ESTIMATION OF DIRECT MEDICAL EXPENDITURES AND HEALTH-RELATED QUALITY OF LIFE (HRQOL) AMONG TYPE-2 DIABETES (T2DM) PATIENTS WITH DEPRESSION USING 2016-2018 MEDICAL EXPENDITURE PANEL SURVEY (MEPS) DATA

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by

UZMA A. PATHAN

Date Submitted:_____ Date Approved: _____

_____ _____

Uzma A. Pathan Dr. Wenchen Kenneth Wu

ABSTRACT

ESTIMATION OF DIRECT MEDICAL EXPENDITURES AND HEALTH-RELATED QUALITY OF LIFE (HRQOL) AMONG TYPE-2 DIABETES (T2DM) PATIENTS WITH DEPRESSION USING 2016-2018 MEDICAL EXPENDITURE PANEL SURVEY (MEPS) DATA

UZMA PATHAN

Background: T2DM patients with depression symptoms (PHQ-2≥3) but without clinical diagnosis remain undiagnosed and untreated. Undiagnosed depression in T2DM patients can exacerbate the patient's health. However, no study has comprehensively evaluated the impact of undiagnosed depression on the direct medical expenditures and HRQoL in T2DM patients.

Objective: To estimate the differences in the total expenditures, expenditures by service type, and HRQoL of T2DM patients with diagnosed, undiagnosed, and no depression.

Methods: A retrospective, cross-sectional study design was implemented using Medical Expenditure Panel Survey data (2016-2018). T2DM patients were stratified using the ICD-10-CM depression code ("F32") and PHQ-2 screener as : (1) Diagnosed (2) Undiagnosed (PHQ-2 ≥ 3 but without depression diagnosis) (3) No depression. The dependent variable was total healthcare expenditures, office-based, hospital outpatient, emergency room, inpatient hospital, prescription, dental, and home health care expenditures for cost-related outcomes. For HRQoL related outcomes, MCS (mental component summary) and PCS (physical component summary) scores were obtained from the SF-12v2/VR-12 questionnaires. Healthcare expenditures were estimated using GLM (generalized linear model) and a two-part model. Regression analysis was used to examine the impact of depression on the HRQoL. Models were adjusted for independent

variables selected using Andersen's behavioral model, and all the expenditures were adjusted to 2018 USD value.

Results: We identified 7078 adults with T2DM, of which 8.99% had undiagnosed depression and 16.30% had diagnosed depression. The incremental expenditure of diagnosed depression was $550 (p=0.755), and for patients with no depression was -$4096 (p=0.005) compared to the undiagnosed depression group. The expenditures based on the service type showed no significant differences in the expenditures between the diagnosed and the undiagnosed depression group. A significant difference of -$563 (p=0.017) was found in the home healthcare expenditures of the no depression group than the undiagnosed depression group.

Compared to adults with undiagnosed depression, the HRQoL scores (MCS: 4.29; PCS: 3.73; p<0.001) were higher for patients with diagnosed depression. Similarly, those with no depression had higher HRQoL scores (MCS: 14.30; PCS 6.59; p<0.001),than the undiagnosed depression patients.

Conclusion: Our findings suggest that if depression symptoms (PHQ≥3) in T2DM patients remain undiagnosed and are not treated, it may contribute to higher expenditures and lower HRQoL. Interventions focused on efficient screening and diagnosis of undiagnosed depression are needed to achieve possible cost savings and better HRQoL.

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LIST OF ABBREVIATIONS

ABM: Andersen Behavioral Model

ADS: Appraisal of Diabetes Scale

ASCVD: Atherosclerotic cardiovascular disease

BRFSS: Behavioral Risk Factor Surveillance System

CAPI: Computer assisted personal interviewing technology

CES-D: Center for Epidemiologic Studies Depression Scale

CPI-M: Consumer Price Index Medical care component

DALY: Disability-adjusted life years

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders-IV

EQ-5D: EuroQoL-5D

FFS: fee-for-service

FPL: Federal Poverty Level

GDS: Geriatric Depression Scale

GHC: Group Health Cooperative

GRH: Green Ribbon Health

HAM-D: Hamilton Rating Scale for Depression

HADS: Hospital Anxiety and Depression Scale

HRQoL: Health related quality of life

ICD9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification

ICD-10 CM: International Classification of Diseases, Tenth Revision, Clinical Modification

IMSS: Mexican Institute of Social Security

MEPS: Medical Expenditure Panel Survey

MHPAEA: The Mental Health Parity and Addiction Equity Act

MCS: Mental Component Summary Score

NHIS: National Health Interview Survey

NHEA: National Health Expenditure Accounts

PA: Physical Activity

PHQ-2: Patient Health Questionnaire-2

PHQ-8: Patient Health Questionnaire-8

PHQ-9: Patient Health Questionnaire-9

PCS: Physical Component Summary Score

PRO: Patient reported outcomes

PHC: Personal Health Care Index

RCT: Randomized control trial

SCID: Structured Clinical Interview for DSM-IV

SCL: Hopkins's symptom checklist

SF-36: Short Form-36

SF-12: Short Form-12

T2DM: Type-2 diabetes

USPSTF: The US Preventive Services Task Force

WMH-CIDI: World Mental Health Survey version of the Composite International Diagnostic Interview

Chapter 1 -Introduction

1.1 Background

According to the National Diabetes Statistics Report, 2020, 34.1 million adults aged 18 years or older—13.0% of all US adults have diabetes. Approximately 90-95% of all diabetes cases can be considered type 2 diabetes(T2DM)[1]. The total estimated cost of diagnosed diabetes in 2017 was $327 billion, $237 billion associated with direct medical expenses, and $90 billion due to reduced productivity[2]. A national representative study found that 88.6% of patients with diabetes have certain comorbid conditions, of which 40.5% are associated with diabetes (concordant comorbidity), and 48.1% are not related to diabetes (discordant comorbidity). Additionally, diabetes patients with discordant comorbidity were found to have higher health care expenditures and lower health-related quality of life (HRQoL) than those with concordant comorbidity[3].

Diabetes-concordant comorbidities (such as cardiovascular and renal diseases) share similar pathophysiologic and management profiles as T2DM. In contrast, diabetes-discordant comorbidities(such as asthma, cancer, and depression) are not associated with the disease pathogenesis, management, or underlying predisposing factor[4]. Treatment of diabetes-discordant comorbidity may interfere with diabetes care management and impair the health outcomes for both conditions. The most common discordant comorbidity in patients with T2DM was found to be depression[5].

The presence of depression is associated with considerable economic burden and poor HRQoL in T2DM patients[6][7]. The financial burden of depression in T2DM patients is related to increased diabetes-related costs due to more inpatient stays, more ambulatory

care visits, and more prescriptions[8]. Studies suggest that successful depression treatment is associated with lower healthcare costs and better HRQoL[9][10][11][12].

Identifying and treating depression in T2DM patients is often recommended, but it is not always done effectively. Previous research indicates that only 28.7% of the US adults with depressive symptoms during the year 2012-2013 received treatment[13]. In addition to this, a 2016 national estimate-based study found that 10.2% of T2DM patients remain undiagnosed for their depression[14]. Because of the lack of a clinical diagnosis, patients might not receive depression treatment, which can exacerbate their health condition. Research attention is therefore warranted to understand the impact of undiagnosed depression in T2DM patients.

1.2 Study Rationale

The likelihood of depression in T2DM is twice that found in the general population [15]. The development of interventions aimed at improving the diagnosis and treatment of depression is necessary to control the depression-associated burden on the healthcare system. Multiple studies have evaluated the impact of clinically diagnosed depression on medical expenditures and the HRQOL in the T2DM population. But individuals without clinical diagnoses may face unique challenges in accessing mental healthcare resources which may prevent them from achieving optimal health state. To our knowledge, no study has comprehensively quantified the effects of undiagnosed depression on healthcare costs and HRQoL in T2DM patients. Therefore, it is essential to evaluate the economic and humanistic burden associated with undiagnosed depression and provide healthcare practitioners and policymakers with up-to-date data for effective planning and implementation of evidence-based interventions. This study aims to examine the total

healthcare expenditures and HRQoL in T2DM patients based on their depression status (diagnosed depression/undiagnosed depression/no depression).

Chapter 2 -Literature Review

The focus of this project is undiagnosed depression in T2DM patients and its impact on the patient's direct medical expenditures and HRQoL. This chapter is divided into two major sections. The first section includes information about the economic burden associated with depression in T2DM patients. The second section describes the humanistic burden associated with depression in T2DM patients. Lastly, the chapter includes information on the covariates and concludes with the identification of research gaps, defining the research objectives and hypothesis.

2.1 Overview of Type 2 Diabetes Mellitus (T2DM)

T2DM is a chronic condition wherein the beta cells in the body do not produce enough insulin – a hormone that regulates blood sugar – or the body does not use insulin well enough (also called insulin resistance), or there is a complete absence of insulin production. T2DM is associated with deleterious microvascular complications (including retinopathy, nephropathy, and neuropathy) and macrovascular complications (such as cardiovascular comorbidities), owing to hyperglycemia and individual components of insulin resistance (metabolic) syndrome[16][17][18]. The high prevalence of T2DM worldwide continues to rise, becoming a serious public health concern. Globally, an estimated 462 million individuals suffer from T2DM, corresponding to 6.28% of the world's population. More than 1 million deaths were associated with diabetes in 2017 alone, ranking it as the ninth leading cause of mortality. In terms of Disability-adjusted life years (DALY's), it ranks as the seventh leading disease. By 2030, the global prevalence of T2DM is expected to rise to 7079 people per 100,000[19].

2.2 Overview of Depression

Depression is a mood disorder characterized by constant sadness and loss of interest. Sometimes called a major depressive disorder, clinical depression, unipolar depression, or simply 'depression' affects how a person may feel, think, and behave and lead to various emotional and physical problems[20]. According to the Diagnostic and Statistical Manual of Mental Disorders(DSM-5) criteria to qualify for depression diagnosis, patients should present a core symptom – (1) depressed mood or (2) loss of interest/pleasure(anhedonia) or both, and at least four of the following symptoms: feelings of guilt or worthlessness, fatigue or loss of energy, concentration problems, suicidal thoughts or thoughts about death, weight loss or weight gain (5% change in weight), psychomotor retardation or activation (change in activity), hypersomnia or insomnia (change in sleep) lasting for at least two weeks[21].

Whenever a clinician suspects depression, the patient should be screened using validated and reliable tools for its identification. The PHQ-2 is useful as a depression screener, with prevalence rates comparable to diagnostic interviews[22]. PHQ-2 inquires about the frequency of depressed mood and anhedonia over the past two weeks by scoring a 0 ("not at all") to 3 ("nearly every day")[23]. PHQ-2 scores can range from 0 to 6, and a cut-off point score ≥3 suggests clinically significant depression. A score of ≥3 has a sensitivity of 83% and a specificity of 92% for depression[24]. However, a score of PHQ-2 ≥3 should prompt either completion of the full PHQ-9 or a clinical interview to provide a clinical diagnosis for depression [23].

2.3 Overview of T2DM with comorbid depression

T2DM and diagnosed depression definition: T2DM patients identified through a standard procedure of clinical interview for depression and having a diagnosis code for depression are referred to as patients with diagnosed depression.

The likelihood of depression in T2DM is twice that found in the general population [15]. Evidence suggests that depression and T2DM are linked through biological mechanisms involving cytokine-mediated inflammatory response, and dysregulation of the hypothalamic-pituitary-adrenal axis, affecting the brain and causing depression[25]. Comorbid depression in T2DM patients is associated with higher rates of macrovascular and microvascular complications, leading to lower HRQoL and higher healthcare costs[26].

To overcome the challenges associated with depression in T2DM patients, identification and treatment of depression are necessary. But depression often goes undiagnosed and thus untreated. A 2016 national estimate-based study found 10.2% of T2DM patients suffer from undiagnosed depression; this lack of clinical diagnosis might prevent the patient from receiving treatment.

T2DM and undiagnosed depression definition: There is no standardized definition for undiagnosed depression; however, in most studies, patients presenting depression symptoms but without a clinical diagnosis are considered to have undiagnosed depression[27][28]. Different studies use the terms for undiagnosed depression such as *unrecognized depression, potential depression, probable depression, and high risk of depression.* Also, different studies use various validated tools like the Beck Depression

Inventory, Hamilton Rating Scale for Depression (HAM-D), Patient Health Questionnaire (PHQ-9), Center for Epidemiologic Studies Depression Scale (CES-D), and Geriatric Depression Scale (GDS-15) for the recognition of depression symptoms[29]. But for the purpose of our study, the term "*undiagnosed depression"* is defined as individuals with PHQ-2 score ≥ 3, i.e., patients with depression symptoms but without ICD-10 diagnosis code of depression ("F32").

2.4 Economic Burden

2.4.1 Costs associated with diagnosed depression

Studies assessing the costs in T2DM patients found that having diagnosed depression is associated with higher expenditures than not having depression. An administrative claims database study identified diabetic (Type 1 and Type 2) patients with and without comorbid depression and analyzed the patient characteristics, treatment patterns, and medical resource use. Results showed that patients with diagnosed depression had greater comorbid conditions, used multiple medications, and used more healthcare services such as inpatient visits, emergency admissions, and outpatient visits. The mean cost of the inpatient($11,275 vs. $9433, $p<0.0001$) and ER visits($692 vs. $443, $p<0.0001$) was higher among those with diagnosed depression than without depression. Overall, total mean costs were higher for those with diagnosed depression($19,707) compared to T2DM patients with no depression($11,237). However, this study included only patients with medical and prescription benefit coverage in a commercially insured plan, and thus the results are not generalizable[30].

Another study was conducted using an 8-year (2004-2011) pooled dataset from Medical Expenditure Panel Survey (MEPS) to understand the economic impact of diagnosed depression in patients with and without diabetes. Inpatient, office-based, and prescription medication costs were the three major components of total medical expenditures. The total mean medical expenditures for patients with diabetes was $10,411 (95% CI 10,005–10,816), and for both depression and diabetes $17,585 (95% CI 16,472–18,699). The next important finding was that while the costs of depression increased over time, and the cost of diabetes decreased over time. The total mean medical expenditures for depression increased from 2004/05 ($7799 95% CI 7319–8280) to 2010/11 ($8500 95% CI 7924–9076). Conversely, the total mean expenditure for diabetes declined from 2004/05 ($11,063 CI 10,065–12,061) to 2010/11 ($10,028 CI 9266–10,790). This particular finding indicates that the emphasis is placed on the treatment of physical complications associated with diabetes leading to lower diabetes-related costs. Whereas a mental condition such as depression may need better screening, diagnosis, and treatment, to slow the increasing expenditures over time. [31].

The next study examined the medical expenditures associated with depression in a nationally representative sample of adults with comorbid diabetes and hypertension. Pooled MEPS data from the year 2013-2015 of adults (≥18 years old) was used, and the presence of depression was identified from the medical condition files using the clinical classification code of "657". The mean expenditures were significantly higher($19,648) for adults with depression than those without depression($11,543). The incremental expenditure of patients with depression was found to be $4607 in comparison to those without depression[7].

