



Disease burden of urinary tract infections among type 2 diabetes mellitus patients in the U.S.



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ABSTRACT

Aims: Type 2 diabetes is a reported risk factor for more frequent and severe urinary tract infections (UTI). We sought to quantify the annual healthcare cost burden of UTI in type 2 diabetic patients.

Methods: Adult patients diagnosed with type 2 diabetes were identified in MarketScan administrative claims data. UTI occurrence and costs were assessed during a 1-year period. We examined UTI-related visit and antibiotic costs among patients diagnosed with UTI, comparing those with versus without a history of UTI in the previous year (prevalent vs. incident UTI cases). We estimated the total incremental cost of UTI by comparing all-cause healthcare costs in patients with versus without UTI, using propensity score-matched samples.

Results: Within the year, 8.2% (6,014/73,151) of subjects had ≥ 1 UTI, of whom 33.8% had a history of UTI. UTI-related costs among prevalent versus incident cases were, respectively, \$603 versus \$447 ($p = 0.033$) for outpatient services, \$1,607 versus \$1,819 ($p = \text{NS}$) for hospitalizations, and \$61 versus \$35 ($p < 0.0001$) for antibiotics. UTI was associated with a total all-cause incremental cost of \$7,045 (95% CI: 4,130, 13,051) per patient with UTI per year.

Conclusions: UTI is common and may impose a substantial direct medical cost burden among patients with type 2 diabetes.

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1. Introduction

Type 2 diabetes is a chronic, progressive metabolic disorder resulting from the loss of early insulin secretion and development of insulin resistance (De Fronzo, 1999). In the United States, the incidence of diabetes nearly tripled between 1990 and 2010, with 1.9 million new cases diagnosed in 2010 (Centers for Disease Control, 2013). Patients with type 2 diabetes are at an elevated risk of a number of other medical conditions compared to non-diabetic individuals, including cardiovascular disease, eye problems and blindness, renal disease, and lower extremity amputations. Type 2 diabetes is also considered an immunocompromised state and is a known risk factor for certain infectious diseases (Muller et al., 2005; Shah & Hux, 2003).

Urinary tract infections (UTIs) are the most common type of bacterial infections (Foxman, 2002). Asymptomatic bacteriuria and

symptomatic UTI are both reported to be more frequent in patients with type 2 diabetes than in the general population (Hoepelman, Meiland, & Geerlings, 2003; Ronald & Ludwig, 2001). Additional evidence suggests that type 2 diabetes increases susceptibility to serious complications of UTI, including emphysematous conditions of the bladder or kidney, renal abscess, and renal papillary necrosis (Griffin, Bergstralhn, & Larson, 1995; Huang & Tseng, 2000; Mnif et al., 2013). Atypical and resistant forms of infection may also be more common in patients with type 2 diabetes (Stapleton, 2002). Several different mechanisms may contribute to the higher frequency of UTI and related complications among diabetic patients, including immune function impairments (Delamaire et al., 1997; Muller et al., 2005), dysfunctional bladder emptying related to autonomic neuropathy (Hosking, Bennett, & Hampton, 1978; Truzzi, Almeida, Nunes, & Sadi, 2008), and higher glucose levels in the urine which may facilitate the growth of pathogenic organisms (Chen, Jackson, & Boyko, 2009).

UTI imposes a substantial economic burden on the health system (Foxman, 2002; Foxman, Barlow, D'Arcy, Gillespie, & Sobel, 2000); nonetheless, formal evidence is limited on the direct medical cost burden of UTI specifically among diabetic patients. Given the increasing prevalence of type 2 diabetes and the clinical link between diabetic status and UTI risk and severity, there is a need to understand

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the frequency and costs associated with UTIs in patients with type 2 diabetes for resource allocation decisions in the U.S. Several large observational studies have examined the risk of UTI in diabetic populations; however, most have been restricted to female subjects due to their significantly higher risk of UTI compared to male patients (Boyko, Fihn, Scholes, Abraham, & Monsey, 2005; Boyko et al., 2002; Foxman, 2002). Other studies have measured the risk of UTI among both men and women with diabetes in settings outside of the U.S. (Al-Rubeann, Moharran, Al-Naqeb, Hassan, & Rafiullah, 2013; Hirji, Guo, Andersson, Hammar, & Gomez-Caminero, 2012; Muller et al., 2005). A recent UK-based analysis found that type 2 diabetes increased UTI incidence for both men and women, but noted variation in the relative risk across different gender and age groups (Hirji et al., 2012). The study also found additional increases in UTI risk among diabetic patients with longer duration of diabetes and among those with poor glycemic control. Given differences in patient characteristics and health care services between countries, additional population-based studies are warranted to describe in detail the age- and gender-specific prevalence of UTI among diabetic patients in the U.S.

Using a large retrospective analysis of commercial claims, we sought to examine the rate of UTI among U.S. patients diagnosed with type 2 diabetes in a managed care setting, and to estimate the additional health care resource use and costs associated with the occurrence and recurrence of UTI in the presence of type 2 diabetes.

