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1 2 Associations Between Immigrant Status and Pharmacological Treatments for Diabetes 3 in U.S. Adults 4 Loretta Hsueh, Elizabeth A. Vrany, Jay S. Patel, Nicole A. Hollingshead, Adam T. Hirsh, 5 6 Mary de Groot, and Jesse C. Stewart Indiana University-Purdue University Indianapolis and Indiana University School of Medicine 7 8 9 10 11 Author Note 12 Loretta Hsueh, Elizabeth A. Vrany, Jay S. Patel, Adam T. Hirsh, and Jesse C. Stewart, 13 Department of Psychology, Indiana University-Purdue University Indianapolis; Nicole A. 14 Hollingshead, Department of Psychology, Indiana University-Purdue University Indianapolis, 15 and Department of Psychiatry and Behavioral Medicine, Ohio State University Wexner Medical 16 17 Center; Mary de Groot, Diabetes Translational Research Center, Indiana University School of Medicine. 18 Correspondence concerning this article should be addressed to Jesse C. Stewart, Ph.D., 19 20 Department of Psychology, Indiana University-Purdue University Indianapolis, 402 North Blackford Street, LD 100E, Indianapolis, IN 46202. Telephone: (317) 274-6761. Fax: (317) 274-21 22 6756. Email: jstew@iupui.edu 23

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#### Abstract

**Objectives:** Although treatment disparities in diabetes have been documented along racial/ethnic 2 3 lines, it is unclear if immigrant groups in the U.S. experience similar treatment disparities. Our primary objective was to determine whether immigrant status is associated with differences in 4 5 pharmacological treatment of diabetes in a nationally representative sample of adults with 6 diabetes. We were specifically interested in differences in treatment with oral hypoglycemic 7 agents (OHA) and insulin. Methods: Respondents were 2,260 adults from NHANES 2003-2012 8 with a self-reported diabetes diagnosis. Immigrant status was indicated by birth within (U.S.-9 born) or outside (foreign-born) the 50 U.S. States or Washington, D.C. Multinomial logistic regression analyses examined associations between immigrant status and (a) treatment with 10 OHAs only and (b) treatment with insulin only or insulin and OHA combination therapy, using 11 12 no treatment as the reference group. Results: Immigrant status was associated with differences in 13 treatment with insulin, but not OHAs, for diabetes. Adjusting for demographics, diabetes severity 14 and duration, CVD, and CVD risk factors, being foreign-born versus U.S.-born was not associated with treatment with OHAs only (OR=1.59; 95% CI: 0.97-2.60). However, being 15 foreign-born was associated with decreased odds (OR=0.53; 95% CI: 0.28-0.99) of treatment 16 17 with insulin. Conclusions: Pharmacological treatment of diabetes differs along immigrant status lines. To understand these findings, studies capturing the processes underlying treatment 18 19 differences in diabetes among immigrants are needed. Findings also raise the possibility that 20 integrating information about a patient's immigrant status, in addition to racial/ethnic identity, 21 may be an important component of culturally sensitive diabetes care. 22 Keywords: diabetes mellitus; hypoglycemic agents; emigrants and immigrants; healthcare 23 disparities.

- 1 Acronyms: U.S. = United States; OHA = oral hypoglycemic agent; NHANES = National Health
- 2 and Nutritional Examination Survey; CVD = cardiovascular disease

1	Over 29 million adults in the U.S. suffer from diabetes, with another 86 million adults
2	facing prediabetes (CDC, 2014). After diabetes onset, poor management can result in serious
3	complications – such as neuropathy, retinopathy, and amputation – and can lead to related
4	chronic medical conditions – such as atherosclerotic cardiovascular disease (CVD; Fowler, 2011)
5	One factor that contributes to poor diabetes management is receiving inadequate diabetes care
6	(Nam, Chesla, Stotts, Kroon, & Janson, 2011; Schmittdiel et al., 2008; Ziemer et al., 2005).
7	High-quality diabetes care involves timely and appropriate treatment with medications, such as
8	oral hypoglycemic agents (OHAs) and insulin (American Diabetes Association [ADA], 2016).
9	Racial/ethnic minority groups face health disparities across many conditions, including
10	diabetes. For instance, the prevalence and incidence of diabetes are higher among certain
11	racial/ethnic minority groups, such as non-Hispanic blacks, Latinos, and Asian Indians (Chinet
12	al., 2012; CDC, 2014; Spanakis & Golden, 2013). Racial/ethnic minority groups are also more
13	likely to experience diabetes-related complications and mortality (Emanuele et al., 2005; Golden
14	et al., 2012; Lanting, Joung, Mackenbach, Lamberts, & Bootsma, 2005; Y. Li, Liao, Fan, Zhang,
15	& Balluz, 2010; Spanakis & Golden, 2013) that may, in part, be consequences of treatment
16	disparities (Golden et al., 2012). Indeed, treatment decision-making for diabetes, including the
17	initiation and intensification of treatment, is complicated by a host of economic, social, and
18	cultural considerations (Davidson, 2005) that operate within and between the patient, provider,
19	and healthcare system and that contribute to racial/ethnic disparities (Brown et al., 2002). What
20	is less understood, however, is whether immigrant groups face health disparities similar to
21	racial/ethnic minorities. This knowledge is important because (1) immigrants are projected to
22	compose about 18% of the U.S. population by 2065 (Pew Research Center, 2015) and (2)
23	immigrants are at an elevated risk of diabetes and shoulder a substantial proportion of the

