

Observational Study

Cost of illness among patients with diabetic foot ulcer in Turkey

Ergun Oksuz, Simten Malhan, Bilge Sonmez, Rukiye Numanoglu Tekin

Ergun Oksuz, Department of Family Medicine, Faculty of Medicine, Baskent University, 06770 Ankara, Turkey

Simten Malhan, Faculty of Health Sciences, Baskent University, 06770 Ankara, Turkey

Bilge Sonmez, Emir Karatekin Family Health Center, Cankiri Karatekin University, 18100 Cankiri, Turkey

Rukiye Numanoglu Tekin, Faculty of Health Sciences, Baskent University, 6770 Ankara, Turkey

Author contributions: Oksuz E contributed to study conception and design, data acquisition, data analysis and interpretation, writing of article, editing, reviewing and final approval of the article; Malhan S, Sonmez B and Numanoglu Tekin R contributed to study conception and design, data acquisition, data analysis and interpretation, and writing of the article.

Institutional review board statement: Not required.

Informed consent statement: Not required.

Conflict-of-interest statement: We have no conflict of interest to declare.

Data sharing statement: None.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Dr. Ergun Oksuz, MD, Professor, Department of Family Medicine, Faculty of Medicine, Baskent University, Baglica Campus, 06770 Ankara, Turkey. eoksuz@baskent.edu.tr

Telephone: +90-312-2466773

Fax: +90-312-2466770

Received: June 17, 2016

Peer-review started: June 23, 2016

First decision: July 4, 2016

Revised: August 5, 2016

Accepted: August 27, 2016

Article in press: August 29, 2016

Published online: October 15, 2016

Abstract

AIM

To evaluate the annual cost of patients with Wagner grade 3-4-5 diabetic foot ulcer (DFU) from the public payer's perspective in Turkey.

METHODS

This study was conducted focused on a time frame of one year from the public payer's perspective. Cost-of-illness (COI) methodology, which was developed by the World Health Organization, was used in the generation of cost data. By following a clinical path with the COI method, the main total expenses were reached by multiplying the number of uses of each expense item, the percentage of cases that used them and unit costs. Clinical guidelines and real data specific to Turkey were used in the calculation of the direct costs. Monte Carlo Simulation was used in the study as a sensitivity analysis.

RESULTS

The following were calculated in DFU treatment from the public payer's perspective: The annual average per patient outpatient costs \$579.5 (4.1%), imaging test costs \$283.2 (2.0%), laboratory test costs \$284.8 (2.0%), annual average per patient cost of intervention, rehabilitation and trainings \$2291.7 (16.0%), annual average per patient cost of drugs used \$2545.8 (17.8%)

and annual average per patient cost of medical materials used in DFU treatment \$735.0 (5.1%). The average annual per patient cost for hospital admission is \$7357.4 (51.5%). The average per patient complication cost for DFU is \$210.3 (1.5%). The average annual per patient cost of DFU treatment in Turkey is \$14287.70. As a result of the sensitivity analysis, the standard deviation of the analysis was \$5706.60 ($n = 5000$, mean = \$14146.8, 95%CI: \$13988.6-\$14304.9).

CONCLUSION

The health expenses per person are \$-PPP 1045 in 2014 in Turkey and the average annual per patient cost for DFU is 14-fold of said amount. The total health expense in 2014 in Turkey is \$-PPP 80.3 billion and the total DFU cost has a 3% share in the total annual health expenses for Turkey. Hospital costs are the highest component in DFU disease costs. In order to prevent DFU, training of the patients at risk and raising consciousness in patients with diabetes mellitus (DM) will provide benefits in terms of economy. Appropriate and efficient treatment of DM is a health intervention that can prevent complications.

Key words: Diabetic foot; Diabetes complications; Cost of illness; Burden of illness; Amputation

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The purpose of this study is to evaluate the annual cost of patients with Wagner grade 3-4-5 diabetic foot ulcer (DFU) in Turkey. Cost-of-illness methodology was used in the generation of cost data. Monte Carlo Simulation was used in the study as a sensitivity analysis. The average annual per patient cost of DFU treatment in Turkey is \$14287.70. As a result of the sensitivity analysis, the standard deviation of the analysis was \$5706.60 ($n = 5000$, mean = \$14146.8, 95%CI: \$13988.6-\$14304.9). Hospital costs are the highest component in DFU disease costs.