Findings from these studies confirm that having depression is associated with higher healthcare expenditures.

2.4.2 Cost-Reduction by diagnosed depression treatment

Cost savings are possible by screening, diagnosis, and treatment of depression in T2DM patients. A study was conducted using nine longitudinal studies between 1991 and 2004 at Group Health Co-operative(GHC), a prepaid health plan in Washington. All the nine studies included were randomized effectiveness trials for comparing depression treatment options. The authors examined the association between outcomes of acute-phase depression treatment and health services cost over subsequent 6 months period. Assessment of depression was done using the Inventory of Depressive Symptoms or the Structured Clinical Interview for DSM-IV. The acute phase treatment outcomes were classified as full remission, partial remission, and persistent depression using the Hamilton rating scale for depression(HAM-D) or Hopkins's symptom checklist(SCL) scale. Full remission was a HAM-D score $\leq$7 or SCL score $\leq$0.7; persistent depression was a HAM-D score $\geq$15 or SCL score $\geq$1.5, and patients not meeting either of the criteria were classified as achieved partial remission.

Data on costs and healthcare service utilization was obtained from the GHC accounting system. Of 1814 patients that met the criteria for depression, only 34% achieved full remission, 37% reported partial remission, and 29% suffered from persistent depression. After adjusting for baseline differences, mean healthcare costs over 6-months following the acute-phase treatment were $2012 for those achieving full remission, $2571 for those who achieved partial remission, and $3094 for those with persistent major depression. The full remission group showed a 10 point decrease(14.0 to 4.3), and the partial

remission group had 4 points decrease(14.5 to 10.9) in the HAM-D scores. Conversely, those with persistent major depression showed no improvement (17.4 to 19.4)in their HAM-D scores. These results reflected that successful depression treatment and achieving full remission were associated with decreased healthcare utilization and expenditures[9]. However, this study comprised of data from randomized clinical trials and included patients only with a single prepaid health plan; thus, the results cannot be generalized to real-world settings.

A retrospective longitudinal cohort study specific to T2DM patients was conducted among working-age (age group 18-64 years) Medicaid beneficiaries with T2DM and newly diagnosed depression. The study examined the association between the depression treatment method and healthcare expenditures. T2DM and depression were identified using diagnosis codes (ICD-9-CM and CPT systems). The study used Medicaid data from 2000–2008 from three states: New York (NY), Texas (TX), and Illinois (IL). The results indicated that, compared to no depression treatment, receiving treatment was associated with a reduction in total healthcare expenditures. The reduction in the total expenditures was between 16%-28% compared to no treatment.[10].

To summarize findings so far, studies demonstrated that T2DM patients with diagnosed depression could have higher healthcare expenditures, and proper treatment can achieve cost reductions. However, the problem is that not enough patients presenting depression symptoms are diagnosed/treated for depression.

Olfson and colleagues examined the prevalence and depression treatment of US adults among a nationally representative household sample using 2012-2013 data. It was found that 34.5% of people presenting depression symptoms are untreated. But, this study

did not investigate if the patients were left untreated due to the absence of clinical diagnosis of depression [32]. Patients that do not have a clinical diagnosis but have depression symptoms suffer from undiagnosed depression.

2.4.3 Costs associated with undiagnosed depression

Studies examining the impact of undiagnosed depression in comparison to diagnosed and no depression have presented inconsistent findings. Luppa and colleagues determined total healthcare costs and service utilization among diagnosed, undiagnosed, and non-depressed primary care patients aged 75 years and older in Germany from a societal perspective. 451 patients were interviewed face-to-face using the Geriatric Depression Scale (GDS-15), a 15-item screening instrument with scores ranging from 0-15. Patients with GDS ≥6 and without clinical diagnosis were identified as undiagnosed depression group. Resource utilization was assessed using a questionnaire of service utilization and costs that was based on cost diaries. Unit costs for all services used and all pharmaceuticals and medical/dental supplies privately purchased or prescribed were estimated to measure healthcare costs. Sixty-three (14%) of the 451 participants in the study had a GDS score≥6. Out of these 63 patients, 38 elderly depressed patients did not receive a diagnosis from their general practitioner and suffered from undiagnosed depression, and 25 had diagnosed depression. Total healthcare costs were €4,722 for the diagnosed depression patients, €5,582 for the undiagnosed depression, and €3,648 for the non-depressed patients. There was no statistically significant difference in the expenditures of diagnosed vs. undiagnosed depression group(p-value=0.911). When comparing the service costs, elderly patients with undiagnosed depression reported higher expenditures for outpatient physician (€415 vs. €339, p=0.911) and non-physician

services(€252 vs. €85, p=0.089), and inpatient care(€2,297 vs. €1,768, p=0.965) than the diagnosed depression group[33]. This study was conducted in the elderly population from Germany; hence the results cannot be extrapolated to the US adults.

An observational study using Medicare claims data of 14,902 participants with diabetes mellitus, congestive heart failure (CHF) was conducted using 12 months (collected between November 2004 and August 2006) data from care management organizations' programs, Green Ribbon Health (GRH), Florida, United States. Patients were classified using the ICD-9 diagnosis code (296.2, 296.3, 298.0, 300.4, 309.0, 309.1, 309.28, 311) from claims data and PHQ-2 score of ≥3 and reports on antidepressants usage. Out of 14,902 patients in the study sample, 2,108 had diagnosed depression,1081 participants had undiagnosed depression(no ICD-9 diagnosis but self-reported antidepressant use/ PHQ-2≥3), and 11,713 were without depression. On comparison, it was found that patients with diagnosed depression ($22,960) had higher total healthcare costs than undiagnosed depression($14,365) and no depression group ($11,956). Participants with diagnosed depression had the highest costs in all service categories. The undiagnosed depression patients had higher home-healthcare($1,322 vs. $790, p<0.001) expenditures than those without depression.[34]. But as this study included only Medicare patients from Florida, the results are not generalizable.

Another study examined the healthcare expenditures among community-dwelling older adults using 2008-2009 MEPS data. Depression was diagnosed using the ICD-9 code("311"), and those without the ICD-9 code but having PHQ-2≥3 was categorized as having undiagnosed depression. The mean expenditures were higher for those with undiagnosed depression($17,603) than those with diagnosed depression($15,928), and

no depression($8,903). Diagnosed depression group had higher expenditures than the undiagnosed depression patients across all service categories, except for home-health care($8,067 vs. $15,561) and ER($1,654 vs. $1,868) costs that eventually contributed to higher total costs associated with undiagnosed depression. Similarly, undiagnosed depression had higher home-health care($15,561 vs $6,394), inpatient($21,375 vs $16,293) and prescription($2,812 vs $2,236) costs than no depression group [35].

The previously mentioned studies mainly included the older population and did not have a representative sample of an adult population. Okunrintemi et al. conducted a study aimed to compare healthcare expenditures among atherosclerotic cardiovascular disease (ASCVD) patients ≥ 18 years of age using (2004–2015) MEPS data. Individuals with an ICD-9-CM code of "311" were classified as having diagnosed depression and those without a clinical diagnosis but having PHQ-2≥ 4 as undiagnosed depression. It was found that out of the total 19,840 ASCVD patients, 3704 had diagnosed depression, 1803 had undiagnosed depression. Those with undiagnosed depression($13221) reported lower total expenditures than the diagnosed depression($14086) group and higher than no depression($10154). After adjustments including relevant covariates, the marginal difference(-$865; 95% CI:− 1828, 136; p=0.07) in the total expenditures of the undiagnosed depression group compared to the diagnosed depression was not statistically significant. Conversely, compared to the patients without depression, the patients with undiagnosed depression had significantly higher expenditures ($2876; 95% CI:2574, 3177; p<0.001) [36].

As the focus of our study is patients with T2DM, to our knowledge, only one study was conducted on T2DM patients to examine the impact of depression status on healthcare

costs. Egede et al. used the MEPS data from the year 2004–2011 to estimate the cost of depression among adults with diabetes (aged ≥18 years). ICD-9 code (diagnostic codes for depression 296, 300, 309, 311) and PHQ-2 scores with a cut point of ≥3 were used to classify patients as those with diagnosed and undiagnosed depression. Patients with diagnosed depression were further subdivided as Asymptomatic diagnosed depression, individuals with an ICD-9 diagnosis of depression but with PHQ-2<3; and Symptomatic depression: individuals with both ICD-9 diagnosis of depression and PHQ-2≥3.

The overall mean medical expenditures for T2DM patients were $15,155 for undiagnosed depression, $16,134 for asymptomatic diagnosed depression, $20,105 for symptomatic diagnosed depression and $10,016 for no depression. The symptomatic diagnosed depression group reported the highest expenditures across all service categories. The undiagnosed depression group had lower costs for all the healthcare services, except for inpatient and outpatient costs, which were slightly higher than asymptomatic diagnosed depression[14]. Whereas, in comparison to the no depression group, undiagnosed depression patients had higher costs across all the service-type. The higher total medical expenditures among patients with diagnosed depression than undiagnosed depression may be the result of receiving treatment. Also, in this study, the ICD-9 diagnoses codes used to identify depression were not specific to major depression and included various mood and anxiety disorders, which might have led to the overestimation of the costs associated with diagnosed depression.

To summarize, results from studies reviewed so far have reported inconsistent information related to the economic burden associated with undiagnosed depression compared to diagnosed and no depression. Studies conducted in the older population

reported higher expenditures in patients with undiagnosed depression than diagnosed depression. On the contrary, studies conducted in the general adult population reported higher expenditures for diagnosed depression than undiagnosed depression. However, in all the studies, undiagnosed depression was associated with higher expenditures than no depression. Only one study by Egede et al. was conducted in T2DM patients, but it used the “no depression” group as a reference for the analysis. At present, no study has done direct comparisons using the undiagnosed depression group as a reference in T2DM patients. Additionally, there is also a need to investigate the healthcare costs by service type to identify the major contributor to the total expenditures. This will help adopt strategies to monitor the use of these services and reduce the total costs accordingly.

2.5 Patient-reported outcome (PRO)

Any report of a patient's health status that comes directly from the patient, without any interpretation of the patient's response by a physician or anyone else, is referred to as a PRO[37]. It contains information on physical functioning, psychological well-being, global health perception, treatment satisfaction, and other subjective outcomes used to measure the HRQoL[38]. HRQoL is a multidomain concept representing the patient's general perception of the effect of illness and treatment on physical, psychological, and social aspects of life. In recent years in patients with T2DM beyond the clinical parameters, HRQoL has been recognized as an essential goal of healthcare. It has been recommended to assess HRQoL in diabetes care routinely. It allows to understand the unmet needs of the patients and carefully address those problems to achieve better outcomes[39].

Different measurement scales that propose to measure HRQoL in T2DM patients have been developed. Some are disease-specific(Audit of Diabetes-Dependent Quality of Life, Diabetes Quality of Life, Appraisal of Diabetes Scale (ADS)), used only for the condition for which they have been developed. Whereas others, termed as generic measurements(Short Form-36 (SF-36), Short Form-12 (SF-12), and EuroQol EQ-5D instruments), have broader applications across illness groups.

As MEPS consists only data related to SF-12v2, for the purpose of our study, it was important to ensure if SF-12 is an appropriate instrument to study the HRQoL measure in T2DM patients. A study was conducted to validate the use of SF-12v2 in diabetic patients using (2011–2013) MEPS data. Reliability (internal consistency and test-retest) and validity (construct, concurrent, criterion, and predictive) of the SF-12v2 were assessed. It was concluded from this study that SF-12v2 is a valid generic instrument for measuring HRQoL measures in T2DM patients[40].

Additionally, just examining if a relationship exists between depression status and HRQOL in people with T2DM is not sufficient and checking for clinical relevance is equally important. As statistical significance does not always translate to clinical relevance, HRQOL research demonstrating a minimally important difference (MID) has become necessary[38]. It is reported that mean differences of 2.0–2.5 points on HRQoL scales among patients with T2DM diabetes are clinically meaningful differences on SF-12 subscales based on Cohen's standardized effect size [41].

2.6 Humanistic Burden

2.6.1 T2DM and Health-related quality of life (HRQoL)

Diabetes is a chronic disease that causes microvascular complications (e.g., retinopathy and neuropathy) and macrovascular complications (e.g., myocardial infarction, angina pectoris, and stroke), leading to a poor HRQoL. Studies have been conducted to assess the impact of diabetes on the HRQoL of individuals suffering from it[42][43].

A study by Graham et al. examined the differences in the HRQoL among community-dwelling older (≥70 years) Mexican Americans with and without T2DM. Participants (n = 619) from the Hispanic Established Population for the Epidemiological Study of the Elderly were interviewed in their homes. HRQoL was measured using the SF-36 questionnaire, where scores range from 0 to 100, with higher values reflecting better HRQoL. Individuals with diabetes reported significantly lower PCS scores (37.50 vs. 43.04, $p<0.001$) than those without diabetes. There were no significant differences in the MCS scores among the groups of patients[42].

A cross-sectional study using data from the 2014-2015 Medical Expenditure Panel Survey (MEPS) was conducted in Hispanic community-dwelling residents with T2DM. HRQoL was assessed using the SF-12 scores. Patients with T2DM reported significantly lower PCS(-5.37, $p<0.001$)and MCS (-2.93, $p<0.001$) scores than those without T2DM [43].

2.6.2 Impact of depression on the HRQoL of T2DM patients

Studies have shown that depression can have a negative impact on the HRQoL in T2DM patients. A cross-sectional study with T2DM patients(aged≥18 years) was conducted to investigate the changes in the HRQoL and the factors related to the changes. Patients were selected from five hospitals belonging to the Mexican Institute of Social Security (IMSS) in different cities in Mexico. The variables related to HRQoL included were age, sex, occupation, marital status, years of T2DM evolution, comorbidities, and presence of depression; identified using Beck Depression Inventory. HRQoL was assessed using the SF-36 where patients were classified according to SF-36 scores as: < 50 (poor HRQoL), 51-75 (acceptable HRQoL), and > 76 (optimal HRQoL)points. Out of 1394 patients, almost half of the patients(49.4%,n= 690) had an HRQOL score lower than 50 points, indicating a poor HRQoL, and only 1.5% (n = 22) of the patients had a score higher than 75, showing an optimum HRQoL. The results suggested that among all the factors studied, depression(OR 4.4, 95% CI 2.03 to 9.9) was one of the most influencing independent factors that lead to the impairment in HRQoL [6]. This study was conducted in the Mexican population, and thus the results cannot be extrapolated to the US population.

Egede et al. conducted a study examining the effects of depression on HRQoL in an indigent population with T2DM in the United States. Depression was examined with the Center for Epidemiological Studies–Depression(CES-D) Scale, a 20-item scale with scores ranging from 0-60; a score ≥16 is considered as having depression. HRQoL was assessed using the MCS and PCS scores computed using SF-12. In the study sample (n=201), 20% (n=40) were depressed with significantly lower SF-12 PCS (36.1 vs.