1	diabetes burden (Oza-Frank, Chan, Liu, Burke, & Kanaya, 2010; Oza-Frank & Narayan, 2010).
2	Because immigrants are clustered within certain racial/ethnic groups, examining treatment
3	disparities along racial/ethnic lines can reveal some information about how to enhance the health
4	of and care for the growing immigrant population. However, it fails to capture unique factors that
5	make immigrant groups particularly vulnerable to healthcare disparities overall and for diabetes
6	in particular (Derose, Escarce, & Lurie, 2007; Lebrun, 2012; Siddiqi, Zuberi, & Nguyen, 2009).
7	The immigrant population in the U.S. is a heterogeneous group that varies in terms of
8	race and ethnicity, English proficiency, pre-migration conditions, and U.S. settlement
9	experiences, among other factors (Brown & Stepler, 2016). Nonetheless, many immigrants
10	encounter similar conditions that can create vulnerabilities to health inequity (Derose, Escarce, &
11	Lurie, 2007). To illustrate, immigrants tend to have lower rates of health insurance, to use
12	healthcare less often, and to receive lower quality of care than those born in U.S. (Derose et al.,
13	2007). In addition, recent trends in local and national immigration policies have not only made it
14	more difficult for immigrants to access care but have also stigmatized certain immigrant groups,
15	including undocumented immigrants and refugees (Karen Hacker, Anies, Folb, & Zallman,
16	2015; K. Hacker et al., 2011; Martinez et al., 2016). As such, we examine immigrant status as a
17	potentially important social determinant of health in general and of diabetes health in particular.
18	The objective of the present study was to determine whether immigrant status is
19	associated with differences in pharmacological treatment of diabetes. The ADA recommends a
20	patient-centered approach to diabetes treatment, which includes considering comorbidities and
21	patient preferences. For people with newly diagnosed type 2 diabetes, the ADA recommends
22	initiating metformin, an oral hypoglycemic agent (OHA). For newly diagnosed people who are
23	symptomatic or who have more severe glycemic measures, the ADA recommends initiating

1 insulin therapy. In addition, for those who have not met or maintained glycemic goals after three months on noninsulin monotherapy, the ADA recommends: (1) adding a second agent, (2) 2 adding a glucagon-like peptide 1 receptor agonist, or (3) adding insulin. Importantly, the ADA 3 4 notes that, for people not achieving glycemic goals, insulin therapy should not be delayed (ADA, 5 2016). Here, we examined immigrant status differences in OHA and insulin treatment. While 6 OHAs are usually the first-line treatment, many patients will need their treatment intensified to achieve or maintain glycemic control (ADA, 2016). Failure to initiate insulin, or failure to 7 8 intensify from OHAs to insulin, can result in an unnecessarily prolonged period of poor glycemic 9 control and, thus, can play a major role in serious diabetes complications (ADA, 2016; Nathan, 2002; Simons-Morton, Genuth, Byington, Gerstein, & Friedewald, 2005). Because U.S. 10 immigrant groups tend to receive lower-quality healthcare (Derose, Bahney, Lurie, & Escarce, 11 12 2009; Derose et al., 2007), we hypothesized that, among people with diabetes, those who were 13 foreign-born would be less likely to receive intensified diabetes treatment (i.e., insulin) 14 compared to their U.S.-born peers. **Methods** 15 **Study Design and Sample** 16 17 The institutional review board at Indiana University-Purdue University Indianapolis (IUPUI) approved this archival study. We examined data from the 2003-2012 survey years of the 18

19 continuous National Health and Nutrition Examination Survey (NHANES). The NHANES

20 program of studies is intended to assess the health and nutritional status of adults and children in

21 the U.S. NHANES employs a cross-sectional, stratified, multistage probability design to capture

22 a nationally representative sample of the civilian, non-institutionalized U.S. population. Detailed

23 descriptions of the survey design and procedures are available on the NHANES website

(www.cdc.gov/nchs/nhanes.htm). Briefly, about 5,000 individuals were recruited each two-year
survey cycle. In NHANES, respondents were first asked to complete a computer-assisted inhome interview conducted by trained personnel to assess demographic, nutrition, and healthrelated factors. Respondents elected to complete the interview in English, in Spanish, or through
an interpreter. Approximately 1-2 weeks after the in-home interview, all respondents were asked
to attend a Mobile Examination Center (MEC) to undergo physical examinations, laboratory
assessments, and additional interviews.

8 From the total sample for the 2003-2012 survey years (N = 50,912), we first selected all 9 respondents aged 18 years or older (n = 29,802). We then selected all respondents who reported a diabetes diagnosis (n = 3,252, 10.9%). Diabetes diagnosis was determined by the question asked 10 during the in-home interview, "Have you ever been told by a doctor or other health professional 11 12 that you have diabetes or sugar diabetes?" Only respondents answering "Yes" were included in our sample. Thus, respondents were excluded if they answered "No," "Borderline or 13 Prediabetes," "Refused," "Don't Know," or did not answer this question. From the cohort of 14 3,252 respondents with self-reported diabetes, we excluded respondents with missing data for 15 country of birth (n = 1) or demographic factors (n = 340). We also excluded respondents with 16 17 missing data for kidney disease (n = 7), retinopathy (n = 15), hemoglobin (Hb) A1c levels (n = 15)123), duration of the diabetes diagnosis (n = 23), clinical CVD (n = 27), hypertension (n = 8), 18 19 hypercholesterolemia (n = 233), smoking status (n = 0), and height/weight measurements (n = 1) 20 179). Because diabetes severity, duration of diabetes diagnosis, and cardiovascular disease and 21 its risk factors can all influence diabetes treatment decisions (Berry, Tardif, & Bourassa, 2007; 22 Uwaifo & Ratner, 2007), it is important to include these factors as covariates in models 23 predicting diabetes treatment received. Finally, we excluded respondents with missing diabetes

medication data (n = 36). The characteristics of our final sample of 2,260 respondents with selfreported diabetes are shown in Table 1.