Oksuz E, Malhan S, Sonmez B, Numanoglu Tekin R. Cost of illness among patients with diabetic foot ulcer in Turkey. *World J Diabetes* 2016; 7(18): 462-469 Available from: URL: <http://www.wjgnet.com/1948-9358/full/v7/i18/462.htm> DOI: <http://dx.doi.org/10.4239/wjd.v7.i18.462>

INTRODUCTION

Diabetes mellitus (DM) is a health problem, the severity of which is gradually increasing all over the world. DM exists in approximately 8.3% of the world's population. In 2013, 10.8% (\$548 billion) of global health expenses were for DM and its complications^[1]. DM amounts to 23% (approximately 10 billion Turkish liras - TL) of the total health expenses of Turkey in 2012^[2].

Diabetic foot ulcer (DFU) is a frequently observed,

serious, and chronic complication of DM. The risk of occurrence during diagnosis can be up to 25%, and 2% of cases require amputation^[3]. Half of the cases of non-traumatic foot amputation are due to DM^[4]. It is estimated that a patient's foot is amputated due to DFU once every 30 s worldwide. The rate of recurring amputation is between 30% and 50% in the following three years in the patients who are amputated once. The rate of death within five years following amputation is 50%^[5].

Approximately 400000 DFU cases are observed in Turkey, and 7700 amputation procedures are performed annually due to DFU^[6]. As the prognosis of cases after amputation is considered, the importance of rational treatment in DFU becomes significant. Surgical and non-surgical basic wound care principles are essential in the efficient recovery of the wounds. Prevention of ulcers and fighting against wound site infections that are difficult to heal are as important as its treatment. DFU treatment requires multidisciplinary treatment procedures. DFU has direct costs as well as indirect costs and it is very important to try to increase quality of life of the patients during treatment, minimize the disease costs, and administer correct treatment that enables the person to remain as a productive and value-adding individual as well as to prevent occurrence of the disease.

The purpose of this study is to evaluate the annual cost of patients with Wagner grade 3-4-5 DFU from the public payer's perspective in Turkey.

MATERIALS AND METHODS

This study was conducted focused on a time frame of 1 year from the perspective of the Turkish reimbursement institution. Cost-of-illness (COI) methodology, which was developed by World Health Organization, was used in the generation of cost data^[7].

COI methodology

Cost is a monetary measure for the sacrifices made for achieving a certain goal. Cost is the value of a source. Economists use the concepts of "opportunity cost" or "monetary cost" in COI studies. Even though no money is spent, it is always considered that scarce resources that can be used in other areas are used. The basic idea behind cost estimation is that once a health service is provided to a person, the resources that are used will not be available anymore for other people or alternative social uses.

COI studies are used by policymakers for budget justification, determining the priorities in financing biomedical research, and development of intervention programs for preventing and treating diseases^[8,9].

Cost studies can be based on either prevalence or incidence, depending on the purpose of the analysis. The approach based on prevalence is more frequently used. In the approach based on prevalence, the total costs are calculated for a patient population in a certain area in a certain period of time^[8,9]. The period of time is usually 1 year. Said studies are required for health policymakers for budget planning and decisions^[8]. Studies based on

incidence calculate the lifetime cost of a patient who has a disease, starting from diagnosis to treatment, or if it is a chronic disease, until death^[8,9]. The analysis perspective determines which resources will be used in the calculation^[8]. Perspective shows who is affected as the resource allocation preference is made and in whose name the decisions are made^[10,11]. COI analyses can be performed with different perspectives, such as societal perspective, patient perspective, or perspective of the third person/public payer^[8].

Health economy research defines the costs in two main categories. The first one is the medical costs that occur due to disease, and the second one is the other disease-associated costs including non-medical costs that occur due to disease^[9-12]. There are direct and indirect costs in each category. Direct costs refer to which payments are made and indirect costs refer to which resources are lost^[9]. The direct medical costs include all types of exclusive and non-exclusive uses of resources (not only monetary expenditures) such as costs related to hospital services, outpatient services, laboratory tests, supplies, prescriptions, physical therapy, care services at home and care centers, caregiver costs, and services such as ambulance, etcetera, and the use of health personnel and departments of hospitals. In addition, they include the future costs or savings such as costs of other tests with false positive or true positive results during monitoring associated with said disease and hospital admissions and treatment costs. Direct medical costs are calculated by classification according to the types of payments and expenses^[10]. Indirect costs are the costs of morbidity and mortality^[9].