39.0,P<0.001) and MCS (41.6 vs. 46.8,P<0.001) scores compared to the non-depressed patients[44].However, this study was conducted in an economically weaker section making the results not generalizable.

2.6.3 Depression treatment improves HRQoL in T2DM patients

Studies have shown that depression treatment in T2DM can improve HRQoL[11][12]. A Finland-based RCT randomized control trial) was conducted to evaluate the effect of the antidepressant paroxetine on HRQoL in depressed T2DM patients(aged 50–70 years). HRQoL was assessed using the overall SF-36 scores. After three months of treatment with paroxetine, there was a statistically significant difference between the treated group versus the placebo group (mean difference = 11.0 points, p = 0.039) [11].

A longitudinal study was conducted using the (2005-2011) MEPS dataset of adults (aged≥21 years) with T2DM and depression. Individuals that received psychotherapy with/without antidepressants had higher PCS scores (beta = 1.28, $p < 0.001$), and those using antidepressants only reported higher MCS scores(beta =0.56, $p < 0.001$) compared to those without any treatment [12].

It should be noted that these studies included patients with diagnosed depression for examining the impact of depression treatment on the HRQoL. However, patients that do not seek treatment due to a lack of diagnoses may be untreated with the worst health outcomes. Patients suffering from undiagnosed depression might not have access to depression treatment leading to poor HRQoL.

2.6.4 Impact of undiagnosed depression on HRQoL

Studies have shown that undiagnosed depression patients have poorer HRQoL compared to patients with diagnosed and no depression. A recent study was conducted on patients with Multiple Sclerosis(MS) to examine the impact of undiagnosed depression on their HRQoL. A total of 742 Canadians over the age of 55 with MS were included in the study. Self-reported depression diagnosis and the Hospital Anxiety and Depression Scale(HADS) depression scale score (range 0-21) was used to categorize patients as diagnosed and undiagnosed. No clinical diagnosis of depression and HADS score> 11 was referred to as undiagnosed depression. HRQoL was measured using a 100 mm visual analog scale in which respondents indicated their health state from 0 (worst possible health state) to 100 (best possible health state).Patients with undiagnosed depression(45.76 ± 23.37) reported lower HRQoL compared to diagnosed depression (55.04 ± 23.53) and no depression patients(60.17 ± 23.05)[45].

Okunrintemi et al. conducted a study using MEPS (2004–2015) data to compare HRQoL status among atherosclerotic cardiovascular disease (ASCVD) patients ≥ 18 years of age. Individuals with an ICD-9-CM code of 311 were classified as having depression and those without a clinical diagnosis but having PHQ-2≥ 4 as undiagnosed depression. HRQoL was assessed using the MCS and PCS scores obtained from the SF-12 questionnaire. Compared to the diagnosed depression group, those with undiagnosed depression presented poor HRQoL estimates (PCS: -4.65, MCS: -8.03, $p<0.006$). Similarly, compared to patients without depression, those with undiagnosed depression presented worse HRQoL scores (PCS: -9.75, MCS: -19.69, $p<0.001$). The authors suggested that patients with a clinical diagnosis of depression were probably on treatment

and, therefore, more likely to have better HRQoL outcomes. Conversely, the undiagnosed patients without any treatment for their depressive symptoms might have reported adverse health outcomes[36].

These studies proved an association between undiagnosed depression and poor HRQoL but were not conducted in T2DM patients. The high prevalence(10.2%) of undiagnosed depression in T2DM patients makes it necessary to evaluate the impact of undiagnosed depression on the HRQoL. Hence, in our study, we will evaluate the impact of undiagnosed depression on the HRQoL of T2DM patients.

2.7 Factors affecting the healthcare expenditures and HRQoL

The purpose of this project is to study the impact of undiagnosed depression on expenditures and HRQoL. Apart from classifying a patient as having diagnosed, undiagnosed, or having no depression, there is a need to identify factors that can influence the costs and outcomes. The selection of these independent variables was based on Andersen's Behavioral Model(ABM) of Health Services Use [46]. The model can be used to predict an individual's use of health services, and studies have also used it as a guide to identifying variables that can affect HRQoL[47][12][48]. The constructs of the model include predisposing, enabling, and need factors. The variables included based on the specific constructs are (1) predisposing factors (gender, race, and age); (2) enabling factors (marital status, education, poverty status, health insurance coverage); (3) need factors (chronic conditions); (4) personal health practices (smoking status and physical activity); and (5) the external environment (region) (*see Figure 1*).

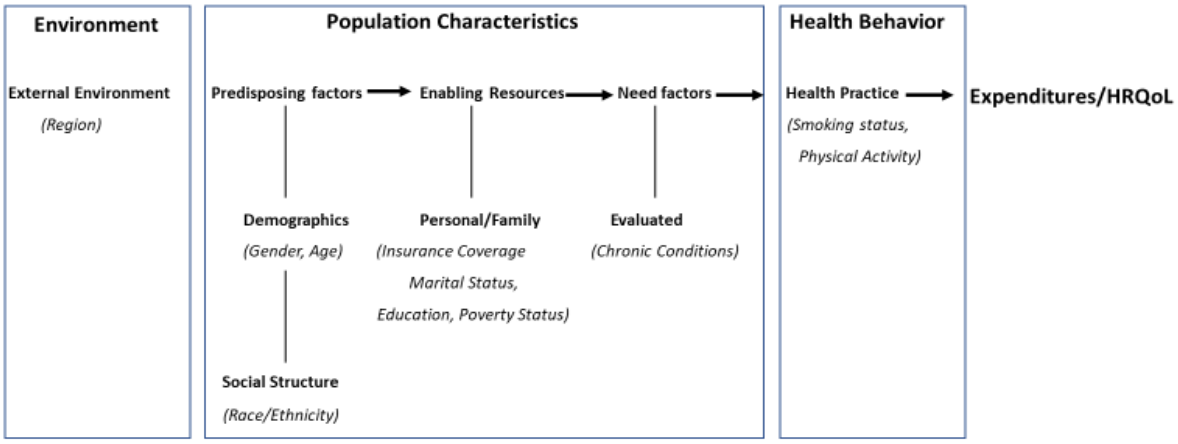


Figure 1: Andersen Behavioral Model

Predisposing factors

Predisposing characteristics influence one's predisposition to use a healthcare resource. These influences include demographics and social structure. Demographic factors include variables such as sex and gender. The social structure includes variables like socioeconomic status and race.

Age: Elderly patients with T2DM have a higher likelihood of having undiagnosed depression than diagnosed and no depression. Egede et al. conducted a study in T2DM patients and reported that patients with undiagnosed depression(41.0%) were more likely to be present in the 65–85 age group than diagnosed depression(37% asymptomatic diagnosed and 28.6% symptomatic diagnosed ; $p<0.001$) and no depression(40.6%) [14].

Gender: A study was conducted using Behavioral Risk Factor Surveillance System(BRFSS) data to assess the prevalence and correlates of undiagnosed depression among adults with diabetes. Depression was assessed using the PHQ-8 questionnaire. It

was found that the female gender (PR, 1.4; 95% CI: 1.1–1.8, P = 0.002) was associated with having undiagnosed depression than males in T2DM patients[49].

Race: A US-based cross-sectional study involving 740 diabetic patients investigated the racial/ethnic variation in the presence of depression and its diagnosis by the physician in a community sample between the years 2004-2005, respectively. The presence of diagnosed depression was based on self-reporting, and undiagnosed depression was identified as a CES-D score≥16 and absence of a clinical diagnosis. Similar rates of depression symptoms were found among White, African-American, and Latino persons. However, African-Americans reported lower rates of physician-diagnosed depression than Whites (OR = 0.470, 95% CI 0.298–0.744). This finding reflected that minorities were likely to remain undiagnosed and untreated for their depression. The reasons for these racial differences were provided as African-American patient's refusal of depression treatment or use of alternative depression therapies, lesser prescription benefits, or physician's uncertainty or bias in prescribing[50].

Enabling factors

Enabling resources are ones that influence an individual's decision to use a healthcare resource, such as the availability of medical facilities and healthcare personnel. The most common enabling factors include measures that examine things such as an individual's geographic location, income level, and insurance coverage.

Marital status: A study conducted in the US to investigate levels and risk of depression symptomatology in T2DM patients reported that unmarried individuals(OR=1.55) were associated with a higher likelihood of being depressed[51]. Similar results were obtained

from a recent study conducted in the Saudi population to determine the predictors of depression among T2DM patients. [52]. However, there is no information available on the association of marital status and undiagnosed depression in T2DM patients.

Education: A US population-based study was conducted to determine the behavioral and clinical characteristics of T2DM that are associated with depression. Data was obtained from nine primary care clinics of a health maintenance organization. PHQ-9 was used to identify depression in these patients. The study results reported that those with less than high school education levels were associated with a higher likelihood (OR= 1.34, 95% CI= 1.04-1.72) of having depression[53]. Similarly, Egede et al. reported that those with less than high school education had a higher likelihood of having undiagnosed depression(39.5% vs. 20.3% (asymptomatic diagnosed), 32.0% (symptomatic diagnosed); $p<0.001$)[14].

Poverty Status: A study was conducted on T2DM patients to examine the association between depression and personal income. Depression was defined as a score of ≥3 on the two-item Patient Health Questionnaire (PHQ-2)[54]. It was found that among adults with T2DM, depression was associated with $2838 lower personal income after adjusting for relevant covariates. As explained by the authors, the reason for this finding was that the individuals with both T2DM and depression have a higher functional disability, which could lead to lower income. Egede et al. analyzed the 2004–2011 MEPS data of T2DM patients with comorbid depression and found that individuals with undiagnosed depression had a significantly higher percentage of low-income individuals. 22.2% of individuals with undiagnosed depression belonged to the low-income category, compared

to 19.6% of those with symptomatic diagnosed depression, 14.1% with asymptomatic diagnosed depression, and 15.5% without depression [14].

Insurance Coverage: A study was conducted using 2014-2015 MEPS data to estimate the prevalence of depression screening/treatment in adults age≥35 and examine how the prevalence varies based on sociodemographic characteristics and depressive symptoms. The presence of depression symptoms was assessed based on the score of ≥3 on the PHQ-2 questionnaire. The study reported that the uninsured individuals with PHQ≥3 were less likely to be assessed(screened/treated) for depression than those with private insurance coverage (OR=0.30; 95% CI=0.18 – 0.51). There was no significant difference between adults with public insurance compared with any private health insurance**.** Similar findings were obtained from the study by Egede et al., a significantly higher proportion (12.4%) of undiagnosed depression patients were uninsured than (4.9%) asymptomatic diagnosed depression, (9.4%) symptomatic diagnosed depression [14].

Need factors

The need construct examines the general health and functional state of an individual and its effect on the use of healthcare resources. These include a person's experience of symptoms of illness, pain, and worries about their health, and their judgment to seek medical care. The presence of various chronic conditions is mostly used as a need factor.

Chronic conditions

A multi-country, cross-sectional study was conducted to estimate the association between depression/undiagnosed depression and chronic diseases(asthma, arthritis, and stroke). Data was obtained from the WHO Study on global AGEing and adult health (SAGE)

Wave 1 (2007–2010). Depression was evaluated based on the World Mental Health Survey version of the Composite International Diagnostic Interview (WMH-CIDI). Undiagnosed depression was defined as a depressed person who did not report a history of diagnosis/treatment for depression. Chronic conditions like arthritis (OR-2.14, 95% CI: 1.82,2.52), asthma (OR-3.36, 95% CI: 2.73,4.14), and stroke (OR-3.14, 95% CI: 2.55,3.86) were found to be associated with depression (p-values < 0.001). Similar odds ratio were found in patients with undiagnosed depression and arthritis (OR-2.37, 95% CI: 1.99,2.81), asthma (OR-3.21, 95% CI: 2.56,4.04]), and stroke (OR-3.11, 95% CI: 2.47,3.91)[55].

In addition to these conditions associated with diagnosed and undiagnosed depression, MEPS includes certain conditions designated as "priority conditions" due to their higher prevalence, expense, or relevance to policy. Some of these are long-term, life-threatening conditions, such as cancer, emphysema, hypertension, and stroke. Others are chronic manageable conditions, including arthritis and asthma[56]. Hence, it is important to evaluate the impact of these comorbid conditions on the medical expenditures and HRQoL in T2DM.

Personal health practices

Smoking: A population-based study was conducted to determine the behavioral and clinical characteristics of T2DM patients that are associated with depression. The study results reported that smoking was associated with a higher likelihood (OR= 2.15, 95% CI= 1.56-2.95) of depression symptoms[53]. Similar results were obtained from a study investigating the association between depression and smoking status of T2DM patients in a Canadian community. The results indicated that in T2DM patients, heavy smokers were

over twice as likely to have major depression compared to non-smokers (OR=2.62; 95% CI=1.43-4.81)[57].

Physical Inactivity: A systematic review based on the association of physical activity and depression in T2DM reported that inactive patients are 1.72 to 1.75 times more likely to be depressed than the more active[58]. A similar finding was observed from a study investigating the correlates of undiagnosed depression in T2DM patients; the absence of physical activity(PR=1.5; 95% CI: 1.2–1.9) was associated with undiagnosed depression[49].

2.8 Gaps in the literature

The studies reviewed so far indicated that having diagnosed depression in T2DM patients is associated with higher healthcare service utilization leading to higher medical expenditures[30][31][7]. It was then recommended that successful treatment of depression could help reduce the costs. Although studies have demonstrated that treatment of depression can lead to cost-savings, but not enough patients are diagnosed and treated for depression [9][10]. To the best of our knowledge, the literature is void of information related to undiagnosed depression.

When considering cost-based studies related to undiagnosed depression, studies have included older populations or patients with other disease conditions like- CHF and ASCVD[33][34][36]. There is only one study that evaluated the costs associated with undiagnosed depression in T2DM patients using 2004–2011 MEPS data. However, the ICD-9 code (diagnostic codes for depression 296, 300, 309, 311) used in this study to identify patients with depression included patients with depression and other mood and

anxiety disorders[14]. Including patients with mood disorders other than depression can overestimate the costs associated with diagnosed depression compared to undiagnosed depression. Hence, our study patients will be identified using a single ICD-10 code (diagnostic code for major depression "F32") and PHQ-2 questionnaire. Also, there is no recently published data on the medical expenditures categorized by the service-type T2DM patients with depression.

Additionally, the presence of depression in T2DM patients can lead to impairment in the HRQoL. Studies so far have evaluated the impact of only diagnosed depression on the HRQoL of T2DM patients, excluding the undiagnosed depressed patients. These undiagnosed patients with depressive symptoms, if left untreated, can have the worst health outcomes. Hence, it is important to investigate both the economic and humanistic consequences of undiagnosed depression in T2DM patients in a nationally representative sample. Findings from this study will help identify the key issues associated with undiagnosed depression and develop healthcare interventions tailored towards the unmet needs of the patients.