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# Measures

4	Immigrant Status. Country of birth was assessed during the in-home interview. Between
5	2003-2006, respondents could identify themselves as being "Born in the 50 U.S. States or
6	Washington, D.C.," "Born in Mexico," "Born Elsewhere," "Refused," or "Don't Know."
7	Between 2007-2010, "Born Elsewhere" was removed and replaced with "Born in Other Spanish
8	Speaking Country" and "Born in Other Non-Spanish Speaking Country." Beginning in 2011-
9	2012, the response options changed to "Born in 50 U.S. States or Washington, D.C.," "Others,"
10	"Refused," and "Don't Know." To maintain consistency across these survey years, we computed
11	a dichotomous immigrant status variable coded as U.Sborn ( $0 =$ respondent reported being born
12	in one of the 50 U.S. States or Washington, D.C.) or foreign-born (1 = respondent reported being
13	born outside of the 50 U.S. States or Washington, D.C., including U.S. territories).
14	Diabetes Medication. During the in-home interview, respondents were asked if they had
14 15	<i>Diabetes Medication.</i> During the in-home interview, respondents were asked if they had taken any prescription medications in the past month. Those who reported taking one or more
14 15 16	<i>Diabetes Medication.</i> During the in-home interview, respondents were asked if they had taken any prescription medications in the past month. Those who reported taking one or more prescription medications were asked to provide the medication containers to the interviewer, who
14 15 16 17	<i>Diabetes Medication.</i> During the in-home interview, respondents were asked if they had taken any prescription medications in the past month. Those who reported taking one or more prescription medications were asked to provide the medication containers to the interviewer, who then recorded the medication name. If the respondent was unable to produce containers, s/he was
14 15 16 17 18	<i>Diabetes Medication</i> . During the in-home interview, respondents were asked if they had taken any prescription medications in the past month. Those who reported taking one or more prescription medications were asked to provide the medication containers to the interviewer, who then recorded the medication name. If the respondent was unable to produce containers, s/he was asked to provide the medication names. Each medication was recorded in an online database,
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14 15 16 17 18 19 20	Diabetes Medication. During the in-home interview, respondents were asked if they had taken any prescription medications in the past month. Those who reported taking one or more prescription medications were asked to provide the medication containers to the interviewer, who then recorded the medication name. If the respondent was unable to produce containers, s/he was asked to provide the medication names. Each medication was recorded in an online database, where it was matched with its drug type, generic name, and therapeutic class code. Using these data, we identified all reported OHAs and insulins in our final sample. We coded respondents as
14 15 16 17 18 19 20 21	<i>Diabetes Medication.</i> During the in-home interview, respondents were asked if they had taken any prescription medications in the past month. Those who reported taking one or more prescription medications were asked to provide the medication containers to the interviewer, who then recorded the medication name. If the respondent was unable to produce containers, s/he was asked to provide the medication names. Each medication was recorded in an online database, where it was matched with its drug type, generic name, and therapeutic class code. Using these data, we identified all reported OHAs and insulins in our final sample. We coded respondents as yes (1) on the OHA treatment variable if they reported taking any of the following medications
14 15 16 17 18 19 20 21 22	<i>Diabetes Medication</i> . During the in-home interview, respondents were asked if they had taken any prescription medications in the past month. Those who reported taking one or more prescription medications were asked to provide the medication containers to the interviewer, who then recorded the medication name. If the respondent was unable to produce containers, s/he was asked to provide the medication names. Each medication was recorded in an online database, where it was matched with its drug type, generic name, and therapeutic class code. Using these data, we identified all reported OHAs and insulins in our final sample. We coded respondents as yes (1) on the OHA treatment variable if they reported taking any of the following medications in the past month: metformin, glipizide, pioglitazone, glyburide, glimepiride, sitagliptin,

1	chlorpropamide, gliclazide, or tolazamide. Otherwise, we coded them as no (0). Similarly, we
2	coded respondents as yes (1) on the insulin treatment variable if they reported taking any of the
3	following forms of insulin in the past month: insulin aspart, insulin aspart protamine, insulin
4	glargine, insulin lispro, insulin lispro protamine, insulin isophane, insulin regular, insulin
5	determir, insulin glulisine, insulin zinc, or insulin zinc extended. Otherwise, we coded them as
6	no (0). From these variables, we created a 3-level variable to capture respondents taking neither
7	OHA nor insulin (none), those taking one or more OHAs without insulin (OHA only), and those
8	taking insulin with or without an OHA (insulin only/insulin+OHA).
9	<i>Covariates.</i> Models included the following demographic covariates: age (years), sex $(0 =$
10	male, 1 = female), four dummy variables for race/ethnicity (reference group: non-Hispanic
11	white), four dummy variables for education level (reference group: college graduate or above),
12	poverty income ratio (PIR), and marital status ( $0 = married/living$ with partner, $1 =$
13	single/widowed/divorced/separated). Between survey years 2003-2010, NHANES included five
14	race/ethnicity categories: non-Hispanic white, non-Hispanic black, Mexican American, other
15	Hispanic, and other race including multi-racial. A sixth category (non-Hispanic Asian) was
16	added in 2011-2012, which we combined with the "other race" category to maintain consistency
17	across survey years. During the in-home interview, respondents reported their highest level of
18	education, from which we created five categories: less than 9 <sup>th</sup> grade, 9-11 <sup>th</sup> grade with no
19	diploma, high school diploma or GED, some college or associate degree, and college graduate or
20	above. Respondents were also asked to report total annual family income or total annual
21	individual income for the last calendar year. From these data, a continuous PIR (possible range:
22	0.0-5.0) was calculated by dividing family or individual annual income by the federal poverty
23	level threshold published in the Census Bureau's Current Population Reports for a specific

