PATIENT ACTIVATION AND MEDICATION ADHERENCE AMONG MEDICARE BENEFICIARIES WITH TYPE 2 DIABETES

by

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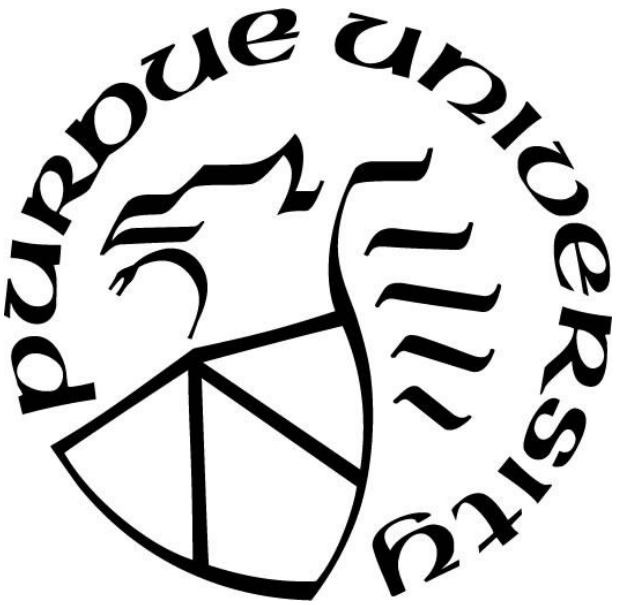

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Dedicated
to
My Family

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ABSTRACT

Zheng, Dandan, M.S., Purdue University, December 2018. Patient Activation and Medication Adherence among Medicare Beneficiaries with Type 2 Diabetes. Major Professor: Joseph Thomas III.

The objectives of this study were to assess patient activation levels, to assess association between sociodemographic characteristics and patient activation, to assess association between health status characteristics and patient activation, and to assess association between patient activation and medication adherence among Medicare beneficiaries with type 2 diabetes. A retrospective cohort study was conducted using data from the 2009 through 2013 Medicare Current Beneficiary Survey (MCBS). Patient activation was measured with the Patient Activation Supplement in the MCBS and was categorized as low, moderate, and high levels based on activation scores. Medication adherence was assessed with proportion of days covered (PDC) using Medicare Part D administrative records from the MCBS within a period of six months after measurement of patient activation. The sample included Medicare beneficiaries who completed the MCBS Patient Activation questionnaire, who were diagnosed with type 2 diabetes, and who were 18 or older. Beneficiaries were excluded if they responded "Not ascertained," "Not Applicable," "Don't know" or "Refused" to more than 50 percent of the Patient Activation questions, did not have continuous Medicare Part A and Part D coverage throughout the assessment period, had less than two Medicare Part D claims for an antidiabetic medication throughout the assessment period, used insulin during the assessment period, resided in long-term care facilities, or had Alzheimer's disease, dementia, mental retardation or mental disorder. All analyses were conducted in SAS 9.4 for Unix environment. An *a priori* alpha level of 0.05 was used to determine significance. Bivariate and multivariable weighted ordinal logistic regression were applied for assessing associations. A total of 571 individuals met sample selection criteria. The mean age was 72.4 years. Of the 571 persons in the sample, 27.5 percent

were at low activation level, 38.7 percent were at moderate activation level, and 33.7 percent were at high activation level. Approximately three-fourths of the sample persons were adherent to antidiabetic medications. Low activation was more likely to be found in males, less educated patients, and patients without arrhythmia. Ex-smokers as compared to non-smokers and overweight patients as compared to those with healthy weight were less likely to report low activation. In multivariable logistic analysis adjusting for race, gender, osteoporosis, Charlson Comorbidity Index score, and number of prescribed medications, patient activation level was not significantly associated with medication adherence. Non-Whites and patients with a Charlson Comorbidity Index score of 1 as compared to those with a score of 0 were more likely to be non-adherent. A lower number of prescribed medications was associated with higher odds of non-adherence.

INTRODUCTION

Diabetes Mellitus

Diabetes Overview

The American Diabetes Association defines diabetes mellitus as "a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both" (American Diabetes Association, 2014). Symptoms of diabetes include excessive urination, thirst and hunger, weight loss, blurred vision and fatigue (World Health Organization, 2016). When diabetes is not well controlled, complications that threaten health and even life develop. Acute complications include diabetic ketoacidosis and nonketotic hyperosmolar coma, which significantly contribute to mortality, costs and poor quality of life (American Diabetes Association, 2014; World Health Organization, 2016). The chronic hyperglycemia of uncontrolled diabetes may lead to serious long-term damage to various organs, especially the eyes, kidneys, nerves, heart, and blood vessels (American Diabetes Association, 2014; World Health Organization, 2016). Such damage can result in long-term complications including neuropathy in the feet with increased risk of foot ulcers, infection and the eventual need for limb amputation, diabetic retinopathy which may cause loss of vision, and nephropathy that may progress to renal failure (American Diabetes Association, 2014; World Health Organization, 2016). Diabetes is often accompanied by hypertension and abnormal lipoprotein metabolism and it nearly doubles the risk of a wide range of cardiovascular diseases (Emerging Risk Factors Collaboration, 2010). Additionally, diabetes has been associated with elevated rates of physical disability (E. Wong et al., 2013), specific cancers, liver disease and infectious disease (Rao Kondapally Seshasai et al., 2011).

Type 1 diabetes and type 2 diabetes constitute the great majority of diabetes cases, accounting for 90 percent to 95 percent and 5 percent to 10 percent of diabetes cases,

respectively (American Diabetes Association, 2017d). The cause of type 1 diabetes is β-cell destruction that leads to an absolute deficiency of insulin secretion so patients with type 1 diabetes require daily insulin treatment to regulate blood glucose level to survive (American Diabetes Association, 2014). Type 2 diabetes, the much more prevalent type, results from a combination of resistance to insulin action and relative insulin deficiency (American Diabetes Association, 2014). Gestational diabetes, characterized by impaired glucose tolerance with onset or first recognition during pregnancy (American Diabetes Association, 2014), has an estimated prevalence of 4.6 percent to 9.2 percent in pregnancy in the U.S. (DeSisto et al., 2014). There are other specific types of diabetes that result from genetic defects of β-cell function, genetic defects in insulin action, drugs or chemicals, infections, other genetic syndromes and so forth (American Diabetes Association, 2014), which may account for 1 percent to 2 percent of all diagnosed cases (Centers for Disease Control and Prevention, n.d.). We focus on type 2 diabetes since the vast majority of diabetes cases (90% to 95%) are type 2 diabetes.

The American Diabetes Association recommends diagnosing diabetes based on: "Fasting plasma glucose ≥ 126 mg/dL (7.0 mmol/L), or 2-hour plasma glucose ≥200 mg/dL (11.1mmol/L) during a 75-g oral glucose tolerance test, or A1C ≥ 6.5 percent (48 mmol/mol), or in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L)" (American Diabetes Association, 2017a).

Type 2 diabetes is a product of the interplay between genetic and metabolic factors (World Health Organization, 2016). Risk factors associated with diabetes include non-modifiable factors such as older age, ethnicity, family history of type 2 diabetes and previous gestational diabetes (World Health Organization, 2016) and modifiable risk factors such as overweight or obesity, unhealthy diet, physical inactivity (Hu et al., 2001) and smoking (Hu et al., 2001; Willi et al., 2007). Overweight and obesity are the strongest risk factors for type 2 diabetes (World Health Organization, 2016).

Burden of Diabetes

Worldwide Prevalence

Diabetes mellitus is a global public health problem. The World Health Organization estimated that 422 million adults (8.5%) all over the world were living with diabetes in 2014, while only 108 million adults (4.7%) had diabetes in 1980 (World Health Organization, 2016).

Prevalence and Incidence in the U.S.

Based on the National Diabetes Statistics Report of the U.S. by the Centers for Disease Control and Prevention, roughly 30.3 million people, or 9.4 percent of the U.S. population, had diabetes in 2015 (Centers for Disease Control and Prevention, 2017). Approximately 23.1 million people among them were diagnosed, but 7.2 million people remained undiagnosed (Centers for Disease Control and Prevention, 2017). Rowley et al. projected that the total number of people with diabetes will increase to 54.9 million, or 15.3 percent of the U.S. population by 2030 despite medical advances and prevention efforts (Rowley et al., 2017).

The prevalence of diabetes in adults increases with age, reaching 25.2 percent among those aged 65 years or older compared with 4.0 percent among those aged 18 to 44 years and 17 percent among those aged 45 to 64 years (Centers for Disease Control and Prevention, 2017). Among patients diagnosed with diabetes, 132,000 were children or adolescents younger than 18 years old with a prevalence of 0.18 percent (Centers for Disease Control and Prevention, 2017). Approximately 5 percent of people with diabetes had type 1 diabetes (Centers for Disease Control and Prevention, 2017).

Among Medicare beneficiaries, diabetes was highly prevalent and 28 percent of the Medicare fee-for-service beneficiaries had diabetes in 2010 (Centers for Medicare and Medicaid Services, 2012).

In terms of the incidence of diagnosed diabetes, it was estimated that 1.5 million new cases of diabetes was diagnosed among U.S adults in 2015, of which more than 50 percent were in persons 45 to 64 years old (Centers for Disease Control and Prevention, 2017).

Burden of Mortality

According to the World Health Organization, 1.5 million deaths worldwide were caused by diabetes directly, and diabetes was recognized as the eighth leading cause of death in 2012 (World Health Organization, 2016). Diabetes was the seventh leading cause of death in the U.S. in 2015, recognized as an underlying cause of death on 79,535 death certificates and as a contributing cause of death on 252,806 death certificates (Centers for Disease Control and Prevention, 2017).

Healthcare Utilization and Economic Burden

Diabetes imposes a substantial burden on healthcare resource utilization and substantial economic costs. In 2014, 7.2 million hospital discharges were associated with diabetes among U.S. adults (Centers for Disease Control and Prevention, 2017). These included 1.5 million inpatient stays attributable to major cardiovascular diseases such as ischemic heart disease and stroke in addition to 108,000 stays due to lower limb amputation and 168,000 stays due to diabetic ketoacidosis (Centers for Disease Control and Prevention, 2017). As to emergency department use, 14.2 million visits were reported with diabetes among adults including hypoglycemia and hyperglycemic crisis (Centers for Disease Control and Prevention, 2017). The U.S. spent approximately $245 billion on diagnosed diabetes in 2012, including $176 billion of direct medical costs and the other $69 billion for productivity reduction (American Diabetes Association, 2013a). Average medical expenditures among people with diagnosed diabetes were

approximately 2.3 times higher than those among people without diabetes (American Diabetes Association, 2013a).

Management of Diabetes

Although there is no known cure for diabetes, diabetes can be treated and controlled with lifestyle management, antidiabetic medications and careful monitoring of blood glucose as well as treatment for complications. Lifestyle management recommended by American Diabetes Association includes nutrition therapy with emphasis on body weight control and healthful eating patterns, physical activities and smoking cessation (American Diabetes Association, 2017b).

Commonly used antidiabetic medications in the U.S consist of a variety of agents classified as biguanides, sulfonylureas, thiazolidinediones (TZD), dipeptidyl peptidase-4 (DPP-4) inhibitors, sodium-glucose cotransporter 2 (SGLT-2) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists and insulin products, and they lower blood glucose level through different pharmacological mechanisms (American Diabetes Association, 2017e). DPP-4 inhibitors, SGLT-2 inhibitors and GLP-1 receptor agonists are new groups of medications. Newer medications may offer moderate glycemic effect but incur high cost based on the cost-effectiveness models (Institute for Clinical and Economic Review, 2014). Additionally, meglitinides, α-glucosidase inhibitors, bile acid sequestrant, dopamine-2 agonists and amylin mimetics may also be used for lowering glucose in specific situations but are not often used due to modest efficacy, frequency of administration and side effects (American Diabetes Association, 2017e). According to the American Diabetes Association, pharmacologic therapy for type 2 diabetes should usually start with metformin monotherapy if not contraindicated (American Diabetes Association, 2017c). If the HbA1c target is not achieved, it should proceed to dual therapy with one add-on agent (American Diabetes Association, 2017c). If HbA1c still not controlled, then triple therapy with two add-on agents should be used (American

Diabetes Association, 2017c). With the progression of diabetes, patients may progress to combination injectable therapy including insulin and GLP-1 receptor agonists agents (American Diabetes Association, 2017c).

As a chronic disease, diabetes requires long-term disease management to control blood glucose levels and prevent development of complications (American Diabetes Association, 2013b). Both lifestyle modification and pharmacologic therapy require patients to be actively engaged in self-management in collaboration with their health care team to gain the best health outcomes (Graffigna et al., 2014).

Patient Activation

Patient Activation Overview

Patient Activation and Patient Engagement

The terms "patient activation" and "patient engagement" are often used interchangeably, while patient engagement is used as a broader concept that includes patient activation, the interventions designed to increase activation, and the patient's actions that results from activation, such as getting preventive care or exercising regularly (Hibbard et al., 2013). Patient activation was defined by Judith Hibbard and colleagues as "understanding one's role in the care process and having the willingness, knowledge, skill, and confidence to manage one's health and healthcare" (Hibbard et al., 2004). Based on a bibliometric analysis, the use of the term "patient activation" increased three-fold from 2004 to 2013 (Menichetti et al., 2016).

Importance of Patient Activation

As Hibbard and colleagues have noted, nearly a decade after the Institute of Medicine called for patient-centeredness to be one of six goals for a 21st century health care system, the Patient Protection and Affordable Care Act recognized patient engagement as a cornerstone of successful health system reform, accountable care

organizations and patient-centered medical homes (Hibbard & Greene, 2013). Optimal treatment of chronic diseases requires not only a healthcare system that recognizes the central role of patients to their care, but also requires activated patients who have the motivation, skills and knowledge needed to manage their health (Remmers et al., 2009). Mosen and colleagues noted that assessing patient activation level is essential because activated, informed, and skilled patients are more likely to make good decisions and get involved in activities which promote their own health (Mosen et al., 2007). A growing body of studies suggest that patient activation may predict health-related quality of life (Gleason et al., 2016), health behaviors, hospitalization, emergency room use (Greene & Hibbard, 2012), medication adherence (Stepleman et al., 2010), and healthcare costs (Hibbard et al., 2013) in chronically ill populations.

Rask et al. have noted that healthcare providers can take advantage of patient activation assessment to tailor health messages and self-management goals (Rask et al., 2009). Hibbard et al. have noted that interventions can be developed and implemented to increase patient activation and engage patients in healthcare planning and healthcare delivery (Hibbard et al., 2015). Tailored intervention has been proved by a few studies to increase patient activation and improve self-management behaviors (Hibbard et al., 2007) and health related outcomes including clinical indicators improvement and utilization rates decline (Hibbard et al., 2009).

Measures of Patient Activation

Patient Activation Measure

Patient activation is commonly measured with the Patient Activation Measure (PAM). It was first developed by Judith Hibbard and colleagues with 22 items (Hibbard et al., 2004) and was later shortened by them to a 13-item scale in order to increase the feasibility of measuring activation in clinical settings and to reduce the burden and cost of survey administration (Hibbard et al., 2005). The PAM is scored on a 0 to 100 scale, and

patients can be categorized into four activation levels depending on the scores: level 1 (PAM ≤ 47.0), level 2 (47.1 ≤ PAM ≤ 55.1), level 3 (55.2 ≤ PAM ≤ 67.0) and level 4 (PAM ≥ 67.1) (Hibbard et al., 2005). Level 1 refers to the least activated patients and level 4 refers to the most activated patients. The 13 items in the PAM measure patients' beliefs, self-perceived knowledge and confidence in self-management of health-related tasks and include items such as "I know what treatments are available for my health problems" and "I am confident that I can tell a doctor my concerns, even when he or she does not ask." Responses are Likert type indicating degrees of agreement or disagreement. The PAM has been commercialized since its technology was transferred to a company called Insignia Health. There is also a version of PAM with only 10 items offered by Insignia Health (Insignia Health, 2018).

Patient Activation Supplement

In addition to the PAM, the Patient Activation Supplement of the Medicare Current Beneficiary Survey (MCBS) can also be used to assess patient activation (Parker et al., 2014). The MCBS is a continuous, nationally representative, longitudinal panel survey of approximately 15,000 Medicare beneficiaries, which could provide a rich resource of patient activation data (Parker et al., 2014). The Patient Activation Supplement was originally comprised of 15 questions but was later redeveloped to include one more question (Parker et al., 2014). The 15-item version consisting of five domains including self-care self-efficacy, doctor relationship and communication, assertiveness with doctor, active and shared decision-making, and health information-seeking was internally validated, with Cronbach's α internal consistency reliability coefficients of 0.72, 0.73, 0.55, 0.51, and 0.69, respectively (Williams & Heller, 2007). Parker et al. suggested three domains in the Patient Activation Supplement, including confidence in managing health, information-seeking, and communication with physicians (Parker et al., 2014). For example, one question asking about confidence is "How

confident are you that you can follow instructions to care for yourself at home?" One question asking about information-seeking is "Do you … bring with you to your doctor visits a list of questions or concerns you want to cover?" One question asking about communication is "Do you … leave your doctor's office feeling that all of your concerns or questions have been fully answered?" (See Parker et al., 2014 for a full list of patient activation questions). Although the Patient Activation Supplement hasn't been externally validated, Parkers et al. considered the questions in it are conceptually similar with those in PAM (Parker et al., 2014). The Patient Activation Supplement has been accepted by other studies to assess patient activation (Butler et al., 2012; Mattingly et al., 2017; Parker et al., 2014).

Patient Activation in Diabetes

In this section, literature is reviewed with regard to patient activation level in diabetes and its association with outcomes such as health behaviors, healthcare utilization, and healthcare costs.

Rask et al. conducted a survey to evaluate patient activation level and correlated patient activation scores with diabetes self-management behaviors and healthcare utilization in 287 adult patients with diabetes (Rask et al., 2009). The patients were from a diabetes clinic based at an urban public hospital, which served a predominantly African American, mostly uninsured and economically disadvantaged population. With the application of PAM-13 scale, 62.2 percent of the patients were reported at level 4, the highest level of activation, 20.7 percent, 9.6 percent and 7.6 percent of the patients were at level 3, level 2 and level 1, respectively. Bivariate analysis was applied to analyze correlations between PAM score and self-management behaviors. Higher activation levels were associated with better behaviors including weekly feet checks ($p = 0.009$), recommended eye examinations ($p = 0.009$), and regular exercise ($p = 0.021$). But daily blood glucose testing, routine check-ups, and blood pressure checking were not

associated with PAM levels. A follow-up survey was completed by 46.3 percent of the participants after 6 months. Mean initial PAM scores were 74.7, while the mean follow-up PAM scores were 76.7 (correlation coefficient = 0.466, $p = 0.182$). Baseline PAM scores did not predict subsequent number of outpatient visits or hospitalizations during the 6-month follow-up period.

Remmers et al. assessed patient activation's associations with future process outcomes, health related outcomes and healthcare utilization among 1,180 adults with diabetes using secondary data sources (Remmers et al., 2009). The data used in the study was obtained by merging two data sources, a descriptive, cross-sectional survey fielded during Fall 2004 of Kaiser Permanente Medical Care program members a diabetes registry with administrative clinical data for 2006, and making appropriate linkage by medical record numbers. Patient activation was assessed with the 22-item PAM. The mean PAM score was 57.1, and 44.4 percent of the participants were at level 2, 26.5 percent were at level 3, 17.4 percent were at level 4, and 11.5 percent were at level 1. The dependent variables including HbA1c testing, LDL-C testing, HbA1c control, all cause inpatient discharges, LDL-C control, and discharges due to acute myocardial infarction were dichotomized based on the frequency of the event, e.g., HbA1c testing (one or more tests or no test during 2006) and HbA1c control (at least 1 test result less than or equal to 8 percent vs. no test result less than or equal to 8 percent during 2006). In multivariable logistic regression, PAM score was positively associated with HbA1c testing (OR = 1.034, 95% CI: 1.009 to 1.060, p =0.008), LDL-C testing (OR = 1.034, 95% CI: 1.010 to 1.058, p =0.005), HbA1c control (OR = 1.108, 95% CI: 1.004 to 1.033, p =0.01), and negatively associated with all cause inpatient discharges (OR = 0.983, 95% CI: 0.967 to 0.998, p =0.03). However, PAM score was not associated with LDL-C control and discharges due to acute myocardial infarction.

Mayberry et al. measured patient activation and assessed its association with glycemic control among adults with type 2 diabetes (Mayberry et al., 2010). The sample

included 21 patients with controlled diabetes and 27 patients with uncontrolled diabetes at a family practice center seeking primary care. A recent A1C greater than 7 percent was regarded as uncontrolled diabetes and a most recent A1C equal to or less than 7 percent was regarded as controlled diabetes. Patient activation was measured with the 13-item PAM. The mean PAM score was 66.0 among patients with uncontrolled diabetes and 63.7 among those with controlled diabetes ($p = 0.607$). No significant association was identified between PAM score and glycemic control with logistic regression.

Begum et al. used cross-sectional data from the Living with Diabetes Study conducted annually in Australia to assess relationships between patient activation and hospitalizations or emergency department visits among 3,951 diabetes patients (Begum et al., 2011). The 13-item PAM was responded to by participants to obtain patient activation scores and to obtain the number of overnight admissions to hospitals and visits to emergency departments in the last 12 months as reported by participants. The overall mean PAM score was 62.7, and 69.9 percent of the total participants (n = 2,739) were at level 3 or level 4 of patient activation. Logistic regression revealed that participants at PAM level 1 were 1.4 times more likely to be hospitalized ($p = 0.023$) and 1.3 times more likely to have visited emergency department ($p = 0.049$) than those at level 4.

Hendriks et al. investigated patient activation level among 1,845 Dutch people with diabetes and its associations with health-related behaviors and outcomes via a paper questionnaire (M. Hendriks & Rademakers, 2014). The participants were selected from claims for diabetes care of six health insurance companies in 2010. Patient activation was measured with PAM 13. The mean PAM score of the respondents was 57.4. The percentage of the respondents at PAM level 1 was 23 percent, 23 percent were at level 2, 31 percent were at level 3 and 24 percent were at level 4. Logistic regression showed patients at level 2 or level 4 were more likely to have feet checks in the last 12 months than those at level 1 ($p = 0.025$, $p = 0.005$, respectively). Patients at level 4 were more

likely to have eye examinations in the last 24 months than those at level 1 ($p = 0.003$). No associations were found between patient activation and HbA1C checks, cholesterol level checks, blood glucose self-checking, blood pressure measurement, self-reported blood glucose level, and blood pressure level.

Hendriks et al. assessed associations between patient activation measured with the PAM-13 and patients' well-being and health-related quality of life among 1,615 type 2 diabetes patients who were treated in primary care in the eastern part of the Netherlands (S. H. Hendriks et al., 2016). Patients' well-being was measured with the World Health Organization-5 Well Being Index and health-related quality of life was measured with EuroQol EQ-5D. Based on multivariable regression, EQ5D score was not significantly associated with patient activation level, while World Health Organization -5 score was positively associated with patient activation level ($b = 0.158$, 95% CI: -0.124 to 0.193, $p < 0.001$).

Woodard et al. investigated the combined effect of functional health literacy and patient activation in predicting HbA1c control through a mail survey among 387 patients with diabetes who received outpatient care at one regional VA medical center (Woodard et al., 2014). Patient activation score was obtained using the PAM-13 and functional health literacy level was dichotomized as low and high using a single-item question, "How confident are you filling out medical forms by yourself?" Neither patient activation nor functional health literacy was independently associated with glycemic control but the interaction between the two was associated with glycemic control (OR = 1.05, 95% CI: 1.01-1.09, $p = 0.02$).

In summary, seven studies have assessed patient activation among diabetes patients and linked patient activation level to self-management behaviors, clinical outcomes or healthcare utilization (Begum et al., 2011; M. Hendriks & Rademakers, 2014; S. H. Hendriks et al., 2016; Mayberry et al., 2010; Rask et al., 2009; Remmers et al., 2009; Woodard et al., 2014). For self-management behaviors, two of the seven

studies found that patient activation was positively associated with the self-management behaviors of having regular feet checks and regular eye examinations, but it was not associated with blood glucose testing (M. Hendriks & Rademakers, 2014; Rask et al., 2009). Remmers et al. found that patient activation was positively associated with HbA1c testing (Remmers et al., 2009), while Hendricks didn't find any association between the two variables (M. Hendriks & Rademakers, 2014). For clinical outcomes, Remmers et al. found patient activation was positively associated with glycemic control (Remmers et al., 2009), while Mayberry et al. and Woodard et al. didn't find any association between them (Mayberry et al., 2010; Woodard et al., 2014). For healthcare utilization, Rask et al. found that patient activation could not predict healthcare utilization, that is, outpatient visits or hospitalizations six months later (Rask et al., 2009). Remmers et al. found patient activation was negatively associated with all cause inpatient discharges (Remmers et al., 2009). Begum et al. found patient activation was negatively associated with hospitalizations and emergency room visits (Begum et al., 2011). For health-related quality of life, Hendricks et al. found that patients' welling being as measured by World Health Organization-5 Well Being Index was positively associated with patient activation, but health-related quality of life as measured with the EuroQol EQ-5D was not associated with patient activation (S. H. Hendriks et al., 2016).

Sociodemographic Characteristics Associated with Patient Activation in Diabetes

Age

Rask et al. conducted a survey to assess association between age and patient activation in 287 adult patients with diabetes (Rask et al., 2009). Age was dichotomized as 50 years old or younger or older than 50, and it was not associated to patient activation scores.

Hendriks et al. assessed association between age and patient activation among 1,845 Dutch people with diabetes via a paper questionnaire (M. Hendriks & Rademakers,

2014). Age was related to patient activation level ($p < 0.001$) and younger people tended to have higher patient activation scores.

Aung et al. assessed the relationship between age and patient activation utilizing data from the Living with Diabetes Study in Australia from 2008 (N = 3761) to 2010 (N = 3040) (Aung et al., 2016). Patient activation level was dichotomized as low (level 1 or level 2) and high level (level 3 or level 4). Age was associated with patient activation ($p = 0.001$) and older patients reported higher patient activation level.

Hendriks et al. assessed relationship between age and patient activation measured with the PAM-13 among 1,615 type 2 diabetes patients who were treated in primary care in the eastern part of the Netherlands (S. H. Hendriks et al., 2016). Based on multivariable regression, age was negatively associated with patient activation score ($b = -0.130$, 95% CI: -0.197 to -0.063, $p < 0.001$).

Mayberry et al. assessed relationship between age and patient activation among adults with type 2 diabetes (Mayberry et al., 2010). The sample included 21 patients with controlled diabetes and 27 patients with uncontrolled diabetes at a family practice center seeking primary care. No significant association was identified between age and PAM score in either patients with controlled diabetes or patients with uncontrolled diabetes.

In summary, five studies assessed association between age and patient activation among diabetes patients (Aung et al., 2016; M. Hendriks & Rademakers, 2014; S. H. Hendriks et al., 2016; Mayberry et al., 2010; Rask et al., 2009). Two studies of the five found that there was no association between age and patient activation (Mayberry et al., 2010; Rask et al., 2009). Two studies found that there were negative relationships between age and patient activation (M. Hendriks & Rademakers, 2014; S. H. Hendriks et al., 2016). One study found that age was positively associated with patient activation (Aung et al., 2016).

Gender

Rask et al. conducted a survey to assess association between gender and PAM scores in 287 adult patients with diabetes (Rask et al., 2009). The patients were from a diabetes clinic based at an urban public hospital, which served a predominantly African American, mostly uninsured and economically disadvantaged population. Gender was not associated with patient activation score.

Hendriks et al. assessed association between gender and patient activation among 1,845 Dutch people with diabetes via a paper questionnaire (M. Hendriks & Rademakers, 2014). The participants were selected from claims for diabetes care of six health insurance companies in 2010. Patient activation was measured with PAM 13. Females had higher patient activation scores compared to males ($p = 0.017$).

Hendriks et al. assessed relationship between gender and patient activation measured with the PAM-13 among 1,615 type 2 diabetes patients who were treated in primary care in the eastern part of the Netherlands (S. H. Hendriks et al., 2016). Based on multivariable regression, gender was not associated with patient activation score.

Mayberry et al. assessed relationship between gender and patient activation among adults with type 2 diabetes (Mayberry et al., 2010). The sample included 21 patients with controlled diabetes and 27 patients with uncontrolled diabetes at a family practice center seeking primary care. No significant association was identified between gender and PAM score in either patients with controlled diabetes or patients with uncontrolled diabetes.

In summary, four studies assessed associations between gender and patient activation among diabetes patients (M. Hendriks & Rademakers, 2014; S. H. Hendriks et al., 2016; Mayberry et al., 2010; Rask et al., 2009). Three studies of the four did not find any association between gender and patient activation (S. H. Hendriks et al., 2016; Mayberry et al., 2010; Rask et al., 2009). Hendriks et al. found that females had higher patient activation scores than males (M. Hendriks & Rademakers, 2014).

Ethnicity/Race

Rask et al. conducted a survey to assess association between race and PAM scores in 287 adult patients with diabetes (Rask et al., 2009). Race was dichotomized as black and other and it was not associated with patient activation score.

Hendriks et al. assessed association between ethnicity and patient activation among 1,845 Dutch people with diabetes via a paper questionnaire (M. Hendriks & Rademakers, 2014). Ethnicity that was classified as Dutch, Western or non-Western was not associated with patient activation score.

Aung et al. assessed relationship between ethnicity and patient activation utilizing data from the Living with Diabetes Study in Australia from 2008 (N = 3761) to 2010 (N = 3040) (Aung et al., 2016). Patient activation level was dichotomized as low (level 1 or level 2) and high level (level 3 or level 4). Ethnicity was not significantly related to patient activation level.

Mayberry et al. assessed relationship between race and patient activation among adults with type 2 diabetes (Mayberry et al., 2010). The sample included 21 patients with controlled diabetes and 27 patients with uncontrolled diabetes at a family practice center seeking primary care. No significant association was identified between race and PAM score among either patients with controlled diabetes or patients with uncontrolled diabetes.