Assessment and evaluation

By following a clinical path with the COI methodology, the main total expenses were reached by multiplying the number of uses of each expense item, the percentage of cases that used them, and unit costs. The direct medical costs, which are the outpatient, laboratory and imaging methods, prescribed drugs, medical supplies that are directly used during the course of treatment of disease, and the amount spent for the hospital admissions and interventions, were calculated, and non-medical direct expenses were ignored, as there were no sufficient data for Turkey. The intangible costs including pain, unhappiness, distress, misery, stress, et cetera, caused by the disease in the individual were also not taken into consideration in this study. The indirect costs including the societal costs caused by the disease, disabilities, or premature deaths were also excluded from the study.

The clinical guidelines were followed in calculating the direct costs and actual data were used for some cases.

The cost of disease was calculated by rating the Wagner classification that shows the grade of foot ulcer^[13]. The Wagner classification rates of patients with DFU in Turkey were as follows: Grade 1: 7.7%, grade 2: 27.2%, grade 3: 35.2%, grade 4: 25.4%, and grade 5: 4.5%^[14-16]. The costs of patients of grades 3-4-5 according to the Wagner classification were calculated.

The Medical Enforcement Declaration (MED), which is officially declared by the institution, is used for the payment of health services by the reimbursement institution in Turkey^[17]. The costs for all medical services used in the calculations were obtained from MED. The drug expenses were based on the 2015 list of the Republic of Turkey Ministry of Health Turkish Medicines and Medical Devices Agency. The drugs were classified according to the active ingredients and all forms of all products included in the reimbursement list related to the active ingredients and were included in the analysis, and their average values were reflected to the calculations. Public discounts, current public paid costs, and costs related to medical materials such as all orthosis and prosthesis devices were obtained from MED. The costs were calculated according to United States dollars by using the foreign exchange rate in 2014 (\$1.00 = 1.179 TL).

The average institution cost was calculated as the admission fee for treatments administered in an outpatient clinic. The health organizations, clinical branches, and surgical branches that can administer DFU treatment were chosen, the prices of related outpatient were obtained from MED, and the average values were calculated. The average costs of pricing per admission of the patients with DFU to the outpatient clinic were included in the analysis according to said average value calculated for each branch. The cost for outpatient to which the patients were transferred for consultation was 10.12 procedure points in accordance with MED. Some of the medical materials used in payment per admission to the outpatient clinic were included in the admission fee. The examinations that were not included in the outpatient clinic admission fee were included in the costs according to MED.

Monte Carlo Simulation (MCS) was used in the study as the sensitivity analysis. MCS is a technique that uses random numbers and a trial-and-error method without using any formula. MCS provides an estimate for the statistical distribution of the possible costs. At the same time, the distribution of variables that constitute the costs is obtained. Simulation technique is a methodology employed to solve problems, not a theory. Approach of this technique to the problems varies depending on system structure and the model to be constructed based on this structure. During the simulation process, a sample is generated by the distribution of the variance observed in the proper distribution forms. Random values are used for uncertain variables. MCS can assign random values to all variables and parameters in accordance with the probabilities. The simulation is based on the random number generation. For example, for a possibility of 66 that requires osteomyelitis treatment, probability distribution according to the random numbers drawn from a normal distribution is as follows: The patient will receive the osteomyelitis treatment if the random number drawn is between 00 and 66, and for the numbers drawn between 67 and 99, the patient will be treated without a need for osteomyelitis treatment. In this study, distribution parameters were calculated at the

Table 1 The average unit cost of outpatient to which the admissions are made in the treatment of diabetic foot ulcer

	Average unit cost (\$-PPP 2014)
Outpatient clinics	
Endocrinology and metabolic diseases	27.1
Orthopedics and traumatology	25.4
Plastic and reconstructive surgery	26.8
Dermatology	22.4
Infectious diseases	27.3
Neurology	27.5
Nephrology	27.4
Cardiovascular surgery	27.8
Physical therapy and rehabilitation	26.4
Algology	31.0
Medical ecology and hydroclimatology	25.6
Consultations	
Infectious diseases - consultation	5.2
Orthopedics and traumatology - consultation	
Cardiovascular surgery - consultation	
Plastic and reconstructive surgery - consultation	
Dermatology - consultation	

rates of diagnosis-treatment and follow-up steps for DFU. In this analysis, the distribution values were provided with the results obtained by performing 5000 simulations for each possible situation. The time horizon is 1 calendar year.