survey year. A PIR value below 1.0 indicates that the family/individual lives below the poverty
 threshold. Because PIR values were capped at 5.0, families/individuals with PIR values above
 this level were recorded as 5.0.

4 Subsequent models further accounted for (a) diabetes severity and duration indicators, and (b) clinical CVD and its risk factors. Diabetes severity and duration indicators were a history 5 6 of kidney disease  $(0 = n_0, 1 = y_{es})$ , presence of retinopathy  $(0 = n_0, 1 = y_{es})$ , HbA1c (%; a measure of blood glucose control over last 120 days; Saudek, Derr, & Kalyani, 2006), and 7 8 duration of diabetes diagnosis (years; current age minus age of diabetes diagnosis). Kidney 9 disease, retinopathy, and age of diabetes diagnosis were assessed during the in-home interview, and HbA1c was measured at the MEC. Respondents were coded as having clinical CVD ( $0 = n_0$ , 10 1 = yes) if they reported a history of coronary artery disease, angina, myocardial infarction, 11 12 stroke, or congestive heart failure during the in-home interview. CVD risk factors were history of hypertension (0 = no, 1 = yes), history of hypercholesterolemia (0 = no, 1 = yes), two dummy 13 variables for smoking status (never versus current smoker and never versus former smoker), and 14 body mass index (BMI;  $kg/m^2$ ). Hypertension, hypercholesterolemia, and smoking status were 15 assessed during the in-home interview, and height and weight for the computation of BMI were 16 17 measured at the MEC.

Supplemental models additionally adjusted for the potential confounders of healthcare factors and language. Healthcare factors were health insurance status, routine healthcare access, and past-year healthcare visits. During the in-home interview, respondents were asked if they were covered by health insurance or another healthcare plan (0 = no, 1 = yes). They were also asked if they had a place where they usually go when sick or needing advice about health (0 =no/don't know, 1 = yes/there is more than one place). In addition, respondents were asked how many times they had seen a doctor or other healthcare professional in the past 12 months, not
including overnight stays, from which we computed two dummy-coded variables (none to three
times versus four to nine times and none to three times versus 10 or more times). Finally,
language of the in-home interview (0 = English without an interpreter, 1 = Spanish or English
through an interpreter) served as an indicator for respondent preference for/comfort with
speaking English.

### 7 Data Analysis

All analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, NC). 8 We first performed *t*-tests and chi-square  $(X^2)$  tests to examine differences between foreign-born 9 and U.S.-born respondents on study variables. To account for survey design factors including 10 oversampling, non-response, and post-stratification, we applied appropriate NHANES sampling 11 12 design weighted variables to all models described below. Applying sample weights allows each respondent to represent the proportion of the population s/he represents, thus providing estimates 13 representative of the U.S. civilian non-institutionalized population (see 14 www.cdc.gov/nchs/tutorials/nhanes/SurveyDesign/Weighting/intro.htm for details). We used 15 sample weights from the MEC subsample because certain covariates (e.g., HbA1c) were 16 17 available for this subsample only.

18 To determine whether immigrant status is associated with differences in diabetes 19 treatment with medications, we ran two multinomial logistic regression models. We first 20 examined the association between immigrant status and our 3-level diabetes treatment variable 21 (none, OHA only, insulin only/insulin+OHA) using none as the reference group. The first model 22 included demographic factors (age, sex, four dummy variables for race/ethnicity, four dummy 23 variables for education level, PIR, and marital status) as covariates. The second model further

1 adjusted for diabetes severity and duration indicators (kidney disease, retinopathy, HbA1c, and duration of diabetes diagnosis), clinical CVD, and CVD risk factors (hypertension, 2 hypercholesterolemia, two dummy variables for smoking status, and BMI). 3 4 Supplemental models additionally adjusted for health insurance status, past-year 5 healthcare visits, and language. To maintain a reasonable predictor-to-event ratio, each of these 6 variables was entered individually and removed before entering the next variable. This resulted in three supplemental models. We also computed a routine access to healthcare variable; 7 however, the number of respondents reporting not having routine access was very low. Thus, we 8 9 did not include this variable in a supplemental model. None of the respondents in our final sample were missing data for healthcare factors or language. 10 11 **Results** 

## **12** Respondent Characteristics

Approximately one quarter (23.4%) of our final sample was foreign-born. As shown in 13 14 Table 1, we observed several significant differences between the foreign-born and U.S.-born groups on the respondent characteristics. First, foreign-born respondents were younger, less 15 likely to be non-Hispanic white or non-Hispanic black, and more likely to be Mexican American, 16 17 other Hispanic, or other race/multi-racial. Foreign-born respondents were more likely to have less than a 9<sup>th</sup> grade education, less likely to have completed up to a high school/GED level of 18 19 education, and less likely to have completed up to some college or associate degree. Foreign-20 born respondents had lower poverty income ratios (i.e., live closer to the poverty line) and were 21 more likely to be married or living with a partner. Second, foreign-born respondents were less 22 likely to have a history of kidney disease, had higher HbA1c levels, and had shorter duration of 23 diabetes diagnosis. Third, foreign-born respondents were less likely to have clinical CVD or a

history of hypertension. Foreign-born respondents were more likely to have never been a
smoker, less likely to be a current smoker, and less likely to be a former smoker and had lower
BMI values. Finally, foreign-born respondents were less likely to have health insurance, more
likely to have used healthcare between 0 and 3 times in the past year, less likely to have used
healthcare more than ten times in the last year, and more likely to have completed the survey in a
language other than English.

