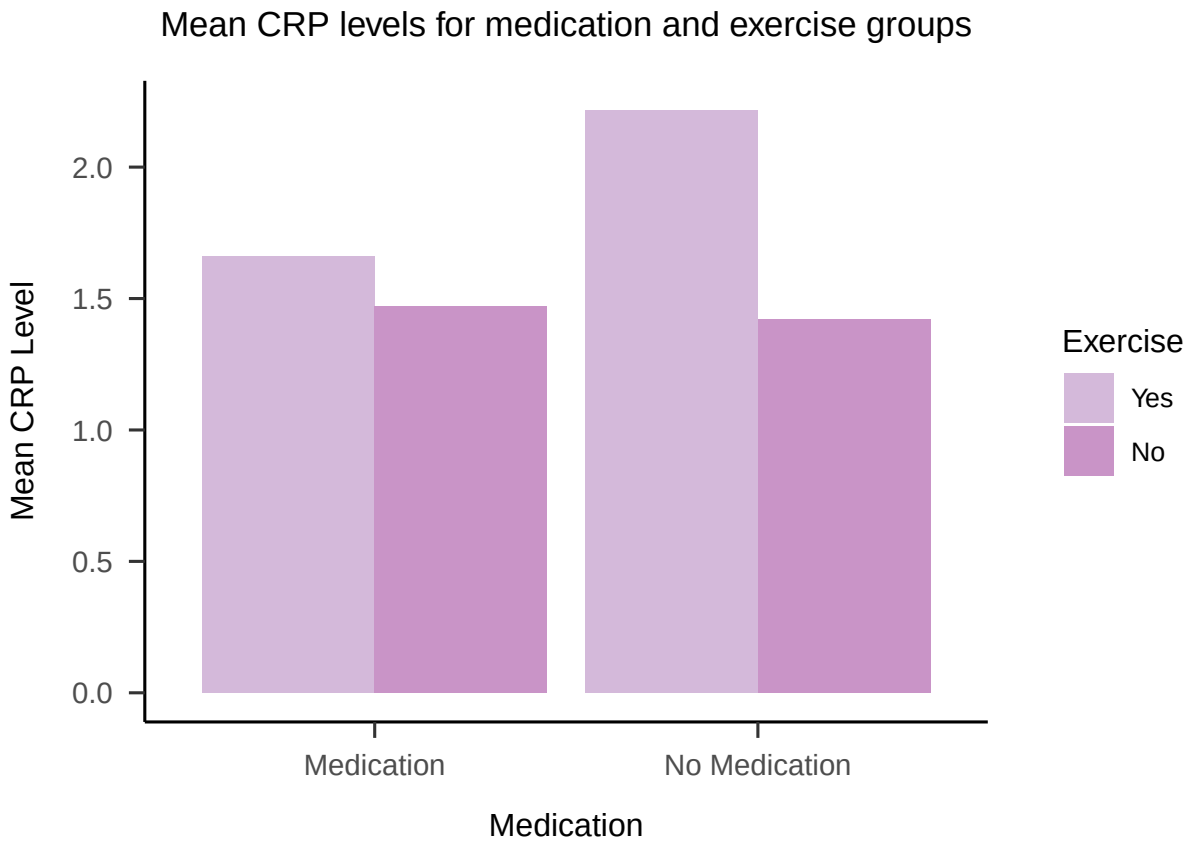

Figure 5. Caption for Figure 5 goes here.

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Table 3

Descriptive statistics.

	Mexico
N_{total}	357
Sex	
male	115 (32.20 %)
female	241 (67.50 %)
unknown	1 (0.30 %)
Age	68 (SD = 8.40)

Introduction

Diabetes and its insidious complications continue to expand as a global health burden at an alarming rate. As of 2021, there were approximately 537 million adults living with diabetes in the world and this number is expected to jump to 783 million by 2045. A disproportionate percentage of these people live in low to middle income countries (LMICs). In light of the COVID-19 pandemic, it is also of great import that we better understand the relationships between diabetes and infectious diseases as diabetes both increased the severity of Covid (in people with elevated a1c levels) and has increased in incidence during the Covid 19 pandemic (Yang et al., 2020) (Rohm, Meier, Olefsky, & Donath, 2022).