RESULTS

The outpatient clinics visited and complications experienced by the patients according to proportional distribution vary during the treatment for DFU, and this creates different cost items in admissions made to the outpatient clinic^[14,18-27]. According to the public payer's perspective, the average annual per patient outpatient cost was \$579.5 in DFU treatment (Table 1).

The distribution of imaging tests and laboratory tests that are required to be performed during the treatment of DFU was obtained from the literature. While bone curettage culture and bone biopsy were required in 66% of the patients^[14,18,25-27] scintigraphy is performed in Wagner grade 4 and 5 gangrene patients (20.6%)^[15,16]. Some of the laboratory tests and imaging procedures performed for the patients with DFU are included in the payment per admission made to the outpatient clinic. The items that are not included in the payment per admission were added to the calculations according to the MED list. Culture, gram staining, and antibiogram analyses must be performed in patients with DFU. In DFU treatment, the average annual per patient cost for imaging tests was \$283.2, and laboratory test cost was \$284.8 (Table 2).

Wagner 3-4-5 DFU patient groups (44.9%) are admitted to inpatient for an average of 23 d a year^[18,19,21,23,26,27]. The average rate of amputation in said patients is 53.9%^[14,18,19,22-24,26,27]. The average hospitalization period for the patients who are amputated is 42 d^[23]. Six percent of patients are hospitalized for five days due to revascularization surgery, and the patients who have

Table 2 Unit costs of imaging - laboratory tests used in the treatment of diabetic foot ulcer

Name of test	Average unit cost (\$-PPP 2014)
Imaging tests	
Direct foot X-ray	Included in outpatient clinic admission fee
Electrocardiogram	
Unilateral chest X-ray	
Doppler ultrasonography	32.4
Magnetic resonance angiography	55.1
Angiography	392.3
Scintigraphy	131.7
Laboratory tests	
Bone biopsy	97.6
Tissue culture	97.6
Aspiration/swab culture	33.8
Bone curettage culture	97.6
HbA1c	3.4
Bleeding profile (Pre-op)	12.2
Glucose	Included in outpatient clinic admission fee
Hemogram	
C-reactive protein	
Red blood cell sedimentation rate	
Albumin	
Kidney function tests	
Liver function tests	
Hepatitis markers	

HbA1c: Hemoglobin A1c.

graft/flap (24%) are hospitalized for an average of 12 d (Table 3)^[28,29].

The average annual per patient cost of inpatient care due to DFU was \$7357.4.

All of the patients received training on a diabetic foot. The average rate of patients receiving treatment for osteomyelitis is 66%^[14,18,25-27]. Wound debridement is performed in patients at an average of 10.1%. The average rate of patients who had graft/flap was 24%. Revascularization surgery is performed in two ways: Percutaneous transluminal angioplasty (6%) or bypass (6%)^[18-20,26]. An average of 8.0% of the patients receives hyperbaric oxygen treatment^[18] over an average of 40 sessions^[20,24]. The rate of patients receiving physical therapy and rehabilitation is 16.6% (30.8% of the amputated patients) (Table 4)^[18,19,22,25,27].

The average annual per patient cost of intervention, rehabilitation, and training for DFU was \$2291.7.

Antibiotic treatment of DFU can be grouped into three categories: Low risk, high risk, and serious risk. In wounds with low risk (24%), clindamycin (4 × 300 mg) or cephalexin (4 × 500 mg) is used for 14 d. In wounds with high risk (60.3%), the patients are admitted to the hospital and one of the following parenteral treatments is administered for 14 d: Piperacillin/tazobactam, ampicillin sulbactam, cephalexin, third generation cephalosporin + clindamycin, or ciprofloxacin + clindamycin. The patients with wounds with serious risk (15.3%) must be admitted to the hospital and one of the following treatments is administered for 14-21 d (for 6 wk if osteomyelitis exists): Ampicillin + gentamicin + clindamycin, imipenem/meropenem, vancomycin, piperacillin/clavulanate, or ticarcillin/clavulanate^[30,31].