Concerning rates of pharmacological treatment for diabetes, 792 respondents (35%)
reported neither an OHA nor an insulin (213 [40.3%] foreign-born; 579 [33.4%] U.S.-born). A
total of 1,106 respondents (48.9%) reported being treated with OHA only (270 [51%] foreignborn; 836 [48.3%] U.S.-born). Three hundred sixty-two respondents (16.0%) reported at least
one form of insulin with or without an OHA (46 [8.7%] foreign-born; 316 [18.3%] U.S.-born).

## 12 Association of Immigrant Status with OHA Only Treatment

As shown in Figure 1, multinomial logistic regression models using no treatment as the 13 14 reference group revealed that the association between immigrant status and the odds of OHA only treatment fell just short of significance in both the demographic-adjusted model (p = 0.060) 15 and the fully-adjusted model (p = 0.065), despite having potentially meaningful effect sizes (ORs 16 17 = 1.58 and 1.59, respectively). In the supplemental models that additionally adjusted for health insurance, past-year healthcare visits, and language one at a time, being foreign-born was 18 19 generally associated with increased odds of OHA only treatment (OR = 1.70, 95% CI: 1.03-2.80, 20 p = 0.038; OR = 1.61, 95% CI: 0.99-2.62, p = 0.058; OR = 1.89, 95% CI: 1.08-3.30, p = 0.026, 21 respectively).

We observed associations, generally in the expected directions, between the covariates and OHA only treatment that are of potential interest (see Table 2). In the fully-adjusted model,

1	less than 9th grade education ( $p = 0.017$ ), 9-11 <sup>th</sup> grade education ( $p = 0.022$ ), and higher poverty			
2	income ratio ( $p = 0.025$ ) were independently associated with an increased odds of OHA only			
3	treatment. In the supplemental models, having health insurance ( $p = 0.002$ ) was also			
4	independently associated with an increased odds of OHA only treatment.			
5	Association of Immigrant Status with Insulin Treatment			
6	As can be seen in Figure 1, multinomial logistic regression models using no treatment as			
7	the reference group indicated that immigrant status was significantly associated with the odds of			
8	insulin treatment (insulin only/insulin+OHA). Compared to being U.Sborn, being foreign-born			
9	was associated with a 53% decreased odds of being treated with insulin in the demographic-			
10	adjusted model ( $p = 0.011$ ) and a 47% decreased odds in the fully-adjusted model ( $p = 0.047$ ). In			
11	supplemental models, adjusting for health insurance, past-year healthcare visits, and language			
12	one at a time attenuated the immigrant status-insulin treatment relationship, but the magnitude of			
13	the association remained large ( <i>OR</i> = 0.60, 95% <i>CI</i> : 0.32-1.13, <i>p</i> = 0.111; <i>OR</i> = 0.56, 95% <i>CI</i> :			
14	0.30-1.07, <i>p</i> = 0.078; <i>OR</i> = 0.60, 95% <i>CI</i> : 0.28-1.28, <i>p</i> = 0.185, respectively).			
15	We again detected associations between the covariates and insulin treatment (see Table			
16	2). A history of retinopathy ( $p < 0.001$ ), higher HbA1c ( $p < 0.001$ ), longer duration of diabetes			
17	diagnosis ( $p < 0.001$ ), clinical CVD ( $p = 0.014$ ), and higher BMI ( $p = 0.046$ ) were independently			
18	associated with an increased odds of insulin treatment, whereas older age ( $p = 0.003$ ) and a			
19	history of hypertension ( $p = 0.017$ ) were independently associated with a decreased odds. In the			
20	supplemental models, having health insurance ( $p < 0.001$ ) and having 10+ past-year healthcare			
21	visits ( $p = 0.021$ ) were also associated with an increased odds of insulin treatment.			
22				

1

#### Discussion

2 Our objective was to determine whether immigrant status is associated with differences in pharmacological treatment of diabetes. In a large, nationally representative sample of adults with 3 diabetes, we found that foreign-born people were only half as likely to be treated with insulin as 4 5 U.S.-born people. Critically, this group difference persisted after adjustment for numerous 6 potential confounders – i.e., age, sex, race/ethnicity, education, income, marital status, diabetes severity and duration, clinical CVD, and CVD risk factors. Although adjusting for healthcare 7 8 factors and language attenuated this relationship, its magnitude remained large. The association 9 between immigrant status and OHA only treatment fell short of significance; however, the observed effect sizes are potentially meaningful and achieved significance in some supplemental 10 models, with being foreign-born people having an increased odds of OHA only treatment. 11 12 Taken together, our findings suggest that differences in pharmacological treatment of diabetes, particularly with insulin, exist along immigrant status lines. Even though the cross-13 14 sectional nature of the data constrains our ability to explore mechanisms underlying these differences, the present findings are provocative. The immigrant status differences we observed 15 may indicate that foreign-born people receive lower intensity diabetes treatment than their U.S.-16 17 born counterparts. If so, the ramifications of these treatment differences are likely to be clinically significant, given that immigrants shoulder a considerable proportion of the diabetes burden 18 19 (Oza-Frank et al., 2010; Oza-Frank & Narayan, 2010) and that lower intensity treatment could 20 hasten the development of serious diabetes complications (Fowler, 2011). To contextualize these findings, future studies should explore the antecedents (e.g., patient preference) and 21 22 consequences (e.g., glycemic control) of immigrant status differences in diabetes treatment.