In summary, four studies assessed relationships between race/ethnicity and patient activation among diabetes patients, but none of them found significant race/ethnicity was associated with patient activation (Aung et al., 2016; M. Hendriks & Rademakers, 2014; Mayberry et al., 2010; Rask et al., 2009).

Education Level

Rask et al. conducted a survey to assess association between education and PAM scores in 287 adult patients with diabetes (Rask et al., 2009). Education was

dichotomized as high school or less and more than high school. Education was not associated with patient activation score.

Hendriks et al. assessed association between education level and patient activation among 1,845 Dutch people with diabetes via a paper questionnaire (M. Hendriks & Rademakers, 2014). Education level ($p < 0.001$) was significantly related to patient activation scores and patients with higher education level had higher patient activation scores.

Mayberry et al. assessed relationship between education level and patient activation among adults with type 2 diabetes (Mayberry et al., 2010). The sample included 21 patients with controlled diabetes and 27 patients with uncontrolled diabetes at a family practice center seeking primary care. No significant association was identified between education and PAM score in patients with controlled diabetes or patients with uncontrolled diabetes.

In summary, three studies assessed the associations between education and patient activation among diabetes patients (Aung et al., 2016; M. Hendriks & Rademakers, 2014; Mayberry et al., 2010; Rask et al., 2009). Two of the four did not find any significant association between education and patient activation (Mayberry et al., 2010; Rask et al., 2009). Hendriks et al. found that patients with higher education level had higher patient activation scores (M. Hendriks & Rademakers, 2014).

Marital Status

Aung et al. assessed relationship between marital status and patient activation utilizing data from the Living with Diabetes Study in Australia from 2008 (N = 3761) to 2010 (N = 3040) (Aung et al., 2016). Patient activation level was dichotomized as low (level 1 or level 2) and high (level 3 or level 4). Marital status was not associated with patient activation level.

Mayberry et al. assessed relationship between marital status and patient activation among adults with type 2 diabetes (Mayberry et al., 2010). The sample included 21 patients with controlled diabetes and 27 patients with uncontrolled diabetes at a family practice center seeking primary care. No significant association was identified between marital status and PAM score among patients with controlled diabetes or patients with uncontrolled diabetes.

In summary, two studies assessed relationships between marital status and patient activation among patients with diabetes (Aung et al., 2016; Mayberry et al., 2010). Neither of them reported significant associations.

Regions

Aung et al. assessed relationship between regions and patient activation utilizing data from the Living with Diabetes Study in Australia from 2008 (N = 3761) to 2010 (N = 3040) (Aung et al., 2016). Patient activation level was dichotomized as low (level 1 or level 2) and high (level 3 or level 4). Accessibility/Remoteness Index of Australia was used to assess regions. Regions were not associated with patient activation level.

In summary, only one study assessed relationship between regions of residence and patient activation among diabetes patients but no significant relationship was found (Aung et al., 2016).

Independent Living

Rask et al. conducted a survey to assess association between independent living and PAM scores in 287 adult patients with diabetes (Rask et al., 2009). Patients living independently had higher activation level ($p = 0.034$).

In summary, only one study reported that independent living was associated with high patient activation levels among diabetes patients (Rask et al., 2009).

Spoken Language at home

Hendriks et al. assessed association between spoken language at home and patient activation among 1,845 Dutch people with diabetes via a paper questionnaire (M. Hendriks & Rademakers, 2014). Spoken language at home was significantly associated with patient activation score ($p = 0.008$) and patients speaking Dutch were more likely to have higher patient activation scores compared to other languages.

In summary, only one study reported an association between spoken Dutch at home and high patient activation among diabetes patients (M. Hendriks & Rademakers, 2014).

Insurance Coverage

Rask et al. conducted a survey to assess association between insurance coverage and PAM scores in 287 adult patients with diabetes (Rask et al., 2009). No significant difference on patient activation scores was between insured and uninsured patients.

In summary, only one study assessed association between insurance coverage and patient activation among diabetes patients, but no significant association was found (Rask et al., 2009).

Health Status Characteristics Associated with Patient Activation in Diabetes

Body Mass Index

Aung et al. assessed relationship between Body Mass Index and patient activation utilizing data from the Living with Diabetes Study in Australia from 2008 (N = 3761) to 2010 (N = 3040) (Aung et al., 2016). Patient activation level was dichotomized as low (level 1 or level 2) and high (level 3 or level 4). Body Mass Index was negatively associated with patient activation level ($p < 0.001$).

Hendriks et al. assessed relationship between Body Mass Index and patient activation measured with the PAM-13 among 1,615 type 2 diabetes patients who were

treated in primary care in the eastern part of the Netherlands (S. H. Hendriks et al., 2016). Based on multivariable regression, a lower Body Mass Index was associated with a higher patient activation score.

In summary, two studies assessed relationships between Body Mass Index and patient activation among diabetes patients and they both reported a negative association between them (Aung et al., 2016; S. H. Hendriks et al., 2016).

Health Status

Rask et al. conducted a survey to assess association between health status and PAM level in 287 adult patients with diabetes (Rask et al., 2009). Health status was measured with a 12-item short-form (SF-12) health survey, which provided a physical health composite score and a mental health composite score. Compared to patients at lower patient activation levels, patients at level 4 had both higher SF-12 physical (p = 0.017) and mental health composite scores (p = 0.000).

Hendriks et al. assessed association between general health status and patient activation among 1,845 Dutch people with diabetes via a paper questionnaire (M. Hendriks & Rademakers, 2014). General health status was significantly associated with patient activation score ($p < 0.001$), patients with better health status reported higher patient activation scores.

In summary, two studies assessed associations between health status and patient activation among diabetes patients (M. Hendriks & Rademakers, 2014; Rask et al., 2009). Rask et al. found patients at level 4 were more likely to report high physical and mental health status (Rask et al., 2009). Hendriks et al. reported that health status was positively associated with patient activation score (M. Hendriks & Rademakers, 2014).

Number of Comorbidities/Presence of Comorbidities

Rask et al. conducted a survey to assess association between depression and PAM scores in 287 adult patients with diabetes (Rask et al., 2009). Presence or absence of depression was not associated with patient activation score.

Aung et al. assessed relationship between number of comorbidities and patient activation utilizing data from the Living with Diabetes Study in Australia from 2008 (N = 3761) to 2010 (N = 3040) (Aung et al., 2016). Patient activation level was dichotomized as low (level 1 or level 2) and high (level 3 or level 4). Number of comorbidities was negatively associated with patient activation level ($p < 0.001$).

In summary, two studies assessed associations between comorbidities and patient activation among diabetes patients (Aung et al., 2016; Rask et al., 2009). Rask et al. found presence or absence of depression was not associated with patient activation score (Rask et al., 2009). Aung et al. reported a negative association between number of comorbidities and patient activation level (Aung et al., 2016).

Diabetes Complications

Aung et al. assessed relationship between number of complications and patient activation utilizing data from the Living with Diabetes Study in Australia from 2008 (N = 3761) to 2010 (N = 3040) (Aung et al., 2016). Patient activation level was dichotomized as low (level 1 or level 2) and high (level 3 or level 4). Number of complications was negatively associated with patient activation level ($p < 0.001$).

Hendriks et al. assessed relationship between macrovascular and microvascular complications and patient activation measured with the PAM-13 among 1,615 patients with type 2 diabetes who were treated in primary care in the eastern part of the Netherlands (S. H. Hendriks et al., 2016). Based on multivariable regression, neither macrovascular nor microvascular complications were associated with patient activation score.

In summary, two studies assessed relationships between complications and patient activation among diabetes patients (Aung et al., 2016; S. H. Hendriks et al., 2016). Aung et al. found that number of complications was negatively associated with patient activation level (Aung et al., 2016). Hendriks et al. reported no significant associations between macrovascular or microvascular complications and patient activation score (S. H. Hendriks et al., 2016).

Smoking Status

Rask et al. conducted a survey to assess association between smoking status and PAM scores in 287 adult patients with diabetes (Rask et al., 2009). Smoking status was not associated with patient activation score.

Hendriks et al. assessed relationship between smoking status and patient activation measured with the PAM-13 among 1,615 type 2 diabetes patients who were treated in primary care in the eastern part of the Netherlands (S. H. Hendriks et al., 2016). Based on multivariable regression, patients who were smoking reported low patient activation scores (b = -0.155, 95% CI: -0.272 to -0.038, p = 0.010).

In summary, two studies assessed associations between smoking status and patient activation among diabetes patients (S. H. Hendriks et al., 2016; Rask et al., 2009). Rask et al. did not find significant association between smoking status and patient activation score (Rask et al., 2009). Hendriks et al. reported that patients who were smoking tended to report low patient activation scores (S. H. Hendriks et al., 2016).

Duration of Diabetes

Rask et al. conducted a survey to assess association between duration of diabetes and PAM scores in 287 adult patients with diabetes (Rask et al., 2009). Patients who had been diagnosed diabetes for more than 5 years had higher patient activation scores compared to those with diabetes for less than 5 years (p = 0.033).

Hendriks et al. assessed association between diabetes duration and patient activation among 1,845 Dutch people with diabetes via a paper questionnaire (M. Hendriks & Rademakers, 2014). Duration of diabetes was not associated with patient activation score.

Aung et al. assessed relationship between duration of diabetes and patient activation utilizing data from the Living with Diabetes Study in Australia from 2008 (N = 3761) to 2010 (N = 3040) (Aung et al., 2016). Patient activation level was dichotomized as low (level 1 or level 2) and high (level 3 or level 4). Duration of diabetes was negatively associated with patient activation level ($p = 0.041$).

Hendriks et al. assessed relationship between diabetes duration and patient activation measured with the PAM-13 among 1,615 type 2 diabetes patients who were treated in primary care in the eastern part of the Netherlands (S. H. Hendriks et al., 2016). Based on multivariable regression, diabetes duration was not associated with patient activation score.

In summary, four studies assessed relationships between diabetes duration and patient activation among diabetes patients (Aung et al., 2016; M. Hendriks & Rademakers, 2014; S. H. Hendriks et al., 2016; Rask et al., 2009). Rask et al. reported a positive association between diabetes duration and patient activation score (Rask et al., 2009). Aung et al. reported a negative association between diabetes duration and patient activation level (Aung et al., 2016). Two other studies found there was no significant association between diabetes duration and patient activation score (M. Hendriks & Rademakers, 2014; S. H. Hendriks et al., 2016).

Type of Treatment

Hendriks et al. assessed relationship between use of insulin and patient activation measured with the PAM-13 among 1,615 type 2 diabetes patients who were treated in primary care in the eastern part of the Netherlands (S. H. Hendriks et al., 2016). Based

on multivariable regression analysis, use of insulin was not associated with patient activation level.

Mayberry et al. assessed relationship between use of insulin and patient activation among adults with type 2 diabetes (Mayberry et al., 2010). The sample included 21 patients with controlled diabetes and 27 patients with uncontrolled diabetes at a family practice center seeking primary care. No significant association was identified between use of insulin and PAM score among patients with controlled diabetes or patients with uncontrolled diabetes.

In summary, two studies assessed relationships between types of antidiabetic treatment and patient activation among diabetes patients (S. H. Hendriks et al., 2016; Mayberry et al., 2010). Hendriks et al. reported use of insulin was not associated with patient activation level (S. H. Hendriks et al., 2016). Mayberry et al. reported use of insulin was not associated with patient activation score (Mayberry et al., 2010).

Patient Activation in Other Diseases

In this section, literature is reviewed with regard to patient activation level in diseases other than diabetes and its association with outcomes such as health behaviors, healthcare utilization, and healthcare costs.

Mosen et al. assessed the patient activation's associations with self-management behaviors and health outcomes among 4,108 adults with chronic conditions from Kaiser Permanente Medical Care program (Mosen et al., 2007). The 22-item Patient Activation Measure (PAM) was employed to assess levels of patient activation. The mean PAM score was 56.8. The distribution of patient activation level was 12.2 percent at level 1, 44.0 percent at level 2, 26.9 percent at level 3, and 16.9 percent at level 4. Compared to patients at level 1 of activation, those at level 4 were over 10 times more likely to report high satisfaction with care (OR = 10.01, 95% CI: 7.49 to 13.39), 5 times more likely to have high self-reported quality of life scores (OR = 5.04, 95% CI: 3.83 to 6.63), and

patients at level 4 reported 48 percent higher self-management behavior index scores ($p < 0.0001$), 26 percent higher physical component score of functional status ($p < 0.0001$) and 29 percent higher mental component score of functional status ($p < 0.0001$).

Stepleman et al. assessed associations between patient activation and quality of life in 199 multiple sclerosis patients recruited from a regional Multiple Sclerosis Center (Stepleman et al., 2010). This study utilized the 13-item PAM to evaluate patient activation. PAM scores ranged from 36.07 to 99.97 with a mean of 63.18. 7.1 percent of the participants were at level 1 of patient activation, followed by 18.9 percent at level 2, 39.8 percent at level 3 and 34.2 percent at level 4. PAM scores were positively correlated to quality of life ($r = 0.42$, $p < 0.01$).

Skolasky et al. conducted a cross-sectional study to examine the relationship between patient activation measured with the PAM-13 and functional status measured with SF-36 (Skolasky et al., 2011). A total of 855 multi-morbid, community-dwelling older participants from eight primary care practices in Baltimore-Washington, D.C. were included in the study. The PAM score ranged from 16.5 to 100 with a mean of 56.6. 18.0, 29.1, 35.7, and 17.2 percent of participants were at PAM level 1 to level 4, respectively. The PAM score was positively associated with functional status including physical and mental health components, with a 10-point change in PAM score leading to a 1.78 and 1.46 change in the two health components, respectively.

Greene et al. assessed patient activation measured with the PAM-13 and its associations with health outcomes and utilization outcomes in 25,047 adult patients from primary care clinics (Greene & Hibbard, 2012). The PAM score had a mean of 66.4, with 7 percent, 14 percent, 33 percent, and 46 percent of patients at level 1 to level 4 of patient activation, respectively. Compared to patients at activation level 1, patients with at level 4 were more likely to take preventive screening of colon cancer, cervical cancer, and breast cancer ($p = 0.03$, $p = 0.003$, $p = 0.01$, respectively), were more likely to achieve normal systolic blood pressure ($p < 0.001$), less likely to achieve diastolic blood

pressure ($p = 0.007$), and were less likely to have costly utilizations of emergency department visits and hospitalizations ($p < 0.01$ for both). However, patient activation level was not associated with HbA1c control.

Hibbard et al. conducted a longitudinal study to assess relationships between patient activation measured with the PAM-13 and billed care costs in 33,163 patients of Fairview Health Services (Hibbard et al., 2013). 7.2 percent, 13.7 percent, 33.2 percent, and 46.0 percent of the patients were at patient activation level 1 to level 4, respectively. At baseline (in 2011), patient activation level was negatively associated with care costs and patients at level 1 had 8 percent higher predicted per capita billed costs compared to those at level 4 ($p < 0.01$). Patient activation level significantly predicted care costs in the first half year of 2011, with a 21 percent higher costs incurred by the patients at level 1 than those at level 4.

Marshall et al. carried out a cross-sectional survey to assess associations between patient activation and clinical outcomes in 433 HIV-infected patients who were receiving care in four HIV clinics (Marshall et al., 2013). The 13-item PAM was used to measure patient activation. The mean PAM score was 72.3 with a range of 34.7 to 100 and 59.6 percent of the patients were at patient activation level 4. Every five-point increase in PAM score was associated with a 10 percent increase in the odds of having a CD4 count greater than 200 cells/mL (adjusted OR = 1.10, 95% CI: 1.01 to 1.21, $p = 0.032$) and an 8 percent increase in the odds of HIV viral suppression (adjusted OR = 1.08, 95% CI: 1.00 to 1.17, $p = 0.046$).

Mitchell et al. analyzed the secondary data of 695 general medical inpatient subjects from a randomized controlled trail conducted at an urban safety net hospital and assessed association between patient activation and total 30-day post-discharge hospital utilization (Mitchell et al., 2014). An adapted, 8-item version of PAM was used. The total 30-day post-discharge hospital utilization included total emergency department visits and hospital readmissions. 9.6 percent, 17.7 percent, 27.8 percent, and 44.9 percent

of the subjects were at activation level 1 to level 4, respectively. Adjusted Poisson regression analysis showed compared to patients at level 4, those at level 1 had a 75 percent increase in the odds of hospital reutilization within 30 days (95% CI: 1.18 to 2.60, $p < 0.001$), those at level 2 had a 50 percent increase in the odds of hospital reutilization within 30 days (95% CI: 1.06 to 2.13, $p < 0.001$), and those at level 3 had a 30 percent increase in the odds of hospital reutilization within 30 days (95% CI: 0.94 to 2.13, $p = 0.03$).

Parker et al. used 2012 MCBS data to evaluate patient activation and assess its association with service utilization and costs among 10,650 Medicare beneficiaries (Parker et al., 2014). Patient Activation Supplement in MCBS was used to measure patient activation. 28.1 percent, 38.1 percent, and 33.8 percent of the beneficiaries were at low, moderate, and high activation levels, respectively. Patient activation level was not significantly associated with inpatient stays and outpatient visits. Patients with moderate or high activation had more physician office visits than those with low activation ($p < 0.05$), but had less home health agencies visits. Patient activation level was not significantly associated with total Medicare Part A and Part B costs.

Young et al. conducted a telephone survey to assess patient activation and its association with asthma outcomes in a low-income rural population with asthma who received medications from the Family Health Center of Marshfield Inc. (Young et al., 2014). Patient activation of 98 adults was assessed with the 13-item PAM. 7.5 percent, 11.8 percent, 33.3 percent, and 47.3 percent were at patient activation level 1 to level 4, respectively. Multivariable regression results indicated that participants at patient activation level 2 and level 3 had better asthma control than those at level 1 ($\beta = 4.65$, 95% CI: 0.38 to 9.45, $p < 0.05$; $\beta = 4.40$, 95% CI: 1.30 to 8.13, $p < 0.05$), while patients at level 4 did not report significantly different asthma control scores from those at level 1.

Greene et al. conducted a longitudinal study to assess patient activation and its association with future health outcomes and costs among primary care patients at

Fairview Health Services (Greene et al., 2015). Patient activation was measured with the PAM-13. One group of participants had a baseline PAM score collected in 2010 and follow-up outcomes collected in 2012 (n = 32,060), and the other group had two PAM scores collected in two consecutive years between 2010 and 2012 (n = 10,957). 58 percent of the PAM levels stayed the same over the two years among patients with two PAM scores. Multivariable regression analysis showed that patients at higher baseline activation levels were more likely to have clinical indicators of HbA1c, high-density lipoprotein, low-density lipoprotein, triglycerides, systolic blood pressure in the normal range two years later. Compared to patients at level 4, those at level 1 (OR = 0.72, $p < 0.001$) and level 2 (OR = 0.79, $p < 0.001$) had higher odds of emergency department visits. Similar for hospitalizations, compared to patients at level 4, those at level 1 (OR = 0.79, $p < 0.01$) and level 2 (OR = 0.86, $p < 0.05$) had higher odds of hospitalizations. Patients at level 3 and level 4 had the same predicted average per capita costs in 2012, while those at level 2 had 12 percent higher costs and those at level 1 had 8 percent higher costs.

Hibbard et al. designed a longitudinal study among 4,865 chronically ill patients from 16 communities to examine whether a baseline patient activation measure could predict outcomes 4 years later and whether changes in patient activation scores are associated with changes in outcomes (Hibbard et al., 2015). PAM-13 was applied to obtain patient activation score, a Health Behaviors Index was used to capture health behaviors, and a Functional Health Index was used to capture functional health. The mean activation score at baseline was 64.3, with 6.8 percent, 19.0 percent, 37.2 percent, and 37.0 percent of the patients at activation level 1 to level 4, respectively. The activation score increased by 2.8 points on average over the 4 years. Compared to patients at level 4, those at lower levels reported worse levels of health behaviors ($r = -0.38$, $p < 0.01$), functional health ($r = 0.48$, $p < 0.01$), any emergency department use ($r = 0.06$, $p < 0.05$), and any hospitalizations ($r = 0.07$, $p < 0.01$) 4 years later. Additionally,

increases in PAM scores over the 4 years were associated with improvements of health-related outcomes including health behaviors ($r = 0.26$, $p < 0.01$) and functional health ($r = -0.06$, $p < 0.01$).

Gleason et al. carried out a survey to assess patient activation and its association with health-related outcomes among 277 older adults (Gleason et al., 2016). The PAM-13 was utilized to measure patient activation, and EuroQol EQ-5D was used to measure health-related quality of life. 12 percent, 20 percent, 41 percent, and 27 percent of the participants were at activation level 1 to level 4, respectively. Patient activation was positively associated with health-related quality of life ($b = -2.4$, $p < 0.001$). Neither number of hospitalizations nor hospitalization in the dichotomous form in the past year was associated with patient activation score.

Hibbard et al. assessed patient activation and examined whether it can predict ambulatory care-sensitive utilization and new diagnosis of a chronic disease in 3 years among 98,142 adult patients from primary care clinics (Hibbard et al., 2016). The 13-item PAM was used to measure baseline patient activation. 6.6 percent, 12.3 percent, 44.5 percent, and 36.7 percent of the patients were at activation level 1 to level 4 in 2011, respectively. Patients at higher level of activation had less visits to emergency departments ($p < 0.001$) and less hospitalizations ($p < 0.001$) in 2011. In multivariable logistic regression, compared to patients at level 4 in 2011, those at level 1 had a significantly higher rate of emergency departments visits in 2013 and 2014 (OR = 1.51, $p < 0.001$; OR = 1.33, $p < 0.05$), and had a significantly higher rate of hospitalizations in 2012, 2013, and 2014 (OR = 1.62, $p < 0.01$; OR = 1.40, $p < 0.05$; OR = 1.30, $p < 0.10$). For predicting a new chronic condition, patients at level 1 in 2011 had a higher rate of getting a new chronic condition in 2012, 2013, and 2014 (OR = 1.25, $p < 0.01$; OR = 1.31, $p < 0.001$; OR = 1.21, $p < 0.01$, respectively), as compared to those at level 4.

Salgado et al. conducted a multicenter cross-sectional study to examine patient activation among 125 respondents from oncology practices in Michigan (Salgado et al.,

2017). PAM-13 was used to assess patient activation. The PAM score had a mean of 65.0 (SD = 18.0), with 17.1 percent of patients at level 1, 8.9 percent at level 2, 41.5 percent at level 3, 32.5 percent at level 4.

In summary, a total of 14 cross-sectional or longitudinal studies explored patient activation and its association with self-management behaviors, health outcomes, healthcare utilization, and costs among diverse chronically ill populations (Gleason et al., 2016; Greene & Hibbard, 2012; Greene et al., 2015; Hibbard et al., 2013; Hibbard et al., 2016; Hibbard et al., 2015; Marshall et al., 2013; Mitchell et al., 2014; Mosen et al., 2007; Parker et al., 2014; Salgado et al., 2017; Skolasky et al., 2011; Stepleman et al., 2010; Young et al., 2014). All of these studies utilized the PAM-13 to measure patient activation except the one using Patient Activation Supplement in MCBS (Parker et al., 2014).

For self-management behaviors, Mosen et al. reported that patients at activation level 4 had higher self-management behavior index scores than those at activation level 1 among chronically ill patients (Mosen et al., 2007); Greene et al. reported that patients at activation level 4 were more likely to take preventive screening of cancer among adult patients from primary care clinics (Greene & Hibbard, 2012); Hibbard et al. reported that patients at lower activation levels at baseline had worse levels of health behaviors 4 years later, and increases in PAM scores over the 4 year period were associated with improvements of health behaviors among chronically ill patients (Hibbard et al., 2015).

For quality of life, Mosen et al. reported that patients at activation level 4 had higher self-reported quality of life scores among chronically ill patients (Mosen et al., 2007); Stepleman et al. reported PAM scores were positively related to quality of life among multiple sclerosis patients (Stepleman et al., 2010); Gleason et al. reported patient activation was positively associated with health-related quality of life among older patients (Gleason et al., 2016).

For health status, Mosen et al. reported that patients at activation level 4 had higher scores of functional status involving physical and mental components compared to patients at activation level 1 among chronically ill patients (Mosen et al., 2007); Skolasky et al. reported that PAM scores were positively associated with functional status among multi-morbid older patients; Hibbard et al. reported that patients at lower activation levels at baseline had worse levels of functional health 4 years later, and increases in PAM scores over the 4 year period were associated with improvements of functional health among chronically ill patients (Hibbard et al., 2015).

For clinical outcomes, Greene et al. reported that patients at activation level 4 were more likely to achieve normal systolic blood pressure and less likely to achieve diastolic blood pressure, but patient activation was not associated with HbA1c control among patients from primary care clinics (Greene & Hibbard, 2012); Marshall et al. reported that PAM score was positively associated with CD4 count and HIV viral suppression among HIV-infected patients (Marshall et al., 2013); Young et al. reported that patients at activation level 2 and level 3 had better asthma control than those at level 1 among low-income rural population with asthma, while patients at activation level 4 did not have significantly different asthma control from those at level 1(Young et al., 2014); Greene et al. reported that patients at higher baseline activation levels were more likely to have clinical indicators of HbA1c, high-density lipoprotein, low-density lipoprotein, triglycerides, systolic blood pressure in the normal range two years later among primary care patients (Greene et al., 2015). Hibbard et al. reported that patients at activation level 1 in 2011 had a higher rate of getting a new chronic condition in 2012, 2013, and 2014 as compared to those at level 4 among primary care patients (Hibbard et al., 2016).

For healthcare utilization, Greene et al. reported that patients at activation level 4 were less likely to have costly utilizations including emergency department visits and hospitalizations than those at level 1 among primary care patients (Greene & Hibbard, 2012); Mitchell et al. reported that patient activation level was negatively associated with

hospital reutilization within 30 days among general medical inpatients (Mitchell et al., 2014); Parker et al. reported that patient activation level was not significantly associated with inpatient stays and outpatient visits, and patients with moderate or high activation had more physician office visits and less home health agencies visits than those with low activation among Medicare beneficiaries (Parker et al., 2014); Greene et al. reported that patients at activation level 1 and level 2 had higher odds of hospitalizations and emergency department visits than those at level 4 among primary care patients (Greene et al., 2015); Hibbard et al. reported that patients at lower activation levels were more likely to have emergency department use and hospitalizations than those at level 4 among chronically ill patients (Hibbard et al., 2015); Gleason et al. did not find any association between patient activation and hospitalizations (Gleason et al., 2016); Hibbard et al. reported that compared to patients at activation level 4 in 2011, those at level 1 had a significantly higher rate of emergency departments visits in 2013 and 2014, and had a significantly higher rate of hospitalizations in 2012, 2013, and 2014 among primary care patients (Hibbard et al., 2016);

For healthcare costs, Hibbard et al. reported that patient activation level was negatively associated with care costs and patients at activation level 1 had higher predicted per capita billed costs than those at level 4 among primary care patients (Hibbard et al., 2013); Parker et al. reported that patient activation level was not significantly associated with total Medicare Part A and Part B costs among Medicare beneficiaries (Parker et al., 2014); Greene et al. reported that
patients at level 3 and level 4 had the same predicted average per capita costs, while those at level 2 had 12 percent higher costs and those at level 1 had 8 percent higher costs among primary care patients (Greene et al., 2015).

Sociodemographic Characteristics Associated with Patient Activation in Other Diseases

In this section, literatures were reviewed in terms of sociodemographic and health status characteristics associated with patient activation among people with conditions other than diabetes.

Age

Marshall et al. carried out a cross-sectional survey to determine the associations between age and patient activation in 433 HIV-infected patients who were receiving care in four HIV clinics (Marshall et al., 2013). The 13-item PAM was used to measure patient activation. Age was not associated with patient activation score.

Mitchell et al. assessed association between age and patient activation among 695 general medical inpatient subjects from a randomized controlled trail conducted at an urban safety net hospital (Mitchell et al., 2014). An adapted, 8-item version of PAM was used. Age in years was not significantly associated with patient activation levels.

Parker et al. used 2012 MCBS data to assess association between age and patient activation among 10,650 Medicare beneficiaries (Parker et al., 2014). Patient Activation Supplement in MCBS was used to measure patient activation. Compared to patients aged from 65 to 74 years old, those aged less than 65 (adjusted OR = 1.18, 95% CI: 1.01 to 1.37, $p = 0.034$), between 75 and 84 years old (adjusted OR = 1.19, 95% CI: 1.09 to 1.30, $p < 0.001$), or 85 or older (adjusted OR = 1.65, 95% CI: 1.47 to 1.85, $p < 0.001$) were found more likely to report low activation.

Hibbard et al. assessed association between age and patient activation measured with PAM-13 at baseline among 4,865 chronically ill patients from 16 communities (Hibbard et al., 2015). Age was not associated with patient activation score.

Eliacin et al. assessed relationship between age and patient activation that are two aspects of patient engagement among 152 veterans with mental health diagnosis (Eliacin et al., 2016). Patient activation was measured with the 13-item PAM of mental health

version. Age and race were significant predictors for PAM scores based on a stepwise selection, explaining 13 percent of the variance in PAM scores ($R^2 = 0.134$, $p < 0.001$).

Gleason et al. carried out a survey to assess association between age and patient activation among 277 older adults (Gleason et al., 2016). The PAM-13 was utilized to measure patient activation. Younger patients were more likely to have high patient activation scores (b = -0.35, $p = 0.002$).

Schmaderer et al. assessed association between age and patient activation in 200 multi-morbid patients discharged to home (Schmaderer et al., 2016). PAM-13 was applied to measure patient activation. Age was not a significant factor correlated to PAM scores.

Salgado et al. conducted a multicenter cross-sectional study to assess association between age and patient activation among 125 respondents from oncology practices in Michigan (Salgado et al., 2017). PAM-13 was used to assess patient activation. No significant difference was found in PAM levels by age.