2.9 Research Objectives and Hypotheses

Based on the reviewed literature and considering the research gaps following research objectives and hypothesis for the proposed study have been developed:

Objective 1: To estimate the total medical expenditures of T2DM patients with diagnosed, undiagnosed, and no depression.

Objective 2: To estimate the differences in the medical expenditures by service type of T2DM patients with diagnosed, undiagnosed, and no depression.

Objective 3: To estimate the differences in the HRQoL of T2DM patients with diagnosed, undiagnosed, and no depression.

Research Hypotheses

Hypothesis 1:

Luppa et al. found that patients with undiagnosed depression(€5,582) had higher healthcare costs than diagnosed(€4,722) and no depression(€3,648)[33]. Another study in community-dwelling older adults using MEPS reported higher expenditures for patients with undiagnosed depression($17,603) compared to diagnosed($15,928) and no depression($8,903)[35]. These findings confirm that patients who may not be treated due to lack of a clinical diagnosis may incur higher costs than those with diagnosed depression. Adults with undiagnosed depression may require other healthcare services like emergency department visits and inpatient stays for other chronic medical conditions that are exacerbated by an untreated depression, which can further increase health care costs. In 2011, Medicaid enrollees with mental health conditions accounted for 27 percent in enrollment but 53 percent in total expenditures due to their intensive health care needs, including office visits, inpatient stays, emergency department visits, and prescription drugs[59]. Hence, our first hypothesis was based on the assumption that T2DM patients with undiagnosed depression may not be treated for depression and thus led to higher expenditures.

H1: "Having undiagnosed depression in T2DM patients is associated with significantly higher total medical expenditures than diagnosed and no depression".

Hypothesis 2:

Choi et al. found that patients with undiagnosed depression had higher home-health care($8,067 vs. $15,561) and emergency costs($1,654 vs. $1,868) than diagnosed depression patients, which contributed to higher overall costs associated with undiagnosed depression. Also, undiagnosed depression had higher home-health care($15,561 vs $6,394), inpatient($21,375 vs $16,293) and prescription($2,812 vs $2,236) costs than no depression group [35]. Another study reported that older patients with undiagnosed depression had higher expenditures for outpatient(€415 vs. €339) and inpatient care(€252 vs. €85) than diagnosed depression. Likewise, these patients with undiagnosed depression had higher costs for all service types than those without depression [33]. Similarly, Egede et al., in a study conducted in T2DM patients, found that undiagnosed depression had higher inpatient and outpatient costs than asymptomatic diagnosed depression patients. Also, undiagnosed depression patients had higher expenditures for all service types than the no depression group. Therefore, our second hypothesis was based on the findings from the previous studies that showed undiagnosed depression could lead to higher expenditures based on the healthcare service type.

H2: "Having undiagnosed depression in T2DM patients is associated with significantly higher medical expenditure by service-type than diagnosed and no depression".

Hypothesis 3:

A study conducted in patients with Multiple sclerosis found that patients with undiagnosed depression(45.76 ± 23.37) reported lower HRQoL compared to diagnosed depression (55.04 ± 23.53) and no depression patients(60.17 ± 23.05) [45]. Similarly,

Okunrintemi et al. found that in ASCVD patients, compared to the patients with diagnosed depression, those with undiagnosed depression(PCS:-4.65, MCS: -8.03) presented lower HRQoL[36]. Hence, our third hypothesis was based on the assumption that T2DM patients with undiagnosed depression may not receive any treatment for their depression symptoms which can worsen their health-related outcomes.

H3: "Having undiagnosed depression in T2DM patients is associated with significantly lower HRQoL than diagnosed and no depression".

Chapter 3 Methods

This chapter provides an overview of the methodology used to conduct the study. The following topics will be discussed in this chapter: (1) study design, (2) data source, (3) study data, (4) description of the variables, (5) and data analysis.

3.1 Study Design

This is a retrospective, cross-sectional study conducted using Medical Expenditure Panel Survey (MEPS), a nationally representative secondary dataset. Data collected from MEPS is available to the public online at https://meps.ahrq.gov/mepsweb/.

3.2 Data Source

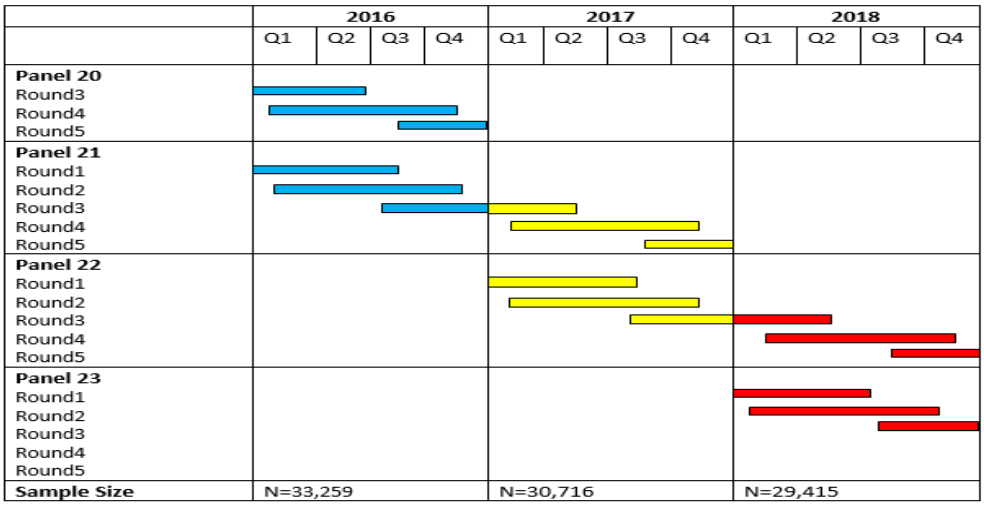
The Medical Expenditure Panel Survey, which began in 1996, is a set of large-scale surveys of families and individuals, their medical providers (doctors, hospitals, pharmacies, etc.), and employers across the United States. MEPS currently has two major components for which data are released: the Household Component and the Insurance Component. The Household Component data are based on questionnaires fielded to individual household members and their medical providers. The Insurance Component estimates come from a survey of employers conducted to collect health insurance plan information[60].

The data for this study comes from the Medical Expenditure Panel Survey Household Component (MEPS-HC). MEPS provides nationally representative estimates of health care use, expenditures, sources of payment, and health insurance coverage for the U.S. civilian noninstitutionalized population. The MEPS Household Component (HC) also provides estimates of respondents' health status, demographic and socio-economic

characteristics, employment, access to care, and satisfaction with health care. Estimates can be produced for individuals, families, and selected population subgroups. An overlapping panel design is used, including five rounds of interviews covering two full calendar years (*refer to figure 2*). Using computer-assisted personal interviewing (CAPI) technology, information about each household member is collected, and the survey builds on this information from interview to interview. All data for a sampled household are reported by a single household respondent. Each annual MEPS-HC sample size is about 15,000 households. Data can be analyzed at either the person or event level. Data must be weighted to produce national estimates.

Upon completion of the household CAPI interview and obtaining permission from the household survey respondents, a sample of medical providers are contacted by telephone to confirm or supplement information received from participants of the MEPS Household Components [61].

Figure 2: MEPS panel design: data reference periods[62]



N is equal to the number of people with the positive person weight on the file

3.3 Study data

3.3.1 Data files used for extraction

In this study, data with all information related to total expenditures and HRQoL was extracted from MEPS Full-year consolidated and Medical Conditions files for the years 2016-2018.

(years 2016-2018).

1. Full-year Consolidated file: This file consists of information pertaining to survey administration, demographics, income, person-level conditions, health status, disability days, quality of care, employment, health insurance, and person-level medical care use and expenditures[61].

2.Medical Conditions file: This file contains information on the medical conditions reported by the Household Component respondent recorded by the interviewer as verbatim text. Professional coders then code these conditions according to ICD-10-CM codes. To preserve confidentiality, all the conditions provided on this file have been coded to 3-digit diagnosis code categories rather than the fully-specified ICD-10-CM code. For example, the ICD10CDX value of F31 "Bipolar disorder" includes the fully-specified subclassifications F3110 through F319[56].

Each survey year has a separate consolidated, and medical conditions file to obtain information on the participants for that particular year. Accordingly, for the three years of our study data, full year-consolidated and medical conditions file specific to that calendar year was used. *(see Table 1)*

Table 1: MEPS files used in this study

Year	Full-year Consolidated Data File	Medical Conditions File
2016	**HC-192**	**HC-190**
2017	**HC-201**	**HC-199**
2018	**HC-209**	**HC-207**

3.3.2 Identification of the study population

Patients with T2DM were identified from the MEPS HC medical conditions file using ICD-10 code "E11," and depression were identified using ICD-10 code "F32". However, it should be noted that MEPS does not differentiate between type (1 or 2) of diabetes, meaning anyone with a current diabetes diagnosis is all coded to T2DM as part of data processing. But, based on data from the Centers for Disease Control and Prevention, 90–95 % of diagnosed diabetes cases are of T2DM[1].

3.3.3 Inclusion and Exclusion criteria

Inclusion criteria

As our study's main sample population involves adults with T2DM, survey participants with a self-reported diagnosis of T2DM were included. The T2DM patients were identified if they responded "yes" to the question-*Other than during pregnancy. have*

you ever been told by a doctor or other health professional that you had diabetes or sugar diabetes? All the participants included were of the age ≥18 years.

Exclusion criteria

Respondents with missing scores for the PHQ-2 and SF-12v2/VR-12 were excluded from the study as we required the PHQ-2 scores to classify the T2DM patients into undiagnosed and no depression. Those with missing PCS and MCS scores were excluded as these scores were required to examine the HRQoL outcome variable. Excluding these patients should not impact much as most of them belonged to the "no depression group."

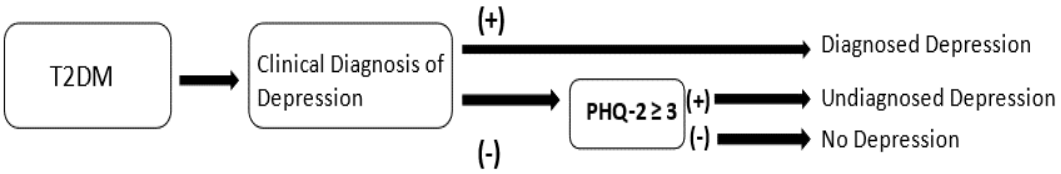
3.3.4 Group classification

ICD-10 code "F32" (clinical diagnosis code of depression) and PHQ-2 ≥3 as the cut-off score were used to categorize the T2DM patients based on their depression status. Responses to the PHQ-2 were used to identify depression symptoms. The PHQ-2 is a two-question self-reporting depression screening tool included in the MEPS questionnaire. The PHQ-2 using a cut-point of ≥3 has a sensitivity of 83 % and specificity of 92 % for identifying depression. Based on the presence/absence of the ICD-10 code for depression, patients were segregated as having diagnosed depression or not. Those without the ICD-10 code were then classified as having undiagnosed depression(PHQ-2≥3) and no depression(PHQ-2<3) using the PHQ-2 scale as mentioned below(*see Figure 3*):

1. Diagnosed depression, individuals with ICD-10 diagnosis code of depression only.

2. Undiagnosed depression, individuals with PHQ-2 depressive symptoms (≥3) but without ICD-10 diagnosis of depression.
3. No depression, individuals with neither depression symptom (PHQ-2<3) nor ICD-10 diagnosis of depression.

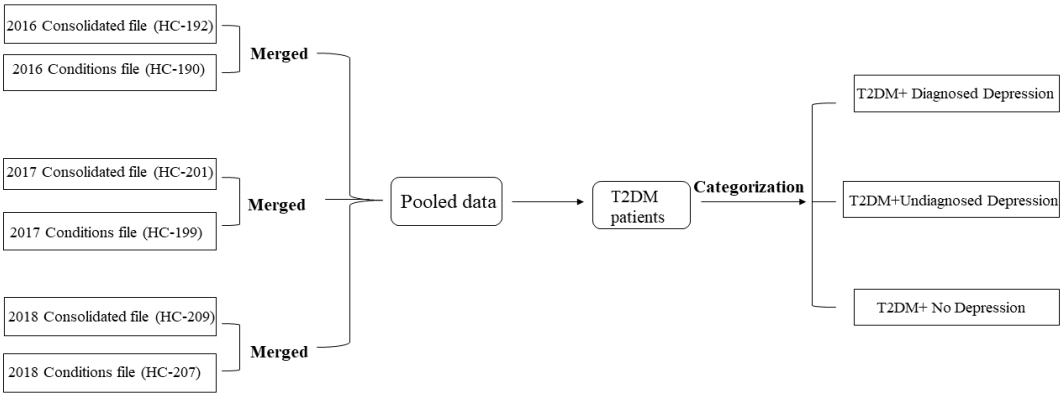
Figure 3: Classification of the study sample based on depression status



3.3.5 Final Analytic Data Set

The data linkage process to create the analytic dataset is shown in Figure 4. For the study, Full-year consolidated files were merged with their respective medical conditions files to obtain the pooled data set. All the files were merged using DUPERSID as a link variable which is a unique patient identifier, across three years of data files (2016, 2017, and 2018). From the pooled data, patients having ICD10 diagnosis codes “E11” for T2DM and “F32” for depression were extracted and categorized as T2DM+Diagnosed depression. The remaining T2DM patients without ICD-10 code “F32” of depression were further classified into undiagnosed(PHQ-2≥3)and no depression(PHQ-2<3) groups using their PHQ-2 scores.

Figure 4: Steps to obtain the final analytic dataset



3.4 Description of Study variables

T2DM and depression in patients were identified using the **ICD10CDX** variable describing medical conditions reported by respondents in the MEPS questionnaire from the Medical conditions file. The ICD10CDX value for T2DM used for our study was "E11," and for depression was "F32". Once T2DM patients with and without depression were obtained, those without depression diagnosis code were then categorized using the PHQ242 variable.

The variable used to classify the patients using their PHQ-2 scores was **PHQ242** obtained from the full-year consolidated files. **PHQ242** is the summation of the values of the two variables below, with scores ranging from 0 through 6. The SAQ includes mental health questions to assess the frequency of the person's depressed mood and decreased interest in usual activities using the following two questions:

ADINTR42 – During the past two weeks, bothered by having little interest or pleasure in doing things

ADDPRS42 – During the past two weeks, bothered by feeling down, depressed, or hopeless

The response score value for each of these two questions ranges from 0-3. Patients having score≥3 without a depression ICD-10 CM diagnosis code ("F32") were identified as patients with undiagnosed depression.

3.4.1 Independent Variables

These variables were selected using the ABM model.

Sex: Data on the gender of each individual was gathered from NHIS. The **SEX** variable was verified for each year during the MEPS interview. When gender was not available from both NHIS interviews and MEPS interviews, the gender was assigned based on the first name of the person. If the first name gave no indication of gender, then family relationships were reviewed. If none of these approaches were effective, then gender was randomly assigned.

