I. REPORT CHECKLIST

The following checklist must be completed and submitted with the project report. By checking an item, *the student(s) are indicating that the work has been done appropriately*.

__X__1. If the research report will be or has been submitted for publication in a journal, provide the name of the journal here: _TBD - please do not publish full report in repository_

__X__2. Project title is concise and clear; lists advisors, course no. & date submitted

__X__3. Abstract is no more than **250 words** and retains headings

__X__4. Introduction provides a definition of the topic under study, the importance of the topic, and the issue addressed by the study and is no more than two (2) pages.

__X__5. There is NO literature review section

__X__6. Purpose(s) of project is clearly and concisely stated

__X__7. Methods section uses headings and represents a summary of the methods used. (Actual methods used should be described if they were modified from the proposal.)

__X__8. Data analysis described is appropriate and responds to the purpose.

__X__9. Appropriate tables are included in the results section.

__X__10. Text of results section interprets the findings reported in the tables, does not repeat them.

__X__11. The discussion section includes a description of the most important findings and relates findings to the literature.

__X__12. The final section of the discussion is the limitations section.

__X__13. The conclusions respond to the purpose statement.

__X__14. Reference list uses style from DI class (PhPr 861C) or is specific to journal.

__X__15. Data collection/recording form(s) and/or questionnaire(s) are included in the appendix.

__X__16. Information is placed in the appropriate section—introduction, methods, results, etc.

__X__17. Report does not exceed 15 pages excluding tables & figures & appendices.

Date report submitted: __April 24, 2019__

Student: Cody Benson, Student (2): Heather Lee, Student (3): Rianne Michael

TITLE PAGE

Title of project:

Investigating the Impact of a Mental Health Adherence Intervention on Mental Health Medication Adherence in Patients with Diabetes

Course title: PhPr 896B

Date: 24 April 2019

Faculty advisor: Dr. Jennifer Bingham, PharmD, BCACP

Students: Cody Benson, Heather Lee, Rianne Michael

ABSTRACT

Specific Aims: Evaluate the impact of targeted psychotropic medication adherence interventions by pharmacists on psychotropic medication adherence rates in patients with type 2 diabetes and determine whether patient-specific variables, such as age, gender, or type of psychotropic medication being taken, influence the degree of impact.

Methods: Adherence, as indicated by proportion of days covered (PDC), was measured before and after face-to-face counseling by a community pharmacist. Pharmacists were alerted to counsel patients receiving Medicare Part D prescription coverage who were prescribed a psychotropic medication and exhibited a PDC of <85%. Data regarding PDC, age, gender, and type of psychotropic medication were analyzed for patients between 18 and 84 years of age with type 2 diabetes.

Main Results: The data set contained 8,167 patients eligible for analysis, including 5,438 women (mean age=63.6 years, SD=11.5) and 2,729 men (mean age=61.6 years, SD=10.3). There was significant improvement in PDC after pharmacist intervention overall (mean PDC increase=13.5%, SD=20.2, $p<0.01$) and for each subgroup, with the exception of nefazodone (n=3, p=0.66). Patients 65 years and older showed the greatest improvement (PDC change=14.5, $p<0.01$), followed by patients aged 40-64 years (PDC change=12.5, $p<0.01$) and then 20-39 years (PDC change=9.1, $p<0.01$).

Conclusions: Targeted face-to-face interventions by pharmacists significantly improved psychotropic medication adherence in adult patients with type 2 diabetes receiving Medicare Part D prescription coverage. Improvement was seen regardless of gender, age, or type of psychotropic medication, except nefazodone, and was greater with increasing age. The degree of improvement also varied among certain psychotropic medications.

INTRODUCTION

Medication non-adherence rates in the United States typically range from 25% to 50% depending on the characteristics of the condition, the treatment, the patient, and the setting.[1] Patient nonadherence to prescribed medications is associated with poor therapeutic outcomes, progression of disease, and an estimated burden of billions per year in avoidable direct health care costs. Adherence to medications used to treat mental health conditions is particularly important, as nonadherence is associated with poor adherence to medications for other chronic conditions as well.[2]

