Epidemiology of Urinary Tract Infections: Incidence, Morbidity, and Economic Costs

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Urinary tract infections (UTIs) are considered to be the most common bacterial infection. According to the 1997 National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey, UTI accounted for nearly 7 million office visits and 1 million emergency department visits, resulting in 100,000 hospitalizations. Nevertheless, it is difficult to accurately assess the incidence of UTIs, because they are not reportable diseases in the United States. This situation is further complicated by the fact that accurate diagnosis depends on both the presence of symptoms and a positive urine culture, although in most outpatient settings this diagnosis is made without the benefit of culture.

Women are significantly more likely to experience UTI than men. Nearly 1 in 3 women will have had at least 1 episode of UTI requiring antimicrobial therapy by the age of 24 years. Almost half of all women will experience 1 UTI during their lifetime. Specific subpopulations at increased risk of UTI include infants, pregnant women, the elderly, patients with spinal cord injuries and/or catheters, patients with diabetes or multiple sclerosis, patients with acquired immunodeficiency disease syndrome/human immunodeficiency virus, and patients with underlying urologic abnormalities. Catheter-associated UTI is the most common nosocomial infection, accounting for >1 million cases in hospitals and nursing homes. The risk of UTI

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increases with increasing duration of catheterization. In noninstitutionalized elderly populations, UTIs are the second most common form of infection, accounting for nearly 25% of all infections.

There are important medical and financial implications associated with UTIs. In the nonobstructed, nonpregnant female adult, acute uncomplicated UTI is believed to be a benign illness with no long-term medical consequences. However, UTI elevates the risk of pyelonephritis, premature delivery, and fetal mortality among pregnant women, and is associated with impaired renal function and end-stage renal disease among pediatric patients. Financially, the estimated annual cost of community-acquired UTI is significant, at approximately $1.6 billion.

Urinary tract infection (UTI) refers to the presence of microbial pathogens within the urinary tract. Usually classified by the site of infection (the bladder [cystitis], kidney [pyelonephritis], or urine [bacteriuria]), UTI can be asymptomatic or symptomatic, characterized by a wide spectrum of symptoms ranging from mild irritative voiding to bacteremia, sepsis, or even death. UTIs that occur in a normal genitourinary tract with no prior instrumentation are considered "uncomplicated," whereas "complicated" infections are diagnosed in genitourinary tracts that have structural or functional abnormalities, including instrumentation such as indwelling urethral catheters, and are frequently asymptomatic.[1,2] Patients with an otherwise normal genitourinary tract who have symptomatic renal infection are diagnosed as having acute uncomplicated pyelonephritis. Asymptomatic bacteriuria (ASB) is defined as the isolation of bacteria from the urine in significant quantities consistent with infection, but without the local or systemic genitourinary signs or symptoms. ASB requires antimicrobial treatment only in specific populations, such as pregnant women. Finally, many women experience frequent recurrent UTIs (RUTIs), designated as either a "relapse" after treatment cessation with the pretherapy isolate or as a "reinfection" with a different organism after initial treatment cessation. Although considered to be a benign condition, RUTI can have a significant impact on quality of life.

UTI is considered to be the most common bacterial infection.[3] How-

TABLE 1. Urinary tract infection epidemiology: measurement concerns

- Not reportable
- Not a single clinical entity
  - —ASB vs. symptomatic infection
  - —Cystitis, bacteriuria, pyelonephritis
  - —Complicated vs. uncomplicated infection
- Diagnostic criteria
  - —Clinical presentation
  - —Clinical presentation + urinalysis
  - —Clinical presentation + urinalysis + culture
  - —Culture
- Source of data
  - —Office visits
  - —Self-report of physician diagnosis
  - —Population screens
  - —Hospital discharges

ASB = asymptomatic bacteriuria.

ever, assessing the accurate incidence of UTI is difficult, because UTIs are not reportable diseases in the United States (Table 1). Further, although accurate diagnosis depends on both the presence of symptoms and a positive urine culture, uncomplicated UTI in outpatient settings are usually diagnosed without the benefit of culture. Thus, there will be errors in most estimates.