2. Materials and methods

2.1. Data source

Data were obtained from the MarketScan Commercial Claims & Encounters and the MarketScan Medicare Supplemental and Coordination of Benefits databases covering the period from January 1, 2008 to September 9, 2011. The MarketScan databases are integrated, de-identified, patient-level data sources representing the health services of approximately 77 million individuals in all age groups since 1996, drawn from 77 employers and 12 U.S. health plans, representing over 126 unique carriers. Enrollees include individuals with primary coverage through fee-for-service or capitated health plans, including comprehensive plans, exclusive provider organizations, preferred provider organizations, point-of-service plans (with and without capitation), and health maintenance organizations. All census regions within the continental U.S. are represented in the database. Data elements capture enrollment history, demographic information, and claims for inpatient, outpatient and pharmacy services (including prescriptions from mail-order and specialty pharmacies). All MarketScan data files are compliant with the patient confidentiality requirements of the Health Insurance Portability and Accountability Act (HIPAA).

2.2. Sample selection

A random sampling of 5 million individuals with at least one recorded diagnosis of type 2 diabetes (International Classification of Disease, 9th Revision, Clinical Modification [ICD-9 CM]: 250.xx) were drawn from the MarketScan database, and within the selected MarketScan population, those with a type 2 diabetes diagnosis between 2008 and 2009 were randomly selected and used as the starting population of the sample selection. This resulted in ~120,000 patients.

The study sample was further restricted to patients who were at least 18 years old as of the start date, defined as the first type 2 diabetes diagnosis date between 1/1/2008 and 9/30/2009, and continuously enrolled in the database for a minimum of 2 years from the start date. Patients were excluded if they had any diagnoses for type 1 diabetes mellitus (ICD-9-CM: 250.x1, 250.x3) or other forms of secondary diabetes (ICD-9-CM: 249.xx). Patients with an observed pregnancy (ICD-9-CM: 630-679, V22) during their 2-year eligibility period were

also excluded from the analysis. The final study sample consisted of 73,151 patients who met the inclusion/exclusion criteria.

2.3. Study design overview

The baseline and study periods were defined respectively as the first and the second year following his/her start date. For each patient, the occurrence of UTI events was separately determined using diagnosis codes during the baseline and study period. Patients were classified into two groups based on presence of UTI events during the baseline period: prevalent cohort if he/she had a UTI event during the baseline period and incident cohort if he/she did not have any UTI event. Furthermore, among patients who had a UTI event during the study period, those who also had a UTI event during the baseline period were referred to as prevalent cases; otherwise incident cases.

The economic burden of UTI was studied in both bottom-up and top-down approaches. The bottom-up approach described UTI-related health care utilization and cost outcomes among the patients with a UTI event during the study period by measuring health care services and costs specifically associated with a UTI diagnosis code or an antibiotic prescription for UTI in prevalent versus incident cases. The top-down approach sought to comprehensively assess and compare any health care service use associated with UTIs, including potential downstream utilization and costs of UTI that may not be coded as UTI-related in the database. We estimated the total incremental burden of UTI among patients with type 2 diabetes by comparing all-cause utilization and cost outcomes in patients with versus without UTI during the study period using a matched sample. The matched sample consisted of the patients with UTIs and their 1:1 matched patients without UTIs using propensity score matching (PSM). The matched adjusted analysis aimed to estimate and compare incremental health care resource uses and cost in patients with versus without a UTI event during the study period, who otherwise had similar characteristics during the baseline period, such as: diagnosis of UTI; hypoglycemia; microvascular complications (retinopathy/blindness, neuropathy, nephropathy); cardiovascular conditions (stroke, transient ischemic attacks, congestive heart failure, myocardial infarction, ischemic heart diseases, peripheral arterial diseases); chronic kidney diseases; and liver diseases.

2.4. Variable measurement

2.4.1. Exposure and covariates

A UTI event was identified in the database using ICD-9-CM diagnosis codes, including chronic pyelonephritis (590.0), acute pyelonephritis (590.1), cystitis (595.x) and urinary tract infection, site not specified (599.0). The study focused specifically on symptomatic UTI diagnoses due to concerns that asymptomatic bacteriuria would be under-diagnosed in retrospective claims data. Patient baseline characteristics regarded as potential risk factors for UTI during the study period were included as covariates, including age, gender, residential location (rural vs. urban), census region, health plan type, Charlson Comorbidity Index (CCI), hypoglycemia, microvascular complications, cardiovascular conditions, chronic kidney diseases and liver diseases.

2.4.2. Outcome variables

Health care utilization and cost outcomes were measured. Utilization outcome variables included hospitalizations, length of stay (in days), outpatient visits and uses of antibiotics for UTI treatment. Hospital and outpatient visits were considered UTI-related if they were recorded with a UTI diagnosis code. UTI-related prescription drugs were defined as any antibiotic prescriptions filled no later than 7 days after a UTI diagnosis, or within the supply days of a previous UTI-related antibiotic drug fill. If a patient had multiple UTI-related antibiotic fills, the days of supply for each fill were combined together to compute total days of supply.

Direct health care costs were disaggregated into hospital, outpatient, and prescription drug costs. Each cost component was

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