Age: The date of birth and age of each individual was asked during the MEPS interview. **AGE16X/17X/18X** were the age variables that were used for this study for the year 2016-2018. The AGE variable indicates an individual's age calculated from its data of birth to the last day of the calendar year. The range for AGE is between 0 and 85. We divided the AGE into the following groups: 18-44, 45-64, and 65+.

Race: The racial background-related questions were asked during the MEPS interview. **RACEV1X** is an imputed variable denoting the six categories of races: White only, Black only, Native American, Asian, Native Hawaiian/Pacific Islander, and multiple

races. The races involving Native Americans, Asians, Native Hawaiian, and others were collapsed into one single category called “others” for the analysis.

Marital Status: Marital Status was collected and updated during every interview. If the marital status of a particular round was different from the previous round, then the marital status for that specific round was updated to reflect the latest status. For this study, **MARRY16X/17X/18X** were the marry variables used for the years 2016-2018. The categories for the marital status were married, widow/divorce/single, and never married. For the study analysis, the marital status(widowed/divorced/separated) was collapsed into a single category as “unmarried.”

Education level: The variable **HIDEG** contains information on the highest degree of education attained at the time the individual entered MEPS. Information was obtained from three questions: highest grade completed, high school diploma, and highest degree, and the variable had seven values. For the purpose of our study analysis, we recoded categories of HIDEG as (No Degree, GED) as **1**, (High school diploma) as **2,** and (Bachelor’s Degree, Master’s Degree, Doctorate Degree, and Other Degree) as **3**. In this recoded categories, category 1 represented education level less than high school; category 2 represented the high school, and category 3 represented education level greater than high school.

Economic Status: Family income as a percentage of the poverty line was determined with the variable **POVCAT16/17/18** for the years 2016-2018. POVCAT variable has the five assigned values to it: negative or poor, near-poor, low income, middle income, and high income. These categories are assigned based on different income levels of people with respect to Federal Poverty Level (FPL), i.e., Poor (less than 100%FPL), Near Poor (100%

to less than 125% FPL), Low income (125% to less than 200% FPL), Middle Income (200% to less than 400% FPL) and high income (greater than or equal to 400%FPL). In this study, the categories: Poor/Negative, Near poor, and Low income were collapsed into a single category called "low-income."

Insurance coverage: The insurance coverage status of the respondents was determined using the INSCOV variable, which summarizes health insurance coverage for the person for the calendar years 2016-2018. The insurance coverage variables used for this study were **INSCOV16/17/18.**

Chronic Conditions

Hypertension: The **HIBPDX** variables indicate that the individual has been diagnosed with high blood pressure. HIBPDX variable was indicated by the 'yes' or 'no' category.

Stroke: **STRKDX** indicates the diagnosis of stroke for an individual. STRKDX variable was indicated by the 'yes' or 'no' category.

Emphysema: **EMPHDX** variable was used to identify persons with emphysema. EMPHDX variable was indicated by the 'yes' or 'no' category.

Cancer: **CANCERDX** variable was used to identify whether the person had ever been diagnosed as having cancer or a malignancy of any kind. After the person responded "yes," the type of cancer was identified. However, for the purpose of our study analysis, the CANCERDX variable was indicated by the 'yes' or 'no' category.

Arthritis: **ARTHDX** asked if the person (aged 18 or older) had ever been diagnosed with arthritis. ARTHDX variable was indicated by the 'yes' or 'no' category.

Asthma: Persons diagnosed with asthma were confirmed with the **ASTHDX** variable. ASTHDX variable was indicated by the 'yes' or 'no' category.

Smoking Status: For the years 2016-2017, the variable **ADSMOK42** was used to identify if the respondent currently smokes or not. ADSMOK42 variable was indicated by the 'yes' or 'no' category. But for the year 2018, the current smoking status variable was replaced with the new variable **OFTSMK53** (how often smoke cigarettes) with response values as *every day, some days, and not at all*. We recoded the OFTSMK53 variable into the 'yes' or 'no' category to make it consistent with the ADSMOK42 variable.

Physical Activity: The variable **PHYEXE53** was used to identify if the respondent currently spends a half hour or more in moderate to vigorous physical activity at least five times a week. PHYEXE53 variable was indicated by the 'yes' or 'no' category.

Census region: The geographic variable of the respondent was determined with the use of the REGION variable. For the calendar years, 2016-2018, the variable used was **REGION16/17/18** and is divided into the following four categories – Northeast, Midwest, South, and West.

3.4.2 Dependent Variables

Total Expenditure Variable

Expenditures in the MEPS-HC files refer to what is paid for health care services. It is defined as the sum of direct payments for care provided during the year, including out-of-pocket payments and payments by private insurance, Medicaid, Medicare, and other sources. Payments for over-the-counter drugs are not collected in MEPS[61]. **TOTEXP** variable was used to identify the total health care expenditure for an individual.

TOTEXP16, TOTEXP17, and TOTEXP18 are the total expenditure variables used for the years 2016 to 2018.

Expenditure Variables by Type of Medical Service

Total Office-Based Visits: Medical provider visits consisting of encounters that took place primarily in office-based settings and clinics and excluding other settings such as a hospital, nursing home, or a person's home are in this category. Expenditure variables associated with all medical provider visits and physician visits were identified using the variable **OBVEXP**. OBVEXP16, OBVEXP17, and OBVEXP18 are the total office-based visit expenditure variables used for the years 2016 to 2018.

Total Outpatient Visits: Expenditure variables associated with all hospital and physician-based outpatient visits were identified using the variable **OPTEXP**. OPTEXP16, OPTEXP17, and OPTEXP18 are the total outpatient visit expenditure variables used for the years 2016 to 2018.

Emergency Room Visits: It represents all emergency room visits reported for the survey year. Expenditure variables associated with emergency room visits were identified using the variable **ERTEXP.** ERTEXP16, ERTEXP17, and ERTEXP18 are the emergency room visit-based expenditure variables used for the calendar years 2016-2018.

Total Inpatient Stays: The expenditure variable associated with inpatient stays was identified using the variable **IPTEXP**. IPTEXP16, IPTEXP17, and IPTEXP18 are the inpatient stay-based expenditure variables used for the years 2016 to 2018.

Home Healthcare: Separate expenditure variables are provided for agency-sponsored home health care (includes care provided by home health agencies, hospitals, and nursing

homes) and care provided by self-employed persons. The expenditure variable associated with home health care was identified using the variables **HHAEXP** and **HHNEXP**. HHAEXP16, HHAEXP17, and HHAEXP18 are the agency-sponsored home healthcare expenditure variables used for the years 2016 to 2017. HHNEXP16, HHNEXP17, and HHNEXP18 are the self-employed home-healthcare expenditure variables used for the years 2016 to 2018.

Total Prescription Medicines: The total expenditure variable sums all amounts paid out-of-pocket and by third-party payers for each prescription purchased in the survey year. The expenditure variable associated with the purchase of prescription medicines was identified using the variable **RXEXP**. RXEXP16, RXEXP17, and RXEXP18 are the prescription medicines purchase expenditure variables used for the years 2016 to 2018.

Determination of HRQoL

The SF-12v2® and VR-12© are 12-item health surveys that are generic instruments to measure HRQoL. These questionnaires assess eight domains of health status: Physical health-related domains include General Health (GH), Physical Functioning (PF), Role Physical (RP), and Body Pain (BP). Mental health-related scales include Vitality (VT), Social Functioning (SF), Role Emotional (RE), and Mental Health (MH). For both surveys, responses are summarized by physical and mental component summary scores (PCS and MCS). The SF-12v2 using norm 98 was contained in the MEPS annual self-administered Questionnaire (SAQ) from 2003 through 2016 and was replaced with the VR-12 beginning in 2017. Corresponding items between the SF-12v2 and VR-12 are similar, but some items differ in potentially important ways, including the number of response choices, the order of response choices, and the wording of questions and

available responses. The comparability of the VR-12 and the SF-12v2 summary scores was aligned by MEPS using a bridging algorithm specific to MEPS. For this study, the PCS and MCS scores were obtained from the variables **PCS42, MCS42** (year 2016) and **VPCS42, VMCS42** (year 2017 and year 2018), respectively.

3.5 Data Analysis

The data for this study was analyzed using SAS version 9.4 University Edition (Copyright © SAS Institute Inc., Cary, NC, USA) and Stata (16.1, StataCorp LLC, College Station, TX)". P-values < 0.05 were considered for statistical significance. We used chi-square tests to determine statistically significant differences across study groups for categorical variables. The adjusted incremental effect of depression status on medical expenditures was estimated using a generalized linear model (GLM) and two-part model while adjusting for relevant covariates. The adjusted incremental effect of depression status on HRQoL was estimated using a linear regression model.

3.5.1 Analysis of Objective 1

Unadjusted mean and standard pairwise comparisons were used to compare the total healthcare expenditures between the three groups using ANOVA and Bonferroni's posthoc tests. The total medical expenditure distribution was found to be right-skewed, but out of the total 7078 observations, only 24 observations had zero costs. So, to model highly skewed positive values of total medical expenditures, we used GLM. The GLM generalizes the ordinary linear regression model by allowing the expectation of the outcome variable to be a function (known as the link function) of the linear index of covariates. The expenditure data usually fits best with a log link; that is, the natural log of

the expected value of the dependent variable is modeled as the linear index of covariates. Hence, for our analysis, after checking with the specification tests (box-cox and modified park test), we used GLM with a log link function and gamma family distribution for expenditure outcomes. Additional advantages of the GLM approach are that predictions are made on the raw cost scale, so no retransformation is required.[63][64].

3.5.2 Analysis of Objective 2

The medical expenditures by service type posed two main statistical challenges: 1) Many patients reported zero medical expenditures 2) rightly skewed distribution (few individuals have very expensive medical expenditures). The expenditure data for the office-based and prescriptions costs included few zero-valued observations(<10%), so it was analyzed using a GLM with a log link and gamma distribution. Whereas other cost variables (inpatient, outpatient, emergency visits, home-healthcare and other) with excessive zero-values were analyzed using a two-part model. A two-part model allows for separate investigation of a logit model for the probability of observing a zero versus positive medical expenditure*(first-part)*, and then a generalized linear model (GLM) to estimate the adjusted association of medical expenditures by service type conditional on having positive medical expenditure*(second part)*[65]. We used the *margins* command in STATA to calculate incremental costs from the combined first and second parts of the final model.

Both the total direct medical expenditures and costs by service type were inflation-adjusted to 2018 US dollars (USD) value using the Personal Health Care Index (CMS Office of the Actuary). The Personal Health Care Index is recommended over the CPI component specific to medical care (CPI-M) as it reflects total personal health care

expenses, which is more appropriate than the CPI-M, which only reflects out-of-pocket expenses[66]. Also, using the CPI-M to adjust total disease-specific costs for inflation leads to overestimates of medical expenditures compared to adjusting with the PHC[67]. The National Health Expenditure Accounts (NHEA) definitions list was used as a reference to determine the price index for the type of expenditure[68].

3.5.3 Analysis of Objective 3

As the distribution of the MCS and PCS scores was nearly normal, a linear regression analysis was used to examine the impact of depression status on the HRQoL. Separate regression models were estimated for each dependent variable (i.e., PCS, MCS) and were adjusted for relevant covariates. However, to perform a linear regression analysis, assumptions of multicollinearity and normality were checked using q-q plots and multicollinearity statistics (Tolerance and VIF). A linear regression model requires normally distributed residuals; a q-q plot with markers close to the diagonal line confirms normal distribution[69]. Tolerance values < 0.1 and VIF>10 were used to check for multicollinearity in the regression model[70].

Chapter 4 Results

This chapter provides information on the study population characteristics, the unadjusted and adjusted results obtained from the statistical analysis tests.

4.1 Patient Population for the study

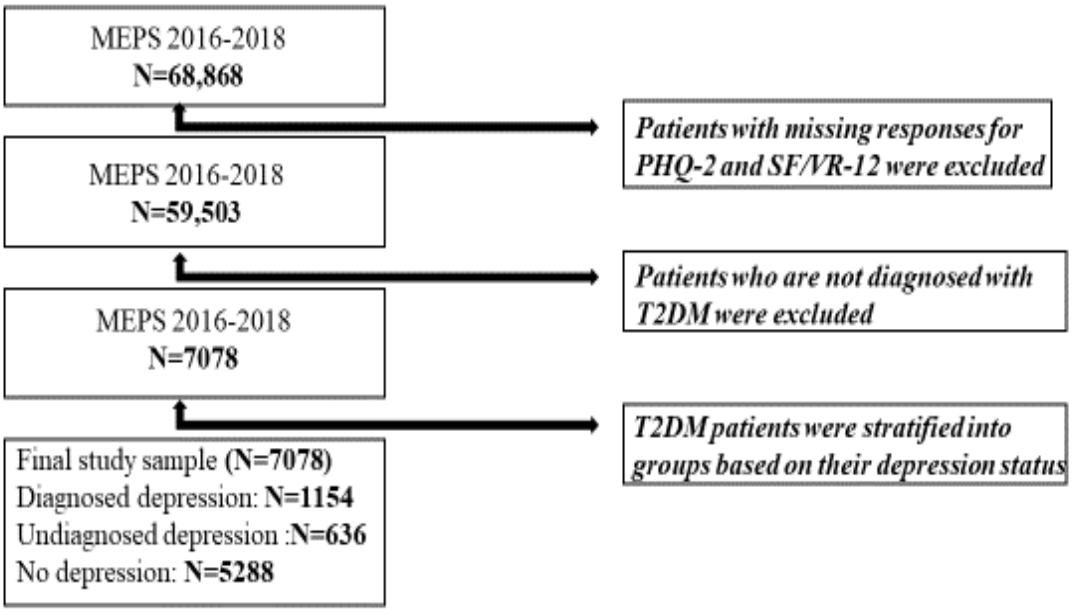


Figure 5: Final study sample

A total of 7078 patients met the study criteria and were included in the data analysis. The selection of the patient population for the study is described in Figure 5. There were 68,868 respondents in panels 20 to 23 (years 2016-2018). Patients with missing responses for PHQ-2 and SF/VR12 questionnaires were excluded. Out of the remaining 59,503 people, patients with T2DM were identified using ICD-10 clinical diagnosis code “E11”. These T2DM patients were then classified using the ICD-10 code “F32” for depression

and PHQ-2 ≥3 as cut-off score. In the final sample of 7078 patients, 16.30% had diagnosed depression, and 8.99% had undiagnosed depression.