Table 3 Hospitalizations in departments for treatment of diabetic foot ulcer

Admission to department	Rate of patients (%)	Hospitalization period
Wound follow-up	44.9	23
Amputation surgery	53.9	42
Revascularization surgery	12.0	5
Plastic and reconstructive surgery - graft/flap	24.0	12

Table 4 Medical and surgical interventions performed in the treatment of diabetic foot ulcer and their costs

Interventions	Rate of patients (%)	Average cost (\$-PPP 2014)
Osteomyelitis treatment	66.0	605.0
Wound debridement	10.1	813.7
Graft/flap	24.0	602.1
Percutaneous transluminal angioplasty	6.0	6250.9
Bypass	6.0	6512.4
Amputation	53.9	961.7
Hyperbaric oxygen treatment	8.0	70.0 ¹
Physical therapy and rehabilitation	16.6	31.3 ¹
Diabetic foot patient training	100.0	1.5

¹Cost per session.

Insulin is used in all of the patients. Furthermore, the cost of anti-thrombotic treatment was added to the calculation for 85% of the patients.

The average annual per patient cost of medication used in the treatment of DFU was \$2545.8.

A total of 42.6% of the patients (non-ischemic wounds) use wound sheath as a medical supply^[18,20,26,27]. For 53.9% of the patients, the costs of orthosis-prosthesis devices were reflected in the calculation by considering the average values for the supplies and their weighted use (Table 5).

The average annual per patient cost of medical supplies used in the treatment of DFU was \$735.0.

Some complications of methods applied in the treatment of DFU can be observed as well. During treatment of DFU, infection can be observed after amputation in 12.8% of the patients and re-amputation can be observed in 11.5% of the patients^[16]. Complications such as barotraumatic otitis (10.26%) and hypoglycemia (0.85%) can be observed in patients treated with hyperbaric oxygen treatment^[20]. The average cost of complications per patient with DFU was \$210.3.

The average annual per patient cost of DFU treatment in our country was \$14287.7 (Table 6).

Sensitivity analysis

DFU includes use of some interventional procedures and pharmacological agents as well as various services provided by outpatient, inpatient, and laboratory units during diagnosis and treatment stages and also includes the cost of side effects of said procedures. Separate calculations were made for each variable for the dis-

Table 5 Distributions of annual drug use of patients regarding drugs and other medical materials

Drugs and medical materials	Average cost (\$-PPP 2014)
Insulin	1118.9
Antibiotics - in the group of wounds with low risk	78.1
Antibiotics - in the group of wounds with moderate risk	240.0
Antibiotics - in the group of wounds with serious risk	764.5
Anti-thrombotic	1348.4
Orthosis and prosthesis devices	961.5
Wound sheath	101.8

Table 6 The average annual cost per patient in diabetic foot treatment (\$-PPP 2014)

Cost components	Average per patient annual cost (\$-PPP)
Outpatient costs	579.5
Laboratory costs	284.8
Imaging test costs	283.2
Inpatient costs	7357.4
Intervention costs	2291.7
Drug costs	2545.8
Medical material costs	735.0
Complication costs	210.3
Total cost per patient	14287.7

tribution and accuracy of the results. Thus, the results of each variable are represented by the probabilities calculated within. As a result of the sensitivity analysis (Table 7), the standard deviation of the analysis was \$5706.6 ($n = 5000$; mean = \$14146.8, 95%CI: \$13988.6-\$14304.9).

The health expenses per person are \$-PPP 1045 in 2014 in Turkey and the average annual per patient cost for DFU is 14-fold of said amount. The total health expense in 2014 in Turkey is \$-PPP 80.3 billion and the total DFU cost has a 3% share in the total annual health expenses for Turkey.