Mental illness is prevalent among the general population, affecting up to 1 in 5 individuals.[3] Of the many challenges seen with mental health, psychiatric disorders among those suffering with diabetes have low rates of detection and subsequently management.[4] This is important as diabetes and mental illness share a bidirectional association, with each having the ability to influence the other in various ways. For instance, conditions such as depression, bipolar disorder, or schizophrenia can act as independent risk factors in the development diabetes. Similarly, onset of new mental illnesses can often lead to suboptimal diabetic management, which increases the risk of adverse consequences including high hemoglobin A1C, neuropathy, retinopathy, and hospitalizations. In addition, anxiety disorders can foster phobias about injectable drugs, creating new difficulties with treatment processes involved with checking blood sugar levels and insulin. Furthermore, severe hypoglycemia or ketoacidosis in diabetic individuals has been associated with a severe comorbid mental health condition, such as schizophrenia or bipolar disorder. Lastly, studies have suggested that comorbidity in diabetes causes a significant increase in health care costs.[5]

The pharmacist plays a critical role in patient adherence due to their ability to intervene and provide counseling related information to improve overall adherence in patients that are not taking their medications as prescribed. When confronting issues of adherence, the patient is educated about enhanced efficacy opportunities in their therapy with the ultimate goal of an improved quality of life.

Communication between the pharmacist and patient is vital to overcome adherence issues. Unfortunately, this may be a challenge for patients with poor mental health as they may be less motivated to seek improvement and manage their conditions.[4] Therefore, the primary purpose of this study was to measure the impact of targeted psychotropic medication adherence interventions performed face-to-face by pharmacists on psychotropic medication adherence rates in adult patients with type 2 diabetes. The secondary purpose was to determine whether patient-specific variables, such as age, gender, or type of psychotropic medication being taken, influences the degree of impact.

METHODS

Design: This study was a retrospective data analysis of a limited data set provided by SinfoniaRx.

Subjects: Patients were selected to be included in data analysis if they were at least 18 years of age or older, had a diagnosis of type 2 diabetes, were prescribed at least one psychotropic medication, and exhibited a PDC of less than 85% for their psychotropic medication(s) at the time the study was initiated; patients 85 years of age or older or who were missing PDC data were excluded. Classes of mental health medications observed included alpha-2 antagonists, typical antipsychotics, atypical antipsychotics, norepinephrine and dopamine reuptake inhibitors (SDRIs), nefazodone, serotonin and norepinephrine reuptake inhibitors (SNRIs), and selective serotonin reuptake inhibitors (SSRIs). The study was approved by the University of Arizona Institutional Review Board.

Intervention: Pharmacists in a community setting were alerted to provide face-to-face counseling interventions to Medicare Part D patients who were prescribed a psychotropic medication that exhibited a PDC value less than 85%. Standardized scripts were utilized by pharmacists to counsel patients about the importance of medication adherence, specific to the psychotropic agent they were prescribed.

Data Collection and Measures: Data collected at specific timepoints in June 2018 and December 2018 were provided as a data set in the form of an Excel spreadsheet by SinfoniaRx that did not contain any protected health information. The data set included gender, age, type of psychotropic medication

prescribed, PDC in June 2018, and PDC at the end of December 2018 for Medicare Part D patients who were diagnosed with type 2 diabetes and were documented to have received the study intervention. Data were subsequently organized according to the data dictionary (Appendix A).

Medical claims data were used to identify patients with a type 2 diabetes diagnosis using codes from the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10). Similarly, pharmaceutical claims data were used to determine PDC values as well as to confirm pharmacist intervention. SinfoniaRx generated the data set as part of their normal quality improvement process to support further analysis of trends in medication non-adherence.

Data analysis: There were 8,167 patients who were included in the study. Demographic characteristics at baseline were compared between females and males. Statistical difference in age between genders was analyzed using a Mann-Whitney test, while differences in the proportion of each psychotropic medication prescribed to each gender were analyzed using a Chi-square test. A Mann-Whitney test was also used to identify statistical differences in PDC values before and after pharmacist intervention, both overall and within each subgroup. Post-hoc analyses to identify which subgroups exhibited differences for age and psychotropic drug class were performed using a Dunn test adjusted by the family-wide error rate procedure of Holm. The a priori p-value for all statistical tests was set at 0.05.