In summary, eight studies assessed associations between age and patient activation among patients with diseases other than diabetes (Eliacin et al., 2016; Gleason et al., 2016; Hibbard et al., 2015; Marshall et al., 2013; Mitchell et al., 2014; Parker et al., 2014; Salgado et al., 2017; Schmaderer et al., 2016). Parker et al. reported that compared to patients aged from 65 to 74 years old, those aged less than 65, between 75 and 84 years old, or 85 or older were found more likely to report low activation (Parker et al., 2014). Gleason et al. reported that younger patients were more likely to have high activation (Gleason et al., 2016). Eliacin et al. reported that age was a significant predictor for PAM score (Eliacin et al., 2016). Another five studies did not find significant associations between age and patient activation (Hibbard et al., 2015; Marshall et al., 2013; Mitchell et al., 2014; Salgado et al., 2017; Schmaderer et al., 2016).

Gender

Marshall et al. carried out a cross-sectional survey to determine the associations between gender and patient activation in 433 HIV-infected patients who were receiving care in four HIV clinics (Marshall et al., 2013). The 13-item PAM was used to measure patient activation. Gender was not associated with patient activation score.

Mitchell et al. assessed association between gender and patient activation among 695 general medical inpatient subjects from a randomized controlled trail conducted at an urban safety net hospital (Mitchell et al., 2014). An adapted, 8-item version of PAM was used. Gender was not significantly associated with patient activation levels.

Parker et al. used 2012 MCBS data to assess association between gender and patient activation among 10,650 Medicare beneficiaries (Parker et al., 2014). Patient Activation Supplement in MCBS was used to measure patient activation. Males were more likely to report low activation level (adjusted OR=1.86, 95% CI: 1.70 to 2.03, $p < 0.001$).

Hibbard et al. assessed association between gender and patient activation measured with PAM-13 at baseline among 4,865 chronically ill patients from 16 communities (Hibbard et al., 2015). Gender was not associated with patient activation score.

Gleason et al. carried out a survey to assess association between gender and patient activation among 277 older adults (Gleason et al., 2016). The PAM-13 was utilized to measure patient activation. Gender was not significantly associated with patient activation score.

Salgado et al. conducted a multicenter cross-sectional study to assess association between gender and patient activation among 125 respondents from oncology practices in Michigan (Salgado et al., 2017). PAM-13 was used to assess patient activation. No significant difference was found in PAM levels by gender.

In summary, six studies assessed associations between gender and patient

activation among patients with diseases other than diabetes (Gleason et al., 2016; Hibbard et al., 2015; Marshall et al., 2013; Mitchell et al., 2014; Parker et al., 2014; Salgado et al., 2017). Parker et al. reported that males were more likely to have low activation (Parker et al., 2014). Another five studies did not find significant associations between gender and patient activation (Gleason et al., 2016; Hibbard et al., 2015; Marshall et al., 2013; Mitchell et al., 2014; Salgado et al., 2017).

Ethnicity/Race

Marshall et al. carried out a cross-sectional survey to determine the associations between race and patient activation in 433 HIV-infected patients who were receiving care in four HIV clinics (Marshall et al., 2013). The 13-item PAM was used to measure patient activation. Race was not associated with patient activation score.

Mitchell et al. assessed association between race and patient activation among 695 general medical inpatient subjects from a randomized controlled trail conducted at an urban safety net hospital (Mitchell et al., 2014). An adapted, 8-item version of PAM was used. Race was not significantly associated with patient activation levels.

Parker et al. used 2012 MCBS data to assess association between race and patient activation among 10,650 Medicare beneficiaries (Parker et al., 2014). Patient Activation Supplement in MCBS was used to measure patient activation. Compared to non-Hispanic White, Hispanic patients and patients of other races were more likely to report low activation level (adjusted OR=1.63, 95% CI: 1.38 to 1.91, $p < 0.001$; adjusted OR=1.28, 95% CI: 1.07 to 1.53, $p = 0.002$, respectively). But race was not a significant predictor comparing non-Hispanic Black with non-Hispanic White.

Hibbard et al. assessed association between race and patient activation measured with PAM-13 at baseline among 4,865 chronically ill patients from 16 communities (Hibbard et al., 2015). Race was significantly associated with patient activation score (*p*

< 0.05). More specifically, White non-Hispanic had higher activation scores compared to African American and Hispanic/Latino.

Eliacin et al. assessed relationship between race and patient activation that are two aspects of patient engagement among 152 veterans with mental health diagnosis (Eliacin et al., 2016). Patient activation was measured with the 13-item PAM of mental health version. White veterans reported significantly higher PAM scores compared to African American veterans ($p = 0.002$).

Gleason et al. carried out a survey to assess association between race and patient activation among 277 older adults (Gleason et al., 2016). The PAM-13 was utilized to measure patient activation. Race was not a significant factor associated with patient activation.

Salgado et al. conducted a multicenter cross-sectional study to assess association between race and patient activation among 125 respondents from oncology practices in Michigan (Salgado et al., 2017). PAM-13 was used to assess patient activation. No significant difference was found in PAM levels by race.

In summary, seven studies assessed associations between ethnicity/race and patient activation among patients with diseases other than diabetes (Eliacin et al., 2016; Gleason et al., 2016; Hibbard et al., 2015; Marshall et al., 2013; Mitchell et al., 2014; Parker et al., 2014; Salgado et al., 2017). Hibbard et al. reported that White non-Hispanic had higher activation scores compared to African American and Hispanic/Latino (Hibbard et al., 2015). Eliacin et al. reported that White veterans reported significantly higher PAM scores compared to African American veterans (Eliacin et al., 2016). Another five studies did not find significant associations between ethnicity/race and patient activation (Gleason et al., 2016; Marshall et al., 2013; Mitchell et al., 2014; Parker et al., 2014; Salgado et al., 2017).

Education Level

Marshall et al. carried out a cross-sectional survey to determine the associations between education and patient activation in 433 HIV-infected patients who were receiving care in four HIV clinics (Marshall et al., 2013). The 13-item PAM was used to measure patient activation. Having high school degree was associated with higher PAM scores ($p < 0.001$).

Mitchell et al. assessed association between education and patient activation among 695 general medical inpatient subjects from a randomized controlled trail conducted at an urban safety net hospital (Mitchell et al., 2014). An adapted, 8-item version of PAM was used. Education was significantly associated with patient activation levels ($p = 0.01$), and patients who had lower level of education were more likely to have low PAM levels (level 1 or level 2).

Parker et al. used 2012 MCBS data to assess association between education and patient activation among 10,650 Medicare beneficiaries (Parker et al., 2014). Patient Activation Supplement in MCBS was used to measure patient activation. Compared to patients with a college degree or greater, those with less than high school education (adjusted OR=2.22, 95% CI: 1.97 to 2.50, $p < 0.001$), those with high school degree (adjusted OR=1.72, 95% CI: 1.53 to 1.93, $p < 0.001$), and those with some college or vocational degree (adjusted OR=1.25, 95% CI: 1.11 to 1.41, $p < 0.001$) were more likely to report low activation level.

Hibbard et al. assessed association between education and patient activation measured with PAM-13 at baseline among 4,865 chronically ill patients from 16 communities (Hibbard et al., 2015). Patients with college graduate or more education had higher patient activation score compared to those with less than college graduate.

Gleason et al. carried out a survey to assess association between education and patient activation among 277 older adults (Gleason et al., 2016). The PAM-13 was

utilized to measure patient activation. Education level was not a significant factor associated with patient activation.

Schmaderer et al. assessed association between education level and patient activation in 200 multi-morbid patients discharged to home (Schmaderer et al., 2016). PAM-13 was applied to measure patient activation. Patients with higher education level had higher PAM scores ($r = 0.21$, $p = .003$).

Salgado et al. conducted a multicenter cross-sectional study to assess association between education and patient activation among 125 respondents from oncology practices in Michigan (Salgado et al., 2017). PAM-13 was used to assess patient activation. Patients with higher education level were more likely to report high PAM levels (Pearson's chi-square $p = 0.01$).

In summary, seven studies assessed associations between education and patient activation among patients with diseases other than diabetes (Gleason et al., 2016; Hibbard et al., 2015; Marshall et al., 2013; Mitchell et al., 2014; Parker et al., 2014; Salgado et al., 2017; Schmaderer et al., 2016). Six studies found that patients with high education levels were more likely to report high activation (Hibbard et al., 2015; Marshall et al., 2013; Mitchell et al., 2014; Parker et al., 2014; Salgado et al., 2017; Schmaderer et al., 2016). But Gleason et al. did not report significant association between education and activation among older adults (Gleason et al., 2016).

Employment Status

Mitchell et al. assessed association between employment status and patient activation among 695 general medical inpatient subjects from a randomized controlled trail conducted at an urban safety net hospital (Mitchell et al., 2014). An adapted, 8-item version of PAM was used. Employment status was significantly associated with patient activation levels, ($p = 0.02$), and patients who were disabled or retired were more likely to have low PAM levels (level 1 or level 2).

In summary, only one study assessed association between employment and patient activation among patients with diseases other than diabetes and reported that patients who were disabled or retired were more likely to have low PAM levels (Mitchell et al., 2014).

Income and Financial Strain

Mitchell et al. assessed association between income and patient activation among 695 general medical inpatient subjects from a randomized controlled trail conducted at an urban safety net hospital (Mitchell et al., 2014). An adapted, 8-item version of PAM was used. Income was not significantly associated with patient activation levels.

Hibbard et al. assessed association between poverty status and patient activation measured with PAM-13 at baseline among 4,865 chronically ill patients from 16 communities (Hibbard et al., 2015). Patients above poverty threshold reported higher patient activation scores than those below poverty threshold did.

Gleason et al. carried out a survey to assess association between financial strain and patient activation among 277 older adults (Gleason et al., 2016). The PAM-13 was utilized to measure patient activation. Financial strain was measured with the 4-item Financial Strain Instrument. Patients with increased financial strain were more likely to have low patient activation scores ($b = -0.53$, $p = 0.008$). While increased financial security at the end of the month was not a significant factor associated with patient activation score.

Schmaderer et al. assessed association between income and patient activation in 200 multi-morbid patients discharged to home (Schmaderer et al., 2016). PAM-13 was applied to measure patient activation. Patients with higher income levels had higher PAM scores in bivariate analysis ($r = 0.22$, $p = .002$). But in multivariable analysis, income was not associated with patient activation.

In summary, assessed association between employment and patient activation among patients with diseases other than diabetes (Gleason et al., 2016; Hibbard et al., 2015; Mitchell et al., 2014; Schmaderer et al., 2016). Hibbard et al. reported that patients above poverty threshold had higher patient activation scores than those below poverty threshold did (Hibbard et al., 2015). Gleason et al. reported that patients with increased financial strain were more likely to have low patient activation scores (Gleason et al., 2016). But Schmaderer et al. and Mitchell et al. did not find significant association between employment and patient activation (Mitchell et al., 2014; Schmaderer et al., 2016).

Marital Status

Mitchell et al. assessed association between marital status and patient activation among 695 general medical inpatient subjects from a randomized controlled trail conducted at an urban safety net hospital (Mitchell et al., 2014). An adapted, 8-item version of PAM was used. Marital status was not significantly associated with patient activation levels.

Parker et al. used 2012 MCBS data to assess association between marital status and patient activation among 10,650 Medicare beneficiaries (Parker et al., 2014). Patient Activation Supplement in MCBS was used to measure patient activation. Compared to married patients, those who were never married (adjusted OR=1.71, 95% CI: 1.44 to 2.02, $p < 0.001$) or widowed (adjusted OR=1.24, 95% CI: 1.13 to 1.36, $p < 0.001$) were more likely to report low activation level. But patients in divorced or separated status did not report significantly different activation from the married patients.

In summary, two studies assessed associations between marital status and patient activation (Mitchell et al., 2014; Parker et al., 2014). Mitchell et al. did not find significant association between marital status and patient activation (Mitchell et al., 2014). Parker et al. reported marital status was significantly associated with patient

activation and compared to married patients, those who were never married or widowed were more likely to report low activation level (Parker et al., 2014).

Independent Living

Gleason et al. carried out a survey to assess association between independent living and patient activation among 277 older adults (Gleason et al., 2016). The PAM-13 was utilized to measure patient activation. Patients who lived alone were more likely to have high patient activation scores (b = 4.9, p = 0.006).

In summary, only one study assessed association between independent living and patient activation and reported that patients who lived alone were more likely to have high activation scores (Gleason et al., 2016).

Family Support

Gleason et al. carried out a survey to assess association between family support and patient activation among 277 older adults (Gleason et al., 2016). The PAM-13 was utilized to measure patient activation and the validated 13-item Family Support Scale was used to measure satisfaction with family support. Patients with increased family support were more likely to have high patient activation scores (b = 0.42, p = 0.02).

In summary, only one study assessed association between family support and patient activation and reported that patients with increased family support were more likely to have high patient activation scores (Gleason et al., 2016).

Insurance Type

Mitchell et al. assessed association between insurance type and patient activation among 695 general medical inpatient subjects from a randomized controlled trial conducted at an urban safety net hospital (Mitchell et al., 2014). An adapted, 8-item version of PAM was used. Insurance type included Free Care, Medicaid, Medicare, and

private insurance. Insurance type was not significantly associated with patient activation levels.

Hibbard et al. assessed association between insurance type and patient activation measured with PAM-13 at baseline among 4,865 chronically ill patients from 16 communities (Hibbard et al., 2015). Insurance type was a significant predictor of patient activation score ($p < 0.01$), with a descending order of private insurance, Medicare, Medicaid, uninsured, and other insurances by mean PAM scores.

Heller et al. assessed association between dual eligibility for Medicaid, managed care enrollment, and patient activation among 236,322 Medicare beneficiaries who responded to the 2007 Medicare Consumer Assessment of Healthcare Providers and Systems Survey (Heller et al., 2009). Patient activation was measured with a 2-item Medicare Segmentation Screening Tool. In a multinomial logistic regression model, dual eligibility for Medicaid was not associated with patient activation, but patients enrolled in managed care tended to be in lower level of activation.

Sheikh et al. assessed association between insurance status and patient activation measured with PAM-13 among 108 adults presenting to an emergency department (Sheikh et al., 2016). Insurance status including public, private, and none was not significantly associated with activation levels.

Smith et al. assessed association between insurance coverage and patient activation measured with PAM-13 using a national survey of 3,400 US adults (Smith et al., 2015). Whether a respondent was insured or not did not influence patient activation significantly.

In summary, five studies assessed association between insurance type or coverage and patient activation among patients with diseases other than diabetes (Heller et al., 2009; Hibbard et al., 2015; Mitchell et al., 2014; Sheikh et al., 2016; Smith et al., 2015). Hibbard et al. reported that insurance type was a significant predictor of patient activation and patients covered by private insurance had higher activation scores (Hibbard et al.,

2015). Heller et al. found managed care enrollment was associated with lower activation, but Medicaid eligibility was not among Medicare beneficiaries (Heller et al., 2009). The other studies found that insurance type was not significantly associated with patient activation (Mitchell et al., 2014; Sheikh et al., 2016; Smith et al., 2015).

Health Status Characteristics Associated with Patient Activation in Other Diseases

Body Mass Index

Greene et al. assessed patient activation measured with PAM-13 and its association with obesity in 25,047 adult patients from primary care clinics (Greene & Hibbard, 2012). Obesity was defined by having a Body Mass Index equal to or greater than 30. Compared to patients at activation level 1, patients with at level 4 were less likely to be obese ($p < 0.001$).

Greene et al. conducted a longitudinal study to assess association between obesity and patient activation among 25,358 primary care patients at Fairview Health Services (Greene et al., 2015). Patient activation was measured with PAM-13. Compared to patients at level 4, those at level 1 (OR = 0.62, $p < 0.001$), level 2 (OR = 0.62, $p < 0.001$), and level 3 (OR = 0.79, $p < 0.001$) were less likely to be not obese.

In summary, two studies assessed association between Body Mass Index and patient activation among patients with diseases other than diabetes and both studies reported that patients at activation level 1 were more likely to be obese based on Body Mass Index (Greene & Hibbard, 2012; Greene et al., 2015).

Health Status

Parker et al. used 2012 MCBS data to assess association between health status and patient activation among 10,650 Medicare beneficiaries (Parker et al., 2014). Patient Activation Supplement in MCBS was used to measure patient activation and a single item question in the questionnaire was used to measure health status. Compared to

patients who reported good, very good, or excellent health status, those who reported fair or poor in health were more likely to have low patient activation level (adjusted OR=1.37, 95% CI: 1.25 to 1.51, $p < 0.001$).

Salgado et al. conducted a multicenter cross-sectional study to assess association between health status and patient activation among 125 respondents from oncology practices in Michigan (Salgado et al., 2017). PAM-13 was used to assess patient activation and a single item question was used to measure health status. No significant difference was found in PAM levels by health status.

In summary, two studies assessed association between health status and patient activation among patients with diseases other than diabetes (Parker et al., 2014; Salgado et al., 2017). Parker et al. found that compared to patients who reported good, very good, or excellent health status, those who reported fair or poor in health were more likely to have low patient activation level among Medicare beneficiaries (Parker et al., 2014). Salgado et al. did not find significant association between health status and patient activation (Salgado et al., 2017).

Comorbidities

Number of Comorbidities

Skolasky et al. conducted a cross-sectional study to examine the relationship between number of comorbidities and patient activation measured with PAM-13 among 855 multi-morbid, community-dwelling older participants from eight primary care practices in Baltimore-Washington, D.C. (Skolasky et al., 2011). Number of comorbidities were not associated with PAM score.

Gleason et al. carried out a survey to assess association between number of chronic conditions, depression and patient activation among 277 older adults (Gleason et

al., 2016). The PAM-13 was utilized to measure patient activation. Number of comorbidities was not a significant factor associated with patient activation.

Schmaderer et al. assessed association between number of comorbidities, severity of comorbidities, depression, anxiety and patient activation in 200 multi-morbid patients discharged to home (Schmaderer et al., 2016). PAM-13 was applied to measure patient activation. Number of comorbidities was not significantly associated with PAM scores.

In summary, three studies assessed associations between number of comorbidities and patient activation and none of them reported significant associations (Gleason et al., 2016; Schmaderer et al., 2016; Skolasky et al., 2011).

Individual Comorbidities

Stepleman et al. assessed association between patient activation and depression in 199 multiple sclerosis patients recruited from a regional Multiple Sclerosis Center (Stepleman et al., 2010). PAM-13 was used to evaluate patient activation. Depression severity of symptoms measured by the Beck Depression Inventory-II was negatively related to PAM scores ($r = -0.43$, $p < 0.01$).

Marshall et al. carried out a cross-sectional survey to determine the associations between depression and patient activation in 433 HIV-infected patients who were receiving care in four HIV clinics (Marshall et al., 2013). The 13-item PAM was used to measure patient activation. Depression symptoms measured with Center for Epidemiologic Studies Depression Scale was negatively associated with PAM scores ($p < 0.001$).

Mitchell et al. assessed association between depression symptoms and patient activation among 695 general medical inpatient subjects from a randomized controlled trail conducted at an urban safety net hospital (Mitchell et al., 2014). An adapted, 8-item version of PAM was used. Patients with a higher level of depressive symptoms were more likely to report low PAM levels (level 1 or level 2) ($p < 0.01$).

Hibbard et al. assessed association between chronic conditions and patient activation measured with PAM-13 at baseline among 4,865 chronically ill patients from 16 communities (Hibbard et al., 2015). Presence of diabetes ($p < 0.05$) and presence of depression ($p < 0.01$) were associated with patient activation score, while presence of hypertension, asthma, and heart disease were not.

Gleason et al. carried out a survey to assess association between number of chronic conditions, depression and patient activation among 277 older adults (Gleason et al., 2016). The PAM-13 was utilized to measure patient activation. Number of comorbidities was not a significant factor associated with patient activation. Diagnosis of depression was not a significant factor associated with patient activation score, whereas the severity of depression measured with the PHQ-9 was negatively associated with patient activation score (b = -0.9, $p < 0.001$).

Hibbard et al. assessed association between presence of five chronic conditions and patient activation among 98,142 adult patients from primary care clinics (Hibbard et al., 2016). The 13-item PAM was used to measure baseline patient activation. Presence of diabetes, hypertension, chronic obstructive pulmonary disease, congestive heart failure, and depression were all found associated with patient activation levels (all $p < 0.001$).

Schmaderer et al. assessed association between number of comorbidities, severity of comorbidities, depression, anxiety and patient activation in 200 multi-morbid patients discharged to home (Schmaderer et al., 2016). PAM-13 was applied to measure patient activation. The Patient Reported Outcomes Measurement Information System-29 was used to measure depression and anxiety. Patients with higher depression scores (r = -0.33, $p = 0.001$) and anxiety scores (r = -0.30, $p = 0.001$) had lower PAM scores.

In summary, seven studies assessed associations between individual comorbidities and patient activation (Gleason et al., 2016; Hibbard et al., 2016; Hibbard et al., 2015; Marshall et al., 2013; Mitchell et al., 2014; Schmaderer et al., 2016; Stepleman et al.,

2010). Five of the seven studies found that the severity of depression symptoms was negatively associated with patient activation (Gleason et al., 2016; Marshall et al., 2013; Mitchell et al., 2014; Schmaderer et al., 2016; Stepleman et al., 2010). Hibbard et al. found that presence of diabetes and presence of depression were associated with patient activation score, while presence of hypertension, asthma, and heart disease were not (Hibbard et al., 2015). Another study by Hibbard et al. reported that presence of diabetes, hypertension, chronic obstructive pulmonary disease, congestive heart failure, and depression were all found associated with patient activation levels (Hibbard et al., 2016).

Charlson Comorbidity Index

Mitchell et al. assessed association between depression symptoms, and Charlson Comorbidity Index and patient activation among 695 general medical inpatient subjects from a randomized controlled trail conducted at an urban safety net hospital (Mitchell et al., 2014). An adapted, 8-item version of PAM was used. Charlson Comorbidity Index was not significantly associated with patient activation levels.

Schmaderer et al. assessed association between number of comorbidities, severity of comorbidities, depression, anxiety and patient activation in 200 multi-morbid patients discharged to home (Schmaderer et al., 2016). PAM-13 was applied to measure patient activation. The Charlson Comorbidity Index was used to measure severity of illness. Severity of comorbidities was not significantly associated with PAM scores.

In summary, two studies assessed associations between Charlson Comorbidity Index and patient activation and neither reported significant associations between the two variables (Mitchell et al., 2014; Schmaderer et al., 2016).

Smoking Status

Skolasky et al. conducted a cross-sectional study to examine the relationship between smoking status and patient activation measured with PAM-13 among 855 multi-morbid, community-dwelling older participants from eight primary care practices in Baltimore-Washington, D.C. (Skolasky et al., 2011). Smoking status was not associated with PAM scores.

Greene et al. assessed association between smoking status and patient activation measured with PAM-13 in 25,047 adult patients from primary care clinics (Greene & Hibbard, 2012). Compared to patients at level 4 of patient activation, patients at level 1 were more likely to be current smokers ($p < 0.001$).

Greene et al. conducted a longitudinal study to assess association between smoking status and patient activation among 25,522 primary care patients at Fairview Health Services (Greene et al., 2015). Patient activation was measured with PAM-13. Compared to patients at level 4, those at level 1 (OR = 0.64, $p < 0.001$), level 2 (OR = 0.65, $p < 0.001$), and level 3 (OR = 0.81, $p < 0.001$) were more likely to be a current smoker.

In summary, three studies assessed associations between smoking status and patient activation (Greene & Hibbard, 2012; Greene et al., 2015; Skolasky et al., 2011). Greene et al. reported that compared to patients at activation level 4, patients at level 1 were more likely to be current smokers (Greene & Hibbard, 2012). Another study by Greene et al. reported that compared to patients at level 4, those at lower levels were more likely to be a current smoker (Greene et al., 2015). Skolasky et al. did not report significant association between smoking status and patient activation (Skolasky et al., 2011).

Prior Hospitalization

Gleason et al. carried out a survey to assess association between hospitalization in the past year, number of hospitalizations in the past year and patient activation among 277 older adults (Gleason et al., 2016). The PAM-13 was utilized to measure patient activation. Neither of them was significantly associated with patient activation.

In summary, only one study assessed association between prior hospitalization and patient activation and no significant association was found (Gleason et al., 2016).

Medication Adherence

Several investigations have reported that approximately 50 percent of patients with type 2 diabetes fail to achieve adequate glycemic control (Ali et al., 2012; Ford, 2011). Medication non-adherence has been recognized as a key factor that affects glycemic control (Egede et al., 2014). The reported prevalence of adherence to antidiabetic drugs ranged from 38 percent to 93 percent based on different methods of adherence measurement (Krass et al., 2015). For the purpose of this study, we focused on adherence rate measured by objective approaches. The medication adherence rate was 47.3 percent for DPP-4 inhibitors initiators, 41.2 percent for sulfonylureas initiators, and 36.7 percent for thiazolidinediones initiators based on a large-scale retrospective cohort study (Farr et al., 2014). A meta-analysis reported an adherence rate for antidiabetic medications of 67.9 percent (Iglay et al., 2015).

The World Health Organization defines adherence as "the extent to which a person's behavior including taking medication, following a diet, and/or executing lifestyle changes corresponds with agreed recommendations from a healthcare provider" (World Health Organization, 2003). Most patients with type 2 diabetes take oral antidiabetic medications or administer insulin to control blood glucose levels. Therefore, it is critical for patients to be adherent with prescribed medication regimens to maintain normal blood glucose level and prevent development of diabetes related complications.

Studies have associated higher medication adherence to antidiabetic medications with improved glycemic control (Aikens & Piette, 2013; Feldman et al., 2014), lower healthcare utilization (Jha et al., 2012) and decreased healthcare costs (E. S. Wong et al., 2014).

Measures of Medication Adherence

Numerous measures are available for measuring medication adherence but none of them can be counted as the gold standard (Lam & Fresco, 2015). Those measures have been designed and validated for different conditions so to choose a most suitable measure is vital for the study design. Measurements of medication adherence can be categorized as subjective and objective measurements (World Health Organization, 2003). Self-report such as using Morisky Medication Adherence Scale and healthcare professional assessments are most commonly used in subjective category. Objective methods include pill counts, electronic monitoring and secondary database analysis etc. (Velligan et al., 2007).

When dealing with secondary databases containing pharmacy insurance claims, medication possession ratio (MPR) and the proportion of days covered (PDC) are the two most common approaches to estimate adherence. MPR is the sum of the days of supply for all fills of a given drug in a particular period, divided by the number of days in the period. However, MPR has been criticized by researchers for overestimating adherence. It is likely to occur when the patient refills medications early or switch medication within the same class, which will result in overlap of days of supply and thus inflate the estimated medication adherence (Crowe, 2015; Nau, 2012). PDC is a more conservative method than MPR. It is the percentage of days in a period “covered” by prescription claims for the same medication or medications in its therapeutic category. Instead of simply summing up the days' supplied across an interval, PDC considers time arrays to reflect the dates covered by each fill and adjusts the start date of each array when arrays

overlap due to early refill. Usually, a patient is considered adherent if his/her PDC value is no less than 0.8.

$$\text{PDC} = \left(\frac{Number\ of\ days\ covered\ by\ prescription\ fills\ in\ period}{Number\ of\ days\ in\ period}\right) * 100\%$$

PDC is the leading method used to calculate medication adherence at a population level, and is endorsed by the Pharmacy Quality Alliance (PQA) and recognized as the Center for Disease Control and Prevention's (CDC) preferred method for medication adherence calculation in populations (Centers for Disease Control and Prevention, 2015; Nau, 2012). Additionally, the U.S. Centers for Medicare and Medicaid Services (CMS) has incorporated PDC measures into its Star Ratings of plan quality used in Medicare Part D plans (Center for Medicare & Medicaid Services, 2017).

Association between Patient Activation and Medication Adherence

Assessing patient activation and its associations with health outcomes will provide greater understanding of the expected gains if patients take active roles in their healthcare (M. Hendriks & Rademakers, 2014). A group of studies has investigated patient activation and its relationship with mediation adherence among various disease conditions and showed benefits for being more activated.

Mosen et al. assessed the patient activation's association with medication adherence among 4,108 adults with chronic conditions from Kaiser Permanente Medical Care program (Mosen et al., 2007). Medication adherence was measured by asking how many days of medication doses were missed in the 7 days prior to the interview. It was analyzed as a dichotomous measure: missed one or fewer medications as high medication adherence vs. more medications as low medication adherence. The 22-item Patient Activation Measure (PAM) was employed to assess levels of patient activation. Patient activation was associated with medication adherence in both bivariate and multiple logistic regression analysis. Each increased stage of PAM was associated with improved medication adherence ($p < 0.0001$). In logistic regression model, participants with Level

4 PAM scores were nearly 3 times more likely to report high medication adherence than those with Level 1 PAM scores (OR = 2.65, 95% CI: 1.74 to 4.03).

Stepleman et al. assessed association between patient activation and medication adherence in 199 multiple sclerosis patients recruited from a regional Multiple Sclerosis Center (Stepleman et al., 2010). To assess medication adherence, patients were asked to respond to the frequency of missing doses of their disease modifying therapies ($r = -0.04$, $p = 0.57$). This study utilized the 13-item PAM to evaluate patient activation. Patient activation was not associated with self-reported medication adherence, which might result from the single-item measurement of adherence, small sample size, skewed sample and measurement and power issues.

Skolasky et al. conducted a cross-sectional study to examine the relationship between patient activation scores and adherence to desirable health-related behaviors (Skolasky et al., 2011). A total of 855 multi-morbid, community-dwelling older participants from eight primary care practices in Baltimore-Washington, D.C. were included in the study. The 13-item version of the PAM was used to classify the patient activation levels of the patients. Several adaptive health-related behaviors were taken into consideration to evaluate patient adherence: frequency of physical activity and structured exercises in past week, number of missed doses during past week as medication adherence and frequency of following recommended diet in past week. Based on the proportional odds regression model, the patient activation score was positively associated with physical activity, structured exercise and medication adherence. A 10-point change in PAM score led to 13 percent increase in the odds of higher level of medication adherence.