DISCUSSION

In this study, the direct medical costs of DFU were investigated from the public payer’s perspective in Turkey. In similar studies conducted on a limited number of patients and in a single center, the estimated treatment costs of DFU patients were investigated in Turkey. In a retrospective study conducted by Keskek *et al*^[21] in 2010 on patients with type 2 diabetes mellitus (T2DM) in Turkey, it was demonstrated that the costs of treatment in the hospital per patient in patients with DFU in a tertiary hospital were higher than those of the patients with T2DM without any chronic complications. The cost of one hospitalization for each patient was calculated in the study conducted by Keskek *et al*^[21]. The cost of the hospital per admission in patients with DFU was \$976.10. The cost of supplies was calculated at 42.6%, and 57.4% was calculated as cost of service. In the cost study related to DM and chronic complications conducted with 7095 patients in 2009 in Turkey, the direct costs of DFU

Table 7 Result of sensitivity analysis for the total costs of diabetic foot ulcer

Cost components	\$-PPP (n = 5000)			
	Average	SD	95%CI	Median
Outpatient costs	576.2	196.1	568.0-584.4	565.5
Cost of imaging tests	279.4	205.6	267.9-291.0	219.2
Laboratory costs	283.3	64.7	278.7-287.7	254.8
Inpatient costs	7290.3	5047.9	6864.8-7715.8	8969.5
Intervention costs	2212.3	2347.7	1980.3-2444.4	1568.2
Drug costs	2554.4	566.3	2490.7-2618.2	2707.4
Cost of medical supplies	742.0	538.0	673.9-810.2	961.5
Cost of complications	208.7	452.7	145.0-272.5	0.0
Total cost	14146.8	5706.6	13988.6-14304.9	14615.4

were TL 1545, and in cases of amputation, the annual cost was TL 2386. In said study, the prevalence of DFU was 9.0% and its incidence was 2.0% in patients with DM, and the incidence of amputation was 0.2% and its prevalence was 1.0% in patients with DM^[32].

The costs of treatment vary according to the distribution of outpatient clinics visited by DFU patients, medication and medical materials used in treatment, laboratory and imaging tests performed, and the need for admission to a hospital and surgical intervention. The period of hospitalization is an important factor that causes high costs. The period of hospitalization is prolonged due to uncontrolled hyperglycemia, long-term wound care, infections, debridement, amputation, and newly occurring complications; therefore, the cost of treatment increases. In our study, the average direct total cost of DFU treatment per patient in our country is \$14287.7. Hospital admissions are \$7357.4 (51.5%) of said cost.

In the studies conducted based on prevalence from the perspective of the health care payer, the cost of DFU in the United States was between \$1892 and \$48354^[33-36]. In the study conducted by Harrington *et al.*^[33], calculations were made using the insurance database of 1995 in the United States. The cost of DFU was \$15309. Inpatient costs are 74% of the total cost^[33]. The study conducted by Stockl *et al.*^[34] was performed by using the insurance database of 2000 and 2001. The cost per episode increases according to the severity of DFU. While the cost of grade 1 was \$1892 per episode, the cost of grade 4/5 was \$27721 per episode. Inpatient costs amount to 77% of the total cost^[34]. In the study conducted by Sargen *et al.*^[35], the cost of DFU was studied using the insurance database of calendar year 2007. In said study, the cost of DFU was \$31363, and if amputation was performed, said cost was \$48354^[35]. In the study conducted by Margolis *et al.*^[36] based on the Medicare database of the United States, the amounts of reimbursement payments made for DFU and lower extremity amputations between 2006 and 2008 were calculated. The cost per patient in patients with DM with DFU was \$31600 for 2006, \$33100 for 2007, and \$35100 for 2008. The cost per patient in patients with DM who had a lower extremity amputation was \$49300, \$51200, and \$54100, respectively^[36].

Kerr *et al.*^[37] calculated the cost of DFU for the National Health Service (NHS) in England in 2010-2011.

Outpatient care, inpatient care, and post-amputation care were calculated in the study conducted by Kerr *et al.*^[37]. Moreover, calculations for materials such as wheelchairs, et cetera, were performed as well. In the study, it was found that 0.6% of the expenditures of NHS consisted of DFU for 2010-2011. Half of the total cost consisted of primary and community care of DFU. Some 8.8% of the total hospital costs associated with diabetes were spent for DFU. The existence of DFU increases the period of hospitalization of the patients by 2.51-fold. The outpatient cost was £4994. The inpatient cost was £3620 per admission. The post-amputation care cost was £2879 per patient.

In the study conducted by Girod *et al.*^[38] in 2003 in France, the monthly cost of DFU was €697 for outpatient care and €1556 for hospital care. While 70% of the total cost consisted of hospital costs in the patients admitted to the hospital, the percentage of drug costs was 10%^[38].