1 Although this study is the first to examine associations between immigrant status and differences in diabetes treatment, our findings indicate that immigrants experience these 2 differences in a fashion analogous to racial/ethnic minority groups. To illustrate, in a sample of 3 people with diabetes, Thackeray and colleagues (2004) found that Hispanics and Asian/Pacific 4 5 Islanders were less likely to take insulin and more likely to take OHAs than non-Hispanic whites. 6 Harris et al. (1999) reported similar results, finding that Mexican Americans with diabetes were 7 more likely to be treated with OHAs than non-Hispanic whites. Our findings are also consistent 8 with evidence of immigrant treatment differences for other medical conditions. Priorresearch 9 has found lower depression (Landa, Skritskaya, Nicasio, Humensky, & Lewis-Fernandez, 2015) and hypertension (Ursua et al., 2014) treatment rates for foreign-born groups versus U.S.-born 10 groups. Differences in treatment adherence have also been investigated. This line of research 11 12 suggests that, among immigrant groups, adherence is lower for radiotherapy (Formenti et al., 1995), substance use treatment (Mancini, Salas-Wright, & Vaughn, 2015), and tuberculosis 13 14 treatment (Ailinger, Moore, Nguyen, & Lasus, 2006) but not for HIV treatment with antiretroviral medications (Vissman, Young, Wilkin, & Rhodes, 2013) or hypertension treatment 15 (W. W. Li, Stewart, Stotts, & Froelicher, 2006). Our findings align with the small but emerging 16 17 literature on immigrant health disparities and highlight the need for future research to examine how these differences develop and the degree to which they contribute to poor health outcomes. 18 19 Several factors may explain the lower odds of insulin treatment in immigrants with 20 diabetes that we observed. Patient-level factors often guide treatment decisions. For instance, foreign-born patients may misunderstand the importance of medication in diabetes management, 21 22 leading to resistance to intensification to insulin therapy (Khunti et al., 2015). In addition, 23 physician-level factors, including beliefs about themselves or their patients, affect treatment

decisions (Khunti et al., 2015). For instance, physicians may believe they lack the time or skill to 1 effectively communicate the importance of safely monitoring insulin therapy. They may also 2 believe that foreign-born patients will demonstrate poor adherence in the event that insulinis 3 4 initiated (Brown et al., 2002). Finally, both patients and physicians are nested within broader 5 healthcare systems that may directly (e.g., through lack of resources to guide appropriate care for 6 diverse populations; Brown et al., 2002) and indirectly (e.g., through policies regarding affordable medication; K. M. Nelson, Chapko, Reiber, & Boyko, 2005) influence the capacity to 7 8 give and receive equitable care. It is worth noting that patient-, physician-, and healthcare 9 systems-level factors likely exert additive and/or interactive effects on treatment decisions. Moreover, these patient-, physician-, and healthcare systems-level factors may be particularly 10 decisive for foreign-born individuals living in the U.S., for whom language discordance, 11 12 differing cultural norms, and fluctuating social and political climates may further complicate medical decisions. 13

14 Some theoretical and clinical implications arise from our findings. Given that U.S. immigrant groups tend to cluster within racial/ethnic minority groups and that racial/ethnic 15 minority groups experience marked health disparities (Nelson, 2002), immigrant groups may be 16 17 a particularly vulnerable and underserved population. Our results suggest that immigrant groups may be susceptible to diabetes treatment disparities. With respect to theory, longitudinal studies 18 19 testing candidate mechanisms that contribute to potential immigrant disparities in diabetes 20 treatment are needed – the significance of such work would be optimized by collecting data at the patient, provider, and healthcare system levels. Concerning clinical practice, our findings 21 22 raise the possibility that integrating information about a patient's immigrant status, in addition to 23 racial/ethnic identity, may be an important component of culturally sensitive diabetes care.

1 Among our study's strengths are the use of a large, nationally representative sample of U.S. adults with diabetes and data collection through interviews, physical examinations, and 2 3 laboratory tests. Particularly important is that respondents who reported past-month medication use were asked to produce medication containers, which were verified by trained interviewers. In 4 5 addition, the physical examination and laboratory components provided objective assessments of 6 key covariates, such as BMI and HbA1c levels. Some limitations are also worth noting. First, although we adjusted our models for many potential confounders including diabetes severity and 7 8 duration, we were not able to match patients on these factors that could affect the odds of 9 receiving either treatment. Thus, we cannot completely rule out the influence of these potential confounders. Second, the cross-sectional nature of the NHANES data did not allow us to 10 rigorously test for mediation, as we could not determine directionality between immigrant status 11 12 and any candidate mediators. Third, because we selected respondents with self-reported, 13 physician-diagnosed diabetes, it is possible that we underestimated treatment differences by 14 immigrant status, as those who are foreign-born are more likely to have unrecognized diabetes (Barcellos, Goldman, & Smith, 2012). Fourth, some characteristics that can make immigrant 15 groups differentially vulnerable to health disparities were not assessed or were not assessed 16 17 consistently in NHANES and could not be examined. Immigrants are an increasingly heterogeneous group (Derose et al., 2007; Hacker et al., 2011; Singh & Hiatt, 2006) varying in 18 19 factors known to affect health outcomes, such as country of origin (Zimmerman, Kiss, & 20 Hossain, 2011), place of arrival (Derose et al., 2007; Zimmerman et al., 2011), age of migration (Angel, Angel, Venegas, & Bonazzo, 2010; Colon-Lopez, Haan, Aiello, & Ghosh, 2009; 21 22 Holmes, Driscoll, & Heron, 2015), and experience with racialization and racism (Viruell-23 Fuentes, 2007, 2011; Viruell-Fuentes, Miranda, & Abdulrahim, 2012). Understanding the