There are several incidence estimates in the literature, which differ in their diagnostic criteria (clinical presentation, urinalysis, culture) and the source of data (office visits, hospital discharges, self-report of physician diagnosis, or population screens). The 1997 National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey[4] estimated that UTI results in nearly 7 million office visits each year in the United States, along with an additional 1 million visits to emergency departments necessitating approximately 100,000 hospitalizations[4] (Figure 1). The number of office visits for UTI among women (1.2%) was twice that among men (0.6%).[4]

Although everyone is susceptible to UTI, there are specific subpopulations that are at increased risk of UTI, including infants,[5] pregnant women,[6] the elderly,[7] patients with spinal cord injuries and/or catheters,[8] patients with diabetes,[9] multiple sclerosis,[10] or acquired immunodeficiency syndrome (AIDS)/human immunodeficiency virus (HIV),[11,12] and patients with underlying urologic abnormalities. Except during the first few months of life, females are far more susceptible than males to UTI. Recently, a retrospective population-based study investigated the incidence rate of first-time symptomatic UTI in children <6 years of age.[13]

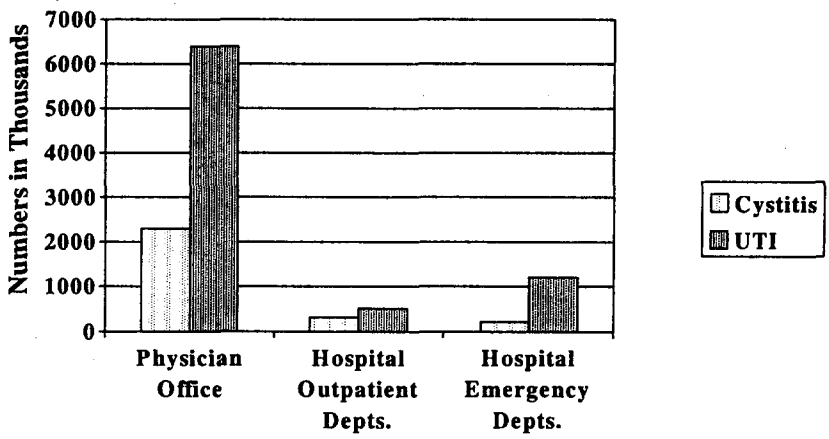

FIG 1. Ambulatory visits for cystitis and urinary tract infection (UTI). (Adapted from *Vital Health Stat 13.*[4])

The cumulative incidence rate of UTI was 3 times greater in girls (6.6%) than boys (1.8%).

Acute, uncomplicated UTIs are generally considered to be benign conditions. However, severe infections may require hospitalization. Long-term ramifications of acute UTI are rare. Significant medical sequelae are more frequently associated with complicated infections or with infections that occur in specific subpopulations, such as pediatric patients, pregnant women, or women with diabetes. Nevertheless, the high prevalence of UTI, combined with the costs associated with medical intervention, have significant financial ramifications: it is estimated that the overall costs associated with UTI are nearly $2 billion each year.[14]

Incidence of Urinary Tract Infection

Symptomatic UTI

Symptomatic UTI is very common among sexually active women[15] and far more common among women than men. An estimated 1 in 3 women will have at least 1 UTI diagnosed by a clinician requiring antimicrobial treatment by the age of 24 years,[16] and 40% to 50% of women will experience at least 1 UTI during their lifetime[16-19] (Figure 2). A recent random digit dialing survey of 2,000 women in the United States found that 10.8% of women >18 years reported at least 1 presumed UTI during the prior 12 months, and the majority of women who had a UTI reported a history of ≥2 UTI episodes in their life.[16]