RESULTS

Over 20,000 (n = 21,536) patients received interventions during the study period, with 8,167 who met inclusion criteria. The demographic characteristics of the study population are shown in Table 1. The study population included more females (n = 5,438) than males (n = 2,729) and the mean age of the female population was significantly greater than that of the male population (63.6 years vs. 61.6 years; p-value = <0.05). In addition, there were significantly more females prescribed a SNRI (23% vs. 19%; $p < 0.01$), whereas there were significantly more males prescribed an alpha-2 antagonist (4% vs 3%; $p < 0.03$), a typical antipsychotic (3% vs. 0%; $p < 0.01$), and an atypical antipsychotic (13% vs. 10%; $p < 0.01$). There were apparent differences in the amount of each psychotropic medication prescribed,

with over 50% of patients prescribed a SSRI, over 20% of patients prescribed a SNRI, and as little as 3 patients prescribed nefazodone.

The PDC values before and after pharmacist intervention are displayed in Table 2. Overall, PDC significantly improved after targeted counseling interventions by pharmacists, with a mean increase in PDC of 13.4% ($p < 0.01$). This effect persisted across all subgroups, with the exception of nefazodone ($n = 3$, $p = 0.66$).

Comparisons between subgroups are depicted in figures 1-3. No significant differences were found in the average PDC change among genders; however, adults >65 years demonstrated a significantly greater change in PDC than adults aged 40-64 years (14.5%, $p < 0.01$), as well as adults aged 20-39 years (12.5%, $p < 0.01$). Similarly, adults aged 40-64 years demonstrated a significantly greater change in PDC than adults aged 20-39 years (9.1%, $p < 0.01$). Among the different drug classes, only the SNRIs and SSRIs subgroups exhibited a significantly greater change in PDC and these effects were only present when compared to the typical antipsychotic subgroup.

DISCUSSION

The most prominent finding in this study is that psychotropic medication adherence significantly improved in patients with type 2 diabetes after targeted face-to-face counseling with a pharmacist. Even when the study population was separated into gender and age subgroups, the intervention continued to display a significant impact in both males and females as well as the various age categories. Interestingly, the results demonstrated a positive association between age and degree of improvement in PDC values, with patients older than 65 years exhibiting significantly greater improvement than those aged 40-64 years and 20-39 years as well as with those aged 40-64 years exhibiting significant improvements compared to those aged 20-39 years. One possible explanation for this trend may be related to the study population containing only patients with Medicare Part D prescription coverage. Since Medicare Part D is available to all adults aged 65 years and older regardless of disability status, but

adults aged <65 years only on the basis of significant disability, the presumed disability status within the age 40-64 years and 20-39 years subgroups may have impacted adherence. Indeed, Medicare patients aged <65 years with disabilities have been shown to be less adherent to medications than adults 65 years and older in populations such as heart failure patients and myocardial infarction survivors.[6,7] Another possible explanation could be the impact of sample size for each subgroup on the results. Although the subgroups of patients 65 years and older and aged 40-64 years are fairly similar, the subgroup of patients aged 20-39 years is <10% of the size of the other two age groups. With a larger sample size for the 20-39 years of age subgroup, it is possible that average increase in PDC value may more closely resemble the other age populations and alter the trend.

When examining the effects of psychotropic drug class on the average change in PDC, significant increases were observed among all drug classes except nefazodone. The lack of a significant increase in PDC for the nefazodone subgroup is presumed to be due to the small population size of 3 patients since the average change in PDC for the nefazodone subgroup was greater than other subgroups with larger populations that demonstrated significance, such as the typical antipsychotic subgroup. The effect of sample size was also apparent when comparing drug classes amongst each other since the SNRI subgroup, which exhibited a mean change in PDC of 13.2%, was significantly different than the typical antipsychotic subgroup, but the alpha-2 antagonist subgroup, which exhibited a mean change in PDC of 13.8% and had a smaller sample size, was not.

Overall, this study demonstrates that pharmacist interventions in a community setting can help improve adherence to psychotropic medications, regardless of age, gender, or type of psychotropic medication prescribed. Community pharmacists have the ability to emphasize and explain the importance of specific medications in managing health conditions with a patient through face-to-face counseling, which can improve patient understanding of why it is critical to take their medications as prescribed. In addition, discussing these topics in person with patients may encourage them to share

any challenges or concerns they are experiencing while taking their medications that act as barriers to adherence. Pharmacists can then clarify any misunderstandings regarding health topics and provide individualized recommendations for how to overcome these barriers. With this additional knowledge, patients may be more likely to be adherent to their medications and be more receptive to the instructions and advice from healthcare providers.