Marshall et al. carried out a cross-sectional survey to determine the associations between patient activation and medication adherence in 433 HIV-infected patients who were receiving care in four HIV clinics (Marshall et al., 2013). The 13-item PAM was used to measure patient activation. Adherence to antiretroviral medications was self-

reported by answering "What percentage of the time would you say you take your anti-HIV medications as prescribed in the last 30 days?" and was dichotomized as 100 percent vs. less than 100 percent. The multivariable logistic regression model manifested that every 5-point increase in PAM was associated with 18 percent increase in the odds of medication adherence (adjusted OR = 1.18, 95% CI: 1.09 to 1.29, $p < 0.001$).

Young et al. conducted a telephone survey to assess association between patient activation and adherence to asthma maintenance medication in a low-income rural population with asthma who received medications from the Family Health Center of Marshfield Inc. (Young et al., 2014). Patient activation of 98 adults was assessed with PAM-13 and medication adherence to long-term controller was assessed using the Morisky Medication Adherence Scale. The score of the scale ranges from 0 to 8 and was dichotomized as low adherence (score < 6) vs. medium/high adherence (score $\geq$ 6). Multivariable regression results indicated that participants at patient activation level 2 had greater adherence than those at level 1 which is the lowest activation level ($\beta = 2.25$, 95% CI: 0.52 to 4.39) and participants at patient activation level 3 or level 4 also had greater adherence than those at level 1 ($\beta = 1.30$, 95% CI: -0.11 to 3.07; $\beta = 1.40$, 95% CI: -0.15 to 3.11, respectively). However, the findings did not support a positive association between the continuous measure of patient activation and adherence to asthma maintenance medication. The most activated participants at level 4 did not report the highest adherence. The authors gave some plausible explanations that individuals at level 4 may have a sense of overconfidence that could impact self-management and outcomes and may have difficulty maintaining appropriate asthma self-management over time or during times of stress or other situations.

Hibbard et al. designed a longitudinal study among 4,865 chronically ill patients from 16 communities to examine whether a baseline patient activation measure could predict medication adherence 4 years later and whether changes in patient activation scores are associated with changes in medication adherence (Hibbard et al., 2015). The

13-item PAM was applied to acquire patient activation score. Medication Adherence Index was applied to assess patient adherence and the respondents were asked to report the frequency at which they could take the medications as their doctors have recommended in the past month. Respondents answered on a 5-point scale from 1 (never) to 5 (always). If one respondent had multiple chronic conditions, the scores of all his adherence questions were averaged to get his final medication adherence score. Both bivariate and multivariable analysis showed that compared with the most activated patients (level 4), the less activated (level 1 to 3) had significantly lower levels of medication adherence so baseline patient activation level was associated with medication adherence at follow-up was concluded. In addition, medication adherence changed in the same direction as the patient activation scores changed over the 4 years.

A multicenter cross-sectional observational study was conducted by Salgado et al. to examine the relationship between patient activation, confidence to self-manage side effects, and adherence to oral oncolytics (Salgado et al., 2017). A total of 125 respondents from oncology practices in Michigan were surveyed online. 13-item PAM was used to assess patient activation and confidence to self-manage symptoms was assessed using item number 5 of that measure: "How confident are you that you can tell when you need to seek medical care and when you can handle the [symptom] yourself?" Medication adherence was self-reported by responding a single item "Thinking about the past four weeks, please rate your ability to take your [oral oncolytic] as prescribed" on a five-point Likert scale. The logistic regression model revealed that the activation level was not a predictor of adherence to oral oncolytics in this convenience sample (Nagelkerke $R^2 = 0.155$). In addition to the limitation of the small convenience sample, some surveys were administered at home but some were in clinic, which could yield a biased estimation of adherence.

In summary, seven prior studies assessed relationship between patient activation and medication adherence in various disease conditions (Hibbard et al., 2015; Marshall et

al., 2013; Mosen et al., 2007; Salgado et al., 2017; Skolasky et al., 2011; Stepleman et al., 2010; Young et al., 2014). Five out of the seven studies reported a positive relationship between patient activation and medication adherence (Hibbard et al., 2015; Marshall et al., 2013; Mosen et al., 2007; Skolasky et al., 2011; Young et al., 2014). The remaining two did not report a significant relationship between patient activation and medication adherence (Salgado et al., 2017; Stepleman et al., 2010). However, no research assessing the relationship between patient activation and medication adherence among patients with diabetes was found.

Sociodemographic Characteristics and Medication Adherence

Age

Aikens et al. assessed association between age and medication adherence measured with the Morisky Medication Adherence Scale in 253 type 2 diabetes patients identified from a large Midwestern urban healthcare system (Aikens, 2012). Poor medication adherence was associated with being younger ($r = 0.15$; $p = 0.012$).

Al-Haj Mohd et al. assessed relationship between age and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 446 patients with type 2 diabetes from Dubai Police Health Services Clinic (Al-Haj Mohd et al., 2015). The mean age of patients at low adherence levels (Morisky Medication Adherence Scale < 6) was significantly different from those at medium (Morisky Medication Adherence Scale = 6 to 7) or high adherence levels (Morisky Medication Adherence Scale = 8) (59 years vs. 64 years, 69 years respectively, $p < 0.05$). In multi-logistic regression model, older age was a significant predictor to adherence (OR = 1.113, 95% CI: 1.045 to 1.185; $p = 0.001$).

Balkrishnan et al. assessed relationship between age and medication adherence measured with MPR across 5 years among 775 type 2 diabetes patients aged at least 65 years who were enrolled in a Medicare health maintenance organization in North

Carolina (Balkrishnan et al., 2003). Age was not associated with medication adherence across 5 years.

Balkrishnan et al. assessed relationship between age and medication adherence calculated by MPR in another longitudinal study using data of 4710 type 2 diabetes patients from the North Carolina Medicaid Program (Balkrishnan et al., 2006). Older age was associated with medication adherence in multiple regression analysis ($\beta = 0.011$, $p < 0.05$) in the cohort of patients followed up for 30 months (n = 3191).

Chew et al. assessed relationship between age and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 668 adult patients with type 2 diabetes who were recruited from three Malaysian public health clinics (Chew et al., 2015). Older age was associated with medication adherence based on multivariable regression (Adjusted OR = 1.003, 95% CI: 1.001 to 1.006, $p = 0.019$).

Curkendall et al. assessed association between age and medication adherence measured with PDC using a cohort of 117,702 adult patients with type 2 diabetes selected from the Truven Health MarketScan Research Databases of healthcare administrative claims (2009 through 2012) (Curkendall et al., 2013). The adherent patients had higher age than those non-adherent patients did ($p < 0.001$). In multivariable logistic regression model, adherence level was lower among younger patients aged 18 through 34 (OR = 0.35, 95% CI: 0.33 to 0.39), 35 through 44 (OR = 0.52, 95% CI: 0.50 to 0.54), and 45 through 54 (OR = 0.78, 95% CI: 0.76 to 0.80) compared with those aged 55 through 64. Adherence level was significantly higher among patients aged 65 through 79 (OR = 1.36, 95% CI: 1.21 to 1.52) and aged 80 years and older (OR = 1.41, 95% CI: 1.25 to 1.59), compared with those aged 55 through 64.

Gonzalez et al. assessed association between age and medication adherence among 104 patients with type 2 diabetes recruited from diabetes specialty and primary care clinics affiliated with a large, urban, academic medical center (Gonzalez et al., 2016). Medication adherence was electronically monitored by Medication Event

Monitoring System bottle cap as well as self-report by answering six questions. Older age was significantly associated with greater electronically monitored and self-reported medication adherence (r =0.33, $p = 0.001$; r =0.21, $p = 0.03$, respectively).

Huber et al. assessed association between age and medication adherence to oral hypoglycemic medication measured with PDC among 10,430 patients with type 2 diabetes identified from a large anonymized health insurance claims database (Huber & Reich, 2016). Except for patients aged more than 85 years, all the other age groups were associated with medication adherence compared to 18 to 44 age group: (45 to 54 years: Adjusted OR = 1.56, 95% CI: 1.27 to 1.92, $p < 0.001$; 55 to 64 years: Adjusted OR = 1.78, 95% CI: 1.47 to 2.17, $p < 0.001$; 65 to 74 years: Adjusted OR = 1.97, 95% CI: 1.63 to 2.38, $p < 0.001$; 75 to 84 years: Adjusted OR = 1.65, 95% CI: 1.36 to 2.00, $p < 0.001$).

Iqbal et al. assessed association between age and medication adherence measured with Drug Attitude Inventory (DAI-10) questionnaire among 300 Pakistani patients with type 2 diabetes attending public and private hospitals in Quetta city (Iqbal et al., 2017). Younger age was associated with medication adherence by Kruskal-Wallis test ($p = 0.006$).

Jamous et al. assessed association between age and medication adherence measured with the 8-item Morisky Medication Adherence Scale among a convenience sample of 131 diabetic patients from Military Medical Services clinic in Nablus, Palestine (Jamous et al., 2011). Age and adherence score were positively correlated by Pearson correlation test (r = 0.22, $p = 0.01$).

Schmittdiel et al. assessed association between age and medication adherence to oral antidiabetic medications measured with PDC among 129,040 diabetes patients aged 65 years and above from 3 Kaiser Permanente regions using data from Surveillance, Prevention, and Management of Diabetes Mellitus (SUPREME-DM) DataLink (Schmittdiel et al., 2015). Age groups were significantly associated with medication adherence. Compared to 65 to 69 age group, 75 to 79 age group, 80 to 84 age group and

age group of 85 years and more were less likely to be adherent (RR= 0.98, p <0.01; RR= 0.97, p <0.001; RR= 0.95, p <0.001, respectively).

Shenolikar et al. assessed association between age and medication adherence measured with MPR among 1,073 type 2 diabetes patients treated with pioglitazone using North Carolina Medicaid database (Shenolikar et al., 2006). Age was not associated with rates of adherence to antidiabetic medications.

Sweileh et al. assessed association between age and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 405 patients with type 2 diabetes at Al-Makhfia governmental diabetes primary healthcare clinic in Nablus, Palestine (Sweileh et al., 2014). Age was not associated with medication adherence.

Wu et al. assessed association between age and medication adherence to oral antidiabetic drugs measured with the 8-item Morisky Medication Adherence Scale among 130 patients with type 2 diabetes from a Chinese tertiary hospital (Wu & Liu, 2016). Age was not associated with medication adherence.

In summary, fourteen studies assessed association between age and medication adherence to antidiabetic drugs (Aikens, 2012; Al-Haj Mohd et al., 2015; Balkrishnan et al., 2003; Balkrishnan et al., 2006; Chew et al., 2015; Curkendall et al., 2013; Gonzalez et al., 2016; Huber & Reich, 2016; Iqbal et al., 2017; Jamous et al., 2011; Schmittdiel et al., 2015; Shenolikar et al., 2006; Sweileh et al., 2014; Wu & Liu, 2016). Eight studies among them reported that older age was associated with medication adherence (Aikens, 2012; Al-Haj Mohd et al., 2015; Balkrishnan et al., 2006; Chew et al., 2015; Curkendall et al., 2013; Gonzalez et al., 2016; Huber & Reich, 2016; Jamous et al., 2011) while two studies found older age was associated with medication non-adherence (Iqbal et al., 2017; Schmittdiel et al., 2015). The four remaining studies, however, did not find significant association between age and medication adherence (Balkrishnan et al., 2003; Shenolikar et al., 2006; Sweileh et al., 2014; Wu & Liu, 2016).

Gender

Adisa et al. assessed association between gender and medication adherence measured with the modified Morisky Adherence Predictor Scale among 176 type 2 diabetes patients from the endocrinology outpatient clinics of two hospitals in southwestern Nigeria (Adisa & Fakeye, 2013). No significant association was found between gender and medication adherence.

Aikens et al. assessed association between gender and medication adherence measured with the Morisky Medication Adherence Scale in 253 type 2 diabetes patients identified from a large Midwestern urban healthcare system (Aikens, 2012). No significant association was found between gender and medication adherence.

Al-Haj Mohd et al. assessed relationship between gender and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 446 patients with type 2 diabetes from Dubai Police Health Services Clinic (Al-Haj Mohd et al., 2015). Females tended to report high adherence levels compared to males (13.5% vs. 4.2%, p =0.001).

Balkrishnan et al. assessed relationship between gender and medication adherence measured with MPR across 5 years among 775 type 2 diabetes patients aged at least 65 years who were enrolled in a Medicare health maintenance organization in North Carolina (Balkrishnan et al., 2003). Gender was not associated with medication adherence across 5 years.

Balkrishnan et al. assessed relationship between gender and medication adherence calculated by MPR in another longitudinal study using data of 4710 type 2 diabetes patients from the North Carolina Medicaid Program (Balkrishnan et al., 2006). Male gender was associated with medication adherence in multiple regression analysis (β = 0.031, $p < 0.05$) in the cohort of patients followed up for 30 months (n = 3191).

Chew et al. assessed relationship between gender and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 668 adult patients

with type 2 diabetes who were recruited from three Malaysian public health clinics (Chew et al., 2015). Gender was not associated with medication adherence.

Curkendall et al. assessed association between gender and medication adherence measured with PDC using a cohort of 117,702 adult patients with type 2 diabetes selected from the Truven Health MarketScan Research Databases of healthcare administrative claims (2009 through 2012) (Curkendall et al., 2013). Adherence was significantly higher among men than women (OR = 1.27, 95% CI: 1.24 to 1.30).

Huber et al. assessed association between gender and medication adherence to oral hypoglycemic medication measured with PDC among 10,430 patients with type 2 diabetes identified from a large anonymized health insurance claims database (Huber & Reich, 2016). Women were found less likely to be adherent to their medication than men (Adjusted OR = 0.89, 95% CI: 0.85 to 0.95, $p < 0.001$).

Iqbal et al. assessed association between gender and medication adherence measured with Drug Attitude Inventory (DAI-10) questionnaire among 300 Pakistani patients with type 2 diabetes attending public and private hospitals in Quetta city (Iqbal et al., 2017). Males were associated with lower medication adherence by Mann-Whitney test ($p = 0.003$).

Jamous et al. assessed association between gender and medication adherence measured with the 8-item Morisky Medication Adherence Scale among a convenience sample of 131 diabetic patients from Military Medical Services clinic in Nablus, Palestine (Jamous et al., 2011). Gender and adherence score were not significantly associated.

Schmittdiel et al. assessed association between gender and medication adherence to oral antidiabetic medications measured with PDC among 129,040 diabetes patients aged 65 years and above from 3 Kaiser Permanente regions using data from Surveillance, Prevention, and Management of Diabetes Mellitus (SUPREME-DM) DataLink

(Schmittdiel et al., 2015). Female was found less likely to be adherent (RR= 0.98, *p* <0.001) compared to male.

Shenolikar et al. assessed association between gender and medication adherence measured with MPR among 1,073 type 2 diabetes patients treated with pioglitazone using North Carolina Medicaid database (Shenolikar et al., 2006). Gender was not associated with rates of adherence to antidiabetic medications.

Sweileh et al. assessed association between gender and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 405 patients with type 2 diabetes at Al-Makhfia governmental diabetes primary healthcare clinic in Nablus, Palestine (Sweileh et al., 2014). Gender was not associated with medication adherence.

Wu et al. assessed association between gender and medication adherence to oral antidiabetic drugs measured with the 8-item Morisky Medication Adherence Scale among 130 patients with type 2 diabetes from a Chinese tertiary hospital (Wu & Liu, 2016). Gender was not associated with medication adherence.

In summary, fourteen studies assessed associations between gender and medication adherence to antidiabetic drugs (Adisa & Fakeye, 2013; Aikens, 2012; Al-Haj Mohd et al., 2015; Balkrishnan et al., 2003; Balkrishnan et al., 2006; Chew et al., 2015; Curkendall et al., 2013; Huber & Reich, 2016; Iqbal et al., 2017; Jamous et al., 2011; Schmittdiel et al., 2015; Shenolikar et al., 2006; Sweileh et al., 2014; Wu & Liu, 2016). Two studies out of the fourteen found females were more adherent than males (Al-Haj Mohd et al., 2015; Iqbal et al., 2017). Four studies out of the fourteen found males were more adherent than females (Balkrishnan et al., 2006; Curkendall et al., 2013; Huber & Reich, 2016; Schmittdiel et al., 2015). The other eight studies did not find significant association between gender and medication adherence (Adisa & Fakeye, 2013; Aikens, 2012; Balkrishnan et al., 2003; Chew et al., 2015; Jamous et al., 2011; Shenolikar et al., 2006; Sweileh et al., 2014; Wu & Liu, 2016).

Ethnicity/race

Aikens et al. assessed association between ethnicity and medication adherence measured with Morisky scale in 253 type 2 diabetes patients identified from a large Midwestern urban healthcare system (Aikens, 2012). No significant association was found between ethnicity (African American or not) and medication adherence.

Al-Haj Mohd et al. assessed relationship between ethnicity and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 446 patients with type 2 diabetes from Dubai Police Health Services Clinic (Al-Haj Mohd et al., 2015). Emirati patients (81.6%) reported lowest adherence level followed by Arab Non-Emirati (47.1%) and Asians (15.4%) (Pearson Chi-Square p <0.001). In multi-logistic regression model, ethnicity was a significant predictor to adherence with Arab Non-Emirati and Asian ethnicities predicting a higher level of adherence compared with Emirati ethnicity (OR = 8.830, 95% CI: 2.052 to 37.995, p = 0.003; OR = 39.4, 95% CI: 1.819 to 853.46, p = 0.19, respectively).

Balkrishnan et al. assessed relationship between race and medication adherence calculated by MPR in another longitudinal study using data of 4710 type 2 diabetes patients from the North Carolina Medicaid Program (Balkrishnan et al., 2006). Black race compared to white race and other race were associated with medication non-adherence in multiple regression analysis (β = -0.024, $p < 0.05$; β = -0.035, $p < 0.05$) in the cohort of patients followed up for 30 months (n = 3191).

Chew et al. assessed relationship between ethnicity and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 668 adult patients with type 2 diabetes who were recruited from three Malaysian public health clinics (Chew et al., 2015). Indian ethnicity had higher adherence level than Malay (OR = 1.08, 95% CI: 1.017 to 1.139, p = 0.011) but in multivariable regression ethnicity was not associated with medication adherence.

Schmittdiel et al. assessed association between race/ethnicity and medication adherence to oral antidiabetic medications measured with PDC among 129,040 diabetes patients aged 65 years and above from 3 Kaiser Permanente regions using data from Surveillance, Prevention, and Management of Diabetes Mellitus (SUPREME-DM) DataLink (Schmittdiel et al., 2015). Compared to white race, Hispanic and black were less likely to be adherent (RR= 0.98, p <0.01; RR= 0.93, p <0.001, respectively) and Asian and missing race were more likely to be adherent (RR= 1.01, p <0.05; RR= 1.02, p <0.01, respectively). American Indian/Alaska native and Native Hawaiian/Pacific Islander were not significantly different from white race on medication adherence.

Shenolikar et al. assessed association between race and medication adherence measured with MPR among 1,073 type 2 diabetes patients treated with pioglitazone using North Carolina Medicaid database (Shenolikar et al., 2006). No difference was found between African American race and all the other races on rates of adherence to antidiabetic medications.

In summary, six studies assessed associations between ethnicity/race and medication adherence (Aikens, 2012; Al-Haj Mohd et al., 2015; Balkrishnan et al., 2006; Chew et al., 2015; Schmittdiel et al., 2015; Shenolikar et al., 2006). Three studies out of the six found that race was associated with medication adherence (Al-Haj Mohd et al., 2015; Balkrishnan et al., 2006; Schmittdiel et al., 2015). The remaining three studies did not find significant association between ethnicity/race and medication adherence (Aikens, 2012; Chew et al., 2015; Shenolikar et al., 2006).

Education

Adisa et al. assessed association between education qualification and medication adherence measured with the modified Morisky Adherence Predictor Scale among 176 ambulatory type 2 diabetes patients recruited from the endocrinology clinics of two

hospitals in southwestern Nigeria (Adisa & Fakeye, 2013). Education qualification was reported not associated with medication adherence.

Al-Haj Mohd et al. assessed relationship between level of education and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 446 patients with type 2 diabetes from Dubai Police Health Services Clinic (Al-Haj Mohd et al., 2015). Patients who reported high adherence levels (Morisky Medication Adherence Scale = 8) were more likely to have a high education level ($p <$ 0.005). In multi-logistic regression model, university level of education was a significant predictor to adherence compared with primary/secondary education level (OR = 19.6, 95% CI: 1.872 to 205.130, $p = 0.013$).

Chew et al. assessed relationship between education and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 668 adult patients with type 2 diabetes who were recruited from three Malaysian public health clinics (Chew et al., 2015). In bivariate regression, having tertiary education was associated with lower adherence level (OR = 0.85, 95% CI: 0.76 to 0.95, $p = 0.004$) but in multivariable regression no association was found.

Iqbal et al. assessed association between education and medication adherence measured with Drug Attitude Inventory (DAI-10) questionnaire among 300 Pakistani patients with type 2 diabetes attending public and private hospitals in Quetta city (Iqbal et al., 2017). Education was associated with medication adherence by Kruskal-Wallis test ($p = 0.032$) and patients with only primary education had the lowest adherence level.

Sweileh et al. assessed association between education and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 405 patients with type 2 diabetes at Al-Makhfia governmental diabetes primary healthcare clinic in Nablus, Palestine (Sweileh et al., 2014). Education level was not associated with medication adherence.

Wu et al. assessed association between education and medication adherence to oral antidiabetic drugs measured with the 8-item Morisky Medication Adherence Scale among 130 patients with type 2 diabetes from a Chinese tertiary hospital (Wu & Liu, 2016). Education was not associated with medication adherence.

In summary, six studies assessed associations between education and medication adherence (Adisa & Fakeye, 2013; Al-Haj Mohd et al., 2015; Chew et al., 2015; Iqbal et al., 2017; Sweileh et al., 2014; Wu & Liu, 2016). Two studies among the six found that tertiary education was associated with higher medication adherence (Al-Haj Mohd et al., 2015; Iqbal et al., 2017). The remaining four studies did not report significant association between education and medication adherence (Adisa & Fakeye, 2013; Chew et al., 2015; Sweileh et al., 2014; Wu & Liu, 2016).

Region

Curkendall et al. assessed association between region and medication adherence measured with PDC using a cohort of 117,702 adult patients with type 2 diabetes selected from the Truven Health MarketScan Research Databases of healthcare administrative claims (2009 through 2012) (Curkendall et al., 2013). U.S. region was significantly associated with increased adherence with Northeast (OR = 1.33, 95% CI: 1.28 to 1.38), North Central (OR = 1.14, 95% CI: 1.10 to 1.17), and West (OR = 1.17, 95% CI: 1.13 to 1.22) compared with the South.

Huber et al. assessed association between cantons of residence and medication adherence to oral hypoglycemic medication measured with PDC among 10,430 patients with type 2 diabetes identified from a large anonymized health insurance claims database (Huber & Reich, 2016). No association was found between cantons of residence and medication adherence.

Iqbal et al. assessed association between locality and medication adherence measured with Drug Attitude Inventory (DAI-10) questionnaire among 300 Pakistani

patients with type 2 diabetes attending public and private hospitals in Quetta city (Iqbal et al., 2017). Locality (urban/rural) was not associated with medication adherence.

In summary, three studies assessed associations between region and medication adherence (Curkendall et al., 2013; Huber & Reich, 2016; Iqbal et al., 2017). Only one of them reported association between region and medication adherence (Curkendall et al., 2013). The other two of them did not report significant association (Huber & Reich, 2016; Iqbal et al., 2017).

Employment

Adisa et al. assessed association between occupation and medication adherence measured with the modified Morisky Adherence Predictor Scale among 176 type 2 diabetes patients from the endocrinology clinics of two hospitals in southwestern Nigeria (Adisa & Fakeye, 2013). No association was found between occupation categories and medication adherence.

Al-Haj Mohd et al. assessed relationship between working status and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 446 patients with type 2 diabetes from Dubai Police Health Services Clinic (Al-Haj Mohd et al., 2015). No association was found between working status of patients and medication adherence.

Chew et al. assessed relationship between employment and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 668 adult patients with type 2 diabetes who were recruited from three Malaysian public health clinics (Chew et al., 2015). Employment was not associated with medication adherence.

Iqbal et al. assessed association between occupation and medication adherence measured with Drug Attitude Inventory (DAI-10) questionnaire among 300 Pakistani patients with type 2 diabetes attending public and private hospitals in Quetta city (Iqbal et al., 2017). Occupation was not associated with medication adherence.

In summary, four studies assessed associations between employment and medication adherence but none of them found that employment was significantly associated with medication adherence (Adisa & Fakeye, 2013; Al-Haj Mohd et al., 2015; Chew et al., 2015; Iqbal et al., 2017).

Income

Chew et al. assessed relationship between income and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 668 adult patients with type 2 diabetes who were recruited from three Malaysian public health clinics (Chew et al., 2015). In bivariate regression analysis, having high level income was associated with lower adherence level compared to medium and low level of income (OR = 0.83, 95% CI: 0.747 to 0.913, $p < 0.0001$; OR = 0.95, 95% CI: 0.910 to 0.999, $p = 0.046$, respectively). In multivariable regression, having high level income was associated with lower adherence compared to low level income (OR = 0.90, 95% CI: 0. 803to 0.999, $p = 0.048$).

Iqbal et al. assessed association between income and medication adherence measured with Drug Attitude Inventory (DAI-10) questionnaire among 300 Pakistani patients with type 2 diabetes attending public and private hospitals in Quetta city (Iqbal et al., 2017). Income was not associated with medication adherence.

Schmittdiel et al. assessed association between household income and medication adherence to oral antidiabetic medications measured with PDC among 129,040 diabetes patients aged 65 years and above from 3 Kaiser Permanente regions using data from Surveillance, Prevention, and Management of Diabetes Mellitus (SUPREME-DM) DataLink (Schmittdiel et al., 2015). Income was not associated with medication adherence.

Wu et al. assessed association between monthly income and medication adherence to oral antidiabetic drugs measured with the 8-item Morisky Medication

Adherence Scale among 130 patients with type 2 diabetes from a Chinese tertiary hospital (Wu & Liu, 2016). Monthly income was not associated with medication adherence.

In summary, four studies assessed associations between income and medication adherence to antidiabetic drugs (Chew et al., 2015; Iqbal et al., 2017; Schmittdiel et al., 2015; Wu & Liu, 2016). Only one of them found that higher income was associated with medication non-adherence (Chew et al., 2015).

Marital Status

Adisa et al. assessed association between marital status and medication adherence measured with the modified Morisky Adherence Predictor Scale among 176 ambulatory type 2 diabetes patients recruited from the endocrinology clinics of two hospitals in southwestern Nigeria (Adisa & Fakeye, 2013). No association was found between marital status and medication adherence.

Al-Haj Mohd et al. assessed relationship between marital status and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 446 patients with type 2 diabetes from Dubai Police Health Services Clinic (Al-Haj Mohd et al., 2015). Significant association was found between marital status and medication adherence levels ($p < 0.001$) and married patients were less adherent than widowed patients were, but the small number of widowed patients was notable. In multi-logistic regression analysis, marital status was not associated with medication adherence.

Chew et al. assessed relationship between marital status and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 668 adult patients with type 2 diabetes who were recruited from three Malaysian public health clinics (Chew et al., 2015). Marital status was not associated with medication.

Sweileh et al. assessed association between marital status and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 405

patients with type 2 diabetes at Al-Makhfia governmental diabetes primary healthcare clinic in Nablus, Palestine (Sweileh et al., 2014). Compared to patients who were single, those who were married were more likely to be adherent (OR = 0.6, 95% CI: 0.4 to 0.9, *p* = 0.021) in bivariate analysis, while it turned out that marital status was not associated with medication adherence in multivariable analysis.

Wu et al. assessed association between marital status and medication adherence to oral antidiabetic drugs measured with the 8-item Morisky Medication Adherence Scale among 130 patients with type 2 diabetes from a Chinese tertiary hospital (Wu & Liu, 2016). Marital status was not associated with medication adherence.

In summary, five studies assessed associations between marital status and medication adherence but none of them found significant association (Adisa & Fakeye, 2013; Al-Haj Mohd et al., 2015; Chew et al., 2015; Sweileh et al., 2014; Wu & Liu, 2016).

Health Status Characteristics and Medication Adherence

Comorbidities and Medication Adherence

Number/Presence of Comorbidities

Aikens et al. assessed association between number of comorbidities and medication adherence measured with the Morisky Medication Adherence Scale in 253 type 2 diabetes patients identified from a large Midwestern urban healthcare system (Aikens, 2012). Comorbidity was dichotomized as two or more comorbid conditions and less than two. Poor medication adherence was associated with having fewer comorbid medical conditions (r = 0.16; *p* = 0.013).

Al-Haj Mohd et al. assessed relationship between other comorbid chronic conditions and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 446 patients with type 2 diabetes from Dubai Police Health Services Clinic (Al-Haj Mohd et al., 2015). Patients who reported low adherence level

were less likely to have comorbid conditions compared to those who reported moderately and highly adherent (46.9% vs. 64.4% vs. 75.0% respectively, p <0.001).

Huber et al. assessed association between number of comorbid conditions and medication adherence to oral hypoglycemic medication measured with PDC among 10,430 patients with type 2 diabetes identified from a large anonymized health insurance claims database (Huber & Reich, 2016). The number of comorbid conditions were significantly associated with adherence. Patients with comorbid conditions were more likely to be adherent than those with no comorbidity (1 comorbidity: Adjusted OR = 1.19, 95% CI: 1.05 to 1.35, $p < 0.010$; 2 comorbidities: Adjusted OR = 1.30, 95% CI: 1.15 to 1.46, $p < 0.001$; 3 comorbidities: Adjusted OR = 1.43, 95% CI: 1.26 to 1.62, $p < 0.001$; 4 comorbidities: Adjusted OR = 1.35, 95% CI: 1.18 to 1.54, $p < 0.001$; more than 5 comorbidities: Adjusted OR = 1.27, 95% CI: 1.12 to 1.44, $p < 0.001$). But there is no linear relationship between number of comorbid conditions and medication adherence.