4.2 Patient Characteristics of the study population

The baseline characteristics of the study sample are summarized in Table 2. A higher proportion of females were present in both diagnosed **(68.02%)** and undiagnosed depression **(55.35%)** groups than males. When considering the racial distribution, a comparatively lower proportion **(61.64% vs. 79.12%, p<0.001)** of white individuals and a higher proportion **(27.04% vs. 14.30%, p<0.001)** of black individuals were found in the undiagnosed depression than diagnosed depression. With respect to the education level, there was a higher percentage of individuals with less than high school education in the undiagnosed depression**(46.63% vs. 28.30%, p<0.001)** group than the diagnosed depression. A higher percentage of undiagnosed depression**(6.29% vs. 4.25%, p<0.001)** group patients were uninsured as compared to the diagnosed. Patients with undiagnosed depression**(21.26%)** had a higher proportion of stroke patients in comparison to those with diagnosed**(15.68%)** and no depression**(10.85%).** In contrast, patients with diagnosed depression had a higher percentage of individuals with asthma**(25.30% vs. 22.33%,p<0.001)** and cancer**(21.58% vs. 18.43%,p<0.001)** than the undiagnosed depression group. The percentage of patients with hypertension**(83.62% vs. 82.83%,p<0.001)** and arthritis**(68.86% vs. 67.67%,p<0.001)** were similar in the diagnosed and undiagnosed depression groups.

When personal health practices were considered, a higher proportion of individuals with undiagnosed depression**(23.74% vs. 17.87%, p<0.001)**were smokers than those with diagnosed depression and **(23.74% vs. 12.40%, p<0.001)** no depression. Also, a higher

proportion of patients with undiagnosed**(72.18%)** and diagnosed depression**(72.61%)**were physically inactive than those without depression**(59.04%)**. Considering the geographical region, a higher proportion**(52.52%)** of undiagnosed depression patients belonged from the southern part of the US compared to those with diagnosed**(37.87%)** and no depression**(42.98%)**.

Table 2: Patient characteristics by depression status in T2DM patients

Variables	**Diagnosed depression** **% *(n)*** 16.30 (n=1154)	**Undiagnosed depression** **% *(n)*** 8.99 (n=636)	**No depression** **% *(n)*** 74.71% (n=5288)	**p-value**
Predisposing factors				
Age category(in years)				
18-44	11.87(137)	10.85(69)	10.93(578)	<0.001
45-64	48.87(564)	44.97(286)	42.02(2222)	
65 and above	39.25(453)	44.18(281)	47.05(2488)	
Gender				
Male	31.98(369)	44.65(284)	49.74(2630)	<0.001
Female	68.02(785)	55.35(352)	50.26(2658)	
Race				
White	79.12(913)	61.64(392)	67.28(3558)	<0.001
Black	14.30(165)	27.04(172)	22.75(1203)	
Others	6.59(76)	11.32(72)	9.97(527)	
Enabling factors				
Marital Status				
Married	38.21(441)	41.04(261)	54.49(2881)	<0.001
Unmarried	44.63(515)	42.45(270)	32.14(1699)	
Never married	17.16(198)	16.51(105)	13.37(707)	
Education				
<High school	28.30(324)	46.63(291)	27.41(1441)	<0.001
High school	44.02(504)	37.50(234)	44.18(2323)	
>High school	27.69(317)	15.87(99)	28.41(1494)	

Poverty status				
Low income	55.55(641)	67.30(428)	40.32(2132)	<0.001
Middle income	23.83(275)	21.23(135)	29.24(1546)	
High income	20.62(238)	11.48(73)	30.45(1610)	
Insurance coverage				
Private	42.03(485)	28.77(183)	54.08(2860)	<0.001
Public	53.73(620)	64.94(413)	40.87(2161)	
Uninsured	4.25(49)	6.29(40)	5.05(267)	
Need factors				
Chronic conditions				
Hypertension	83.62(965)	82.83(526)	76.14(4024)	<0.001
Stroke	15.68(181)	21.26(135)	10.85(574)	<0.001
Emphysema	9.88(114)	10.71(68)	3.37(178)	<0.001
Asthma	25.30(292)	22.33(142)	12.71(672)	<0.001
Arthritis	68.86(794)	67.67(429)	46.37(2452)	<0.001
Cancer	21.58(249)	18.43(117)	16.86(891)	<0.001
Personal Health Practices				
Smoking Status				
Yes	17.87(203)	23.74(146)	12.40(645)	<0.001
No	82.13(933)	76.26(469)	87.60(4558)	
Physical Activity				
Yes	27.82(316)	27.39(169)	40.96(2147)	<0.001
No	72.18(820)	72.61(448)	59.04(3095)	
External Environment				
Census region				
Northeast	15.68(181)	13.52(86)	14.77(781)	<0.001
Midwest	24.09(278)	16.19(103)	18.68(988)	
West	22.36(258)	17.77(113)	23.56(1246)	
South	37.87(437)	52.52(334)	42.98(2273)	

4.3 Analysis of Total Medical Expenditures *(Objective 1)*

Table 3 below summarizes the unadjusted mean medical expenditure obtained using ANOVA for the years 2016-2018 for T2DM patients with diagnosed, undiagnosed, and no depression. Unadjusted mean and standard pairwise comparisons were used to compare the expenditures by depression categories[71].

Table 3. Unadjusted Total Healthcare expenditures by depression status (reported in 2018 dollars)

Category	Unadjusted Mean Expenditures	(95% CI)
Diagnosed depression	$22,059	($20,172-$23,945)
Undiagnosed depression	$21,089	($18,548-$23,630)
No depression	$14,016	($13,135-$14,898)

The overall mean medical expenditures for patients with T2DM were $22,059 (95% CI 20,172-23,945)for those with diagnosed depression, $21,089(95% CI 18,548-23,630) for those with undiagnosed depression, and $14,016(95% CI 13,135-14,898) for those without depression, respectively .Pairwise comparison tests using the Bonferroni test showed significant differences in mean expenditures between all paired groups except those between diagnosed and undiagnosed depression.

As shown in Figure 6, Between 2016 and 2017, the mean direct medical expenditure for the undiagnosed depression group increased from $18,236 to $22,304 (an increase of 22.3%) as compared to the 6.49% and increase of the diagnosed depression group. The

undiagnosed depression group showed minimal change (1.53%) in the mean expenditures between 2017 and 2018. However, the expenditures for the diagnosed depression group increased from $21,066 to $26,261(an increase of 24.66%).

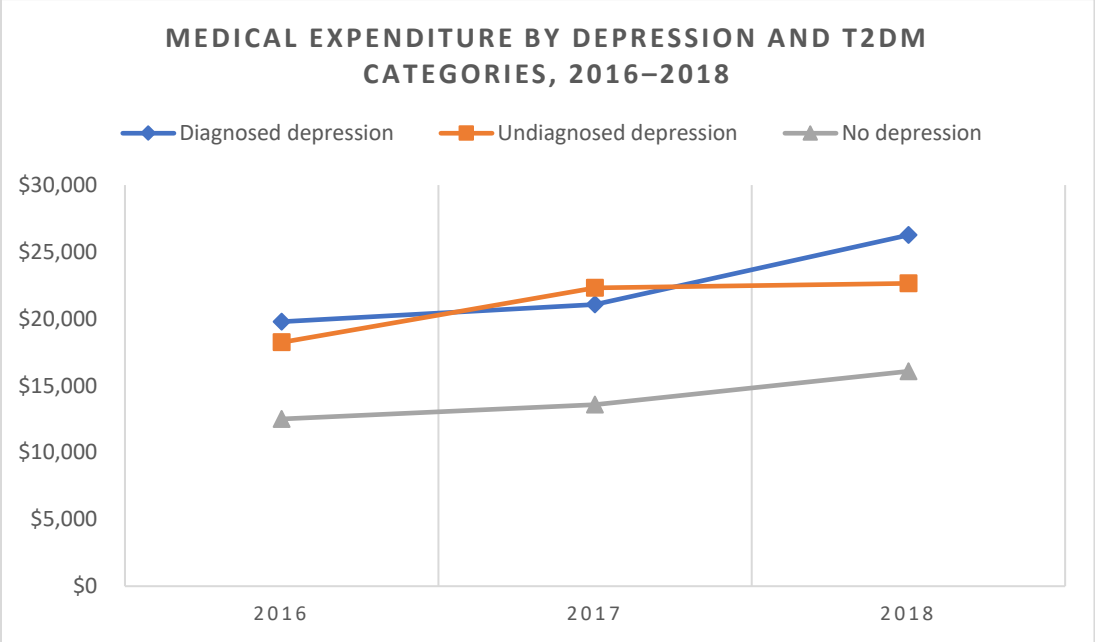
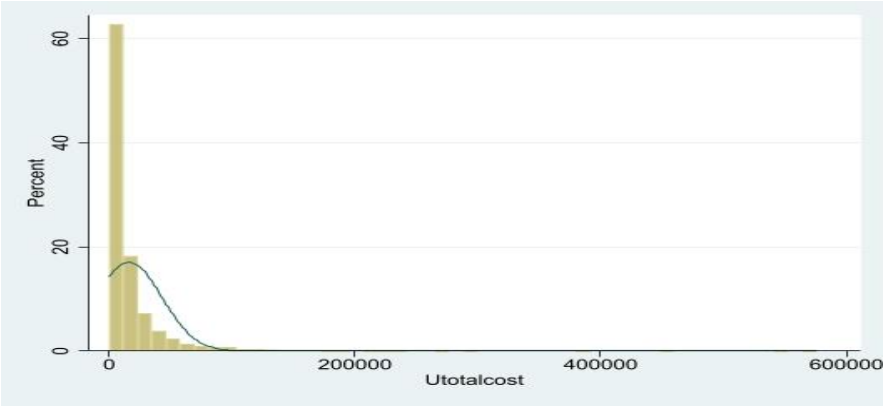


Figure 6: Changes in the total healthcare expenditures by depression categories, 2016-2018.

As shown in Figure 7, the total healthcare expenditure data displayed highly skewed values and is not normally distributed. Since our data had only 24 observations with zero total expenditures, we used the glm model with log-link function and gamma distribution for analysis to tackle the rightly skewed distribution problem. The results of the specification tests for the model choice of the link function and distribution family can be found in the appendix A section.

Figure 7: Distribution of the total healthcare expenditures.



The results of the adjusted model on the incremental costs associated with the depression status and the relevant covariates are shown in Table 4. Those with diagnosed depression presented higher total expenditures ($550, p=0.755) compared with the undiagnosed depression group. Conversely, those without depression showed significantly lower (-$4096, p=0.005) total expenditures than the undiagnosed depression group. Compared with men, women had lower total direct medical expenditures (-$1626, p=0.029). With respect to race, black individuals were associated with decreased total costs (-$2216, p=0.011) in comparison to white individuals. Patients with at least high school education had significantly higher(high school: $2609, >High school: $4187, p<0.001) costs than those who received less than high school education. Participants with public insurance had increased total direct medical expenditures ($8114, p<0.001), followed by private insurance($6277, p<0.001), compared to the uninsured patients. Physically active patients had significantly lesser healthcare costs (-$2722,p<0.001) than those who were not active.

Table 4: Incremental total medical expenditures by depression status among T2DM adults, adjusted for relevant covariates (2018-dollar value)

Variables	**Incremental cost ($)**	**(95% CI)**	**p-value**
Undiagnosed depression (ref)	-	-	-
Diagnosed depression	550	(-2902,4001)	0.755
No depression	-4096	(-6978,-1214)	0.005
Age category(in years)			
18-44	-3649	(-5743, -1556)	0.001
45-64	354	(-1245,1954)	0.664
65 and above(ref)	-	-	-
Gender			
Male(ref)	-	-	-
Female	-1626	(-3087,-164)	0.029
Race			
White(ref)	-	-	-
Black	-2216	(-3918,-514)	0.011
Others	-3125	(-5222,-1028)	0.003
Marital Status			
Married	-5417	(-7945,-2889)	<0.001
Unmarried	-3290	(-5932,-649)	0.015
Never married(ref)	-	-	-
Education			
<High school(ref)	-	-	-
High school	2609	(1033,4185)	0.001
>High school	4187	(2127,6248)	<0.001
Poverty status			
Low income	579	(-1487,2647)	0.583
Middle income	-475	(-2367,1417)	0.623
High income(ref)	-	-	-
Insurance coverage			
Private	6277	(4165,8389)	<0.001
Public	8114	(5999,10230)	<0.001

Uninsured(ref)	-	-	-
Chronic conditions			
Hypertension	3072	(1527,4616)	<0.001
Stroke	6430	(3695,9164)	<0.001
Emphysema	3553	(-329,7436)	0.073
Asthma	3224	(1006,5442)	0.004
Arthritis	2933	(1488,4379)	<0.001
Cancer	4784	(2601,6967)	<0.001
Smoking Status	-2383	(-4191,-575)	0.010
Physical Activity	-2722	(-4081,-1362)	<0.001
Census region			
Northeast	2681	(428,4934)	0.020
Midwest	276	(-1575,2127)	0.770
West	422	(-1374,2218)	0.645
South(ref)	-	-	-

4.4 Analysis of Medical Expenditures by service type *(Objective 2)*

Table 5 below summarizes the mean medical expenditure by service type for the years 2016-2018 for T2DM patients with diagnosed, undiagnosed, and no depression. Unadjusted mean and standard pairwise comparisons were used to compare these expenditures by depression categories. The results from pairwise comparisons are as follows:

1. *Office-based*- Pairwise comparison tests showed significant differences in the office expenditures between the diagnosed and no depression only.

2. *Hospital outpatient*- No statistically significant differences were found in the mean outpatient expenditures in the study groups.

3. *Hospital inpatient*- Pairwise comparisons showed significant differences between all groups except diagnosed versus the undiagnosed depression group.

4. *Emergency room*- Pairwise comparison tests showed significant differences between all groups except diagnosed versus the undiagnosed depression group.

5. *Prescription*-Pairwise comparison tests showed significant differences in the mean expenditures for all the groups.

6. *Home healthcare*- Pairwise comparison tests showed significant differences between all groups except the diagnosed versus the undiagnosed depression group.

Table 5: Unadjusted expenditures by service type among adults with T2DM and depression (reported in 2018 US dollars)

Service type	Diagnosed depression	Undiagnosed depression	No depression
Office-based	$3821($3244-$4398)	$3543($2766-$4321)	$2836($2566-$3105)
Hospital outpatient	$1432($886-$1977)	$1157($423-$1892)	$904($649-$1158)
Hospital Inpatient	$4941($3820-$6062)	$5851($4340-$7361)	$3220($2696-$3744)
Emergency room	$564($459-$669)	$541($400-$683)	$361($312-$411)
Prescription	$8142($7411-$8873)	$6676($5691-$7661)	$5105($4764-$5447)
Home healthcare	$2165($1679-$2651)	$2619($1964-$3274)	$891($664-$1118)
Others	$935($797-$1073)	$665($479-$851)	$668($603-$733)

Those with diagnosed depression presented increased expenditures in all the categories compared to the undiagnosed and no depression groups. But for the inpatient service category, the costs of the undiagnosed depression group were the highest. Similarly, the

undiagnosed depression patients had higher costs in all the categories than those without depression.