The overall findings in this study are consistent with similar studies that have researched the effects of pharmacist counseling on patient adherence to medications. For example, Singleton et. al (2017) demonstrated improvement in patient adherence to diabetic medications after pharmacist intervention via telephone, with an average PDC increase of 65.2% to 78.7%.[8] In addition, Akinbosoye et. al (2016) examined the effect of motivational interviewing techniques utilized by pharmacists in a community pharmacy on patient PDC rates.[9] When PDC was assessed 6 months after the intervention, they found that the overall PDC rate was 3% higher in the intervention group than the control group. Furthermore, Taitel et. al (2012) investigated the effects of face-to-face counseling performed by a community-based pharmacist on adherence in patients starting statin therapy.[10] The intervention consisted of two face-to-face counseling sessions where the pharmacist addressed common patient barriers to adherence. Patients who were in the intervention group were observed to have greater medication adherence and persistency. For instance, the intervention group demonstrated a continuous medication possession ratio (MPR) of 61.8%, whereas the comparison group had a MPR of 56.9% ($p < 0.01$), 12 months after counseling. In addition, 40.9% of the intervention group versus 33.7% of the comparison group had a MPR greater than 80% ($p < 0.01$).

The results of this study have several implications for encouraging the pharmacist involvement in improving a patient adherence rates. Due to the association between medication adherence and enhanced health outcomes, community pharmacists are in a unique position to reduce health consequences by providing targeted counseling about adherence to specific medications during each

patient encounter. Through these interactions, pharmacists can identify trends in patient challenges regarding adherence and utilize this information to address potential barriers when a patient is being initiated on a new medication. Further research is necessary to verify whether PDC values are an appropriate measure of adherence and whether these values correlate with improved clinical outcomes or control of health conditions, such as hemoglobin A1C in diabetes.

Several limitations were identified during the course of this study. Firstly, the dependent variable is not a strict measurement of medication adherence since PDC values are generated based on the timeliness of medication refills and represent the amount of days a patient likely had enough medication to take as prescribed. In some cases, this value may overestimate adherence if a patient continues to pick up refills on time but forgets to take or chooses not to take their medication as prescribed. In other cases, this value may underestimate adherence if a patient was instructed to take less of their medication by their provider but has not obtained an updated prescription or if the medication is prescribed as needed.

Secondly, although all the patients included in this study were prescribed a psychotropic medication, the data set received could not be used to confirm whether the patient was prescribed the psychotropic medication to improve mental health or for another indication. While the most common medications prescribed to the study population, SSRIs, are only approved by the Food and Drug Administration (FDA) for psychological conditions, they may be used off-label in the treatment of vasomotor symptoms of menopause, such as hot flashes, and in sexual dysfunction, such as premature ejaculation. Furthermore, the second most commonly prescribed medications, SNRIs, contain drugs that are FDA-approved for non-psychological conditions, such as neuropathy and musculoskeletal pain, as well as drugs that are used off-label for tension headache, vasomotor symptoms of menopause, and urinary incontinence.

Finally, this study only included adults with type 2 diabetes on Medicare Part D prescription coverage and is therefore not generalizable to all patients with type 2 diabetes since patients must be over the age of 65 and/or demonstrate significant disability to be eligible for this program. Arguments could be made for improved or reduced adherence among the general type 2 diabetes population compared to those included in this study.

CONCLUSIONS

Targeted face-to-face interventions by community pharmacists that addressed adherence to psychotropic medications significantly improved psychotropic medication adherence rates in adults with type 2 diabetes receiving Medicare Part D prescription coverage. Improvement was seen regardless of gender, age, or type of psychotropic medication, except nefazodone, and was greater with increasing age. The degree of improvement also varied among certain psychotropic medications.

REFERENCES

1. Iuga AO, McGuire MJ. Adherence and health care costs. *Risk Manag Healthc Policy*. 2014;7:35–44. Published 2014 Feb 20. doi:10.2147/RMHP.S19801

2. Katon W, Cantrell CR, Sokol MC, Chiao E, Gdovin JM. Impact of Antidepressant Drug Adherence on Comorbid Medication Use and Resource Utilization. *Arch Intern Med.* 2005;165(21):2497–2503. doi:10.1001/archinte.165.21.2497

3. Learn About Mental Health - Mental Health - CDC. (n.d.). Retrieved March 2019, from https://www.cdc.gov/mentalhealth/learn/index.htm

4. Balhara YP. Diabetes and psychiatric disorders. *Indian J Endocrinol Metab*. 2011;15(4):274–283. doi:10.4103/2230-8210.85579