Jamous et al. assessed association between presence of comorbid disease and medication adherence measured with the 8-item Morisky Medication Adherence Scale among a convenience sample of 131 diabetic patients from Military Medical Services clinic in Nablus, Palestine (Jamous et al., 2011). Patients with comorbid diseases were more adherent than those without comorbidity were ($p = 0.03$) by Chi-square test.

Sweileh et al. assessed association between presence of comorbid diseases and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 405 patients with type 2 diabetes at Al-Makhfia governmental diabetes primary healthcare clinic in Nablus, Palestine (Sweileh et al., 2014). Compared to patients who had no comorbidities, those who had were more likely to be non-adherent (OR = 1.2, 95% CI: 0.8 to 1.8, $p = 0.02$) in bivariate analysis, while it turned that presence of comorbidity was not associated with medication adherence in multivariable analysis.

In summary, five studies assessed associations between number of comorbidities or presence of comorbidities and medication adherence (Aikens, 2012; Al-Haj Mohd et

al., 2015; Huber & Reich, 2016; Jamous et al., 2011; Sweileh et al., 2014). Aikens et al. found patients with two or more comorbidities were more adherent than those with less comorbidities (Aikens, 2012). Three of the five studies found that having comorbid conditions were associated with higher adherence level compared with no comorbid conditions (Al-Haj Mohd et al., 2015; Huber & Reich, 2016; Jamous et al., 2011). One study out of the eight did not find any association between comorbidities and mediation adherence (Sweileh et al., 2014).

Charlson Comorbidity Index

Balkrishnan et al. assessed relationship between comorbidity severity and medication adherence measured with MPR across 5 years among 775 type 2 diabetes patients aged at least 65 years who were enrolled in a Medicare health maintenance organization in North Carolina (Balkrishnan et al., 2003). An increase in the score of comorbidity severity measured with Charlson Comorbidity Index was associated with a 0.0062-point decrease in MPRs ($p < 0.05$).

Curkendall et al. assessed association between comorbidities and medication adherence measured with PDC using a cohort of 117,702 adult patients with type 2 diabetes selected from the Truven Health MarketScan Research Databases of healthcare administrative claims (2009 through 2012) (Curkendall et al., 2013). Comorbidities were measured with specific diseases and Deyo-Charlson Comorbidity Index. Patients with higher Deyo-Charlson Comorbidity Index score was significantly more adherent ($p < 0.001$).

In summary, two studies used Charlson Comorbidity Index to measure severity of comorbidities but gave opposite results: one found that higher level of severity was associated with decreased medication adherence (Balkrishnan et al., 2003) whereas another one found higher level of severity was associated with increased medication adherence (Curkendall et al., 2013).

Individual Comorbidities

Chew et al. assessed relationship between comorbidities and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 668 adult patients with type 2 diabetes who were recruited from three Malaysian public health clinics (Chew et al., 2015). Neither hypertension nor dyslipidemia was associated with medication adherence.

Curkendall et al. assessed association between comorbidities and medication adherence measured with PDC using a cohort of 117,702 adult patients with type 2 diabetes selected from the Truven Health MarketScan Research Databases of healthcare administrative claims (2009 through 2012) (Curkendall et al., 2013). Comorbidities were measured with specific diseases and Deyo-Charlson Comorbidity Index. Renal impairment was associated with increased adherence (OR = 1.14, 95% CI: 1.10 to 1.20) and macrovascular disease was associated with decreased adherence (OR = 0.95, 95% CI: 0.92 to 0.99). Microvascular disease was not associated with medication adherence. Patients with higher Deyo-Charlson Comorbidity Index score was significantly more adherent ($p < 0.001$).

Aikens et al. assessed association between depressive symptoms, diabetes-related distress and medication adherence measured with the Morisky Medication Adherence Scale in 253 type 2 diabetes patients identified from a large Midwestern urban healthcare system (Aikens, 2012). Depressive symptoms severity was measured with Patient Health Questionnaire-9 (PHQ-9) and diabetes-related distress was evaluated by Problem Areas in Diabetes scale (PAID). Depressive symptoms were associated with poorer medication adherence ($\beta = 0.24$, $p = 0.001$) and diabetes-related distress was associated with lower medication adherence ($\beta = 0.26$, $p < 0.001$).

Al-Haj Mohd et al. assessed relationship between depression and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 446 patients with type 2 diabetes from Dubai Police Health Services Clinic (Al-Haj Mohd et

al., 2015). The Depression, Anxiety and Stress scale (DASS) was applied to measure depression, anxiety and stress condition. Patients at low medication adherence level were less likely to report normal depression scores ($p = 0.004$) and were more likely to report severe level of anxiety scores ($p < 0.001$) and severe levels of stress scores ($p = 0.004$).

Balkrishnan et al. assessed relationship between depression level and medication adherence measured with MPR across 5 years among 775 type 2 diabetes patients aged at least 65 years who were enrolled in a Medicare health maintenance organization in North Carolina (Balkrishnan et al., 2003). The short-form Center for Epidemiologic Studies Depression scale was used to measure level of depression on a scale of 0 to 100. Depression level was not associated with medication adherence.

Chew et al. assessed relationship between depression and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 668 adult patients with type 2 diabetes who were recruited from three Malaysian public health clinics (Chew et al., 2015). Depression measured with the PHQ-9 was negatively associated with medication adherence in multivariable regression model (OR = 0.988, 95% CI: 0.981 to 0.994, $p < 0.0001$). Diabetes-related distress measured with Diabetes Distress Scale was not associated with medication adherence.

Gonzalez et al. assessed association between depression, distress and medication adherence among 104 patients with type 2 diabetes recruited from diabetes specialty and primary care clinics affiliated with a large, urban, academic medical center (Gonzalez et al., 2016). Depression symptoms were measured with the PHQ-9 and diabetes-related distress was measured with 17-item Diabetes Distress Scale. Medication adherence was electronically monitored by Medication Event Monitoring System bottle cap as well as self-report by answering six questions. Greater levels of diabetes distress were significantly associated with lower electronically monitored and self-reported adherence after covariate adjustment ($\beta = -0.29$, $p = 0.001$; $\beta = -0.24$, $p = 0.02$, respectively). After adding depression symptoms in the model, depression symptoms was associated with

lower electronically monitored and self-reported adherence after covariate adjustment (β = -0.25, $p = 0.02$; β = -0.35, $p = 0.004$, respectively).

Gonzalez et al. assessed association between depression symptoms and medication adherence among 879 type 2 diabetic patients from two primary care clinics (Gonzalez et al., 2007). Depression was evaluated by 10-item Harvard Department of Psychiatry/National Depression Screening Day Scale (HANDS) on a 0 to 30 score range with ≥ 9 as major depression. Medication adherence was obtained by responding a question: "In the past 7 days, on how many days did you miss taking any one of your prescribed medicines?" Logistic regression showed that major depression was associated with a 2.31-fold increase in the odds of missing one or more doses of medication over the previous 7 days (95% CI: 1.50 to 3.56, $p < 0.001$) and each 1-point increase in the HANDS symptom severity score was associated with a 1.10-fold increase in the odds of missing at least one doses over the previous 7 days (95% CI: 1.07 to 1.14, $p < 0.001$). In patients with unlikely major depression, each 1-point increase in the HANDS score was associated with 1.12-fold increase in the odds of missing one or more doses over the previous 7 days (95% CI: 1.03 to 1.22, $p = 0.007$).

Osborn et al. assessed association between depression symptoms measured with the PHQ-9 and medication adherence measured with the 4-item Morisky Medication Adherence Scale among 139 patients with type 2 diabetes who were recruited from the internal medicine clinic of an academic medical center in the Southeastern United States (Osborn & Egede, 2012). More depressive symptoms were associated with medication non-adherence ($p < 0.001$) from the result of bias corrected bootstrapping.

In summary, nine studies assessed associations between individual comorbidities and medication adherence (Aikens, 2012; Al-Haj Mohd et al., 2015; Balkrishnan et al., 2003; Chew et al., 2015; Curkendall et al., 2013; Gonzalez et al., 2016; Gonzalez et al., 2007; Osborn & Egede, 2012). For depression, six out of the nine studies found that depression was negatively associated with medication adherence (Aikens, 2012; Al-Haj

Mohd et al., 2015; Chew et al., 2015; Gonzalez et al., 2016; Gonzalez et al., 2007; Osborn & Egede, 2012). One of the nine studies did not find any significant associations between depression and medication adherence (Balkrishnan et al., 2003). For anxiety, one out of the nine studies found that anxiety was negatively associated with medication adherence (Al-Haj Mohd et al., 2015). For diabetes-related distress, four studies out of the nine assessed its relationship with medication adherence (Aikens, 2012; Al-Haj Mohd et al., 2015; Chew et al., 2015; Gonzalez et al., 2016). Three out of the four studies found a negative association between distress and mediation adherence (Aikens, 2012; Al-Haj Mohd et al., 2015; Gonzalez et al., 2016). The other one study did not find significant association between distress and medication adherence (Chew et al., 2015). For hypertension and dyslipidemia, Chew et al. found neither of them was associated with medication adherence (Chew et al., 2015). For renal impairment, Curkendall et al. found its presence was associated with medication adherence (Curkendall et al., 2013). For cardiovascular diseases, Curkendall et al. found the presence of macrovascular disease was associated with increased adherence while the presence of microvascular disease was not (Curkendall et al., 2013).

Diabetes Complications

Aikens et al. assessed association between number of complications and medication adherence measured with the Morisky Medication Adherence Scale in 253 type 2 diabetes patients identified from a large Midwestern urban healthcare system (Aikens, 2012). Complications were identified using a self-report checklist of visual, cardiovascular, kidney, genitourinary, and other common diabetic complications. As a continuous variable, number of complications was not associated with medication adherence.

Chew et al. assessed relationship between diabetic complications and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 668

adult patients with type 2 diabetes who were recruited from three Malaysian public health clinics (Chew et al., 2015). Diabetic complications were classified as microvascular complications including retinopathy, nephropathy, and diabetic foot problems, and macrovascular complications including ischemic heart disease and cerebrovascular disease or stroke. No association was found between medication adherence and binary variables of any diabetes complication, any microvascular and any macrovascular complication.

In summary, two studies assessed relationships between diabetic complications and medication adherence and they both reported no significant relationships (Aikens, 2012; Chew et al., 2015).

Type of Antidiabetic Medications

Adisa et al. assessed association between type of antidiabetic medications and medication adherence measured with the modified Morisky Adherence Predictor Scale among 176 ambulatory type 2 diabetes patients recruited from the endocrinology clinics of two hospitals in southwestern Nigeria (Adisa & Fakeye, 2013). Type of antidiabetic medications was categorized as oral medication alone, insulin plus oral medication and insulin alone. It was not associated with medication adherence.

Aikens et al. assessed association between type of antidiabetic medications and medication adherence measured with the Morisky Medication Adherence Scale in 253 type 2 diabetes patients identified from a large Midwestern urban healthcare system (Aikens, 2012). Type of antidiabetic medications was dichotomized as oral hypoglycemic medication alone and insulin plus oral medication. No association was reported between being on insulin or not and medication adherence.

Al-Haj Mohd et al. assessed relationship between type of antidiabetic therapy and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 446 patients with type 2 diabetes from Dubai Police Health Services Clinic (Al-

Haj Mohd et al., 2015). Patients at low adherence level were more likely to use insulin compared with those who were at medium and high adherence level (58.7% vs. 37.3% vs. 27.5% respectively, $p < 0.001$). Insulin use was associated with non-adherence in multi-logistic regression (OR = 0.188, 95% CI: 0.05 to 0.709, $p = 0.014$). Additionally, patients at low adherence level were more likely to be on combination antidiabetic therapy rather than monotherapy compared to those at medium and high adherence level (68.1% vs. 89.8%, $p < 0.001$).

Balkrishnan et al. assessed relationship between oral antidiabetic medication use and medication adherence measured with MPR across 5 years among 775 type 2 diabetes patients aged at least 65 years who were enrolled in a Medicare health maintenance organization in North Carolina (Balkrishnan et al., 2003). Oral antidiabetic medication use was associated with a 0.28-point increase in the MPR ($p < 0.001$).

Balkrishnan et al. assessed relationship between type of antidiabetic medication and medication adherence calculated by MPR in another longitudinal study using data of 4710 type 2 diabetes patients from the North Carolina Medicaid Program (Balkrishnan et al., 2006). Treatment of TZD was significantly associated with medication adherence in multiple regression analysis ($\beta = 0.057$, $p < 0.001$) in the cohort of patients followed up for 30 months (n = 3191). Having been prescribed metformin was also associated with medication adherence ($\beta = -0.36$, $p < 0.01$). Combination therapy with TZD was not associated with medication adherence compared to monotherapy of TZD.

Chew et al. assessed relationship between type of antidiabetic medication and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 668 adult patients with type 2 diabetes who were recruited from three Malaysian public health clinics (Chew et al., 2015). Oral hypoglycemic agent use and type of insulin use were both found not associated with medication adherence.

Gonzalez et al. assessed association between type of antidiabetic medication and medication adherence among 104 patients with type 2 diabetes recruited from diabetes

specialty and primary care clinics affiliated with a large, urban, academic medical center (Gonzalez et al., 2016). Medication adherence was electronically monitored by Medication Event Monitoring System bottle cap as well as self-report by answering six questions. Patients taking insulin had significantly lower electronically monitored adherence compared with those taking oral medications only ($p = 0.005$), while their self-reported adherence was not significantly different.

Huber et al. assessed association between type of antidiabetic therapy and medication adherence to oral hypoglycemic medication measured with PDC among 10,430 patients with type 2 diabetes identified from a large anonymized health insurance claims database (Huber & Reich, 2016). Patients taking combined drug therapy were 6 to 10-fold more likely to be adherent than those with metformin-only therapy (metformin and another oral hypoglycemic medication: Adjusted OR = 9.86, 95% CI: 9.21 to 10.55; other combination of oral hypoglycemic medications: Adjusted OR = 5.73, 95% CI: 5.35 to 6.14).

Jamous et al. assessed association between type of antidiabetic therapy and medication adherence measured with the 8-item Morisky Medication Adherence Scale among a convenience sample of 131 diabetic patients from Military Medical Services clinic in Nablus, Palestine (Jamous et al., 2011). No association was found between patients on monotherapy or combination therapy.

Sweileh et al. assessed association between type of antidiabetic therapy and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 405 patients with type 2 diabetes at Al-Makhfia governmental diabetes primary healthcare clinic in Nablus, Palestine (Sweileh et al., 2014). Patients with combination therapy were not significantly different from those with monotherapy on medication adherence.

In summary, ten studies assessed associations between type of antidiabetic therapy and medication adherence (Adisa & Fakeye, 2013; Aikens, 2012; Al-Haj Mohd

et al., 2015; Balkrishnan et al., 2003; Balkrishnan et al., 2006; Chew et al., 2015; Gonzalez et al., 2016; Huber & Reich, 2016; Jamous et al., 2011; Sweileh et al., 2014). Six studies out of the ten found that type of antidiabetic therapy was associated with medication adherence (Adisa & Fakeye, 2013; Aikens, 2012; Al-Haj Mohd et al., 2015; Balkrishnan et al., 2003; Gonzalez et al., 2016; Huber & Reich, 2016). Four studies out of the ten did not find significant association between type of antidiabetic therapy and medication adherence (Balkrishnan et al., 2006; Chew et al., 2015; Jamous et al., 2011; Sweileh et al., 2014). However, the type of antidiabetic therapy variable was categorized differently in each article.

Number of Prescribed Medications

Adisa et al. assessed association between number of prescribed medications and medication adherence measured with the modified Morisky Adherence Predictor Scale among 176 ambulatory type 2 diabetes patients recruited from the endocrinology clinics of two hospitals in southwestern Nigeria (Adisa & Fakeye, 2013). Number of prescribed medications was dichotomized into more than 4 medications and no more than 4 medications. Adisa et al. reported that patients who took more than 4 medications had higher proportion in being adherent than those with no more than 4 medications (p = 0.05) by Chi-square test.

Iqbal et al. assessed association between number of prescribed drugs and medication adherence measured with Drug Attitude Inventory (DAI-10) questionnaire among 300 Pakistani patients with type 2 diabetes attending public and private hospitals in Quetta city (Iqbal et al., 2017). The number of prescribed drugs was not associated with medication adherence.

Schmittdiel et al. assessed association between number of medications and medication adherence to oral antidiabetic medications measured with PDC among 129,040 diabetes patients aged 65 years and above from 3 Kaiser Permanente regions

using data from Surveillance, Prevention, and Management of Diabetes Mellitus (SUPREME-DM) DataLink (Schmittdiel et al., 2015). Number of medications at study start was positively associated with medication adherence (RR= 1.02, p <0.001).

Sweileh et al. assessed association between number of medications and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 405 patients with type 2 diabetes at Al-Makhfia governmental diabetes primary healthcare clinic in Nablus, Palestine (Sweileh et al., 2014). More medications patients had, more likely they were non-adherent (OR = 1.1, 95% CI: 1.0 to 1.2, p = 0.042) in bivariate analysis. But the weak association disappeared in multivariable analysis.

Wu et al. assessed association between number of medications and medication adherence to oral antidiabetic drugs measured with the 8-item Morisky Medication Adherence Scale among 130 patients with type 2 diabetes from a Chinese tertiary hospital (Wu & Liu, 2016). Number of medications was not associated with medication adherence.

In summary, a total of five studies assessed associations between the number of medications and medication adherence to antidiabetic drugs (Adisa & Fakeye, 2013; Iqbal et al., 2017; Schmittdiel et al., 2015; Sweileh et al., 2014; Wu & Liu, 2016). Two studies out of the five found that number of medications was positively associated with medication adherence (Adisa & Fakeye, 2013; Schmittdiel et al., 2015). The other three studies did not find any association between number of medications and medication adherence (Iqbal et al., 2017; Sweileh et al., 2014; Wu & Liu, 2016).

Duration of Diagnosis

Adisa et al. assessed association between duration of diabetes and medication adherence measured by modified Morisky Adherence Predictor Scale among 176 ambulatory type 2 diabetes patients recruited from the endocrinology clinics of two

hospitals in southwestern Nigeria (Adisa & Fakeye, 2013). Duration of diabetes in year groups was not associated with medication adherence.

Al-Haj Mohd et al. assessed relationship between duration of diabetes and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 446 patients with type 2 diabetes from Dubai Police Health Services Clinic (Al-Haj Mohd et al., 2015). Patients at low adherence level had shorter duration of diabetes compared with those at medium and high adherence level (Mean 2 years vs. 4 years vs. 7 years respectively, $p < 0.05$). Duration of diabetes was recognized as a predictor of medication adherence in multi-logistic regression model (OR = 1.830, 95% CI: 1.270 to 2.636, $p = 0.001$).

Chew et al. assessed relationship between duration of diabetes and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 668 adult patients with type 2 diabetes who were recruited from three Malaysian public health clinics (Chew et al., 2015). No association was found between diabetes duration and medication adherence.

Iqbal et al. assessed association between duration of diabetes and medication adherence measured with Drug Attitude Inventory (DAI-10) questionnaire among 300 Pakistani patients with type 2 diabetes attending public and private hospitals in Quetta city (Iqbal et al., 2017). Duration of diabetes was not associated with medication adherence.

Jamous et al. assessed association between duration of diabetes and medication adherence measured with the 8-item Morisky Medication Adherence Scale among a convenience sample of 131 diabetic patients from Military Medical Services clinic in Nablus, Palestine (Jamous et al., 2011). A significant positive correlation was reported between duration of diabetes and adherence level by Spearman correlation test ($p = 0.047$).

Sweileh et al. assessed association between duration of diabetes and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 405 patients with type 2 diabetes at Al-Makhfia governmental diabetes primary healthcare clinic in Nablus, Palestine (Sweileh et al., 2014). No association was found between duration of diabetes and medication adherence.

Wu et al. assessed association between duration of diabetes and medication adherence to oral antidiabetic drugs measured with the 8-item Morisky Medication Adherence Scale among 130 patients with type 2 diabetes from a Chinese tertiary hospital (Wu & Liu, 2016). Duration of diabetes was not associated with medication adherence.

In summary, seven studies assessed associations between duration of diabetes and medication adherence (Adisa & Fakeye, 2013; Al-Haj Mohd et al., 2015; Chew et al., 2015; Iqbal et al., 2017; Jamous et al., 2011; Sweileh et al., 2014; Wu & Liu, 2016). Two of the seven studies reported positive association between duration of diabetes and medication adherence (Al-Haj Mohd et al., 2015; Jamous et al., 2011). Five of the seven studies did not report significant association between those two variables (Adisa & Fakeye, 2013; Chew et al., 2015; Iqbal et al., 2017; Sweileh et al., 2014; Wu & Liu, 2016).

Smoking Status

Balkrishnan et al. assessed relationship between current smoking status and medication adherence measured with MPR across 5 years among 775 type 2 diabetes patients aged at least 65 years who were enrolled in a Medicare health maintenance organization in North Carolina (Balkrishnan et al., 2003). No significant association was found between current smoker and medication adherence.

Chew et al. assessed relationship between smoking status and medication adherence measured with the 8-item Morisky Medication Adherence Scale among 668

adult patients with type 2 diabetes who were recruited from three Malaysian public health clinics (Chew et al., 2015). No association was found between smoking status and medication adherence.

In summary, two studies assessed relationships between smoking status and medication adherence but neither of them found significant relationship (Balkrishnan et al., 2003; Chew et al., 2015).

Prior Hospitalization

Huber et al. assessed association between preceding hospitalization and medication adherence to oral hypoglycemic medication measured with PDC among 10,430 patients with type 2 diabetes identified from a large anonymized health insurance claims database (Huber & Reich, 2016). Patients with preceding hospitalization was less likely to be medication adherent (Adjusted OR = 0.67, 95% CI: 0.61 to 0.74, $p < 0.001$).

Balkrishnan et al. assessed relationship between hospitalization during previous year and medication adherence measured with MPR across 5 years among 775 type 2 diabetes patients aged at least 65 years who were enrolled in a Medicare health maintenance organization in North Carolina (Balkrishnan et al., 2003). No significant relationship was found.

Balkrishnan et al. assessed relationship between presence of an event requiring emergency department visit or hospitalization and medication adherence calculated by MPR in another longitudinal study using data of 4710 type 2 diabetes patients from the North Carolina Medicaid Program (Balkrishnan et al., 2006). Presence of an event requiring emergency department visit or hospitalization was negatively associated with medication adherence (b = -0.073, $p < 0.01$).

In summary, three studies assessed relationship between prior hospitalization and adherence to antidiabetic medications (Balkrishnan et al., 2003; Balkrishnan et al., 2006; Huber & Reich, 2016). Two studies of them found negative association between prior

hospitalization and medication adherence (Balkrishnan et al., 2006; Huber & Reich, 2016), but one study didn't find any significant association (Balkrishnan et al., 2003).

Significance

Diabetes mellitus is a widespread public health problem with increasing incidence and prevalence (Cheng et al., 2013; Selvin et al., 2014). Among patients with type 2 diabetes, approximately 50 percent fail to achieve adequate glycemic control, which is a HbA1c less than 7% (Ali et al., 2012; Ford, 2011). Medication non-adherence has been recognized as a key factor that affects glycemic control (Egede et al., 2014). The medication adherence rate for oral antidiabetic drugs ranged from 36.7 percent to 47.3 percent based on a large-scale retrospective cohort study (Farr et al., 2014).

Several studies have reported associations between patient activation and medication adherence among chronically ill patients (Hibbard et al., 2015; Marshall et al., 2013; Mosen et al., 2007; Skolasky et al., 2011). However, those studies were quite limited by subjective adherence measurement or lack of sample generalizability. The results also were mixed. Some studies reported positive relationships between patient activation and medication adherence (Hibbard et al., 2015; Marshall et al., 2013; Mosen et al., 2007; Skolasky et al., 2011) but some did not report significant relationships (Salgado et al., 2017; Stepleman et al., 2010; Young et al., 2014). Moreover, no studies assessing association between patient activation and medication adherence specifically among diabetes patients were found. It's urgent to fill the gap, because once accomplished, it will provide further insight into potential benefits for diabetes patients if their activation can be improved (M. Hendriks & Rademakers, 2014). It will also identify potential predictors of patient activation, which may help to guide interventions to improve activation levels of patients with diabetes and accordingly their health outcomes. Continued existence of lack of understanding of the potential role of patient activation in medication adherence among diabetes patients will hinder the improvement

of long-term self-management of patients with diabetes and the improvement of health outcomes.

Objectives

The goal of this study was to assess association between patient activation and medication adherence among Medicare beneficiaries with type 2 diabetes. The specific objectives are listed below.

1) To assess patient activation levels of Medicare beneficiaries with type 2 diabetes;
2) To assess association between sociodemographic characteristics and patient activation;
3) To assess association between health status characteristics and patient activation;
4) To assess association between patient activation and medication adherence in Medicare beneficiaries with type 2 diabetes.

Notes

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METHODS

Data Source

Medicare Current Beneficiary Survey (MCBS) data was used to complete the project objectives. The MCBS is conducted by the Centers for Medicare and Medicaid Services (CMS), and is a continuous, in-person, nationally representative survey of approximately 15,000 Medicare beneficiaries (Parker et al., 2014). The MCBS is a longitudinal panel survey, with sample beneficiaries interviewed three times a year starting from each fall and continuing over up to four consecutive years to form a continuous profile of their health care experience (NORC at the University of Chicago). The MCBS includes Access to Care files with self-reported survey data and Cost and Use files with Medicare claims that can be linked to survey-reported events (U.S. Department of Health and Human Services, 2017).

Study Design

A retrospective cohort study was conducted to assess association between patient activation and medication adherence to antidiabetic medications among Medicare beneficiaries with type 2 diabetes. The MCBS files from 2009 through 2013 were used in this study.

The patient activation measure was the MCBS Patient Activation Supplement conducted in each summer round and present in MCBS Access to Care files. Patient Activation Supplements are available in the MCBS only for the years 2001, 2004, 2009, 2011, 2012 and 2013. The beneficiary interview in each survey year starts from its fall to the summer in the following year, which means the 2011 Access to Care file has the patient activation data which was actually collected in summer 2012. Medication adherence was assessed with proportion of days covered (PDC) using Medicare Part D administrative records from MCBS Cost and Use files within a period of six months after measurement of patient activation. Assessment of patient activation takes place from

May through August, but the exact dates for each beneficiary are unknown. Therefore, the start date of the assessment period of medication adherence was September 1 and the ending date was the end of February in the following year. Medicare Part D administrative records are on a calendar year basis, that is, the 2012 file contains records from January 1, 2012 to December 31, 2012. For example, for patients who completed the Patient Activation Supplement in summer 2012, we used the Part D administrative records in the 2012 and 2013 files to measure medication adherence from September 1, 2012 to February 28, 2013.

Study Sample

Inclusion Criteria

The sample included Medicare beneficiaries who completed the MCBS Patient Activation questionnaire, who were diagnosed with type 2 diabetes, and who were 18 or older. Individuals with type 1 diabetes were not included because patients with type I diabetes must use insulin and it's difficult to measure medication adherence to insulin products whose doses might be adjusted frequently.

Exclusion Criteria

Beneficiaries were excluded if they responded "Not ascertained," "Not Applicable," "Don't know" or "Refused" to more than 50 percent of the Patient Activation questions, did not have continuous Medicare Part A and Part D coverage throughout the assessment period, had less than two Medicare Part D claims for an antidiabetic medication throughout the assessment period, used insulin during the assessment period, resided in long-term care facilities during the medication adherence assessment period, or had Alzheimer's disease, dementia, mental retardation or mental disorder.

Continuous Medicare Part A enrollment was required because inpatient stays must be adjusted for PDC calculation. At least two Medicare Part D claims are needed because that is the minimum amount needed to calculate medication adherence using the PDC method. Patients with any insulin prescriptions were excluded because doses of insulin might be frequently adjusted, making it difficult to accurately measure adherence with administrative data. Institutionalized beneficiaries were also excluded because detailed pharmacy information is collected in the MCBS only for community-dwelling persons. Also facility staff instead of beneficiaries were interviewed for respondents in facilities so subjective and attitudinal questions including patient activation were not asked. Patients with Alzheimer's disease, dementia, mental retardation or mental disorder were excluded because they were less likely to provide accurate responses.

Identification of Type 2 Diabetes

Type 2 diabetes was identified if the beneficiaries had at least one Medicare Part A claim or at least two Medicare Part B claims with International Classification of Diseases Clinical Modification codes, 9th edition (ICD-9-CM): 250.x0 or 250.x2, or if they self-reported that they had been diagnosed with type 2 diabetes by a physician, that is, they answered "Yes" to the survey question "Has a doctor ever told you that you had any type of diabetes, including sugar diabetes, high blood sugar, borderline diabetes, pre-diabetes, or pregnancy-related diabetes?" and answered "Type 2 diabetes" to the survey question "Which type of diabetes did the doctor say that you have?"