Additionally, diabetes is associated with a steep increase in cardiovascular disease risk and is a leading cause of death in many low to middle income countries (LMICs) including Mexico. Although the precise classification of diabetes remains controversial because of the complex nature of its pathogenesis, there are three universally acknowledged subtypes: type 1 diabetes, type 2 diabetes, and gestational diabetes. Diabetes is a progressive disease in that the longer one has it, the more complications ensue. Therefore, it is helpful to conceptualize diabetes as a process that can be stopped, but not reversed. Research that contributes to slowing down or stopping the process can be extremely valuable to global health regardless of its contribution to cure and prevention because of the astronomical rates of diabetes in our world today.

Inflammation is a strong indicator of diabetes development and progression. Inflammation predicts the development of diabetes (Dilys J. Freeman et al., 2002) (Dilys J. Freeman et al., 2001) (Schmidt et al., 1999). Specifically, trials for drugs directed at inflammation among people with type 2 diabetes have indicated that drugs targeted at inflammation may be a therapeutic option for preventing diabetes (Agrawal & Kant, 2014).Retinopathy and focal neuropathy (Said, 2007) have also been linked to inflammatory processes. Additionally, the direct damage caused by high blood glucose leads to more

inflammation and creates a nasty feedback loop wherein inflammation causes more insulin resistance which leads to high blood glucose.

Diabetes treatment and inflammation

The ability of cells to absorb insulin can be increased through diet, exercise, and oral pills.Increasing exercise and dieting can cause major decreases in inflammation. Some of the drugs for type 2 diabetes aimed at increasing insulin sensitivity also decrease inflammation (e.g., drugs that cause weight loss). In the opposite direction, insulin can cause severe low blood glucose levels that initiate a stress response causing more inflammation.

Methods

Procedures and Sample

357 participants were included in our analyses. Of those, 115 were assessed to be male (32.20 %), 241 were identified to be female (67.50 %). Sex data for 1 participant was missing (see Table 3). This indicates that females were overrepresented in our sample, assuming binary sexes are represented equally in the population ($\chi(1) = 44.60$, $p < 0.0001$). The age in our sample was $M = 68$ years (SD = 8.40 years). Because of missing values in the variables of interest in some of our analyses, subjects were excluded. Thus, N is reported separately for each analysis.

Variables

The original WHO dataset contains more than 1,600 variables, not all of which are relevant to our research questions. Therefore, we have limited our analysis to 10 variables, listed below in Table 1. In our analysis, we only included participants who reported that they already have a formal diabetes diagnosis from a doctor, since our research questions revolve around diabetes treatments. Figure (plot_all) shows the raw data and the data that we selected for our analysis (the colorful points on the far left).

filtering. A variable was created called "diabetes treatment" wherein anyone who answered yes to

[edit this to describe the three we use in our analysis] A variable was created to indicate whether or not someone fell into one of the four following categories: diagnosed and treated diabetes, diagnosed and untreated diabetes, undiagnosed diabetes, or no diabetes. This variable was created using 3 questions from the in-person survey portion of the study. If participants answered yes to "Have you ever been diagnosed with diabetes (high blood sugar)?" and also answered yes to either "Have you been taking insulin or other blood sugar lowering medications in the last 2 weeks?" or "Have you been following a special diet, exercise regime or weight control program for diabetes during the last 2 weeks?", then they were in the diagnosed and treated group (China: n = 448, Mexico: n = 165). If they answered yes to diagnosis, but no to both treatment questions then they were placed in the untreated diabetes group (China: n = 43, Mexico: n = 39). If they answered no to the diagnosis question and their HbA1c was under 6.5% then they were placed in the no diabetes group (China: n = 5,246, Mexico: n = 1,241). Lastly, if they answered no to the diagnosis question but their HbA1c was 6.5% or higher, then they were placed into the undiagnosed diabetes group (China: n = 444, Mexico: n = 181). There was a group of people in both countries who answered "no" to both treatment options but still had an HbA1c level below 6.5% (China: n = 29, Mexico: n = 17). These people were excluded from the analysis.