5. Grenard JL, Munjas BA, Adams JL, et al. Depression and medication adherence in the treatment of chronic diseases in the United States: a meta-analysis. *J Gen Intern Med*. 2011;26(10):1175–1182. doi:10.1007/s11606-011-1704-y

6. Zhang Y, Baik SH. Race/Ethnicity, disability, and medication adherence among medicare beneficiaries with heart failure. *J Gen Intern Med*. 2013;29(4):602–607. doi:10.1007/s11606-013-2692-x

7. Zhang Y, Baik SH, Chang CC, Kaplan CM, Lave JR. Disability, race/ethnicity, and medication adherence among Medicare myocardial infarction survivors. *Am Heart J*. 2012;164(3):425–433.e4. doi:10.1016/j.ahj.2012.05.021

8. Singleton J, Veach S, Catney C, Witry M. Analysis of a Community Pharmacy Intervention to Improve Low Adherence Rates to Oral Diabetes Medications. *Pharmacy*. 2017;5(4):58. doi:10.3390/pharmacy5040058.

9. Akinbosoye OE, Taitel MS, Grana J, Hill J, Wade RL. Improving Medication Adherence and Health Care Outcomes in a Commercial Population through a Community Pharmacy. *Popul Health Manag*. 2016;19(6):454–461. doi:10.1089/pop.2015.0176

10. Taitel M, Jiang J, Rudkin K, Ewing S, Duncan I. The impact of pharmacist face-to-face counseling to improve medication adherence among patients initiating statin therapy. *Patient Prefer Adherence*. 2012;6:323–329. doi:10.2147/PPA.S29353

TABLES AND FIGURES

Table 1.

Demographic Characteristics of Study Population

	Gender		
Characteristics	**Female**	**Male**	**P-value**
Number	5438	2729	--
Age (mean, SD)	63.6 (11.5)	61.6 (10.3)	<0.05[a]
Class of Psychotropic Medication (n, %)			
Alpha-2 Antagonist	164 (3%)	108 (4%)	<0.03[b]
Typical Antipsychotic	0 (0%)	92 (3%)	<0.01[b]
Atypical Antipsychotic	558 (10%)	351 (13%)	<0.01[b]
NDRI	506 (9%)	276 (10%)	0.24[b]
Nefazodone	3 (<1%)	0 (0%)	0.22[b]
SNRI	1258 (23%)	517 (19%)	<0.01[b]
SSRI	2895 (53%)	1439 (53%)	0.66[b]

SD = standard deviation, n = number, NDRI = Norepinephrine and Dopamine Reuptake Inhibitor, SNRI = Serotonin and Norepinephrine Reuptake Inhibitor, SSRI = Selective Serotonin Reuptake Inhibitor. Percentages may not add up to 100 due to rounding error.

[a]p-value for a Mann-Whitney test

[b]p-value for Chi-square test

Table 2.