Identification of Antidiabetic Medications

Antidiabetic medications except insulin were compiled as shown in Table 1 by reviewing 2018 Quality Rating System Measure Technical Specifications by CMS (Centers for Medicare & Medicaid Services, 2017). Use of any of the medications was

Table 1. List of Antidiabetic Medications

Antidiabetic Drug Category	Generic Names
Alpha-glucosidase inhibitors	Acarbose, Miglitol
Amylin analogs	Pramlintide
Biguanides	Metformin
Dipeptidyl peptidase-4 ((DPP-4) inhibitors	Alogliptin[1], Linagliptin, Saxagliptin, Sitaglipin
Glucagon-like peptide-1 (GLP-1) receptor agonists	Exenatide, Liraglutide, Albiglutide[1], Dulaglutide[1]
Meglitinides	Nateglinide, Repaglinide
Sodium glucose cotransporter 2 (SGLT-2) inhibitors	Dapagliflozin, Canagliflozin, Empagliflozin[1]
Sulfonylureas	Chlorpropamide, Glimepiride, Glipizide, Glyburide, Tolazamide, Tolbutamide
Thiazolidinediones (TZD)	Pioglitazone, Rosiglitazone
Antidiabetic combinations	Alogliptin-metformin[1], Alogliptin-pioglitazone[1], Canagliflozin-metformin[1], Dapagliflozin-metformin[1], Empaglifozin-linagliptin[1], Empagliflozin-metformin[1], Glimepiride-pioglitazone, Glimepiride-rosiglitazone, Glipizide-metformin, Glyburide-metformin, Linagliptin-metformin, Metformin-pioglitazone, Metformin-repaglinide, Metformin-rosiglitazone, Metformin-saxagliptin, Metformin-sitagliptin, Sitagliptin-simvastatin[2]

[1] The medication was introduced to the market after 2013.
[2] The medication was discontinued since September 2013.

Reference:

Centers for Medicare & Medicaid Services. (2017). 2018 Quality Rating System Measure Technical Specifications.

identified by generic names from Medicare Part D administrative records in Cost and Use files.

Study Variables

Patient Activation

Patient activation level was derived from the MCBS Patient Activation Supplement of sixteen questions. The items were designed to capture the "confidence," "communication," and "information seeking" domains within patient activation (Parker et al., 2014). All items have Likert-type response scales such as "Always," "Usually," "Sometimes," and "Never." Whole number values were assigned to each response based on the order within the structure of the survey questions, so a higher number indicates higher level of patient activation. For example, "Always" = 4 points, "Usually" = 3 points, "Sometimes" = 2 points, and "Never" = 1 point. According to the method developed by Parker et al., responses of "Not Applicable," "Not Ascertained," "Don't know" or "Refused" were regarded as missing, and items with such responses were left out (Parker et al., 2014). Beneficiaries were excluded if eight or more questions had missing values. Patient activation score was obtained by dividing the sum of the scores by the number of non-missing items for each beneficiary. Patient activation was then categorized as "low," "moderate," or "high" based on activation score. Based on Parker and colleagues' approach, low activation is determined if the activation score is below the mean minus one-half of the standard deviation, high activation is determined if the activation score is above the mean plus one-half of the standard deviation, and moderate activation is determined if the activation score is between the cutoff points for high and low (Parker et al., 2014).

Medication Adherence

Medication adherence was evaluated using PDC which ranges from 0 to 1. PDC was dichotomized as a binary variable. A value of 0.80 or more was regarded as adherent to antidiabetic medications, while a value less than 0.80 was regarded as nonadherent, consistent with general practice for use of PDC (Nau, 2012). If a patient took more than one medication, a weighted average of PDCs for each individual medication was calculated to represent the PDC for that patient. Weighted PDC was calculated by sum of days covered by each medication divided by sum of number of days each medication was to be taken. PDC considers time arrays to reflect the dates covered by each fill and adjustments were made when there were overlapping fills, medication discontinuations, medication switches, add-on medications, or inpatient stays during the assessment period.

Overlapping fills. It was assumed that if a patient refilled a prescription before the days of supply of the preceding prescription for that medication ended, he or she would not start to take the new refill until he or she used up the previously obtained medication. Such overlaps in the period covered by medication supply were adjusted by shifting forward the refill use start date.

Discontinuation. A discontinuation was defined as not refilling a medication within 90 days after previous supply had been used up. The day after the day in which previous supply was used up was defined as the discontinuation date. The days starting from a discontinuation date were not included in the PDC calculation of that medication. If a medication was discontinued, the PDC was calculated by the number of days covered by the medication divided by the number of days from the first fill date within the assessment period to the day before the discontinuation day.

Medication switch. A switch was defined as discontinuing a medication and starting another medication. If a patient switched medications before the previous supply was used up, the PDC of the former medication was calculated as the number of days covered by the former medication prior to medication switch divided by the number of

days from the start of the former medication to the discontinuation of that medication. If a patient switched medications after the previous supply was used up, the PDC of the former medication was calculated as the number of days covered by the former medication divided by the number of days from the start of the former medication to the start of the medication to which the patient was switched. The PDC of the latter medication was calculated as the number of days covered by the latter medication divided by the number of days from its start to the end of the assessment period or discontinuation of the medication.

Add-on medication. If a patient started a new medication but continued all the previous medications, we defined the new medication as an add-on medication. If a patient added a medication, PDC of that medication was calculated as the number of days covered by the add-on medication divided by the number of days from the its start to the end of the assessment period or discontinuation of the medication.

Consideration on days from the start date through the first fill date in the assessment period. We looked at one additional prescription prior to the start date and made inferences accordingly. If a medication was unavailable to a patient for more than 90 days prior to the first fill date in the assessment period, it was considered as an add-on medication and the days from the PDC assessment start date through the first fill date in the assessment period were excluded from PDC calculation. If a medication was unavailable to a patient for 90 days or less prior to the first fill date in the assessment period, we incorporated the previous one prescription before the PDC assessment start date to determine if those days before the first fill date in the assessment period were covered by the medication or not. We also shifted back the first fill date if the previous prescription fill was not used up yet at the first fill date in the assessment period. Therefore, we had a pre-observe window before the six-month assessment period. The pre-observe window was 190 days which reflected the drug discontinuation gap of 90 days and the maximum days of supply of 100 days. Similarly, we had a post-observe

window of 90 days when the adjusted last day that a patient was covered by a medication was prior to the PDC assessment ending date so that we could determine if the medication was discontinued or not.

Adjustment for inpatient stays. If a patient was admitted to a hospital during the assessment period, Medicare covered medications would be dispensed directly from the hospital rather than filled through Part D contractors (Center for Medicare & Medicaid Services, 2017). Thus, medication fills during an inpatient stay would not be included in Medicare Part D claims. In order to estimate the PDC, the number of days of that stay were added to the days of supply, which assumes the patient received relevant medications from other sources during the hospital stay (Center for Medicare & Medicaid Services, 2017).

If the last day that a patient was covered by a prescription was before the assessment ending date after all adjustments were made, one more prescription fill after the assessment ending date was taken into consideration to evaluate medication coverage on those days from the last day a patient was covered by the prescription to the assessment ending date.

Sociodemographic Variables

Age

Age was calculated at the start date of medication adherence assessment using date of birth and was categorized into age groups of "Under 65 years," "65 to 69 years," "70 to 74 years," "75 to 79 years," "80 to 84 years," or "85 years or older."

Race

Race is recorded in the MCBS as "Asian," "African American," "Native Hawaiian or Pacific Islander," "White," "American Indian or Alaska Native," "other

race," and "more than one race." Race was collapsed down to "White" and "Non-White."

Gender

Gender is recorded in the MCBS as "male" and "female."

Marital Status

Marital status in the MCBS includes four categories: "married," "widowed," "divorced," "separated," and "never married." It was collapsed down to "single," "married," and "widowed."

Region

Region of residence is recorded in the MCBS based on nine census divisions and Puerto Rico. The census divisions include New England, Middle Atlantic, East North Central, West North Central, South Atlantic, East South Central, West South Central, Mountain, and Pacific. Region was collapsed down to the standard four Census Regions of Northeast, Midwest, South, and West based on the beneficiary's residence. Northeast consists of New England and Middle Atlantic divisions, which includes Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont, New Jersey, New York, and Pennsylvania. Midwest consists of East North Central, and West North Central divisions, which includes Indiana, Illinois, Michigan, Ohio, Wisconsin, Iowa, Kansas, Minnesota, Missouri, Nebraska, North Dakota, and South Dakota. South consists of South Atlantic, East South Central and West South Central divisions, which includes Delaware, District of Columbia, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, West Virginia, Alabama, Kentucky, Mississippi, Tennessee, Arkansas, Louisiana, Oklahoma, and Texas. West consists of Mountain and Pacific divisions, which includes Arizona, Colorado, Idaho, New Mexico, Montana, Utah, Nevada, Wyoming, Alaska, California, Hawaii, Oregon, and Washington.

Employment

Employment status is recorded in the MCBS as "working at a job or business for pay" and "not working," and was recoded as "employed" and "unemployed."

Education

Education achieved is recorded in the MCBS as "no formal schooling," "elementary (1st to 8th grades)," "some high school (9th to 12th grades) but no diploma," "completed high school but no college," "vocational, technical or business," "some college but no degree," "associate's degree," "bachelor's degree" or "post-graduate degree." Education was collapsed down to "Less than high school," "High school but no diploma," "High school graduate," "Post high school, but no degree," "Associate's or bachelor's degree," and "Post-graduate degree."

Income

The MCBS collects data on beneficiaries' annual total household income before taxes in the categories of "less than $5,000," "$5,000 to $9,999," "$10,000 to $14,999," "$15,000 to $19,999," "$20,000 to $24,999," "$25,000 to $29,999," "$30,000 to $39,999," "$40,000 to $49,999," "and "$50,000 or more." Income level was collapsed down to "$9,999 or less," "$10,000 to $19,999," "$20,000 to $29,999," "$30,000 to $39,999," "$40,000 to $49,999," and "$50,000 or more" so that the income ranges at each level were equal and number of individuals at each level could reach 50 or greater to ensure adequate cell sizes.

Independent Living Status

Living independently or not was obtained from a single survey question asking the total number of people in the household. If the answer was "1," then the beneficiary was living independently. If the answer was more than 1, then the beneficiary was not living independently.

Health Insurance Coverage

Health insurance coverage was constructed from three survey questions including managed care enrollment, Medicaid eligibility, and private insurance coverage. Managed care enrollment was obtained from a survey question: "Are you currently covered by any Medicare HMO plans?" If a patient answered "Yes", he or she was enrolled in Medicare HMO. If a patient answered "No", he or she only was enrolled in a traditional Medicare plan. The MCBS records respondents' Medicaid eligibility and sources of data in a single question. Medicaid eligibility was coded as "Yes" if the answer of the question was "Survey data only," "CMS administrative data," or "Both survey data and administrative data," or "No" if the answer of the question was "No entitlement." Whether a patient was covered by any private health insurance plan is recorded as "Yes" or "No."

The categories of insurance coverage include traditional Medicare only, Medicare HMO (Health Maintenance Organization) only, traditional Medicare and Medicaid eligibility, traditional Medicare and private insurance coverage, Medicare HMO and Medicaid eligibility, Medicare HMO and private insurance coverage.

Health Status Variables

Obesity

Self-reported height and weight was obtained from survey questions. Body Mass Index was calculated by dividing a patient's weight in kilograms by height in meters squared. A Body Mass Index of 18.5 or greater and below 25 was classified as "Healthy," a Body Mass Index of 25 or greater and below 30 was classified as "Overweight," and a Body Mass Index of 30 or higher was classified as "Obese."

Perceived Health Status

Perceived health was accessed through a survey question: "In general, compared to other people at your age, would you say your health is excellent, very good, good, fair, or poor?"

Individual Comorbidities

Comorbidities were obtained through respondents' self-report based on a single survey question: "Has a doctor ever told you that you had [a specific illness or condition]?" Illnesses or conditions covered included hypercholesterolemia, hypertension, coronary heart disease, valvular heart disease, arrhythmia, stroke, osteoporosis, non-skin cancer, and depression. Respondents answered "Yes" or "No" to each of the illnesses or conditions. One variable was made for each of the individual comorbidities with response categories of "Yes" and "No."

Charlson Comorbidity Index

A Charlson Comorbidity Index score was calculated to assess comorbidities. It is a weighted index taking into consideration the number and severity of comorbid conditions and was first developed by Charlson and colleagues to predict one-year mortality (Charlson et al., 1987). It contains nineteen conditions and each of them was assigned a weight based on their relative risks on mortality (Charlson et al., 1987). It was adapted to seventeen conditions for use with ICD-9-CM administrative databases by Deyo et al. and Romano et al. (Deyo et al., 1992; Romano et al., 1993). To improve accuracy, an updated list of ICD-9-CM diagnosis codes for each of the conditions developed by Quan et al (Quan et al., 2005) was used to identify comorbidities from Medicare Part A and Part B claims prior to the start date of adherence measurement. Self-reported conditions were also used to facilitate identification of comorbidities.

Number of Prescribed Medications

The total number of prescribed medications at the start date of the adherence assessment period was calculated based on the Medicare Part D administrative data. If a prescription claim covered the start date of the adherence period, the medication was counted towards the number of prescribed medications. The total number of prescribed medications was then calculated and was a continuous variable.

Smoking Status

Smoking status was obtained through two survey questions: (1) "Have you ever smoked cigarettes, cigars, or pipe tobacco?" and (2) "Do you smoke cigarettes, cigars, or pipe tobacco now?" A beneficiary who answered "No" to the first question was classified as a non-smoker. A beneficiary who answered "Yes" to the second question was classified as a current smoker. A beneficiary who answered "Yes" to the first question but answered "No" or "No, but originally yes" to the second question was classified as an ex-smoker.

Prior Hospitalization

Prior hospitalization was identified based on any hospital inpatient stay within one year prior to medication adherence assessment. It was coded as "Yes" if the beneficiary had any inpatient stay, or as "No" otherwise.

Statistical Analysis

All analyses were conducted in SAS 9.4 for Unix environment. An *a priori* alpha level of 0.05 was used to determine significance for all the analyses. The MCBS utilizes a stratified, clustered, unequal-probability, and multi-stage sample design (Centers for Medicare and Medicaid Services, 2017). Bivariate and multivariable ordinal logistic regression were conducted to assess association between patient characteristics and patient activation, with cross-sectional survey weights used to account for overall

selection probability of each sample person and adjust for survey nonresponse and coverage error (Koenig et al., 2016). One-year backward longitudinal survey weights were used in bivariate and multivariable logistic regression assessing association between patient activation and medication adherence. The Fay's balanced repeated replication method was applied for variance estimation with a Fay coefficient of 0.3, adjusting for stratification and clustering design (Loganathan et al., 2017). The balanced repeated replication method draws multiple replicates, or subsamples from the full sample and replicate weights are created in each replicate by modifying the original weights. Fay's balanced repeated replication is a modified balanced repeated replication method by imposing a perturbation of the original weights with a Fay coefficient, which is less conservative in estimating variances than the traditional balanced repeated replication method (Zhang et al., 2001). The coefficient can be no less than 0 and below 1. Fay's method is equivalent to the traditional balanced repeated replication method when the coefficient is 0. The larger the coefficient is, the less conservative the variance estimates are. A value of 0.3 used in this study was recommended by the MCBS data file user guide (Center for Medicare & Medicaid Services, 2018). A series of replicate weights provided by the MCBS were used in REPWEIGHTS statement under SURVEY procedures.

Sample Characteristics

The SAS procedure PROC FREQ was used to obtain frequency and percentage tabulations for the sociodemographic variables and health status variables identified in this study. Sociodemographic variables included age, gender, race, education, employment, income, marital status, independent living, and health insurance coverage type. Health status Characteristics included obesity, perceived health status, hypercholesterolemia, hypertension, coronary heart disease, valvular heart disease,

arrhythmia, stroke, osteoporosis, non-skin cancer, depression, Charlson Comorbidity Index, number of prescribed medications, and smoking status.

Patient Activation

Distribution of Patient Activation

The SAS procedure PROC FREQ was used to obtain the percentage of beneficiaries at "low," "moderate," or "high" level of patient activation. The SAS procedure PROC MEANS was used to obtain the means and standard deviations of activation scores at each level.

Bivariate Associations between Sociodemographic Variables and Patient Activation

The SAS procedure PROC SURVEYFREQ was applied to obtain weighted frequencies in each category of sociodemographic variables. The SAS procedure PROC SURVEYLOGISTIC was used to conduct ordinal logistic regression to assess bivariate associations between sociodemographic variables and patient activation. Cross-sectional survey weights including general-purpose weights and a series of replicate weights were applied. Sociodemographic variables included age, gender, race, education, employment, income, marital status, independent living, and health insurance coverage type.

Bivariate Associations between Health Status Variables and Patient Activation

The SAS procedure PROC SURVEYFREQ was applied to obtain weighted frequencies for each health status variable. The SAS procedure PROC SURVEYLOGISTIC was used to conduct ordinal logistic regression to assess bivariate associations between health status variables and patient activation. Cross-sectional survey weights including general-purpose weights and a series of replicate weights were applied. Health status Characteristics included obesity, perceived health status, hypercholesterolemia, hypertension, coronary heart disease, valvular heart disease,

arrhythmia, stroke, osteoporosis, non-skin cancer, depression, Charlson Comorbidity Index, and smoking status.

Multivariable Association between Patient Characteristics and Patient Activation

Multivariable ordinal logistic regression was carried out to assess association between patient characteristics and patient activation adjusting for risk factors with SAS procedure PROC SURVEYLOGISTIC. Cross-sectional survey weights including general-purpose weights and a series of replicate weights were applied. Manual backward model selection in combination with Akaike Information Criteria were used to select a multivariable model reflecting significant predictors of patient activation that had the best model fit. We started with the full model with all demographic variables and health status variables in and eliminated the least significant variable in each step. When most of the variables in the model were significant and there was a big "jump" in the value of the Akaike Information Criteria if one more variable was eliminated, that multivariable was selected.

Medication Adherence

Distribution of Medication Adherence

Medication adherence was measured as PDC for diabetes medications for each beneficiary within an interval of six months starting from September 1 after patient activation measurement. A beneficiary was considered adherent to antidiabetic medications if the PDC was 0.80 or greater. A binary variable was created to represent medication adherence level. The SAS procedure PROC MEANS can be used to obtain means and standard deviations of PDCs for adherent and non-adherent groups. The SAS procedure PROC FREQ was used to generate a frequency table for medication adherence.

Bivariate Associations between Sociodemographic Variables and Medication Adherence

The SAS procedure PROC SURVEYFREQ was applied to generate weighted frequencies for each sociodemographic variable. The SAS procedure PROC SURVEYLOGISTIC was used to conduct ordinal logistic regression to assess bivariate associations between sociodemographic variables and medication adherence. Longitudinal survey weights including general-purpose weights and a series of replicate weights were applied. Sociodemographic variables included age, gender, race, education, employment, income, marital status, independent living, and health insurance coverage type.

Bivariate Associations between Health Status Variables and Medication Adherence

The SAS procedure PROC SURVEYFREQ was applied to generate weighted frequencies for each health status variable. The SAS procedure PROC SURVEYLOGISTIC was used to conduct ordinal logistic regression to assess bivariate associations between health status variables and medication adherence. Longitudinal survey weights including general-purpose weights and a series of replicate weights were applied. Health status Characteristics included obesity, perceived health status, hypercholesterolemia, hypertension, coronary heart disease, valvular heart disease, arrhythmia, stroke, osteoporosis, non-skin cancer, depression, Charlson Comorbidity Index, smoking status, number of prescribed medications, and prior hospitalization.

Association between Patient Activation and Medication Adherence

Bivariate Association between Patient Activation and Medication Adherence

Bivariate ordinal logistic regression was carried out to assess associations between patient activation and medication adherence with SAS procedure PROC SURVEYLOGISTIC. Longitudinal survey weights including general-purpose weights

and a series of replicate weights were applied for variance estimation. Medication adherence was the response variable and patient activation was the predictor variable.

A series of sensitivity analyses were conducted using patient activation score instead of categorized levels and using alternate patient activation categorizations to evaluate their impacts on the bivariate association between patient activation and medication adherence. Five changes in patient activation were made, including using patient activation score as the predictor variable, categorizing activation as "low," "moderate," and "high" levels using two different cutoff points: the mean activation score minus 0.75 times the standard deviation of activation scores and the mean score plus 0.75 times the standard deviation, categorizing activation as "low" and "high" levels using the mean score of patient activation as a cutoff point, categorizing activation as "low" and "high" levels using the mean activation score plus one-half of the standard deviation of activation scores as a cutoff point, and categorizing activation as "low" and "high" levels using the mean activation score minus one-half of the standard deviation as a cutoff point. Sensitivity analyses were also performed on PDC cutoff values of 0.90 and 0.70.

Multivariable Association between Patient Activation and Medication Adherence

Multivariable ordinal logistic regression was carried out to assess associations between patient activation and medication adherence adjusting for risk factors with SAS procedure PROC SURVEYLOGISTIC. Longitudinal survey weights including general-purpose weights and a series of replicate weights were applied for variance estimation. Medication adherence is the response variable and patient activation is the predictor variable. The model adjusted for sociodemographic and health status variables that were significant from bivariate analyses as covariates including race, gender, osteoporosis and number of medications.

A series of sensitivity analyses were conducted using patient activation score instead of categorized levels and using alternate patient activation categorizations to

evaluate their impacts on the bivariate association between patient activation and medication adherence, which is the same as described in the bivariate association section above. Sensitivity analyses were also performed on PDC using alternate cutoff values of 0.90 and 0.70.

Notes

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RESULTS

Study Sample

Figure 1 shows the sample selection flow chart. A total of 24,056 Medicare beneficiaries who completed the Patient Activation Supplement in the 2009, 2011, 2012, and 2013 MCBS were identified. All of them were 18 years old or older. There were 23,929 individuals who responded to more than 50 percent of patient activation questions. Among the 23,929 individuals, 6,608 individuals had a diagnosis of type 2 diabetes. We excluded 780 individuals with Alzheimer's disease, dementia, mental retardation, mental disorder, 4,231 individuals without continuous Medicare Part A and Part D coverage, 2 individuals who resided in long-term care facilities, 386 individuals who used insulin products, and 638 individuals with less than two Medicare Part D claims for antidiabetic drugs. The final sample consisted of 571 individuals. With the application of survey weights, results from this sample can be generalized to 2,663,304 Medicare beneficiaries with type 2 diabetes.

Sample Demographic Characteristics

Age

Age was calculated at the start date of medication adherence assessment using date of birth. The mean age was 72.4 years with a standard deviation of 9.6 years. Age was categorized into age groups of "Under 65 years," "65 to 69 years," "70 to 74 years," "75 to 79 years," "80 to 84 years," or "85 years or older." Table 2 presents the sample distribution by age. Eleven percent of the patients were under 65 years old, twenty-five percent were age 65 to 69 years, twenty-one percent were age 70 to 74 years, twenty percent were age 75 to 79 years, seventeen percent were age 80 to 84 years. Only approximately six percent were 85 years or older.

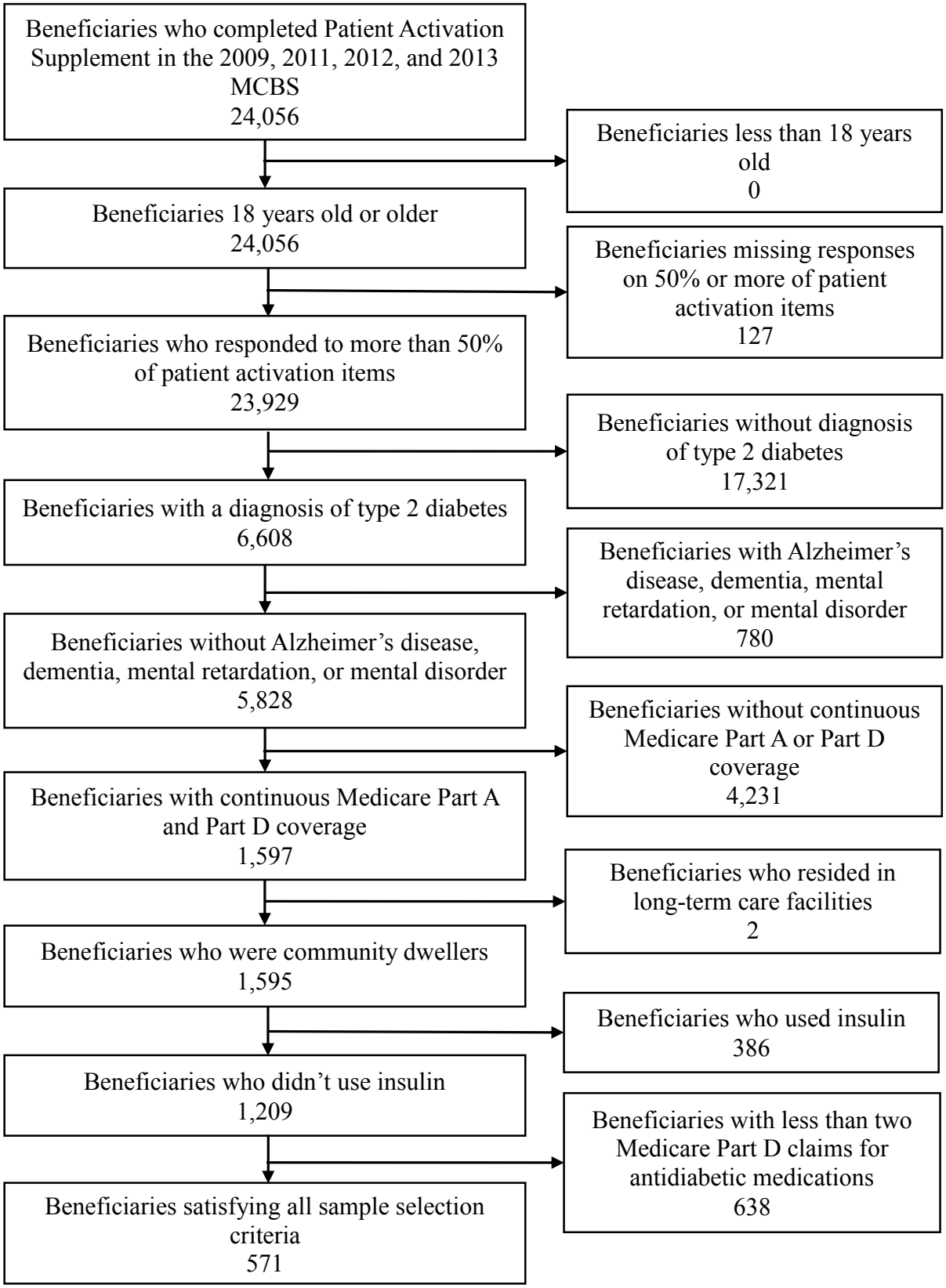

Figure 1. Sample Selection Results

Table 2. Sample Distribution by Age

Age	Frequency (N=571)	Percent
Under 65 years	62	10.9
65 to 69 years	144	25.2
70 to 74 years	122	21.4
75 to 79 years	116	20.3
80 to 84 years	95	16.6
85 years or older	32	5.6

Race

Race was coded as "White" and "Non-White." As shown in Table 3, a majority of the patients were White (77.5%), and the others were non-White (22.5%).

Gender

Gender is recorded in the MCBS as "male" and "female." Forty-three percent of the sample persons were male, and fifty-seven percent were female (Table 4).

Marital Status

Marital status in the MCBS includes four categories: "married," "widowed," "divorced," "separated," and "never married." It was collapsed down to "single," "married," and "widowed." As shown in Table 5, nearly one-half of the sample persons were married (49.7%). Twenty-six percent were widowed, and twenty-four percent were single.

Region

Region was categorized as the standard four Census Regions of Northeast, Midwest, South, and West based on the beneficiary's residence. As shown in Table 6, over two-fifth of the sample resided in the South region (42.0%), and approximately one-fourth resided in the Midwest (23.5%). Sixteen percent lived in the Northeast, and eighteen percent lived in the West.

Employment

Employment status is recorded in the MCBS as "working at a job or business for pay" and "not working," and was recoded as "employed" or "unemployed." As shown in Table 7, most of the sample persons were unemployed (89.7%). It was not surprising because the sample was Medicare beneficiaries.

Table 3. Sample Distribution by Race

Race	Frequency (N=556)	Percent
White	431	77.5
Non-White	125	22.5

Table 4. Sample Distribution by Gender

Gender	Frequency (N=571)	Percent
Male	243	42.6
Female	328	57.4

Table 5. Sample Distribution by Marital Status

Marital Status	Frequency (N=571)	Percent
Married	284	49.7
Widowed	151	26.4
Single	136	23.8

Table 6. Sample Distribution by Region

Region	Frequency (N=548)	Percent
Northeast	89	16.2
Midwest	129	23.5
South	230	42.0
West	100	18.3

Table 7. Sample Distribution by Employment

Employment	Frequency (N=571)	Percent
Unemployed	512	89.7
Employed	59	10.3

Education

Education was categorized as “Less than high school,” “High school but no diploma,” “High school graduate,” “Post high school, but no degree,” “Associate's or bachelor's degree,” and “Post-graduate degree.” As shown in Table 8, 15.3 percent had a less than high school education, 19.5 percent went to high school but had no diploma, 24.1 percent were high school graduates, and 23.9 percent received post high school education without a degree. Only 11.6 percent of the sample had associate’s or bachelor’s degree, and 5.5 percent had post-graduate degree.

Income

The MCBS collects data on beneficiaries’ annual total household income before taxes. Income level was recoded as “$9,999 or less,” “$10,000 to $19,999,” “$20,000 to $29,999,” “$30,000 to $39,999,” “$40,000 to $49,999,” and “$50,000 or more.” As shown in Table 9, approximately one-fourth of the sample had an income of $9,999 or less (23.4%), and over one-fourth had an income between $10,000 and $19,999 (28.9%). Eighteen percent had an income between $20,000 and $29,999, ten percent had an income between $40,000 and $39,999, eight percent had an income between $40,000 and $49,999, and eleven percent had an income of $50,000 or more.

Independent living status

Independent living status was coded as “Yes” or “No.” The sample distribution by independent living status is shown in Table 10. Nearly two-thirds of the sample persons were living with others (67.6%), and the other one-third were living independently (32.4%).

Health Insurance Coverage

Health insurance coverage was constructed from three survey questions on managed care enrollment, Medicaid eligibility, and private insurance coverage. The

Table 8. Sample Distribution by Education

Education	Frequency (N=568)	Percent
Less than high school	87	15.3
High school but no diploma	111	19.5
High school graduate	137	24.1
Post high school, but no degree	136	23.9
Associate's or bachelor's degree	66	11.6
Post-graduate degree	31	5.5

Table 9. Sample Distribution by Annual Household Income

Household Income	Frequency (N=453)[1]	Percent
$9,999 or less	106	23.4
$10,000 to $19,999	131	28.9
$20,000 to $29,999	85	18.8
$30,000 to $39,999	46	10.2
$40,000 to $49,999	34	7.5
$50,000 or more	51	11.3

[1] N was less than 571 due to missing responses.