[This is good as is] A variable was then created that indicated "unknown treatment" if the diabetes treatment variable indicated that there was no treatment but hba1c was below 6.5 and otherwise "Known treatment" was indicated. All "unknown treatment" variables were then removed (n = 17). See plot.all2 and plot.all_filtered to see the data before and after these data points were filtered out.

Biomarkers. A subset of people participating in the SAGE study underwent biomarker analysis in Mexico (n = 1831) and in China (n = 12,077). Exclusions included

people for incomplete data, ### people for having an elevated CRP value that might indicate injury or infection. The sample was ##% female and ##% male. Participant ages for this analysis ranged from 50 to 105 years old (M = 68.27, SD = 9.23).

Biomarkers were analyzed using dried blood spot (DBS) procedures, and collected via standard venipuncture into an EDTA tube. In order to go from venous blood to DBS, the samples of whole blood were homogenized and then pipetted in 20uL aliquots onto standard Whatman 903 filter paper. The samples were left to dry for 24 hours at room temperature before they were analyzed. We punched out a 6mm spot from the DBS card and used 250 uL of PBS buffer pH = 7 to elute for 14 hours. The Abbott Architect CI8200 chemistry analyzer was used to analyzed the DBS eluates in order to obtain CRP values and it was used for HbA1c as well.

Hemoglobin A1c (HbA1c) is a measure of average blood glucose values over the past 3 months. HbA1c also required a 6 mm DBS punch. This one was eluted in 400uL MULTIAGEN Hemoglobin Denaturant for 14 hours. The Architect blood chemistry analyzer was loaded with a cuvette with eluent and was then used to determine HbA1c and total hemoglobin by measuring absorbance at 700 for Hba1cnm and 604nm for total hemoglobin. The analyzer's program calculated percent HbA1c using the following formula:[(HbA1c/TotHb)×100] - 3+(0.2 × TotHb).

Self-report surveys conducted by trained interviewers.

Data are from the World Health Organization's Study on Adult Health and Ageing (SAGE). Our data is from 1 of 5 countries where the data were collected.

All analyses were conducted in R with the following packages: here (Müller, 2020), rio(**chanRioSwissarmyKnife2021?**), tidyverse[re], ggpubr (**kassambaraGgpubrGgplot2Based2022?**),bibtex (**francoisBibtexBibtexParser2022?**),papja (**austPapajaPrepareReproducible2022?**),

psych (**revellePsychProceduresPsychological2022?**),and forcats (**wickhamForcatsToolsWorking2022?**).

comment 495 # Results

Discussion

We see diet and exercise predicting CRP over and above the effects of age such that those who said that they do diet and exercise (insert direction based in RQ2 results).

Ultimately we see that inflammation is impacted by diabetes treatments. Access to care does not appear to explain (summarize baed on RQ3). However, it is important that further exploration between diabetes, inflammation, and diabetes treatments take place.

Limitations

We were not able to look at pills and insulin separately and some their effects have the potential to cancel each other out. The sex variable was established through interviewer discernment. * combination therapy is a possibility that we could not account for. Additionally we do not know exactly which medications people were taking.

Appendix

Despite the documented limitations of the World Health Organization Health State Description scale (**asadaMedicalTechnologiesNonhuman2005?**), it is worth exploring in future studies whether or not this scale captures diabetes complications in such a way that we might be able to analyze connections between inflammation and diabetes complications cross-sectionally in the SAGE data.

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Figure captions

Figure 1.

Figure 2.

Figure 3. This is the caption of figure 3.

Figure 4.

Figure 5. Caption for Figure 5 goes here.

Table captions

Table 1. Effect of Medication on CRP, controlling for Age.

Table 2. Effect of Diet and Exercise on CRP, controlling for Age.

Table 3. Descriptive statistics.