Change in PDC After Counseling

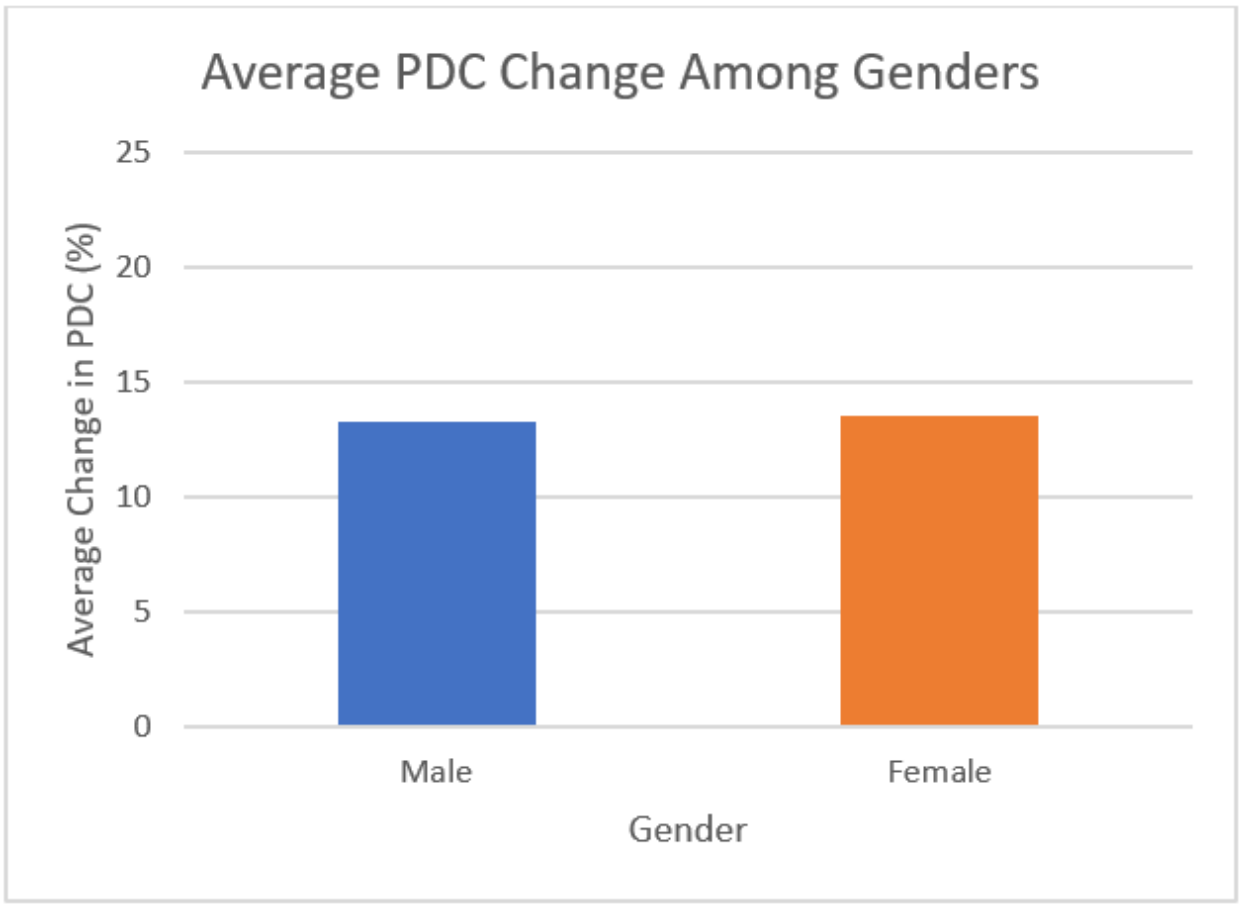
	PDC[a] (%)			
Characteristic	**Pre-Intervention**	**Post-Intervention**	**Difference in PDC**	**P-value[b]**
Overall	66.1 (12.1)	79.5 (19.1)	13.4 (20.2)	<0.01
Gender				
Male (n = 2,729)	65.9 (12.0)	79.2 (18.9)	13.3 (20.5)	<0.01
Female (n = 5,438)	66.2 (12.1)	79.7 (18.9)	13.5 (20.0)	<0.01
Age (years)				
≥ 65 (n = 4,277)	66.5 (11.9)	80.9 (18.5)	14.5 (19.6)	<0.01
40 - 64 (n = 3,634)	65.7 (12.6)	78.2 (19.4)	12.5 (20.6)	<0.01
20 - 39 (n = 256)	65.0 (12.3)	74.1 (20.8)	9.1 (22.5)	<0.01
Class of Psychotropic Medication				
Alpha-2 Antagonist (n = 272)	65.4 (13.2)	79.2 (17.8)	13.8 (19.9)	<0.01
Typical Antipsychotic (n = 92)	62.2 (12.4)	68.8 (20.5)	6.6 (20.6)	<0.05
Atypical Antipsychotic (n = 909)	65.1 (12.6)	77.8 (20.6)	12.2 (21.0)	<0.01
NDRI (n = 782)	65.1 (12.4)	77.7 (19.6)	12.7 (20.4)	<0.01
Nefazodone (n = 3)	67.0 (9.0)	78.0 (19.2)	11.3 (20.8)	0.66
SNRI (n = 1,775)	66.8 (11.6)	80.0 (18.6)	13.2 (20.2)	<0.01
SSRI (n = 4,334)	66.3 (11.9)	80.3 (18.7)	14.1 (19.9)	<0.01

n = number, PDC = Proportion of Days Covered, NDRI = Norepinephrine and Dopamine Reuptake Inhibitor, SNRI = Serotonin and Norepinephrine Reuptake Inhibitor, SSRI = Selective Serotonin Reuptake Inhibitor