Table 10. Sample Distribution by Independent Living Status

Independent Living	Frequency (N=571)	Percent
No	386	67.6
Yes	185	32.4

categories created for insurance coverage were traditional Medicare only, Medicare HMO only, traditional Medicare and Medicaid, traditional Medicare and private insurance, Medicare HMO and Medicaid, Medicare HMO and private insurance.

Table 11 shows that over one-third, or thirty-five percent of the sample persons were enrolled in Medicare HMO only, and 6.5 percent were enrolled in traditional fee-for-service Medicare only. As for dual coverage, 16.7 percent were dual eligible for traditional Medicare and Medicaid, 2 8.6 percent were covered by both traditional Medicare and private insurance, 9.3 percent were covered by both Medicare HMO and Medicaid, and only 4.3 percent were covered by both Medicare HMO and private insurance.

Sample Health Status Characteristics

Smoking Status

Smoking status was recoded as "non-smoker," "ex-smoker," and "current smoker." The sample distribution is presented in Table 12. Approximately one-half of the sample persons were ex-smokers (47.3%), 41.7 percent were non-smokers, and the remaining 11 percent were current smokers.

Obesity

Body Mass Index was calculated using self-reported height and weight, which is a patient's weight in kilograms divided by height in meters squared. A Body Mass Index of 18.5 or greater and below 25 was classified as "Healthy," a Body Mass Index of 25 or greater and below 30 was classified as "Overweight," and a Body Mass Index of 30 or higher was classified as "Obese." As shown in Table 13, over one-half of the sample persons were obese (52.6%), and over one-third were overweight (35.4%). Only 12 percent had a healthy weight.

Table 11. Sample Distribution by Insurance Coverage

Insurance Coverage	Frequency (N=557)[1]	Percent
Traditional Medicare	36	6.5
Medicare HMO	193	34.7
Traditional Medicare and Medicaid	93	16.7
Traditional Medicare and Private Insurance	159	28.6
Medicare HMO and Medicaid	52	9.3
Medicare HMO and Private Insurance	24	4.3

[1] N was less than 571 due to missing responses.

Table 12. Sample Distribution by Smoking Status

Smoking Status	Frequency (N=571)	Percent
Non-smoker	238	41.7
Ex-smoker	270	47.3
Current Smoker	63	11.0

Table 13. Sample Distribution by Obesity

Obesity	Frequency (N=557)	Percent
Healthy	67	12.0
Overweight	197	35.4
Obese	293	52.6

Perceived Health Status

Perceived health was coded as “excellent,” “very good,” “good,” “fair,” or “poor.” Table 14 shows the sample distribution by perceived health status. Approximately 8 percent of the sample perceived they had excellent health, 24.7 percent perceived they had very good health, 36.0 percent perceived they had good health, 22.6 percent perceived they had fair health, and 8.4 percent perceived they had poor health.

Individual Comorbidities

Comorbidities were identified through a self-reported survey question: “Has a doctor ever told you that you had [a specific illness or condition]?” The illnesses or conditions included hypercholesterolemia, hypertension, coronary heart disease, valvular heart disease, arrhythmia, osteoporosis, depression, non-skin cancer, and stroke. One variable was made for each of the individual comorbidities with response categories of “Yes” and “No.” Table 15 shows the sample distribution by presence of individual comorbidities. Over two-thirds of the sample had hypercholesterolemia (69.7%). Over four-fifths of the sample had hypertension (83.5%). Only 12.6 percent had coronary heart disease. Eleven percent self- reported presence of valvular heart disease (10.7%). Nineteen percent self-reported presence of arrhythmia (18.8%). There were 14.3 percent of the sample with osteoporosis, 22.2 percent with depression, 16.3 percent with non-skin cancer, and 11.9 percent with stroke.

Charlson Comorbidity Index

Charlson Comorbidity Index was used to assess severity of comorbid conditions. The score of Charlson Comorbidity Index was calculated and was categorized as five levels, “0,” “1,” “2,” “3,” “4 or greater.” Table 16 presents the sample distribution by Charlson Comorbidity Index score. Approximately one-third, or 32.1 percent of the sample had a score of 0. Of the 571 patients, 17.5 percent had a score of 1, 17.0 percent

Table 14. Sample Distribution by Perceived Health Status

Perceived Health	Frequency (N=570)	Percent
Excellent	47	8.3
Very good	141	24.7
Good	205	36.0
Fair	129	22.6
Poor	48	8.4

Table 15. Sample Distribution by Presence of Individual Comorbidities

Individual Comorbidities	Frequency	Percent
Hypercholesterolemia (N=570)[1]		
No	173	30.4
Yes	397	69.7
Hypertension (N=570)[1]		
No	94	16.5
Yes	476	83.5
Coronary Heart Disease (N=570)[1]		
No	498	87.4
Yes	72	12.6
Valvular heart disease (N=570)[1]		
No	509	89.3
Yes	61	10.7
Arrhythmia (N=570)[1]		
No	463	81.2
Yes	107	18.8
Osteoporosis (N=566)[1]		
No	485	85.7
Yes	81	14.3
Depression (N=571)[1]		
No	444	77.8
Yes	127	22.2
Cancer (Non-skin) (N=571)[1]		
No	478	83.7
Yes	93	16.3
Stroke (N=571)[1]		
No	503	88.1
Yes	68	11.9

[1] Sample size N's vary due to missing responses.

Table 16. Sample Distribution by Charlson Comorbidity Index Score

Charlson Comorbidity Index Score	Frequency (N=571)	Percent
0	183	32.1
1	100	17.5
2	97	17.0
3	64	11.2
4 or greater	127	22.2

had a score of 2, 11.2 percent had a score of 3, and 22.2 percent had a score of 4 or greater.

Number of Prescribed Medications

The total number of prescribed medications at the start date of adherence measurement, i.e., September 1st of the survey year, was calculated based on the Medicare Part D administrative data. If a prescription claim covered the start date of the adherence period, the medication was counted towards the number of prescribed medications. The total number of prescribed medications was then calculated and was made as a continuous variable. Table 17 shows that the mean number of prescribed medications was 5.6 with a standard deviation of 2.7. It also shows that 22.1 percent of the sample took 3 or less prescribed medications. Nearly half, or 46.6 percent of the sample had 4 to 6 prescribed medications, 22.7 percent had 7 to 9 prescribed medications, and 8.5 percent had 10 or more prescribed medications.

Prior Hospitalization

Prior hospitalization was identified based on any hospital inpatient stay within one year prior to the medication adherence assessment. It was coded as "Yes" if the beneficiary had any inpatient stay, or as "No" otherwise. Only 7.7 percent of the sample had a prior hospitalization one year prior to the medication adherence assessment (Table 18).

Patient Activation

Sample Distribution by Patient Activation

A patient activation score was calculated by dividing the sum of the rating on each patient activation item by the number of non-missing items for each beneficiary. Patient activation was then categorized as "low," "moderate," or "high" based on

Table 17. Sample Distribution by Number of Prescribed Medications

Number of Prescribed Medications[1]	Frequency (N=551)	Percent
3 or less	122	22.1
4 to 6	257	46.6
7 to 9	125	22.7
10 or more	47	8.5

[1] The mean was 5.6 with a standard deviation of 2.7.

Table 18. Sample Distribution by Prior Hospitalization Status within One Year Prior to the Medication Adherence Assessment

Prior Hospitalization	Frequency (N=571)	Percent
No	527	92.3
Yes	44	7.7

activation score. The mean patient activation score was 3.20 with a standard deviation of 0.42. Table 19 presents the sample distribution by patient activation level. Of the 571 Medicare beneficiaries, 27.5 percent were at low activation level, 38.7 percent were at moderate activation level, and 33.7 percent were at high activation level.

Bivariate Associations between Sociodemographic Characteristics and Patient Activation

Bivariate associations between sociodemographic variables and patient activation level among Medicare beneficiaries with type 2 diabetes are presented in Table 20. Cross-sectional survey weights including general-purpose weights and a series of replicate weights were applied in the models for variance estimation. Age, race, marital status, region, employment status, independent living status, and insurance coverage were not significantly associated with low patient activation. Males were more likely to report low activation than females (O.R. = 1.39, $p = 0.041$). Compared to patients with post-graduate degrees, those with less than high school education were 5.22 times more likely to report low activation ($p < 0.001$), and those who graduated from high school were 2.14 times more likely to report low activation ($p = 0.030$). The lower the income, the more likely patients had low activation. Compared to patients with an income of $50,000 or more, those with an income between $10,000 and $19,999 were 2.11 times more likely to have low activation ($p = 0.014$), and those with an income of $9,999 or less were 2.47 times more likely to have low activation ($p = 0.014$).

Bivariate Associations between Health Status Characteristics and Patient Activation

Bivariate associations between health status variables and patient activation level among Medicare beneficiaries with type 2 diabetes are presented in Table 21. Cross-sectional survey weights including general-purpose weights and a series of replicate weights were applied in the models for variance estimation. Smoking status, obesity,

Table 19. Sample Distribution by Patient Activation Level

Patient Activation Level	Frequency (N=571)	Percent
Low	162	27.5
Moderate	222	38.7
High	187	33.7

Table 20. Bivariate Associations between Demographic Variables and Low Patient Activation Level

Variables	Weighted Number	Odds Ratio	95% C.I.	*p* value[1]
Age (N=571)[2]				
Under 65 years	253,580	0.58	0.24 – 1.39	0.217
65 to 69 years	585,059	0.54	0.22 – 1.30	0.169
70 to 74 years	434,526	0.65	0.29 – 1.42	0.273
75 to 79 years	346,842	0.55	0.26 – 1.20	0.130
80 to 84 years	217,642	0.83	0.36 – 1.91	0.665
85 years or older	78,480	Ref.		
Race (N=556)[2]				
White	1,459,818	Ref.		
Non-White	394,345	1.37	0.94 – 2.00	0.103
Gender (N=571)[2]				
Female	1,113,838	Ref.		
Male	802,291	1.39	1.01 – 1.91	0.041
Marital Status (N=571)[2]				
Married	954,519	Ref.		
Widowed	471,913	1.66	0.74 – 1.84	0.097
Single	489,697	1.39	0.94 – 2.05	0.507
Region (N=548)[2]				
Northeast	341,812	1.50	0.90 – 2.50	0.117
Midwest	387,682	1.30	0.84 – 2.03	0.241
South	763,101	1.16	0.74 – 1.82	0.504
West	359,385	Ref.		
Employment (N=571)[2]				
Unemployed	1,709,540	Ref.		
Employed	206,589	1.11	0.71 – 1.75	0.643

Table 20. Continued

Variables	Weighted Number	Odds Ratio	95% C.I.	*p* value[1]
Education (N=568)[2]				
Less than high school	285,342	5.22	2.36 –	<0.001
High school but no diploma	351,348	1.85	0.86 – 3.98	0.112
High school graduate	457,758	2.14	1.08 – 4.25	0.030
Associate's or bachelor's degree	484,811	0.71	0.29 – 1.72	0.445
Post high school, but no degree	224,395	0.97	0.47 – 2.02	0.938
Post-graduate degree	101,453	Ref.		
Income (N=453)[2]				
$9,999 or less	342,510	2.47	1.21 – 5.05	0.014
$10,000 to $19,999	446,877	2.11	1.17 – 3.79	0.014
$20,000 to $29,999	294,965	1.80	0.89 – 3.64	0.099
$30,000 to $39,999	168,128	1.12	0.51 – 2.45	0.779
$40,000 to $49,999	118,895	0.99	0.41 – 2.40	0.981
$50,000 or more	175,901	Ref.		
Independent Living (N=571)[2]				
No	1,300,857	Ref.		
Yes	615,272	0.90	0.63 – 1.30	0.576
Insurance Coverage (N=557)[2]				
Traditional Medicare	140,040	Ref.		
Medicare HMO	662,402	0.85	0.38 – 1.93	0.701
Traditional Medicare and Medicaid	298,024	1.31	0.53 – 3.20	0.556
Traditional Medicare and Private Insurance	510,728	0.87	0.42 – 1.84	0.720
Medicare HMO and Medicaid	176,090	0.93	0.30 – 2.86	0.891
Medicare HMO and Private Insurance	79,931	0.63	0.19 – 2.02	0.431

[1] *p* values were obtained from ordinal logistic regression. $p < 0.05$ indicates significance.
[2] Sample size N's vary due to missing responses.

Table 21. Bivariate Associations between Health Status Variables and Low Patient Activation Level

Variables	Weighted Number	Odds Ratio	95% C.I.	*p* value[1]
Smoking Status (N=571)[2]				
Non-smokers	807,508	Ref.		
Ex-smokers	868,157	0.76	0.54 – 1.07	0.115
Current Smokers	240,464	1.20	1.64 – 2.22	0.566
Obesity (N=557)[2]				
Healthy	200,205	Ref.		
Overweight	650,233	0.55	0.30 – 1.02	0.057
Obese	1,019,618	0.66	0.36 – 1.20	0.171
Perceived Health (N=570)[2]				
Excellent	149,412	Ref.		
Very good	454,311	0.88	0.52 – 1.48	0.619
Good	711,768	0.95	0.53 – 1.71	0.871
Fair	432,374	1.40	0.73 – 2.70	0.306
Poor	166,740	1.00	0.44 – 2.24	0.997
Hypercholesterolemia (N=570)[2]				
Yes	1,370,354	Ref.		
No	544,446	0.98	0.65 – 1.49	0.933
Hypertension (N=570)[2]				
Yes	1,589,223	Ref.		
No	321,996	1.24	0.72 – 2.12	0.437
Coronary Heart Disease (N=570)[2]				
Yes	228,959	Ref.		
No	1,684,934	0.90	0.52 – 1.57	0.717
Valvular heart disease (N=570)[2]				
Yes	208,019	Ref.		
No	1,703,753	1.01	0.58 – 2.10	0.751

Table 21. Continued

Variables	Weighted Number	Odds Ratio	95% C.I.	*p* value[1]
Arrhythmia (N=570)[2]				
Yes	340,211	Ref.		
No	1,572,939	1.65	1.10 – 2.48	0.016
Osteoporosis (N=566)[2]				
Yes	276,252	Ref.		
No	1,624,847	1.29	0.83 – 2.00	0.260
Depression (N=571)[2]				
Yes	417,588	Ref.		
No	1,498,541	0.86	0.58 – 1.26	0.433
Cancer (Non-skin) (N=571)[2]				
Yes	281,554	Ref.		
No	1,634,575	1.46	0.92 – 2.31	0.105
Stroke (N=571)[2]				
Yes	207,441	Ref.		
No	1,708,688	0.76	0.41 – 1.40	0.369
Charlson Comorbidity Index (N=571)[2]				
0	657,961	Ref.		
1	334,153	1.03	0.67 – 1.59	0.892
2	321,434	1.02	0.62 – 1.69	0.921
3	200,606	1.13	0.57 – 2.24	0.732
4 or greater	401,975	1.04	0.71 – 1.54	0.824

[1] *p* values were obtained from ordinal logistic regression. $p < 0.05$ indicates significance.
[2] Sample size N's vary due to missing responses.

perceived health, presence of hypercholesterolemia, hypertension, coronary heart disease, valvular heart disease, osteoporosis, depression, non-skin cancer, stroke, and Charlson Comorbidity Index score were not significantly associated with low activation level. Patients without arrhythmia were 1.65 times more likely to report low activation than those with arrhythmia ($p = 0.016$).

Multivariable Association between Patient Characteristics and Patient Activation

Table 22 presents a multivariable model that was fit to assess multivariable association between patient characteristics and low activation among Medicare beneficiaries with type 2 diabetes. Cross-sectional survey weights including general-purpose weights and a series of replicate weights were applied in the model for variance estimation. Backward model selection in combination with Akaike Information Criteria were used to select a multivariable model reflecting significant predictors of patient activation that had the best model fit. The global likelihood ratio test was significant, which indicates good model fit ($p < 0.001$). Gender, education, smoking status, obesity, and arrhythmia were included in the model. Two-way interaction effects were examined, and no significant interaction term was found. In contrast to bivariate regression results, income level was not found significantly associated with activation level, but smoking status and overweight were found significantly associated with activation level.

Similar with bivariate results, males were 1.83 times more likely to report low activation ($p = 0.005$). Low education level was strongly associated with having low activation. Compared to patients with post-graduate degrees, those with education less than high school were 7.40 times more likely to report low activation ($p < 0.001$), those who went to high school but had no diploma were 2.45 times more likely to report low activation ($p = 0.036$), and who graduated from high school were 2.63 times more likely to report low activation ($p = 0.012$). Ex-smokers were 0.37 times less likely to have low

Table 22. Multivariable Association between Patient Characteristics and Low Patient Activation Level

Variables (N=553)[1]	Weighted Number	Odds Ratio	95% C.I.	*p* value[2]
Gender				
Female	1,065,326	Ref.		
Male	790,729	1.83	1.21 – 2.78	0.005
Education				
Less than high school	276,502	7.40	3.24 – 16.88	<0.001
High school but no diploma	342,067	2.45	1.06 – 5.68	0.036
High school graduate	438,275	2.63	1.24 – 5.58	0.012
Post high school, but no degree	482,206	1.14	0.53 – 2.45	0.730
Associate's or bachelor's degree	217,806	0.93	0.38 – 2.28	0.872
Post-graduate degree	99,199	Ref.		
Smoking Status				
Non-smokers	779,922	Ref.		
Ex-smokers	842,778	0.63	0.43 – 0.94	0.023
Current Smokers	233,355	1.03	0.53 – 1.98	0.940
Obesity				
Healthy	200,205	Ref.		
Overweight	647,663	0.48	0.26 – 0.88	0.018
Obese	1,008,187	0.65	0.36 – 1.18	0.155
Arrhythmia				
Yes	335,046	Ref.		
No	1,521,009	1.55	1.02 – 2.34	0.040

[1] Sample size N was less than 571 due to missing responses.

[2] *p* values were obtained from ordinal logistic regression. $p < 0.05$ indicates significance.

activation than non-smokers ($p = 0.023$), while current smokers were not significantly different from non-smokers in terms of having low activation. Compared to patients with a healthy weight, those who were overweight were 0.52 times less likely to report low activation ($p = 0.018$), while those who were obese did not report a significant different likelihood of reporting low activation. Similar with bivariate results, patients without arrhythmia were 1.55 times more likely to report low activation than those with arrhythmia ($p = 0.040$).

Medication Adherence

Sample Distribution by Medication Adherence

Medication adherence was measured as PDC for diabetes medications for each beneficiary within an interval of six months. A beneficiary was considered adherent to antidiabetic medications if the PDC was 0.80 or greater. Table 23 shows the sample distribution by adherence to antidiabetic medications. Of the 571 Medicare beneficiaries with type 2 diabetes, approximately three-fourths, or 74.2 percent were adherent to antidiabetic medications.

Bivariate Associations between Sociodemographic Characteristics and Medication Adherence

Table 24 presents bivariate associations between sociodemographic variables and medication non-adherence among Medicare beneficiaries with type 2 diabetes. Longitudinal survey weights including general-purpose weights and a series of replicate weights were applied in the models for variance estimation. Race was strongly associated with medication non-adherence. Non-Whites were 3.39 times more likely to report non-adherence to antidiabetic medications than Whites ($p < 0.001$). Males were 0.60 times less likely to report non-adherence than females ($p = 0.029$). Age, marital

Table 23. Sample Distribution by Adherence to Antidiabetic Medications

Medication Adherence	Frequency (N=571)	Weighted Frequency (N=2,663,304)	Percent
Adherence	424	1,966,975	74.2
Non-adherence	147	696,329	25.7

Table 24. Bivariate Associations between Demographic Variables and Medication Non-Adherence

Variables	Weighted Number	Odds Ratio	95% C.I.	*p* value[1]
Age (N=571)[2]				
Under 65 years	342,165	1.52	0.52 – 4.45	0.440
65 to 69 years	741,465	0.85	0.31 – 2.33	0.750
70 to 74 years	645,609	1.09	0.36 – 3.27	0.882
75 to 79 years	505,477	1.08	0.41 – 2.84	0.871
80 to 84 years	309,221	1.20	0.45 – 3.23	0.711
85 years or older	119,367	Ref.		
Race (N=556)[2]				
White	2,019,318	Ref.		
Non-White	554,247	3.39	2.07 – 5.54	<0.001
Gender (N=571)[2]				
Female	1,535,854	Ref.		
Male	1,127,450	0.60	0.38 – 0.95	0.029
Marital Status (N=571)[2]				
Married	1,344,191	Ref.		
Widowed	663,381	0.87	0.52 – 1.45	0.579
Single	655,732	1.13	0.70 – 1.83	0.619
Region (N=548)[2]				
Northeast	500,016	1.01	0.47 – 2.16	0.986
Midwest	531,892	1.06	0.56 – 1.98	0.864
South	1,045,566	1.16	0.63 – 2.13	0.630
West	502,103	Ref.		
Employment (N=571)[2]				
Unemployed	2,378,086	Ref.		
Employed	285,218	1.22	0.64 – 2.34	0.535

Table 24. Continued

Variables	Weighted Number	Odds Ratio	95% C.I.	*p* value[1]
Education (N=568)[2]				
Less than high school	390,297	1.18	0.35 – 3.98	0.787
High school but no diploma	483,623	1.33	0.40 – 4.44	0.636
High school graduate	634,249	0.85	0.25 – 2.93	0.793
Post high school, but no degree	669,892	1.73	0.54 – 5.48	0.352
Associate's or bachelor's degree	326,219	1.56	0.46 – 5.34	0.471
Post-graduate degree	141,413	Ref.		
Income (N=453)[2]				
$9,999 or less	468,596	1.37	0.50 – 3.73	0.531
$10,000 to $19,999	621,819	0.84	0.29 – 2.46	0.753
$20,000 to $29,999	395,378	0.83	0.27 – 2.54	0.746
$30,000 to $39,999	237,774	0.68	0.23 – 2.00	0.484
$40,000 to $49,999	168,378	0.99	0.29 – 3.39	0.989
$50,000 or more	241,448	Ref.		
Independent Living (N=571)[2]				
No	1,825,902	Ref.		
Yes	837,402	0.99	0.64 – 1.53	0.971
Insurance Coverage (N=557)[2]				
Traditional Medicare	186,099	Ref.		
Medicare HMO	900,960	1.34	0.54 – 3.29	0.526
Traditional Medicare and Medicaid	403,417	1.40	0.50 – 3.96	0.521
Traditional Medicare and Private	729,453	1.00	0.41 – 2.46	0.994
Medicare HMO and Medicaid	250,626	1.24	0.39 – 3.87	0.715
Medicare HMO and Private Insurance	119,322	0.69	0.10 – 4.92	0.711

[1] *p* values were obtained from ordinal logistic regression. $p < 0.05$ indicates significance.
[2] Sample size N's vary due to missing responses.

status, region, employment status, education level, income level, independent living status, and insurance coverage were not significantly associated with medication non-adherence.

Bivariate Associations between Health Status Characteristics and Medication Adherence

Table 25 presents bivariate associations between health status variables and medication non-adherence among Medicare beneficiaries with type 2 diabetes. Longitudinal survey weights including general-purpose weights and a series of replicate weights were applied in the models for variance estimation. Patients without osteoporosis were 1.93 times more likely to be non-adherent to antidiabetic medications ($p = 0.018$). Compared to patients who had a Charlson Comorbidity Index score of 0, those who had a score of 1 were 2.64 times more likely to be non-adherent to antidiabetic medications ($p = 0.004$). Every one unit increase in the number of prescribed medications was associated with a 74 percent increase in the odds of being non-adherent to antidiabetic medications (O.R. = 1.74, $p = 0.023$). Smoking status, obesity, perceived health status, presence of hypercholesterolemia, hypertension, coronary heart disease, valvular heart disease, arrhythmia, depression, non-skin cancer, and stroke, and prior hospitalization were not significantly associated with non-adherence to antidiabetic medications.

In summary, race, gender, absence of osteoporosis, Charlson Comorbidity Index score, and number of prescribed medications were significant risk factors for medication non-adherence.

Table 25. Bivariate Associations between Health Status Variables and Medication Non-Adherence

Variables	Weighted Number	Odds Ratio	95% C.I.	*p* value[1]
Smoking Status (N=571)[2]				
Non-smokers	1,115,983	Ref.		
Ex-smokers	1,226,655	0.80	0.52 – 1.24	0.316
Current Smokers	320,666	1.18	0.63 – 2.23	0.600
Obesity (N=557)[2]				
Healthy	278,306	Ref.		
Overweight	921,500	1.76	0.88 – 3.52	0.108
Obese	1,394,750	1.22	0.61 – 2.49	0.576
Perceived Health (N=570)[2]				
Excellent	214,895	Ref.		
Very good	621,864	1.28	0.49 – 3.30	0.614
Good	993,460	1.88	0.81 – 4.39	0.139
Fair	602,844	1.32	0.54 – 3.21	0.536
Poor	227,744	2.13	0.75 – 6.04	0.155
Hypercholesterolemia (N=570)[2]				
Yes	1,884,013	Ref.		
No	777,793	1.26	0.80 – 1.97	0.309
Hypertension (N=570)[2]				
Yes	2,222,081	Ref.		
No	435,424	1.10	0.65 – 1.85	0.733
Coronary Heart Disease (N=570)[2]				
Yes	317,823	Ref.		
No	2,342,580	1.06	0.53 – 2.13	0.860
Valvular heart disease (N=570)[2]				
Yes	284,991	Ref.		
No	2,371,501	0.90	0.48 – 1.70	0.741

Table 25. Continued

Variables	Weighted Number	Odds Ratio	95% C.I.	*p* value[1]
Arrhythmia (N=570)[2]				
Yes	481,888	Ref.		
No	2,177,031	1.24	0.76 – 2.04	0.384
Osteoporosis (N=566)[2]				
Yes	397,906	Ref.		
No	2,244,743	1.93	1.12 – 3.31	0.018
Depression (N=571)[2]				
Yes	584,491	Ref.		
No	2,078,813	0.65	0.39 – 1.07	0.091
Cancer (Non-skin) (N=571)[2]				
Yes	417,532	Ref.		
No	2,245,772	0.86	0.50 – 1.49	0.598
Stroke (N=571)[2]				
Yes	301,427	Ref.		
No	2,361,877	1.09	0.57 – 2.11	0.783
Charlson Comorbidity Index (N=571)[2]				
0	881,953	Ref.		
1	471,232	2.64	1.38 – 5.03	0.004
2	453,706	1.66	0.92 – 3.00	0.090
3	282,299	1.84	0.92 – 3.71	0.086
4 or greater	574,114	1.33	0.74 – 2.39	0.329
Number of Medications[3] (N=551)[2]	2,567,984	1.74	1.08 – 2.81	0.023
Prior Hospitalization (N=571)[2]				
No	2,466,852	0.87	0.39 – 1.94	0.731
Yes	196,452	Ref.		

[1] *p* values were obtained from ordinal logistic regression. $p < 0.05$ indicates significance.
[2] Sample size N's vary due to missing responses.
[3] Variable is continuous.

Association between Patient Activation and Medication Adherence

Bivariate Association between Patient Activation and Medication Adherence

Bivariate association between patient activation and medication non-adherence among Medicare beneficiaries with type 2 diabetes is shown in Table 26. Longitudinal survey weights including general-purpose weights and a series of replicate weights were applied in the models for variance estimation. A PDC value equal to or greater than 0.80 was considered adherent to medications, and a PDC value less than 0.80 was considered non-adherent to medications. Patient activation level was found not significantly associated with non-adherence to antidiabetic medications ($p = 0.698$).

Sensitivity Analyses on Patient Activation

A series of sensitivity analyses were conducted using patient activation scores and using alternate patient activation categorizations to evaluate how they affected the bivariate association between patient activation and medication adherence. First, the predictor variable, patient activation level was changed to be patient activation score that is a continuous variable. There was still no significant association between patient activation score and medication non-adherence ($p = 0.362$). Second, patient activation level was categorized as "low," "moderate," and "high" levels using two different cutoff points, the mean activation score minus 0.75 times the standard deviation of activation scores and the mean plus 0.75 times the standard deviation. No significant association was found between patient activation level and medication non-adherence ($p = 0.219$). Third, patient activation level was categorized as "low" or "high" using the mean score of patient activation as a cutoff point. No significant association was found between patient activation level and medication non-adherence ($p = 0.612$). Fourth, patient activation level was categorized as "low" or "high" using the mean activation score plus one-half of the standard deviation as a cutoff point. No significant association was found between

Table 26. Bivariate Association between Patient Activation and Medication Non-Adherence (PDC less than 0.80)

Patient Activation (N=571)	Weighted Number	Odds Ratio	95% C.I.	*p* value[1]
High	726,396	Ref.		
Moderate	1,028,043	0.83	0.54 – 1.28	0.397
Low	908,865	0.89	0.57 – 1.39	0.599

[1] *p* values were obtained from ordinal logistic regression. $p < 0.05$ indicates significance.

patient activation level and medication non-adherence ($p = 0.411$). Fifth, patient activation level was categorized as "low" and "high" levels using the mean activation score minus one-half of the standard deviation as a cutoff point. No significant association was found between patient activation level and medication non-adherence ($p = 0.914$). Based on the analyses above, we confirmed that whether patient activation scores or categorized levels were used and how patient activation level was categorized did not have significant impacts on the association between patient activation and adherence to antidiabetic medications among Medicare beneficiaries with type 2 diabetes.

Sensitivity Analyses on Medication Adherence

Sensitivity analyses were also conducted to evaluate how different cutoff values for PDC might affect the bivariate association between patient activation level and medication adherence. As shown in tables in Appendix A, patient activation level was not significantly associated with non-adherence to antidiabetic medications using PDC cutoff values of either 0.90 or 0.70 ($p = 0.704$; $p = 0.950$).