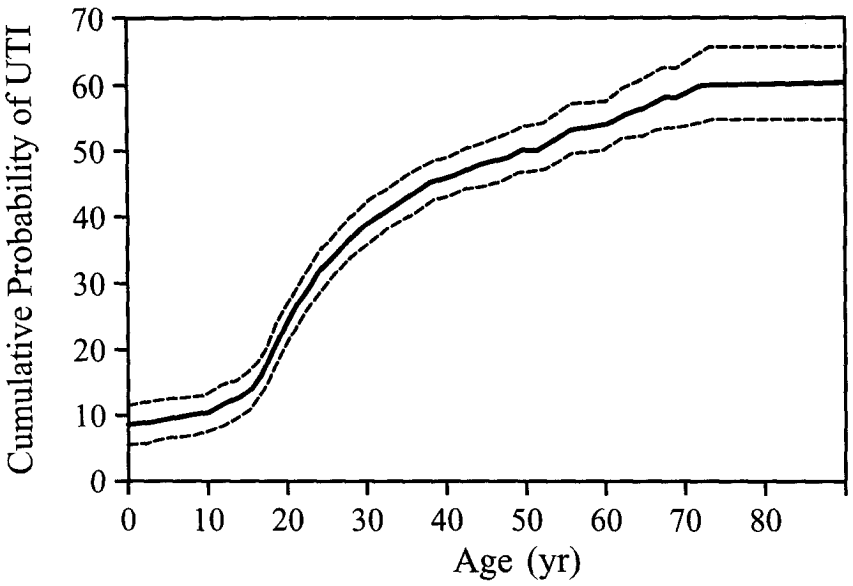

FIG 2. Cumulative probability of self-reported, physician diagnosed urinary tract infection (UTI) by age among US women. Dashed curves indicate 95% Hall-Wellner Confidence Bands. (Adapted from *Ann Epidemiol.*[16])

Earlier research demonstrated that despite the presence of symptoms, women do not immediately seek medical intervention for UTI.[20,21] Results from a self-administered questionnaire sent to all women who were registered with a rural medical practice in England for the prior 2 years and were at least 25 years of age found 27% of respondents experienced dysuria and 34% experienced urinary frequency.[20] However, many women waited up to 5 days before seeking medical attention. The symptoms were least common among older (55 to 74 years) women.[21]

A wide range of factors have been identified that can increase susceptibility to UTI. Among the specific genetic factors known to increase susceptibility are nonsecretor status or ABO blood-group antigens[22,23] (Table 2). Biologic factors that have been identified include congenital abnormalities,[24,25] the presence of a urinary obstruction,[26] and a prior history of UTI.[2,25,27] Modifiable behavioral risk factors include the use of diaphragms, condoms and/or spermicides for contraception, and frequency of sexual intercourse among premenopausal women.[28-33] Postcoital prophylaxis can minimize RUTI among susceptible women. Estrogen deficiency has been associated with an increased risk of UTI, and the postmenopausal use of intravaginal estriol cream can reduce the

TABLE 2. Factors that increase susceptibility to urinary tract infection (UTI)

Genetic	Biologic	Behavioral	Other
Nonsecretor status	Congenital abnormalities	Sexual intercourse	Urogenital surgery
ABO blood-group antigens	Urinary obstruction Prior history of UTI Diabetes Incontinence	Diaphragm use Condom use Spermicide use Recent antibiotic use	Estrogen deficiency

risk of recurring RUTI.[34] Finally, women of all ages are at increased risk of UTI after antimicrobial use.[16,19,35]

A prospective study monitored nearly 800 sexually active young women seeking contraception at either a university health clinic or health maintenance organization (HMO) for 6 months.[36] The incidence of UTI was 70 of 100 person-years among the university coeds and 50 of 100 person-years among the HMO cohort. The risk of infection was significantly associated with both recent use of the diaphragm with spermicide ($P < 0.001$ for the university cohort and $P = 0.04$ for the HMO cohort) and recent sexual intercourse ($P < 0.001$ for university students and $P = 0.002$ for HMO women). Similarly, women with a history of UTI demonstrated an increased risk of acute UTI. In comparison, another study estimated the risk of UTI among healthy university men at $P = 0.049$ of 100 person-years.[37]