[a]Results are presented as means with standard deviations in parentheses

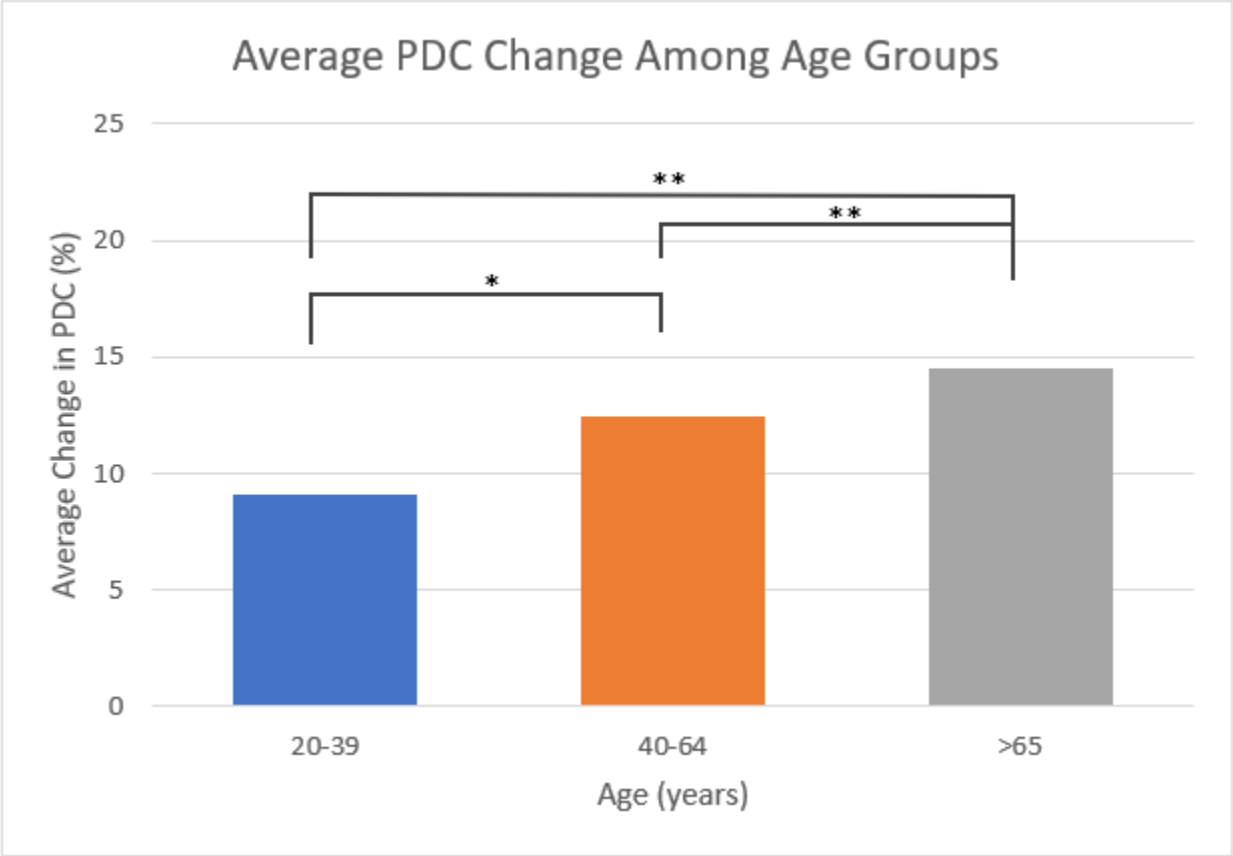
[b]All p-values are for a Mann-Whitney test