Multivariable Associations between Patient Activation and Medication Adherence

Multivariable association between patient activation and medication non-adherence among Medicare beneficiaries with type 2 diabetes is shown in Table 27. The multivariable model was adjusted for race, gender, presence of osteoporosis, Charlson Comorbidity Index, and number of prescribed medications based on the significant predictor variables found in bivariate analysis between patient characteristics and medication adherence. Longitudinal survey weights including general-purpose weights and a series of replicate weights were applied in the model for variance estimation. The global likelihood ratio test was significant, which indicated good model fit ($p < 0.001$).

With a PDC cutoff value of 0.80 for medication adherence, patient activation level was not significantly associated with non-adherence to antidiabetic medications

Table 27. Multivariable Association between Patient Activation and Medication Non-Adherence (PDC less than 0.80)

Variables (N=531)[1]		Weighted Number	Odds Ratio	95% C.I.	*p* value[2]
Patient Activation					
High		497,535	Ref.		
Moderate		678,641	0.85	0.49 – 1.48	0.556
Low		598,014	0.87	0.49 – 1.56	0.644
Race					
White		1,397,211	Ref.		
Non-White		376,979	3.57	2.04 – 6.26	<0.001
Gender					0.126
Female		1,031,179	–	–	
Male		743,011	–	–	
Osteoporosis					0.023
Yes		254,210	–	–	
No		1,519,980	–	–	
Gender*Osteoporosis			–	–	<0.001
Charlson Comorbidity Index					
0		611,819	Ref.		
1		314,409	2.36	1.07 – 5.20	0.034
2		302,003	1.60	0.80 – 3.19	0.185
3		187,347	2.24	0.85 – 5.90	0.102
4 or greater		358,612	1.66	0.83 – 3.30	0.148
Number of Medications		1,774,190	0.90	0.81 – 0.99	0.039
Interaction Effects					
Gender=Male	Osteoporosis: No vs Yes		>999.9	232.08 – >999.9	<0.001
Gender=Female	Osteoporosis: No vs Yes		0.46	0.24 – 0.90	0.023
Osteoporosis=Yes	Gender: Male vs Female		<0.001	<0.001 – 0.001	<0.001
Osteoporosis=No	Gender: Male vs Female		0.64	0.36 – 1.14	0.126

[1] Sample size N was less than 571 due to missing responses.

[2] p values were obtained from ordinal logistic regression. $p < 0.05$ indicates significance.

Note: – Due to complexity of interaction effects, comparisons between levels of gender depend on the level of presence of osteoporosis, and vice versa. So odds ratio estimates of variables included in the interaction term were not reported here but were reported by slicing at the bottom of the table.

after adjusting for other risk factors. Similar with the bivariate result, non-White patients were 3.57 times more likely to be non-adherent to antidiabetic medications ($p < 0.001$). Compared to patients with a Charlson Comorbidity Index score of 0, those with a score of 1 were 2.36 times more likely to be non-adherent ($p = 0.034$). A one unit increase in the number of prescribed medications was associated with a 10 percent decrease in the odds of reporting non-adherence (O.R. = 0.90, $p = 0.039$), which is opposite from the result in bivariate analysis.

There was a significant interaction effect of gender and osteoporosis, which is shown at the bottom of Table 27. When slicing by gender, male patients without osteoporosis were more likely to be non-adherent than those with osteoporosis (O.R. >999.9, $p < 0.001$), and female patients without osteoporosis were less likely to be non-adherent than those with osteoporosis (O.R. = 0.46, $p = 0.021$). When slicing by presence of osteoporosis, patients with osteoporosis who were male were less likely to be non-adherent than those who were female (O.R. < 0.001, $p < 0.001$), patients without osteoporosis who were male were not significantly different from those who were female on medication adherence (O.R. = 0.64, $p = 0.126$).

Sensitivity Analyses on Patient Activation

Sensitivity analyses were conducted on using patient activation score instead of categorized levels as the predictor variable and using different categorizations of patient activation level. Five alternate approaches for patient activation categorization were examined, including using patient activation score as the predictor variable, categorizing activation as “low,” “moderate,” and “high” levels using two different cutoff points: the mean activation score minus 0.75 times standard deviation of activation scores and the mean score plus 0.75 times standard deviation, categorizing activation as “low” and “high” levels using the mean score of patient activation as a cutoff point, categorizing activation into two levels as “low” or “high” using the mean activation score plus one-

half of the standard deviation of activation scores as a cutoff point, and categorizing activation as “low” and “high” levels using the mean activation score minus one-half of the standard deviation of activation scores as a cutoff point. None of the approaches had a significant impact on the multivariable association between patient activation and medication adherence.

Sensitivity Analyses on Medication Adherence

Sensitivity analyses were also performed on PDC cutoff values of 0.90 and 0.70 (Appendix B). When the PDC cutoff value was 0.90, no significant interaction term was found. Patient activation level was found not significantly associated with medication non-adherence, which is consistent with the result when PDC cutoff value was 0.80. When the PDC cutoff value was 0.70, interaction of gender and osteoporosis was found significant and patient activation level was still not significantly associated with medication non-adherence. Therefore, PDC cutoff values did not have a significant impact on the association between patient activation level and medication adherence to antidiabetic drugs.

SUMMARY AND DISCUSSION

Background

Approximately 50 percent of patients with type 2 diabetes fail to achieve adequate glycemic control (Ali et al., 2012; Ford, 2011). Lack of glycemic control decreases patients' quality of life and increases risk of life-threatening complications. Medication non-adherence, a key factor in glycemic control (Egede et al., 2014) is high among patients with type 2 diabetes and has been reported to range from 38 percent to 93 percent (Krass et al., 2015). As a chronic disease, diabetes requires patients to be actively engaged in self-care management in collaboration with their health care team to obtain good health outcomes (American Diabetes Association, 2013b; Graffigna et al., 2014). Emerging studies indicate that patient activation, "understanding one's role in the care process and having the willingness, knowledge, skill, and confidence to manage one's health and healthcare" (Hibbard et al., 2004) may influence medication adherence in chronically ill populations (Stepleman et al., 2010). However, studies that have examined association between patient activation and medication adherence are quite limited by self-reported adherence measurement or lack of sample generalizability. Moreover, no studies assessed association between patient activation and medication adherence specifically among diabetes patients.

Objectives

The goal of this study was to assess association between patient activation and medication adherence among Medicare beneficiaries with type 2 diabetes. The specific objectives were:

1) To assess patient activation levels of Medicare beneficiaries with type 2 diabetes;
2) To assess association between sociodemographic characteristics and patient activation;
3) To assess association between health status characteristics and patient activation;

4) To assess association between patient activation and medication adherence in Medicare beneficiaries with type 2 diabetes.

Methods

A retrospective cohort study was conducted to assess association between patient activation and medication adherence to antidiabetic medications among Medicare beneficiaries with type 2 diabetes. Data from the 2009 through 2013 Medicare Current Beneficiary Survey (MCBS) was used in this study.

Medication adherence was assessed with proportion of days covered (PDC) using Medicare Part D administrative records from MCBS Cost and Use files within a period of six months after measurement of patient activation. Assessment of patient activation takes place from May through August but the exact dates for each beneficiary are unknown. Therefore, the assessment period of medication adherence was from September 1 to the end of February in the following year.

The sample included Medicare beneficiaries who completed the MCBS Patient Activation Supplement, who were diagnosed with type 2 diabetes, and who were 18 or older. Beneficiaries were excluded if they responded "Not ascertained," "Not Applicable," "Don't know" or "Refused" to more than 50 percent of the Patient Activation questions, had no continuous Medicare Part A and Part D coverage throughout the assessment period, had less than two Medicare Part D claims for an antidiabetic medication throughout the assessment period, used insulin during the assessment period, resided in long-term care facilities, or had Alzheimer's disease, dementia, mental retardation or mental disorder.

Patient activation level was derived from the MCBS Patient Activation Supplement of sixteen questions. The items were designed to capture the "confidence," "communication," and "information seeking" domains within patient activation (Parker et al., 2014). All items have Likert-type response scales such as "Always," "Usually,"

"Sometimes," and "Never." Whole number values were assigned to each response based on the order within the structure of the survey questions, so a higher number indicates higher level of patient activation. A patient activation score was obtained by dividing the sum of the scores by the number of non-missing items for each beneficiary. Based on Parker and colleagues' approach, low activation is determined if the activation score is below the mean minus one-half of the standard deviation, high activation is determined if the activation score is above the mean plus one-half of the standard deviation, and moderate activation is determined if the activation score is between the cutoff points for high and low (Parker et al., 2014).

Medication adherence was evaluated using PDC which ranges from 0 to 1. PDC was dichotomized as a binary variable. A value of 0.80 or more was regarded as adherent to antidiabetic medications, while a value less than 0.80 was regarded as nonadherent, consistent with general practice for use of PDC (Nau, 2012). If a patient took more than one medication, a weighted average of PDCs for each individual medication was calculated to represent the PDC for that patient. Weighted PDC was calculated by sum of days covered by each medication divided by sum of number of days each medication was to be taken. PDC considers time arrays to reflect the dates covered by each fill and adjustments were made when there were overlapping fills, medication discontinuations, medication switches, add-on medications, and inpatient stays during the assessment period.

Sociodemographic variables included age, gender, race, education, employment, income, marital status, independent living, and health insurance coverage type. Health status Characteristics included obesity, smoking status, perceived health status, hypercholesterolemia, hypertension, coronary heart disease, valvular heart disease, arrhythmia, stroke, osteoporosis, non-skin cancer, depression, Charlson Comorbidity Index, number of prescribed medications, and prior hospitalization.

All analyses were conducted in SAS 9.4 for Unix environment. An *a priori* alpha level of 0.05 was used to determine significance for all the analyses. Bivariate and multivariable ordinal logistic regression were conducted using cross-sectional survey weights to assess association between patient characteristics and patient activation. One-year backward longitudinal survey weights were used in bivariate and multivariable logistic regression assessing association between patient activation and medication adherence. The Fay's balanced repeated replication method was applied for variance estimation with a Fay coefficient of 0.30, adjusting for clustering and stratification design of the MCBS (Loganathan et al., 2017).

Results

Sample Characteristics

A total of 571 individuals were included in the final sample after sample selection. With the application of survey weights, the sample represents 2,663,304 Medicare beneficiaries with type 2 diabetes. The mean age was 72.4 years. Most of the sample persons were female, White, unemployed, and living with others. Nearly one-half of the sample persons were married. Forty-two percent resided in the South of the U.S. Approximately 60 percent had high school education or lower. Over one-half of the sample had less than $20,000 annually in household income. Over one-third was enrolled in Medicare HMO only and 28.6 percent was enrolled in both traditional Medicare and private insurance. Only 11.0 percent was current smokers and 47.3 percent was past smokers. Only 12 percent had a healthy weight. Approximately seventy percent perceived their health status as good, very good, or excellent. A majority of the beneficiaries had hypercholesterolemia and hypertension. Nearly one-third had a Charlson Comorbidity Index score of 0 and 22.2 percent had a score of 4 or greater. The mean number of prescribed medications taken by the sample was 5.6. Only 7.7 percent

of the sample had inpatient stays during one year prior to the medication adherence assessment.

Patient Activation

Sample Distribution by Patient Activation

The mean patient activation score was 3.20 with a standard deviation of 0.42. Of the 571 Medicare beneficiaries, 27.5 percent were at low activation level, 38.7 percent were at moderate activation level, and 33.7 percent were at high activation level. Approximately one-third of beneficiaries with type 2 diabetes reported low activation, i.e., not actively engaged in their own health care. Our finding raises concerns about low activation among Medicare beneficiaries with type 2 diabetes and shows a great need for increasing activation levels for those low activated patients.

Bivariate Associations between Sociodemographic Characteristics with Patient Activation

Sociodemographic variables were examined for associations with patient activation level. Only gender, education, and income were significantly associated with low activation. Low activation level was more likely to be found in males and patients with an annual household income level of less than $20,000. Lower education was also associated with low activation level, but the trend was not monotonic. Age, race, marital status, region, employment status, independent living status, and insurance coverage were not significantly associated with low patient activation.

Bivariate Associations between Health Status Characteristics with Patient Activation

Health status variables were also examined for associations with patient activation level. Only absence of arrhythmia was significantly associated with low activation. Smoking status, obesity, perceived health, presence of hypercholesterolemia, hypertension, coronary heart disease, valvular heart disease, osteoporosis, depression,

non-skin cancer, and stroke, and Charlson Comorbidity Index score were not significantly associated with low activation level.

Multivariable Association between Patient Characteristics and Patient Activation

A multivariable model was fit to assess multivariable association between patient characteristics and low activation using backward model selection in combination with Akaike Information Criteria. Gender, education, smoking status, obesity, and arrhythmia were included in the model as significant predictors of patient activation level. Low activation was more likely to be found in males, less educated patients, and patients without arrhythmia.

Males were more likely to report low activation among Medicare beneficiaries with type 2 diabetes. Being male has been found associated with low activation in prior studies (M. Hendriks & Rademakers, 2014; Parker et al., 2014), which is in line with our finding. Literature has suggested that females reported higher level of concerns about diabetes (Berenguera et al., 2016), took diabetes more seriously (Mosnier-Pudar et al., 2009), and had more engagement in seeking health information than males (Bidmon & Terlutter, 2015). Mathew et al. and Mosnier-Pudar et al. have suggested that males identified their wives as a main source of support in their disease management, while females were more engaged in self-management (Mathew et al., 2012; Mosnier-Pudar et al., 2009).

Consistent with prior studies, low education was recognized as a predictor of low patient activation (M. Hendriks & Rademakers, 2014; Marshall et al., 2013; Mitchell et al., 2014). There might be several reasons. Zimmerman et al. have suggested that individuals with low education have limited opportunities or resources to learn about health (Zimmerman et al., 2015). Mandpe et al. suggested that less educated patients with diabetes tend to have less knowledge of disease (Mandpe et al., 2014), and Jackson

et al. suggested that less educated patients with diabetes tended to have less knowledge of diabetes self-care (Jackson et al., 2014).

Low income was associated with low activation in bivariate results. Duke and Stanik reported that low-income status discouraged patients from seeking care from providers due to concerns about receiving low-quality care, disrespect, or costs, and low-income patients had limited health information access (Duke & Stanik, 2016). This may account for the association between low income and low activation in bivariate analysis. In contrast to bivariate results, income level was not significantly associated with activation level after adjusting for other risk factors. Prior research had similar findings that income became not significant after adjusting for other risk factors (Schmaderer et al., 2016). Since education has been reported to have a strong positive association with income (Wolla & Sullivan, 2017) and was positively associated with patient activation in this study, the change in significance might be due to a positive confounding effect of education.

Patients without arrhythmia were more likely to have low activation than those with arrhythmia, but this has not been found in other studies. Based on a qualitative study conducted by McCabe et al., patients with atrial fibrillation, a common form of arrhythmia, experience unpredicted palpitations, dyspnea, and fatigue, which leads to fear and diminished quality of life, and reported to seek treatment with hopes to get free from the burden of atrial fibrillation (McCabe et al., 2011). Because of the fear and diminished quality of life, patients with arrhythmia may take a more active role in self-care management than those without arrhythmia.

Ex-smokers as compared to non-smokers were less likely to report low activation. This may be due to the stronger willpower and self-control that ex-smokers have than never smokers as reported by Fenske (Fenske, 2011), which may give ex-smokers more confidence in managing their health care.

Overweight patients as compared to those with healthy weight were less likely to report low activation, while obese patients did not report significantly different activation level from those with healthy weight. Aung et al. and Hendriks et al. both found higher Body Mass Index was associated with lower activation level (Aung et al., 2016; S. H. Hendriks et al., 2016), which is not consistent with this study. The reason for the conflicting is unclear.

Medication Adherence

Medication adherence was measured over a period of six months after patient activation measurement. The length of the assessment period was limited by the availability of the MCBS data since only data from 2009 through 2013 was available. The sample size would decrease a lot if an assessment period of a year was adopted. A beneficiary was considered adherent to antidiabetic medications if the PDC was no less than 0.80. Approximately three-fourths, or 74.2 percent were adherent to antidiabetic medications. The adherence rate was higher than prior reports in type 2 diabetes, which was 67.9 percent using MPR as reported by a meta-analysis (Iglay et al., 2015). But MPR overestimates adherence. The adherence rate was reported as 47.3 percent, 41.2 percent, and 36.7 percent for DPP-4 inhibitors initiators, sulfonylureas initiators, and thiazolidinediones initiators respectively using PDC based on a large-scale retrospective cohort study (Farr et al., 2014). The higher adherence rate in this study than Farr et al's work might be explained by our older population and longer duration of diabetes.

Bivariate Associations between Sociodemographic Characteristics and Medication Adherence

Bivariate associations between sociodemographic characteristics and medication adherence were assessed to identify factors that were influential on medication adherence. Being non-white or being females were significantly associated with medication non-adherence to antidiabetic medications in bivariate regression analysis.

Bivariate Associations between Health Status Characteristics and Medication Adherence

Bivariate associations between health status characteristics and medication adherence were assessed. Absence of osteoporosis and higher number of prescribed medications were significantly associated with medication non-adherence to antidiabetic medications in bivariate regression analysis. Compared to patients who had a Charlson Comorbidity Index score of 0, those who had a score of 1 were 2.64 times more likely to be non-adherent to antidiabetic medications. Age, marital status, region, employment status, education level, income level, independent living status, and insurance coverage were not significantly associated with medication non-adherence.

Association between Patient Activation and Medication Adherence

Bivariate Associations between Patient Activation and Medication Adherence

In bivariate logistic analysis, patient activation level was not significantly associated with medication adherence. A series of sensitivity analyses were performed on using patient activation scores as the predictor variable, categorizing activation level differently, and using 0.90 and 0.70 as PDC cutoff points. These changes had no significant impact on the bivariate association between patient activation and medication adherence.

Multivariable Associations between Patient Activation and Medication Adherence

In multivariable logistic analysis adjusting for race, gender, presence of osteoporosis, Charlson Comorbidity Index score, and number of prescribed medications, patient activation level was not significantly associated with medication adherence. The same sensitivity analyses as in bivariate analysis were performed using patient activation scores as the predictor variable, using alternate activation level categorizations, and using 0.90 and 0.70 as PDC cutoff points. These changes had no significant impact on findings.

Several prior studies have found significant associations between patient activation and medication adherence in populations other than patients with type 2 diabetes, including multi-morbid populations (Hibbard et al., 2015; Mosen et al., 2007; Skolasky et al., 2011), asthma population (Young et al., 2014), and HIV-infected population (Marshall et al., 2013). Apart from difference in target population, the inconsistency in findings may result from different measurements of patient activation and medication adherence. This study used the Patient Activation Supplement in the MCBS rather than the PAM to assess patient activation. For medication adherence, this study used objective adherence measurement, PDC, rather than self-reported measurements. Future research can utilize the PAM-13 and PDC approach with a longer adherence assessment period in Medicare beneficiaries with type 2 diabetes to provide more evidence whether or not patient activation is associated with adherence to antidiabetic drugs.

Similar with results of bivariate analysis between sociodemographic characteristics and medication adherence, non-adherence to antidiabetic medications was more likely to be found in non-Whites. The finding is in line with Balkrishnan et al.'s study that assessed association between race and medication adherence among Medicaid enrolled patients with type 2 diabetes (Balkrishnan et al., 2006). As Gellad et al. have suggested, the racial/ethnical disparity in medication adherence may attribute to cost concerns (Gellad et al., 2007).

Compared to patients with a Charlson Comorbidity Index score of 0, those with a score of 1 were more likely to have non-adherence, but those with scores higher than 1 did not have significantly different odds of being non-adherent. In type 2 diabetes, Balkrishnan et al. found that higher Charlson Comorbidity Index score was associated with lower MPRs (Balkrishnan et al., 2003), whereas Curkendall et al. found higher Charlson Comorbidity Index score was associated with medication adherence measured by PDC (Curkendall et al., 2013). The reason for the conflicting is unclear. But the

difference in findings may be because a longer adherence assessment period, one year instead of one-half year, was used in prior studies. Also, Balkrishnan et al. did not exclude insulin users in their sample, and Curkendall et al. studied new users of antidiabetic medications.

In bivariate analysis, higher number of prescribed medications was associated with non-adherence. After adjusting for other risk factors, higher number of prescribed medications was associated with lower odds of non-adherence, which is opposite to the bivariate result. Confounders may reverse an association between a predictor variable and a response variable (Kamangar, 2012). Number of prescribed medications has been reported positively associated with Charlson Comorbidity Index scores (Dominick et al., 2005; Szeto et al., 2006) and Charlson Comorbidity Index was associated with medication adherence in this study, so Charlson Comorbidity Index score might have confounded the association between number of medications and medication adherence and led to a reversed association.

In bivariate analysis, males were more likely to be adherent. Association between gender and medication adherence in diabetes has not been consistently shown in the literature. Some studies found females were more adherent than males (Al-Haj Mohd et al., 2015; Iqbal et al., 2017), others found males were more adherent than females (Balkrishnan et al., 2006; Curkendall et al., 2013; Huber & Reich, 2016; Schmittdiel et al., 2015) while some studies did not find significant association between gender and medication adherence (Adisa & Fakeye, 2013; Chew et al., 2015; Sweileh et al., 2014; Wu & Liu, 2016). Interestingly, all studies that found males were more adherent used objective adherence measurements including MPR and PDC (Balkrishnan et al., 2006; Curkendall et al., 2013; Huber & Reich, 2016; Schmittdiel et al., 2015) and all other studies mentioned above used self-reported adherence. So our finding was quite consistent with prior studies that used objective adherence measurements.

In bivariate analysis, patients with osteoporosis were more likely to be adherent. In multivariable analysis, gender and osteoporosis interacted with each other in the model. For males, patients without osteoporosis were more likely to be non-adherent than those with osteoporosis, which is consistent with bivariate analysis. But for females, patients with osteoporosis were more likely to be non-adherent than those without osteoporosis. For patients with osteoporosis, females were more likely to be non-adherent. For patients without osteoporosis, gender was not associated with medication adherence. Female diabetes patients with osteoporosis may need more education and monitoring to increase medication adherence and achieve adequate glycemic control. The interaction effect has not been reported by other studies. More efforts should be taken to study the interaction effect between gender and osteoporosis on medication adherence to antidiabetic drugs.

Limitations

The findings should be interpreted in light of several limitations. The MCBS is a representative survey of Medicare beneficiaries, but this study was restricted to non-institutionalized patients who were healthy enough to complete the survey on their own and patients who had continuous Medicare Part A and Part D coverage and had at least two Medicare Part D claims. Therefore, the findings of this study can only be generalized to ambulatory Medicare Part D beneficiaries with type 2 diabetes.

We were unable to assess some variables potentially influential to patient activation or medication adherence using the MCBS data, including duration of diabetes, diabetes complications and dosing frequency of medications. Literature has shown that longer duration of diabetes was associated with higher patient activation (Aung et al., 2016; Rask et al., 2009) and also medication adherence (Al-Haj Mohd et al., 2015). Aung et al. have suggested that smaller number of complications was associated with higher patient activation (Aung et al., 2016). Srivastava et al. have suggested that lower

dosing frequency was associated with improved medication adherence (Srivastava et al., 2013).

PDC values may be affected when patients' claims for prescribed medications were filed through insurances other than Medicare Part D or were not filed by physicians. But the missing claims would not affect association between patient activation and medication adherence unless missing claims were associated with patient activation level.

Most prior studies used the PAM to evaluate activation scores or levels. Although the PAM developed by Judith Hibbard is a more common measure of patient activation, the items in the MCBS Patient Activation Supplement are regarded conceptually similar (Parker et al., 2014). The PAM captures three key domains of knowledge, skills, and confidence, and the Patient Activation Supplement captures domains of confidence, communication, and information-seeking behaviors. The Patient Activation Supplement evaluates patients' behaviors of obtaining health-related information to reflect their knowledge rather than asking their abilities directly as the PAM does. Williams and Heller validated the 15-item Patient Activation Supplement with good internal reliability and construct validity (Williams & Heller, 2007). The Patient Activation Supplement has been used by other studies as a good source to assess patient activation (Butler et al., 2012; Mattingly et al., 2017; Parker et al., 2014).

All sociodemographic variables and health status variables except Charlson Comorbidity Index, number of prescribed medications, and prior hospitalization came from survey data of the MCBS, which subject to the accuracy of respondents' self-report.

Conclusions and Implications

Patient Activation Levels of Medicare Beneficiaries with Type 2 Diabetes

Of the 571 Medicare beneficiaries with type 2 diabetes, 27.5 percent of the were at low activation level, 38.7 percent were at moderate activation level, and 33.7 percent

were at high activation level. A large portion of patients reported low activation, which raises concerns about low activation among Medicare beneficiaries with type 2 diabetes. It shows a great need for increasing activation levels for those low activated patients given the benefits of high activation from literature.

Associations between Sociodemographic Characteristics with Patient Activation

Males and low education were associated with low patient activation. Healthcare providers may pay more attention to male or less-educated patients and implement tailored interventions to enhance patients' involvement in their self-care as well as their ability to manage their own health, which may lead to increased patient activation level and improved health outcomes ultimately.

Associations between Health Status Characteristics with Patient Activation

Absence of arrhythmia was associated with low patient activation. Ex-smokers as compared to non-smokers and overweight patients as compared to those with a healthy weight tended to report higher activation. For patients with the same disease burden, healthcare providers may allocate less labor-intensive support to patients with arrhythmia but offer more to those without arrhythmia to optimize use of healthcare resources by matching support with patients' needs (Hibbard et al., 2015).

Association between Patient Activation and Medication Adherence

We did not find a significant association between patient activation level and medication adherence among Medicare beneficiaries with type 2 diabetes. Future research might adopt a longer assessment period of medication adherence and also account for more risk factors such as duration of diabetes, number of complications, and dosing frequency.

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APPENDICES

Appendix A

Sensitivity Analyses on Bivariate Association between Patient Activation and Medication Adherence

Table A1. Bivariate Association between Patient Activation and Medication Non-Adherence (PDC less than 0.90)

Patient Activation (N=571)	Weighted Number	Odds Ratio	95% C.I.	*p* value[1]
High	726,396	Ref.		
Moderate	1,028,043	0.99	0.68 – 1.46	0.973
Low	908,865	1.16	0.76 – 1.78	0.478

[1] *p* values were obtained from ordinal logistic regression. $p < 0.05$ indicates significance.

Table A2. Bivariate Association between Patient Activation and Medication Non-Adherence (PDC less than 0.70)

Patient Activation (N=571)	Weighted Number	Odds Ratio	95% C.I.	*p* value[1]
High	726,396	Ref.		
Moderate	1,028,043	1.09	0.63 – 1.87	0.759
Low	908,865	1.02	0.59 – 1.77	0.929

[1] *p* values were obtained from ordinal logistic regression. $p < 0.05$ indicates significance.

Appendix B

Sensitivity Analyses on Multivariable Association between Patient Activation and Medication Adherence

Table B1. Multivariable Association between Patient Activation and Medication Non-Adherence (PDC less than 0.90)

Variables (N=531)[1]	Weighted Number	Odds Ratio	95% C.I.	*p* value[2]
Patient Activation				
High	497,535	Ref.		
Moderate	678,641	1.04	0.65 – 1.67	0.872
Low	598,014	1.04	0.63 – 1.74	0.863
Race				
White	1,397,211	Ref.		
Non-White	376,979	2.40	1.42 – 4.07	0.001
Gender				
Female	1,031,179	Ref.		
Male	743,011	0.79	0.51 – 1.22	0.284
Osteoporosis				
Yes	254,210	1.71	0.92 – 3.19	0.092
No	1,519,980	Ref.		
Charlson Comorbidity Index				
0	611,819	Ref.		
1	314,409	2.79	1.51 – 5.15	0.001
2	302,003	1.70	0.88 – 3.28	0.109
3	187,347	2.08	0.93 – 4.65	0.073
4 or greater	358,612	2.46	1.44 – 4.21	0.001
Number of Medications	1,774,190	0.87	0.81 – 0.94	<0.001

[1] Sample size N was less than 571 due to missing responses.

[2] *p* values were obtained from ordinal logistic regression. $p < 0.05$ indicates significance.

Table B2. Multivariable Association between Patient Activation and Medication Non-Adherence (PDC less than 0.70)

Variables (N=531)[1]		Weighted Number	Odds Ratio	95% C.I.	*p* value[2]
Patient Activation					
High		497,535	Ref.		
Moderate		678,641	1.26	0.64 – 2.47	0.504
Low		598,014	1.18	0.58 – 2.38	0.644
Race					
White		1,397,211	Ref.		
Non-White		376,979	4.15	2.30 – 7.50	<0.001
Gender					0.003
Female		1,031,179	–	–	
Male		743,011	–	–	
Osteoporosis					0.034
Yes		254,210	–	–	
No		1,519,980	–	–	
Gender*Osteoporosis			–	–	0.003
Charlson Comorbidity Index					
0		611,819	Ref.		
1		314,409	3.81	1.64 – 8.83	0.002
2		302,003	2.19	0.88 – 5.49	0.092
3		187,347	2.20	0.72 – 6.72	0.166
4 or greater		358,612	1.98	0.82 – 4.80	0.128
Number of Medications		1,774,190	0.88	0.77 – 1.01	0.063
Interaction Effects					
Gender=Male	Osteoporosis: No vs Yes		>999.9	50.03 – >999.9	0.004
Gender=Female	Osteoporosis: No vs Yes		0.45	0.21 – 0.94	0.034
Osteoporosis=Yes	Gender: Male vs Female		<0.001	<0.001 – 0.004	<0.001
Osteoporosis=No	Gender: Male vs Female		0.33	0.16 – 0.69	0.003

[1] Sample size N was less than 571 due to missing responses.

[2] p values were obtained from ordinal logistic regression. $p < 0.05$ indicates significance.

Note: – Due to complexity of interaction effects, comparisons between levels of gender depend on the level of presence of osteoporosis, and vice versa. So odds ratio estimates of variables included in the interaction term were not reported here but were reported by slicing at the bottom of the table.