A prospective study in Finland followed 179 women for 12 months after an initial UTI episode caused by *Escherichia coli*.[38] There were 147 recurrent UTI episodes diagnosed during that period, of which 131 were classified as recurrences occurring at least 1 month after the index episode. Nearly half of the women (44%) experienced recurrences, and women with a history of UTI were most likely to experience RUTI from the index episode. Among 285 college women in the United States with first UTI, 24% had a symptomatic episode within 6 months; infection occurred twice as frequently as relapse (16% vs. 8%).[15]

Finally, a 1-day point prevalence study performed in intensive care units (ICU) throughout Europe found UTI to be the third most common ICU-acquired infection (17.6%), after pneumonia (46.9%) and lower respiratory tract infections (17.8%).[39] Prolonged duration in the ICU (>48 hours) and urinary catheterization were among the 7 identified risk factors for ICU-acquired infections. It should be noted that ICU-acquired UTI did not significantly increase the risk of mortality.

TABLE 3. Incidence of urinary tract infection among children

	Girls	Boys
Infancy	0.4%–1.0%	0.188% (circumcised)* 0.702% uncircumcised
1–5 yr†	0.9%–1.4%	0.1%–0.2%
Cumulative incidence through age 6	6.6%	1.8%
School age	0.7%–2.3%	0.04%–0.2%
Overall incidence in prepubertal children‡	3%	1%

*Data from *Lancet.*[51]
†Data from *Acta Paediatr.*[13]
‡Data from *Kidney Int Suppl.*[5]

ASB

The overall prevalence of ASB among the general population is estimated at 3.5%, and the prevalence increases with age in a linear trend.[40] Other risk factors for ASB include parity, diabetes in women, a history of UTI, and lower education.[41] An estimated 4% to 10% of pregnant women are diagnosed with ASB.[42,43] ASB is more prevalent among women with diabetes than women without diabetes. However, diabetes does not appear to increase the risk of ASB among men.[44]

The incidence of ASB among elderly (>70 years) persons living independently is 3 times greater in women (16% to 18%) than men (6%).[45] Similarly, the incidence is higher among elderly women living in nursing homes (17% to 55%) than men (15% to 31%).[45] However, the incidence is nearly comparable among elderly men (12.6 of 1,000 person-years) and women (14 of 1,000 person-years) if prostatitis is categorized as a UTI.[7]

Incidence of Urinary Tract Infection in Special Subpopulations

Pediatrics

Approximately 3% of prepubertal girls and 1% of prepubertal boys are diagnosed with UTI[5] (Table 3). Many girls who do not undergo radiographic evaluation after an initial UTI experience a recurrence within 1 year,[5] and girls who experience recurrent UTI are at increased risk of renal scarring,[46] which then increases their risk of progressive renal disease in adulthood.[47] A retrospective study recently found that 35% of boys and 32% of girls who had their first UTI at <1 year of age contracted a recurrent UTI during the next 3 years.[48] Eighteen percent of infants who experience a UTI during their first 12 months will experience

a recurrence within the subsequent few months, and infants who do not experience a recurrence rarely have additional episodes 1 year later.[5]

There is strong evidence indicating a protective effect of circumcision against UTIs among male infants. Noncircumcised boys <6 months have a significantly greater quantity of both *E coli* and gram-negative uropathogens in their urethras as compared with circumcised cohorts.[49] Noncircumcised boys also have an overall 12-fold increased risk of UTI compared with circumcised boys during the first 6 months.[50] Uncircumcised boys have a significantly higher probability of hospital admission for UTI (7.02 of 1,000) than circumcised boys (1.88 of 1,000; $P < 0.0001$), according to a population-based cohort study.[51]

Patients with Catheters or Spinal Cord Injuries

Catheter-associated UTI is the most common nosocomial infection, accounting for >1 million cases each year in US hospitals and nursing homes.[52] Nosocomial UTI among newly catheterized patients is frequently asymptomatic (90%),[52] and the risk of UTI increases with increasing duration of catheterization.[53] The overall incidence of bacteriuria is 8% and ranges from 3% to 10% per day.