Prompers *et al.*^[39] prospectively calculated the societal disease cost for DFU in Europe in 2003-2004 with the approach based on incidence. In the study, in which 14 sites from 10 European countries were included, the direct cost of DFU per patient was €9446 and the cost per patient in amputated patients was €24540. The indirect cost of DFU was €645 per patient and said cost was €681 in the amputated patients. Hospital costs were 39% of the total cost of DFU^[39].

In the study conducted by Rezende *et al.*^[40] in 2008 in Brazil with a simulated hypothetical cohort, approximately 30% of patients with DFU were admitted to the hospital. It was stated that extremity amputation was performed in 14% of patients with DFU. The total annual cost of patients admitted to the hospital due to DFU was approximately \$264 million (\$51 million-461 million) and said cost was \$128 million (\$24.5 million-\$222.3 million) for the amputated patients^[40].

In a study conducted in Pakistan in 2005 for investigating the direct cost of DFU treatment in a tertiary hospital, it was demonstrated that the cost of treatment increases as DFU progresses. The cost for University of Texas Classification grade 1 phase B was £21 and the same cost was £288 for grade 2 phase D and £378 for grade 3 phase D. In the study, in which 62% of the patients had a grade 2 ulcer, the average cost was £376 for major amputations and £389 for minor amputations. The average annual health expense per patient was £1.7

in Pakistan for the period the study was conducted^[41].

In a study comparing the costs of United States Medicare and private insurance patients in 2013, it was calculated that the annual treatment cost of DFU was \$11296 for Medicare (\$27040 vs \$15743) and \$15329 for privately insured (\$25931 vs \$10602) patients^[42].

In conclusion, despite the fact that it is difficult to compare the costs between countries due to the social and economic differences in terms of methods used in the treatment of DFU, said disease is a complication that decreases the quality of life of the patient, is life threatening, and significantly increases the socio-economic costs of DM.

The annual cost of DFU in Turkey was found to be similar to the results of cost studies conducted based on prevalence for the other countries.

DM-related complications are severe and will often require hospitalization for long periods. In some cases, it exposes a necessity for major surgery. The highest cost component was the hospital cost in the COI for DFU. Improvements in inpatient durations and health interventions will reduce the costs of related disease. The second leading cost component was found to be the pharmacy costs. Among these costs, antithrombotic drugs have the largest share. Increased use of generic anti-thrombotic drugs may be a powerful factor for reducing this cost.

The most effective way of reducing the costs related to DFU is the prevention of the complication itself. Another alternative is delaying the complication as long as possible. In order to prevent DFU, it will be helpful to provide training to the patients at risk and to raise awareness in patients with DM in terms of economy. Appropriate and efficient treatment of DM is a health intervention that can prevent complications. Further studies may help in discovering more effective healthcare strategies and improving the healthcare quality.

COMMENTS

Background

Diabetes mellitus (DM) has the highest proportion in health expenses globally. A major part of these expenses are caused by DM complications. Diabetic foot ulcer (DFU) is a frequent and severe DM complication. DFU might cause disability by going all the way to amputation. Studies have shown that DFU substantially increases mortality rates. The study has been done from Turkey Healthcare Payer's perspective. In Turkey, there are no previous studies of DFU costs done according to cost-of-illness (COI) methodology.

Research frontiers

The current research hotspot is to identify how much DFU's cost is among all DM complications that are high in cost and which resources cost the highest among all the components of DFU costs. This way, the areas that should be intervened to lower the DFU costs will be easier to determine.

Innovations and breakthroughs

DFU's annual mean per patient cost is \$14287.7. Hospitalization costs constitute 51.5% of these expenses. Studies done in United States and Europe report that hospitalization costs for DFU are approximately 70%. This rate is lower in Turkey. Also, hospitalization costs are a major part of DFU costs. Pharmacy costs, which are mostly anti-thrombotic drugs and insulin treatment, constitute 18% of all

costs. In Turkey, DM constitutes 23% of all healthcare costs, and 1/6 of this is DFU expenses, which are approximately 3% of all health care expenses in Turkey.

Applications

With this study, it has been shown that DFU constitutes 3% of all health care costs in Turkey. Shortening the time spent hospitalized and improving the interventions done in hospitals should lower the costs substantially. Using generic anti-thrombotic agents and manufacturing insulin locally in Turkey are powerful moves that might decrease these costs. The study, which is done by COI methodology, will supply the convenient data needed to compare the costs between Turkey and other countries.