1 influence of these factors is an important goal for future research and will help identify

2 modifiable targets for interventions and policy changes designed to reduce immigrant health3 disparities.

In sum, the present study identified differences in pharmacological treatment of diabetes
along immigrant status lines, with foreign-born individuals being about half as likely to receive
insulin than their U.S.-born counterparts. This, in turn, could result in poorer glycemic control
and, ultimately, an elevated incidence of serious diabetes complications among immigrants.

8

## **Figure Legends**

**Figure 1.** Forest Plot Summarizing Odds Ratio Estimates of Association of Being Foreign-Born with OHA Only Treatment and Insulin (Insulin Only/Insulin+OHA) Treatment. The reference group is none (no OHA or insulin treatment). The demographics-adjusted model is adjusted for age, sex, race/ethnicity, education, poverty income ratio, marital status, and the NHANES sampling design. The fully-adjusted model is further adjusted for kidney disease, retinopathy, hemoglobin A1c level, duration of diabetes diagnosis, clinical cardiovascular disease, hypertension, hypercholesterolemia, smoking status, and body mass index. OHA = oral hypoglycemic agent; OR = odds ratio; CI = confidence interval; NHANES = National Health and Nutrition Examination Survey.

Table 1. Differences in Respondent Characteristics Between Immigrant Status Groups

Characteristics	Total Sample	U.SBorn	Foreign-Born	Test Value
	(N = 2260)	(n = 1731)	(n = 529)	
Demographic Factors	· · · · ·			
Age, years	62.8 (12.3)	63.2 (12.5)	61.3 (11.5.7)	t = 3.06, p = 0.002
Female, %	1090 (48.2)	836 (48.3)	254 (48.0)	$\chi^2(1) = .01, p = 0.910$
Race/Ethnicity, %				
Non-Hispanic White	915 (40.5)	875 (50.5)	40 (7.6)	$\chi^2(1) = 191.55, p < 0.001$
Non-Hispanic Black	629 (27.8)	582 (33.6)	47 (8.9)	$\chi^2(1) = 308.71, p < 0.001$
Mexican American	404 (17.9)	196 (11.3)	208 (39.3)	$\chi^2(1) = 216.38, p < 0.001$
Other Hispanic	174 (7.7)	39 (2.3)	135 (25.5)	$\chi^2(1) = 123.43, p < 0.001$
Other/Multi-racial	138 (6.1)	39 (2.3)	99 (18.7)	$\chi^2(1) = 310.82, p < 0.001$
Education, %				
Less Than 9th Grade	446 (19.7)	224 (12.9)	222 (42.0)	$\chi^2(1) = 215.50,  p < 0.001$
9-11th Grade	419 (18.5)	336 (19.4)	83 (15.7)	$\chi^2(1) = 3.73, p = 0.054$
High School Graduate/GED	500 (22.1)	436 (25.2)	64 (12.1)	$\chi^2(1) = 40.32, p < 0.001$
Some College or AA Degree	569 (25.2)	479 (27.7)	90 (17.0)	$\chi^2(1) = 24.40, p < 0.001$
<b>College Graduate or Above</b>	326 (14.4)	256 (14.8)	70 (13.2)	$\chi^2(1) = 0.79, p = 0.37$
Poverty Income Ratio	2.3 (1.5)	2.4 (1.5)	1.9 (1.4)	t = 7.66, p < 0.001
Single/Widowed/Divorced, %	927 (41.0)	752 (43.4)	175 (33.1)	$\chi^2(1) = 17.98,  p < 0.001$
Diabetes Severity Indicators				
Kidney Disease, %	195 (8.6)	161 (9.3)	34 (6.4)	$\chi^2(1) = 4.24, p = 0.039$
Retinopathy, %	469 (20.8)	360 (20.8)	109 (20.6)	$\chi^2(1) = 0.01, p = 0.92$
Hemoglobin A1c Level, %	7.3 (1.7)	7.3 (1.7)	7.5 (1.8)	t = -3.25, p = 0.001
Duration of Diabetes Diagnosis, years	11.8 (11.9)	12.1 (12.0)	10.8 (11.3)	t = 2.17, p = 0.030
Cardiovascular Disease and Risk Factors				
Cardiovascular Disease, %	699 (30.9)	595 (34.4)	104 (19.7)	$\chi^2(1) = 41.06,  p < 0.001$
Hypertension, %	1616 (71.5)	1293 (74.7)	323 (61.1)	$\chi^2(1) = 36.99,  p < 0.001$
Hypercholesterolemia, %	1439 (63.7)	1117 (64.5)	322 (60.9)	$\chi^2(1) = 2.35, p = 0.12$
Smoking Status, %				
Never	1082 (47.9)	758 (43.8)	324 (61.2)	$\chi^2(1) = 49.42,  p < 0.001$
Current	360 (15.9)	311 (18.0)	49 (9.3)	$\chi^2(1) = 22.94, p < 0.001$
Former	818 (36.2)	662 (38.2)	156 (29.5)	$\chi^2(1) = 13.47,  p < 0.001$
Body Mass Index, kg/m <sup>2</sup>	32.3 (7.5)	33.0 (7.7)	30.0 (6.0)	t = 8.22, p < 0.001
II. dd Frat				
Healincare Factors and Language	1000 (00 0)	1599 (01 7)	401 (75.9)	$u^{2}(1) = 0.750 = 0.001$
Dest Veen Healtheans Visite 9/	1989 (88.0)	1388 (91.7)	401 (75.8)	$\chi^{2}(1) = 97.30, p < 0.001$
rast rear meannicare visits, %	617 (29 6)	451 (26 1)	106 (27.1)	$w^{2}(1) = 24.01$ m < 0.001
U 10 3 4 to 0	04/(28.0)	431 (20.1)	190 (37.1)	$\chi^{-}(1) = 24.01, p < 0.001$ $\chi^{2}(1) = 2.21, p = 0.060$
4 10 9	933 (42.2) 660 (20.2)	148 (43.2) 522 (20.7)	203 (38.8)	$\chi^{-}(1) = 5.51, p = 0.009$
10+ Longuage 9/ Non Ext-P-h	000 (29.2)	332(30.7)	128 (24.2)	$\chi^{-}(1) = 8.55, p = 0.004$
Language, % Non-English	326 (14.4)	19 (1.1)	307 (38.0)	$\chi^{2}(1) = 1064.06, p < 0.001$