Patients with spinal cord injuries (SCIs) are predominantly young males. UTIs are very common among patients with SCIs and are always complicated in nature. Unlike UTIs in most other subpopulations, UTIs among patients with SCIs are associated with significant morbidity and mortality. In fact, approximately 40% of patients with SCIs will die of renal-related problems.[54] Approximately 1 in 3 patients with SCI have bacteriuria ($\geq 10^5$ colony-forming units/mL) at any time.[55] *E coli* remains a common uropathogen among SCI patients, in addition to enterococci, *Pseudomonas*, and *Proteus mirabilis*.

Factors that increase susceptibility to UTI among patients with SCI include overdistension of the bladder, increased risk of urinary obstruction, impaired voiding, and increased incidence of stones.[56] Similarly, quadriplegics and patients with high-level spinal cord injuries are at increased risk for UTI because of their elevated risk for autonomic dysreflexia and the greater need for indwelling (versus intermittent) catheterization.

Patients with Diabetes

Diabetes increases the risk of UTI and bacteriuria among female but not male patients.[57] Patients with diabetes generally have a 2-fold to 4-fold increased incidence of bacteriuria over patients without diabetes. The etiology of UTI among persons with diabetes includes more unusual

uropathogens than UTI among persons without diabetes.[9] Further, UTI with diabetes can lead to severe complications, such as emphysematous cystitis and emphysematous pyelonephritis.[57] UTIs in ambulatory patients with diabetes are considered to be complicated, and patients are at risk of developing upper tract involvement, obstruction, and/or severe or unusual complications. In a population-based study of hospitalization rates for pyelonephritis in Manitoba, women with diabetes were 6 to 24 times more likely than nondiabetic women, and men with diabetes were 3 to 17 times more likely than nondiabetic men, to be hospitalized for pyelonephritis.[58] Nondiabetic younger women (aged 25 to 44 years) were 4 times more likely than similarly aged men (8.62 of 10,000 vs. 1.68 of 10,000) to be hospitalized for pyelonephritis. The difference was less apparent at older ages (45 to 64 years, 5.98 of 10,000 vs. 4.01 of 10,000; ≥65, 11.20 of 10,000 vs. 10.00 of 10,000).[58]

Persons with HIV/AIDS

The incidence of UTI among both women[59] and men who are seropositive for HIV is greater than among women and men who are HIV seronegative.[11,12] The incidence of UTI is believed to be even greater among patients with AIDS or who have low CD4 counts ($<0.2 \times 10^9$/L).[11] However, earlier research involving female commercial sex workers in Africa found no significant relation between HIV status, CD4 count, and symptomatic UTI.[60] Nevertheless, research consistently reports that patients with HIV are more likely to have *Enterococcus* species as the predominant uropathogen, in contrast to *E coli* as the most common uropathogen isolated among seronegative patients.[12,60]

Patients with Multiple Sclerosis

The risk of UTI and bacteriuria is significantly increased (90% and 74%, respectively) among patients with multiple sclerosis.[10] UTI frequently precedes multiple sclerosis relapse, and recurrent UTI is associated with acute exacerbation and neurologic progression of the disease.

Pregnant Patients

UTIs are the most common bacterial infections during pregnancy, and pyelonephritis is the most common severe bacterial infection complicating pregnancy.[6] Approximately 4% to 10% of pregnant women will have ASB, and 1% to 4% of pregnant women will develop acute cystitis for the first time during pregnancy[43] (Table 4). A history of childhood UTI without renal scarring increases the risk for ASB during pregnancy to 27%, and 47% with renal scarring.[47] Acute pyelonephritis affects 1% to

TABLE 4. Incidence of urinary tract infection (UTI) during pregnancy

• ASB	4%–10%
—History of childhood UTI without scarring	7%
—History of childhood UTI with scarring	7%
• Cystitis	4%
• Pyelonephritis	1%–2%