Figure 1



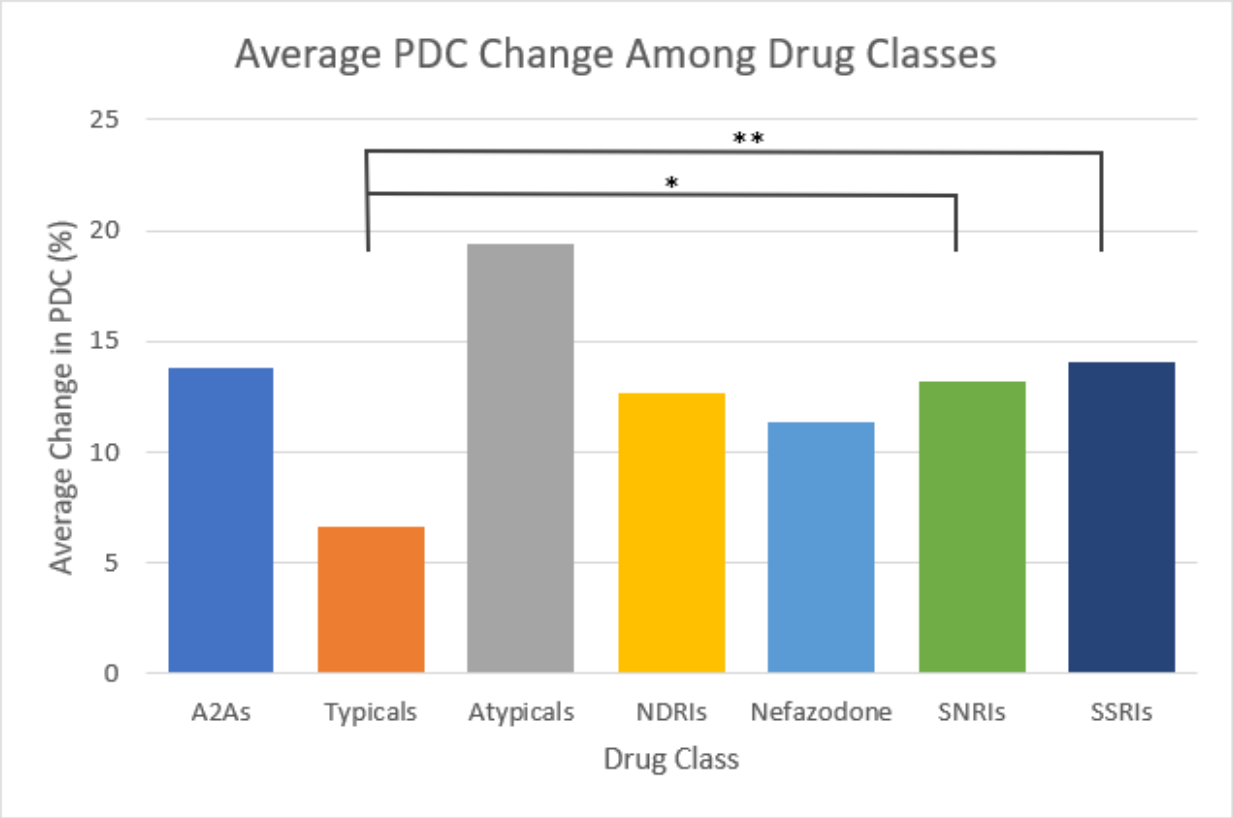
PDC = Proportion of Days Covered

Figure 2



PDC = Proportion of Days Covered
* Dunn p-value adjusted by the family-wide error rate procedure of Holm <0.04
** Dunn p-value adjusted by the family-wide error rate procedure of Holm <0.01

Figure 3



PDC = Proportion of Days Covered, A2As = Alpha-2 Antagonist, Typicals = Typical Antipsychotics, Atypicals = Atypical Antipsychotics, NDRIs = Norepinephrine and Dopamine Reuptake Inhibitors, SNRIs = Serotonin and Norepinephrine Reuptake Inhibitors, SSRIs = Selective Serotonin Reuptake Inhibitors
* Dunn p-value adjusted by the family-wide error rate procedure of Holm <0.05
** Dunn p-value adjusted by the family-wide error rate procedure of Holm <0.01

APPENDICES

Appendix A.

Data Dictionary

	A	B	C	D	E	F	G
1	**Variable Name**	**Code**					
2	Face-to-Face Counseling	Yes = 1, No = 0					
3	Type 2 Diabetes	Yes = 1, No = 0					
4	Proportion of Days Covered Before	%					
5	Proportion of Days Covered After	%					
6	Gender	F = 1, M = 0					
7	Age	Years					
8	Class of Mental Health Medication	None = 0					
9		Alpha-2 Antagonist = 1					
10		Typical Antipsychotic = 2					
11		Atypical Antipsychotic = 3					
12		NDRI = 4					
13		Nefazodone = 5					
14		SNRI = 6					
15		SSRI = 7					
16							
17							
18							

F = female, M = male, NDRIs = Norepinephrine and Dopamine Reuptake Inhibitors, SNRI = Serotonin and Norepinephrine Reuptake Inhibitor, SSRI = Selective Serotonin Reuptake Inhibitor