Note: Continuous variables presented as mean and *SD*, categorical variables presented as n and %. GED = General Education Diploma; AA = associate degree.

Table 2. Independen	nt Associations of	of Covariates	with Oral	Hypoglycemic	Agent Only	and Insulin (Ins	ulin
Only/Insulin+OHA)	Treatment						

None (Ref)	OHA Only	Insulin Only/Insulin+OHA
	OR (95% CI)	OR (95% CI)
Demographic Factors		
Age	1.01 (0.99-1.02)	0.97* (0.95-0.99)
Sex (Ref: Male)	1.06 (0.83-1.35)	0.93 (0.64-1.35)
Race/Ethnicity (Ref: Non-Hispanic White)		
Non-Hispanic Black	1.00 (0.63-1.58)	0.80 (0.48-1.32)
Mexican American	0.62 (0.34-1.12)	0.64 (0.31-1.35)
Other Hispanic	0.62 (0.29-1.34)	0.39 (0.14-1.11)
Other/Multi-racial	0.69 (0.35-1.39)	0.49 (0.19-1.29)
Education (Ref: College Graduate or Above)		
Less Than 9th Grade	1.97* (1.14-3.40)	0.77 (0.37-1.59)
9-11th Grade	1.75* (1.15-2.68)	0.79 (0.41-1.54)
High School Graduate/GED	1.36 (0.82-2.27)	0.69 (0.33-1.47)
Some College or AA Degree	1.16 (0.78-1.74)	1.00 (0.61-1.64)
Poverty Income Ratio	1.11* (1.01-1.22)	1.10 (0.98-1.23)
Marital Status (Ref: Married/Living with Partner)	0.82 (0.64-1.06)	0.87 (0.56-1.37)
Diabetes Severity Indicators		
Kidney Disease (Ref: No)	0.63 (0.37-1.07)	1.21 (0.61-2.44)
Retinopathy (Ref: No)	1.30 (0.97-1.76)	3.18** (2.08-4.85)
Hemoglobin A1c Level	1.01 (0.92-1.10)	1.34** (1.21-1.47)
Duration of Diabetes Diagnosis	0.99 (0.97-1.00)	1.04** (1.03-1.06)
Cardiovascular Disease and Risk Factors		
Cardiovascular Disease (Ref: No)	1.01 (0.74-1.39)	1.86* (1.13-3.04)
Hypertension	1.18 (0.89-1.57)	0.61* (0.41-0.92)
Hypercholesterolemia	1.10 (0.78-1.53)	0.98 (0.63-1.55)
Smoking Status (Ref: Never)		
Current	0.90 (0.65-1.25)	0.62 (0.38-1.02)
Former	0.96 (0.67-1.11)	1.14 (0.78-1.64)
Body Mass Index	1.01 (0.99-1.03)	1.03* (1.00-1.05)
Healthcare Factors and Language		
Health Insurance (Ref: No)	$1.67*(1.05-2.63)^{a}$	3.26** (1.69-6.28) <sup>a</sup>
Past-Year Healthcare Visits (Ref: 0 to 3)		
4 to 9	$1.12 (0.81 - 1.53)^{a}$	$1.56 (0.99-2.46)^{a}$
10+	$1.07 (0.73 - 1.56)^{a}$	$1.86^* (1.10-3.14)^a$
Language (Ref: English)	$0.58 (0.32 - 1.07)^{a}$	$0.68 (0.27 - 1.72)^{a}$

Note: N = 2,260. Results are from the fully-adjusted model unless otherwise indicated. <sup>a</sup>Results are from individual supplemental models.

OHA = oral hypoglycemic agent; GED = General Education Diploma; AA = associate degree. \*p < .05, \*\*p < .001



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