ASB = asymptomatic bacteriuria.
Adapted from *J Miss State Med Assoc*[43] and *Pediatr Nephrol.*[47]

2% of pregnant women, particularly during the end of the second and beginning of the third trimesters.[42]

Women with a history of UTI are at increased risk of UTI during pregnancy. Risk factors for ASB or acute cystitis during pregnancy include lower socioeconomic status, sickle-cell trait and anemia, increased parity or older age, and minimal medical care throughout the pregnancy. Functional urinary tract abnormalities and diabetes mellitus can also increase susceptibility to UTI during pregnancy.[61-64]

Geriatric Patients

Among the noninstitutionalized elderly populations, genitourinary infections are the second most common form of infection, accounting for nearly 25% of all identified infections.[7] Asymptomatic bacteriuria is believed to affect up to 50% of geriatric women[65] and 30% of geriatric men. Approximately 11% to 25% of elderly noncatheterized patients develop asymptomatic bacteriuria that generally spontaneously resolves.[66] Similarly, 12% of elderly ambulatory men are determined to have ASB, frequently with gram-positive uropathogens.[67] Although the majority of cases (76%) spontaneously resolve, infections with urea-splitting bacteria (such as *Proteus*) are more likely to have significant sequelae, including stone formation and permanent renal damage.[68]

Medical Implications of UTI

Uncomplicated UTI

Acute uncomplicated UTI (cystitis) in the nonobstructed adult, nonpregnant woman is believed to be a benign illness with no long-term medical sequelae. To date, however, there are no large-scale prospective studies verifying this assumption. There are data highlighting significant short-term ramifications of acute uncomplicated UTI. Research on college women found that UTI resulted in 6.1 symptomatic days, 2.4 days of restricted activity, and 0.4 days of bed rest.[30] Within 3 to 4 months of an initial UTI, 20% to 30% of women will experience a recurrence of the

TABLE 5. Urinary tract infection (UTI) in pregnancy: morbidity

Condition	Potential Ramifications
Untreated ASB	Pyelonephritis Low birth-weight infants Anemia Pregnancy-induced hypertension
Third-trimester UTI	Mental retardation in infant Developmental delays in infant Cerebral palsy in infant Fetal death

ASB = asymptomatic bacteriuria.

infection[69] with additional concomitant short-term morbidity. Despite short-term morbidity, there is no indication that UTI or RUTI among women leads to chronic renal failure, renal scarring, or hypertension.

UTI During Pregnancy

The ramifications of UTI during pregnancy can be significant, including an elevated risk of pyelonephritis, premature delivery, and fetal mortality (Table 5). If left untreated, ASB can result in acute pyelonephritis and infants with low birth weight,[6,70-72] anemia, and pregnancy-induced hypertension/preeclampsia.[6,72] As a result, early screening for ASB during pregnancy is highly recommended.[73-75]

In some women, pyelonephritis during pregnancy can present as only lower tract symptoms. More commonly, women present with the traditional symptoms of pyelonephritis, including fever with flank pain, costovertebral angle tenderness (especially on the right side), and possible vomiting and nausea. Women with pyelonephritis during pregnancy generally should be hospitalized for aggressive hydration and parenteral antibiotic therapy. A majority (86%) of women will experience uterine contractions during the first hour after antimicrobial therapy has been initiated, and 50% will continue to have uterine contractions after ≥5 hours of therapy.[76]

Recent research suggests UTI during pregnancy may increase the risk of cerebral palsy[77] or mental retardation[78] among offspring. Data from a retrospective cohort study found an increased relative risk for mental retardation or developmental delay, as well as fetal death, with maternal UTI specifically during the third trimester.[78] Treatment for third-trimester UTI did not impact on fetal morbidity. The authors recommended early and aggressive screening and treatment for ASB during pregnancy.