Results from the adjusted analyses of the healthcare expenditures based on the service type for each depression category in T2DM patients are presented in Table 6. There were no significant differences in the expenditures between the diagnosed and the undiagnosed depression group across all the cost categories. Significant differences were found only in the home healthcare expenditures between the undiagnosed depression and no depression groups.

Table 6: Incremental expenditures of health care services among adults with T2DM with depression (reported in 2018 US dollars)

Service type	Undiagnosed depression (1)	Diagnosed depression (2)	No depression (3)	p-value (1 vs. 2)	p-value (1 vs. 3)
Office-based[a]	Reference	24(-924, 972)	-788(-1594, 18)	0.961	0.055
Hospital outpatient[b]	Reference	218(-340, 776)	-246(-699, 208)	0.443	0.288
Hospital Inpatient[b]	Reference	-331(-1613, 952)	-750(-1853, 354)	0.613	0.183
Emergency room[b]	Reference	4(-131, 140)	-87(-205, 32)	0.949	0.151
Prescription[a]	Reference	1204(-70, 2479)	-687(-1710, 336)	0.064	0.188
Home healthcare[b]	Reference	151(-444, 746)	-563(-1024, -103)	0.618	0.017
Others[b]	Reference	70(-120, 261)	-127(-290, 35)	0.467	0.125

[a] *Results were obtained from a generalized linear model with a log link function and gamma-distribution.*

[b] *Results were obtained from a two-part model.*

4.5 Analysis of HRQoL *(Objective 3)*

Results for the assumptions of the regression model are provided in Appendix A. As shown in Table 7, T2DM patients with undiagnosed depression reported the lowest MCS and PCS scores compared to those with diagnosed and no depression, respectively. Also, pairwise comparison tests showed significant differences in the MCS and PCS scores across all the groups.

Table 7:Unadjusted mean (95% CI) of PCS and MCS for T2DM patients by depression category

	PCS	MCS
Diagnosed depression	36.11(35.28-36.93)	41.49(40.87-42.12)
Undiagnosed depression	31.63(30.53-32.74)	36.69(35.85-37.54)
No depression	42.49(42.11-42.88)	53.04(52.75-53.33)

Adjusted analyses indicated that, compared to adults with undiagnosed depression, the MCS scores were 4.29 points, and the PCS scores were 3.73 points higher for patients with diagnosed depression. Alternatively, those with no depression had MCS scores of 14.30 points, and the PCS scores 6.59 points higher than the undiagnosed depression patients(Table 8).

Table 8: Adjusted parameter estimates of PCS and MCS for T2DM patients by depression category

Adjusted Parameter estimates				
	PCS	p-value	MCS	p-value
Undiagnosed depression	Reference	-	Reference	-
Diagnosed depression	3.73	<0.001	4.29	<0.001
No depression	6.59	<0.001	14.30	<0.001
Age category				
18-44	3.23	<0.001	-3.17	<0.001
45-64	0.99	0.0004	-2.16	<0.001
65 and above(ref)				
Gender				
Male(ref)				
Female	-0.35	0.1739	-0.21	0.3388
Race				
White(ref)				
Black	0.58	0.1733	0.70	0.05
Others	0.98	0.0450	1.31	0.001
Marital status				
Married	-0.46	0.2396	-0.15	0.6419
Unmarried	-0.17	0.6644	-0.31	0.3657
Never married(ref)				
Education				
<High school(ref)				
High school	-0.15	0.6294	0.55	0.033
>High school	0.24	0.5122	0.34	0.2626
Poverty Status				
Low income	-4.23	<0.001	-1.97	<0.001
Middle income	-1.99	<0.001	-0.74	0.011
High income(ref)				
Insurance Coverage				
Private	-1.00	0.0917	-0.60	0.2378
Public	-3.13	<0.001	-2.01	<0.001
Uninsured(ref)				
Hypertension	2.15	<0.001	0.44	0.096

Stroke	4.47	<0.001	0.96	0.002
Emphysema	3.19	<0.001	0.72	0.1464
Asthma	1.80	<0.001	1.04	0.0005
Arthritis	5.60	<0.001	1.61	<0.001
Cancer	2.22	<0.001	0.23	0.4233
Smoking Status	0.58	0.1090	1.32	<0.001
Physical Activity	-3.77	<0.001	-1.38	<0.001
Census Region				
Northeast	1.64	<0.001	-0.09	0.7640
Midwest	0.64	0.061	0.47	0.1010
West	1.04	0.0015	0.29	0.2880
South(ref)				

Chapter 5 Discussion

This chapter is divided into four main sections. The first section provides information on the population characteristics and its discussion. The second section includes our research hypothesis and its discussion. The third section describes the implications of our research findings. The final section includes the strengths, limitations, future research suggestions, and conclusion.

5.1 Study population characteristics and discussion

Prevalence

In our study, out of the 7,078 T2DM patients, 8.99% had undiagnosed depression. Our findings correspond to the previous studies of T2DM patients who reported having a similar percentage of undiagnosed depression patients. A 2006 BRFSS study reported 8.7% of the T2DM population had undiagnosed depression, and the 2016 MEPS study reported 10.2% suffered from undiagnosed depression[49][14]. It is evident from our finding that even after the 2016 US Preventive Services Task Force (USPSTF) recommendation suggested for the regular screening of depression in the adult population to ensure the accurate diagnosis of depression, a large proportion(8.99%)of T2DM patients remains undiagnosed[72].

Race

Our results reflect that the minorities(black patients) were more affected by undiagnosed depression. A higher percentage of black patients were identified as suffering from undiagnosed depression than diagnosed (27.04% vs. 14.30%, $p<0.001$) and (27.04% vs. 22.75%, $p<0.001$) no depression. This can be explained by the finding of a study that

showed among patients with similar rates of depression symptoms, African-American reported lower odds(OR=0.470) of receiving a diagnosis from a physician and lower odds(OR=0.415) of treatment than Whites. The reasons for the racial differences were mentioned as African-American patient's refusal of depression treatment or use of alternative depression therapies, lesser prescription benefits, or physician's uncertainty or bias in prescribing [50].

Income status and Insurance coverage

It was found having undiagnosed depression was associated with lower income and lack of access to healthcare services. In our study, 67.30% of undiagnosed depression patients were low-income patients compared to 55.55% in the diagnosed and 40.32% in the no depression group. Similarly, patients with undiagnosed depression(6.29%) had a significantly higher percentage of uninsured patients than those with (4.25%) diagnosed and (5.05%) no depression.

Findings from previous studies indicated that uninsured individuals with depression symptoms are less likely to have their depression diagnosed than those with private or public insurance. Kato et al. reported that uninsured individuals with depression symptoms(PHQ≥3) were less likely to be assessed(screened/treated) for depression than those with private insurance coverage (OR=0.30; 95% CI=0.18 – 0.51) [32]**.** Similar findings were obtained from the study in which Egede et al., among T2DM adults, a significantly higher proportion (12.4%) of undiagnosed depression patients were uninsured than those with (4.9%) asymptomatic, (9.4%) symptomatic diagnosed depression, and (7.9%) no depression[14].

Another interesting finding from our study was that there was a substantially higher proportion of publicly insured(64.94% vs. 53.73%, $p<0.001$) patients with undiagnosed depression than diagnosed depression. This finding indicates the existence of disparity in access to mental healthcare services among these patients. In recent years, multiple national policy changes involving publicly funded insurance programs were made. Like, the Medicaid expansion that might have expanded coverage for lower-income individuals, a group among whom the likelihood of undiagnosed depression is potentially high[73]. Next, in the year 2008, the MHPAEA(The Mental Health Parity and Addiction Equity Act) was enacted to prevent insurance plans from imposing less favorable benefit limitations on mental health conditions than on any other medical condition [74]. Lastly, the Medicare Improvements for Patients and Providers Act of 2008 reduced mental health treatment cost-sharing from 45% in 2010 to 20% in 2014 onward[75]. Although these policy changes were made, our study findings raise questions on the proper implementation of these policies in real-world settings.

5.2 Study hypothesis and discussion

H1: "Having undiagnosed depression in T2DM patients is associated with significantly higher total medical expenditures than diagnosed and no depression".

The total expenditures of T2DM patients in our study were the highest for the ($22,059) diagnosed depression patients, followed by the ($21,089) undiagnosed depression and ($14,016) no depression group. These findings are consistent with the results reported in the previous studies. Unutzer et al., in a study of Medicare patients with T2DM and CHF, found the expenditures to be $22,960 for diagnosed depression, $14,365 for undiagnosed

depression, and $11,956 for those without depression [34]. However, this study included extremely ill Medicare patients, and thus the findings are not generalizable.

Similarly, a recent study specific to T2DM patients reported higher mean medical expenditures for patients with symptomatic($20,105) and asymptomatic($16,134) diagnosed depression than undiagnosed($15,155) depression and no depression($10,016). Although this study reported higher expenditures for patients with diagnosed depression, it may have overestimated the costs by including patients with anxiety and other mood disorders. The ICD-9 code for major depression is "296" and "311", roughly converts to ICD-10 code "F32" and "F33". This study reporting higher costs for diagnosed depression than undiagnosed depression included patients with various other ICD-9 codes (300, 309) comprising a spectrum of mood disorders[76].

Conversely, studies that used a specific depression diagnosis code, i.e., "311" for identifying diagnosed depression, have reported higher mean expenditures for undiagnosed depression than diagnosed and no depression groups. Choi et al. used the MEPS data to compare the healthcare expenditures for diagnosed depression (ICD 9- "311") and undiagnosed depression in older adults. The mean expenditures were higher for those with ($17,603) undiagnosed depression than ($15,928) diagnosed and no depression($8,903) [35]. This study was conducted in community-dwelling older adults and not in the T2DM population specifically.

After adjusting the model for relevant covariates, it was found that total medical expenditures in T2DM patients with diagnosed depression presented higher total expenditures ($550, p=0.755) compared with the undiagnosed depression group. This result did not confirm our first hypothesis; undiagnosed depression is associated with

significantly higher expenditures than diagnosed depression. However, comparable findings were obtained from a study conducted in ASCVD patients where the undiagnosed depression patients reported lower expenditures (-$865, p=0.07) compared to the diagnosed depression patients[36].

Conversely, the T2DM with no depression showed significantly lower (-$4096, p=0.005) total expenditures than the undiagnosed depression group. This finding suggests that having undiagnosed depression can lead to higher expenditures than no depression. Our results are consistent with the study conducted by Egede et al., where T2DM patients with undiagnosed depression($2872, p<0.001) had significantly higher total expenditures than no depression[14].

H2: "Having undiagnosed depression in T2DM patients is associated with significantly higher medical expenditure by service-type than diagnosed and no depression".

The largest contributors to the cost of T2DM are prescription medications ($71.2 billion), hospital inpatient services ($69.7 billion), medications and supplies to treat diabetes ($34.6 billion), and office visits ($30.0 billion)[2]. In our study the major contributors to the total costs($57,164) in T2DM patients were prescription medications($19,923), inpatient($14,012) and office-based visit($10,200) costs.

The results of expenditures based on service type did not support our second hypothesis as the diagnosed depression patients had higher costs than undiagnosed depression across all service categories except for inpatient stays. The incremental cost of the diagnosed depression group for inpatient services was lesser (-$331, p=0.613) than the undiagnosed depression. This finding is similar to the study by Egede et al., where the inpatient costs

were higher for the undiagnosed depression patients than the asymptomatic diagnosed depression patients. The possible explanation for this finding is that patients with undiagnosed depression might extend their hospital stay due to lack of treatment and access to care to manage the negative impact of depression on their health state.

Similarly, patients without depression had significantly lower (-$563, p=0.017)incremental costs for home-healthcare services than patients with undiagnosed depression. This is comparable to the finding from a study by Choi et al., where patients with undiagnosed depression had higher ($638, p<0.05) home-health care costs than the no depression group [35].

H3: "Having undiagnosed depression in T2DM patients is associated with significantly lower HRQoL than diagnosed and no depression".

The HRQoL among undiagnosed depression groups was significantly lower than the diagnosed and no depression group. This finding was in accordance with our third research hypothesis. In our study, results from the adjusted analysis indicated that patients with diagnosed depression had higher MCS (4.29 points; p<0.001) and PCS(3.73 points; p<0.001) than those with undiagnosed depression. These findings are comparable to the study with ASCVD patients, where the undiagnosed depression group reported lower MCS(8.03 points; p=0.006) and PCS(4.65 points; p=0.006) than the diagnosed depression group [36]. One of the logical reasons for this finding is that patients with diagnosed depression might be receiving depression treatment and thus are more likely to have better HRQoL. Conversely, undiagnosed depression patients might

remain untreated for depression which may worsen their health and diminish their HRQoL.

Also, patients without depression reported better HRQoL (PCS: 6.59, MCS: 14.30, $p<0.001$) than those with undiagnosed depression. These results correspond to the findings from the study by Okunrintemi et al., where patients with undiagnosed depression presented worse HRQoL scores (PCS: -9.75, MCS: -19.69, $p<0.001$)than those without depression [36].

5.3 Study Implications

Findings from our study have implications for developing interventions to improve the diagnosis and treatment of depression. It is evident from our results that T2DM patients with undiagnosed depression have significantly higher expenditures than those without depression. These patients, when left undiagnosed with depression, may later increase the economic burden on the healthcare system. To reduce the total expenditures, developing interventions that can effectively identify patients with undiagnosed depression is required.

No significant differences in the expenditures of diagnosed and undiagnosed depression indicate that there is a lack of appropriate depression treatment among those diagnosed. Depression treatment focused on the specific needs of diagnosed depression patients should be designed to reduce expenditures. Also, our study indicates that it is crucial to investigate the use of inpatient services in T2DM patients. As T2DM patients with undiagnosed depression due to the negative impact of their untreated depression might extend their inpatient stays, incurring higher expenditures. As pointed out in a systematic

review that depression symptoms are associated with higher rates of readmission. Compared to inpatients without depression, those discharged with depression symptoms were more likely to be readmitted (20.4% vs. 13.7%, risk ratio [RR]: 1.73), creating a substantial burden on the healthcare system[77]. Thus, monitoring the depression symptoms in T2DM can help get their depression diagnosed and treated, thus reducing their costs and sufferings.

The study findings also have implications in the context of home healthcare services. Undiagnosed depression patients with T2DM incurred higher home-healthcare expenditures than those without depression. A framework should be in place for the home healthcare providers with emphasis on T2DM patients to diagnose and treat depression in home care patients.

Lastly, the differences in the HRQoL scores among T2DM patients with undiagnosed diagnosed and no depression have clinical relevance. It is reported that mean differences of 2.0–2.5 points on HRQoL scales among patients with T2DM are clinically meaningful on SF-12 subscales[41]. Our study results showed that patients with undiagnosed depression reported the worst HRQoL outcomes than patients with diagnosed and no depression. The mean differences in the HRQoL scores between the undiagnosed depression compared to diagnosed and no depression group was greater than 2.0-2.5 points. This finding calls for timely diagnosis and treatment of undiagnosed depression in T2DM to improve health outcomes.