Pediatric UTI

UTIs among pediatric patients are associated with significantly greater morbidity and long-term sequelae than UTIs among adults, including impaired renal function and end-stage renal disease. UTI in prepubertal girls can eventually lead to potential complications during pregnancy. Recurrent UTI in girls is associated with renal scarring[79] and a concomitant increased risk of progressive renal disease in adulthood.[80] Children diagnosed with vesicourethral reflux are at increased risk of developing pyelonephritis from UTI. However, circumcision has been shown to strongly protect against UTI among infant boys.

Childhood UTI does not appear to increase the risk of hypertension up to 20 years later,[81] and unilateral renal scarring after childhood UTI does not appear to impact on renal function.[82] However, bilateral scarring is associated with a more severe prognosis.[82] Pediatric patients diagnosed with pyelonephritis and a positive dimercaptosuccinic acid (DMSA) scan (renal scintigraphy using DMSA as a tracer) have a 33% risk of renal scarring.[83] Many children with abnormal DMSA scans have reflux and/or dysfunctional voiding.

UTI in the Elderly

There are many factors that predispose elderly persons to UTI, including chronic diseases, functional abnormalities, and specific medications.[34,84] ASB is prevalent among this population,[65,85] but it frequently resolves without treatment and has no long-term sequelae. However, symptomatic UTI among the elderly requires antimicrobial therapy.[86-88]

Financial Implications of UTI

The financial implications of UTI are enormous, predominantly a result of the high incidence of UTI. Direct costs include the costs of outpatient doctor visits, antimicrobial prescriptions, and hospitalization expenses, as well as the nonmedical costs associated with travel, sick days, and morbidity. The indirect costs of lost output must also be considered. Although acute uncomplicated UTI is considered to be a benign condition with minimal long-term sequelae, it is associated with significant short-term morbidity. Approximately 11.3 million women in the United States had $\geq$1 presumed acute community-acquired UTI resulting in antimicrobial therapy in 1995, with direct costs estimated at $659 million and indirect costs totaling $936 million (Table 6). The estimated annual cost of community-acquired UTI is approximately $1.6 billion.[15]

In addition, there has been a significant increase in hospitalizations for UTI among women from 1970 to 1990, with longer average lengths of

TABLE 6. Financial implications of urinary tract infection (UTI)

Community-Acquired UTI	Nosocomial UTI
Direct: $659 million	Average cost/infection: $558–$593
Indirect: $936 million	1 extra hospital day/patient = ~1 million days
Total: $1.6 billion	Estimated annual cost: $424–$451 million

stay.[89] Of the 2 million nosocomial infections each year, 30% are UTIs,[53,90] predominantly (80%) secondary to an indwelling urethral catheter.[53] Nosocomial UTI necessitates 1 extra hospital day per patient, or nearly 1 million extra hospital days per year. It is estimated that each episode of symptomatic UTI adds $676 to a hospital bill,[91] and the estimated annual cost of nosocomial UTI in the United States ranges between $424 and $451 million.[92] Catheter-related bacteremia is estimated to cost nearly $2,900 per episode.[91] At nearly $2 billion, the total cost of community-acquired plus nosocomial UTI in the United States alone is significant.

Summary

UTI is the most common bacterial infection. It is generally associated with minimal morbidity except among specific subpopulations. However, there is a significant absence of data regarding its accurate incidence, factors that increase susceptibility to UTI, and the long-term medical sequelae of UTI.

There are many areas for future investigational effort. There is a need for accurate data regarding the incidence of symptomatic UTI and pyelonephritis among all populations. There is an increasing population of immunocompromised individuals potentially at risk for UTI. Researchers should investigate the implications to the overall epidemiology of UTI: are these groups more susceptible to UTI by any pathogen or will there be an increase in the number of uropathogens transmitted through the general population?

Finally, the clinical ramifications of UTI are significant. There is a high incidence of symptomatic UTI necessitating antimicrobial therapy, as well as an increasing population of highly susceptible patients who require antimicrobials for UTI and/or other infections, resulting in an increased risk of developing antimicrobial resistance among common uropathogens. As a result, there is a growing need to ensure appropriate therapy with agents that maximize success for both community-acquired and nosocomial UTI while minimizing risk of the development of antimicrobial resistance.

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