5.4 Strengths

Our study is strengthened by using a large sample of non-institutionalized individuals obtained from MEPS data, a nationally representative dataset that makes our results highly generalizable. Also, the information related to costs obtained from MEPS survey participants is confirmed by the medical care providers making it a good quality data. To our knowledge, it is the first study to comprehensively evaluate the impact of undiagnosed depression on the direct medical expenditures and HRQoL of T2DM patients. Using a specific ICD-10 code for depression "F32" ensured that we did not overestimate the costs associated with diagnosed depression. Using the ABM model framework ensured that we included all the relevant independent variables that can impact an individual's healthcare costs and HRQoL. Also, using GLM and the two-part model to estimate expenditures allowed us to overcome challenges like zero expenditures and highly skewed distribution in healthcare costs data.

5.5 Limitations

Although our study provides important findings that make it an essential addition to the literature, the results should be interpreted with its limitations. As MEPs have a cross-sectional study design, causality cannot be established between the depression status and the outcome variables. Our sample population includes self-reported diagnoses of T2DM and depression; thus, there is a possibility of recall bias. Also, we did not examine if those diagnosed were treated/untreated for their depression. Similarly, we did not check if the undiagnosed depression patients received any form of antidepressant treatment or not. Although we controlled for most of the relevant covariates, confounding associated with the severity of T2DM, and depression could not be eliminated. Additionally, the ICD-10

depression diagnosis code “F32”, to preserve patient confidentiality, was coded to a 3-digit code in MEPS rather than a fully-specified code (e.g., F32.1 for moderate single episode depression F32.5 single episode of depression in complete remission). This 3-digit code prevented us from identifying if the patients have had single/recurrent episodes of depression and whether the patient was in full/partial remission.

5.6 Future research recommendation

Our study focused only on direct medical expenditures, other nonmedical costs related to caregiving, indirect costs such as presenteeism and absenteeism are important to estimate the total economic burden. Future researchers can investigate the impact of undiagnosed depression on all these cost components and provide a more accurate estimate of the total costs.

We did not confirm if the patients with diagnosed depression received any depression treatment or not. Similarly, we did not check if undiagnosed depression patients received any antidepressants for conditions other than depression. Future researchers can investigate the differences in expenditures and HRQoL in T2DM patients based on the depression treatment status.

5.7 Conclusion

This study demonstrates the importance of screening, diagnosing, and treating depression among T2DM patients. Undiagnosed depression in T2DM patients can negatively impact healthcare expenditures and HRQoL. Our findings suggest that if depression symptoms(PHQ≥3) in T2DM patients remain undiagnosed and are not treated, it may potentially contribute to higher expenditures and lower HRQoL. Evidence-based

interventions focused on efficient screening and diagnosis of depression symptoms in undiagnosed depression are needed to achieve possible cost savings and better HRQoL. Lastly, as the results demonstrate that minority groups, uninsured and lower-income patients have a higher proportion of patients with undiagnosed depression, such groups may require increased monitoring by clinicians to achieve better outcomes.

Appendix A

Specificity Tests for the analysis of healthcare expenditures:

Table 9: Box-Cox Test

The TRANSREG Procedure

Box-Cox Transformation Information for totalcost				
Lambda		**R-Square**	**Log Like**	
-1.0		0.01	-85035.3	
-0.5		0.08	-68079.2	
0.0	+	0.15	-61963.9	<
0.5		0.11	-63418.4	
1.0		0.05	-69123.2	
1.5		0.02	-78151.6	
2.0		0.01	-89692.2	
< - Best Lambda * - 95% Confidence Interval + - Convenient Lambda				

The lamba value suggested using box-cox test was 0, so log-link function was used for the expenditures.

Table 10: Modified Park test

Parameter Estimates							
Variable	**DF**	**Parameter Estimate**	**Standard Error**	**t Value**	**Pr > |t|**	**95% Confidence Limits**	
Intercept	**1**	1.79133	0.58499	3.06	0.0022	0.64456	2.93809
Lnp	**1**	1.69734	0.06096	27.84	<.0001	1.57784	1.81683

The estimated power is 1.7 with a 95% confidence interval of (1.56, 1.82). This estimate is very near 2, hence a gamma distribution was used.

Testing Assumptions of Regression model:

Figure 8: Q-Q plots of Residuals (MCS)

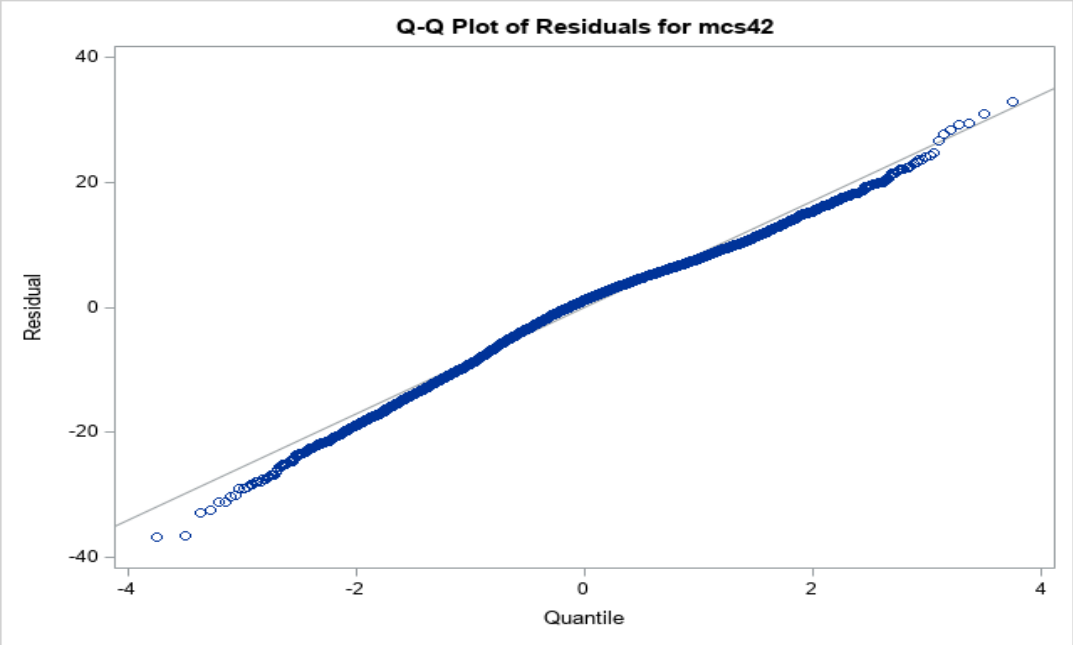
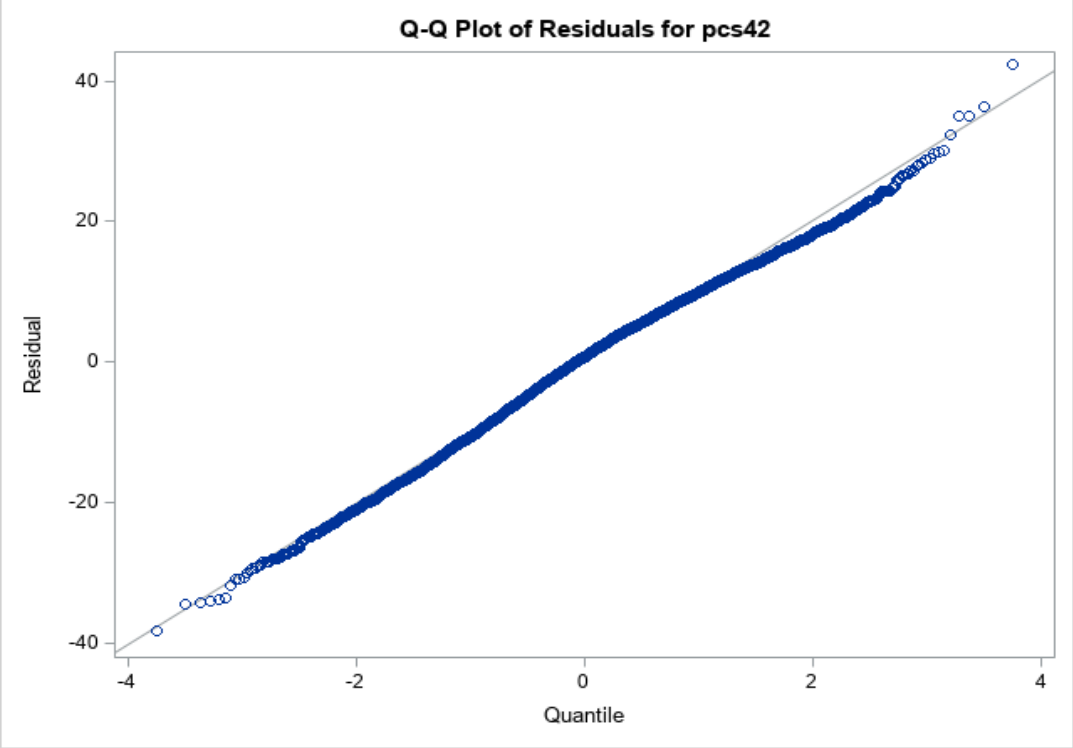


Figure 9: Q-Q plots of Residuals (PCS)



Multicollinearity Investigation

Table 11: Parameter estimates for MCS

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|	Tolerance	Variance Inflation
Intercept	**1**	36.85786	1.64116	22.46	<.0001	.	0
sex	**1**	-0.20948	0.21898	-0.96	0.3388	0.88909	1.12474
smoking	**1**	1.31505	0.30468	4.32	<.0001	0.93277	1.07208
exercise	**1**	-1.38382	0.21620	-6.40	<.0001	0.96754	1.03355
hibp	**1**	0.43714	0.26307	1.66	0.0966	0.89086	1.12252
asth	**1**	1.04420	0.29924	3.49	0.0005	0.89224	1.12077
arth	**1**	1.60953	0.22571	7.13	<.0001	0.83347	1.19980
stroke	**1**	0.95630	0.32126	2.98	0.0029	0.93931	1.06462
cancer	**1**	0.22643	0.28275	0.80	0.4233	0.91052	1.09828
emph	**1**	0.72239	0.49728	1.45	0.1464	0.90120	1.10963
cat1	**1**	4.29667	0.43919	9.78	<.0001	0.40342	2.47883
cat3	**1**	14.30620	0.38163	37.49	<.0001	0.38810	2.57667
adult1	**1**	-3.17414	0.39190	-8.10	<.0001	0.69372	1.44151
adult2	**1**	-2.16232	0.23921	-9.04	<.0001	0.75322	1.32763
race1	**1**	0.70296	0.36160	1.94	0.0519	0.37832	2.64329
race2	**1**	1.31103	0.41491	3.16	0.0016	0.36419	2.74578
marry1	**1**	-0.15294	0.32888	-0.47	0.6419	0.39210	2.55039

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|	Tolerance	Variance Inflation
marry2	**1**	-0.30747	0.33988	-0.90	0.3657	0.40387	2.47606
hideg2	**1**	0.55074	0.25857	2.13	0.0332	0.64571	1.54869
hideg3	**1**	0.34031	0.30375	1.12	0.2626	0.58005	1.72399
povstat1	**1**	-1.97030	0.30203	-6.52	<.0001	0.46980	2.12856
povstat2	**1**	-0.73503	0.28884	-2.54	0.0110	0.63578	1.57288
inscov1	**1**	-0.59727	0.50590	-1.18	0.2378	0.16567	6.03603
inscov2	**1**	-2.01444	0.50428	-3.99	<.0001	0.16859	5.93154
region1	**1**	-0.09432	0.31420	-0.30	0.7640	0.85205	1.17364
region2	**1**	0.47137	0.28738	1.64	0.1010	0.81933	1.22050
region4	**1**	0.29472	0.27733	1.06	0.2880	0.77915	1.28346

Table 12: Parameter estimates for PCS

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|	Tolerance	Variance Inflation
Intercept	**1**	14.11010	1.93849	7.28	<.0001	.	0
sex	**1**	-0.35176	0.25866	-1.36	0.1739	0.88909	1.12474
smoking	**1**	0.57685	0.35988	1.60	0.1090	0.93277	1.07208
exercise	**1**	-3.77263	0.25537	-14.77	<.0001	0.96754	1.03355
hibp	**1**	2.15099	0.31073	6.92	<.0001	0.89086	1.12252
asth	**1**	1.79109	0.35346	5.07	<.0001	0.89224	1.12077

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|	Tolerance	Variance Inflation
arth	**1**	5.60279	0.26660	21.02	<.0001	0.83347	1.19980
stroke	**1**	4.47313	0.37946	11.79	<.0001	0.93931	1.06462
cancer	**1**	2.21967	0.33398	6.65	<.0001	0.91052	1.09828
emph	**1**	3.19319	0.58738	5.44	<.0001	0.90120	1.10963
cat1	**1**	3.72882	0.51876	7.19	<.0001	0.40342	2.47883
cat3	**1**	6.58920	0.45077	14.62	<.0001	0.38810	2.57667
adult1	**1**	3.23292	0.46290	6.98	<.0001	0.69372	1.44151
adult2	**1**	0.99313	0.28255	3.51	0.0004	0.75322	1.32763
race1	**1**	0.58170	0.42711	1.36	0.1733	0.37832	2.64329
race2	**1**	0.98259	0.49008	2.00	0.0450	0.36419	2.74578
marry1	**1**	-0.45690	0.38847	-1.18	0.2396	0.39210	2.55039
marry2	**1**	-0.17420	0.40145	-0.43	0.6644	0.40387	2.47606
hideg2	**1**	-0.14738	0.30542	-0.48	0.6294	0.64571	1.54869
hideg3	**1**	0.23517	0.35878	0.66	0.5122	0.58005	1.72399
povstat1	**1**	-4.22745	0.35675	-11.85	<.0001	0.46980	2.12856
povstat2	**1**	-1.99976	0.34117	-5.86	<.0001	0.63578	1.57288
inscov1	**1**	-1.00789	0.59756	-1.69	0.0917	0.16567	6.03603
inscov2	**1**	-3.12903	0.59564	-5.25	<.0001	0.16859	5.93154
region1	**1**	1.64450	0.37112	4.43	<.0001	0.85205	1.17364

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|	Tolerance	Variance Inflation
region2	**1**	0.63613	0.33944	1.87	0.0610	0.81933	1.22050
region4	**1**	1.04322	0.32758	3.18	0.0015	0.77915	1.28346

As we can see from the above results, none of our values match the criteria for multicollinearity, it is verified that no multicollinearity exists in our regression model.

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VITA

Name	Uzma A Pathan
Baccalaureate Degree	Bachelor of Pharmacy, NCRD's Sterling Institute of Pharmacy, Mumbai, India. Major: Pharmacy
Date Graduated	May, 2016
Master's degree	Master of Pharmacy, Bombay College of Pharmacy, Mumbai, India. Major: Pharmacology
Date Graduated	August, 2018