Terminology

Cost in health economics refers to the resources consumed during the provision of health care. COI study aims to determine the total economic impact of a disease or health condition on society through the identification, measurement, and valuation of all direct and indirect costs. Sensitivity analysis is a way to analyze the impact of uncertainty on an economic analysis or a decision. Simulation is a modeling technique that makes it possible to observe the causation in the system and the actions of the real system under different circumstances. Monte Carlo Simulation (MCS) is a technique that uses random numbers and a trial-and-error method without using any formula. MCS provides an estimate for the statistical distribution of the possible costs.

Peer-review

In the present study, the authors evaluate the annual cost of patients with diabetic foot ulcers in Turkey. In general, the manuscript is well written, straightforward and very descriptive.

REFERENCES

- 1 **International Diabetes Federation.** IDF Diabetes Atlas. 6th ed. Basel, Switzerland: International Diabetes Federation, 2013: 11-16
- 2 **Public Health Institution of Turkey.** National Diabetes Programme 2015-2020. Ankara, Turkey: Republic of Turkey Ministry of Health, 2014: 25-38
- 3 **Singh N, Armstrong DG, Lipsky BA.** Preventing foot ulcers in patients with diabetes. *JAMA* 2005; **293**: 217-228 [PMID: 15644549 DOI: 10.1001/jama.293.2.217]
- 4 **Reiber GE, Vileikyte L, Boyko EJ, del Aguila M, Smith DG, Lavery LA, Boulton AJ.** Causal pathways for incident lower-extremity ulcers in patients with diabetes from two settings. *Diabetes Care* 1999; **22**: 157-162 [PMID: 10333919]
- 5 **Ollendorf DA, Kotsanos JG, Wishner WJ, Friedman M, Cooper T, Bittoni M, Oster G.** Potential economic benefits of lower-extremity amputation prevention strategies in diabetes. *Diabetes Care* 1998; **21**: 1240-1245 [PMID: 9702427 DOI: 10.2337/diacare.21.8.1240]
- 6 **Ministry of Health and Turkish Diabetes Foundation.** Diabetes 2020: Vision and Targets - Turkey Final Report. Ankara, Turkey: Turkish Diabetes Foundation, 2010: 57-60
- 7 **Cowley P, Bodabilla L, Musgrove P, Saxenian H.** Content and Financing of an Essential National Package of Health Services, Global Assessments in the Health Sector. World Health Organization, 1994: 171-181
- 8 **Kobelt G.** Forms of Health Economic Evaluation. In: Kobelt G. Health economics: An introduction to economic evaluation. 3rd ed. London: Office of Health Economics, 2013: 12-31
- 9 **Rice DP.** Cost-of-illness studies: fact or fiction? *Lancet* 1994; **344**: 1519-1520 [PMID: 7983947 DOI: 10.1016/S0140-6736(94)90342-5]
- 10 **Rice DP.** Cost of illness studies: what is good about them? *Inj Prev* 2000; **6**: 177-179 [PMID: 11003181 DOI: 10.1136/ip.6.3.177]
- 11 **Russell LB, Siegel JE, Daniels N, Gold MR, Luce BR, Mandelblatt JS.** Cost-effectiveness analysis as a Guide to resource allocation in Health: Roles and limitations. In: Gold MR, Siegel JE, Russell LB, Weinstein MC, editors. Cost-effectiveness in health and medicine. New York: Oxford University Press, 1996: 3-24
- 12 **Luce BR, Manning WG, Lipscomb J.** Estimating costs in Cost-

- effectiveness analysis. In: Gold MR, Siegel JE, Russell LB, Weinstein MC, editors. Cost-effectiveness in health and medicine. New York: Oxford University Press, 1996: 176-213
- 13 **Wagner FW.** The dysvascular foot: a system for diagnosis and treatment. *Foot Ankle* 1981; **2**: 64-122 [PMID: 7319435 DOI: 10.1177/107110078100200202]
 - 14 **Yesil S, Akinci B, Yener S, Bayraktar F, Karabay O, Havitcioglu H, Yapar N, Atabey A, Kucukyavas Y, Comlekci A, Eraslan S.** Predictors of amputation in diabetics with foot ulcer: single center experience in a large Turkish cohort. *Hormones (Athens)* 2009; **8**: 286-295 [PMID: 20045802 DOI: 10.14310/horm.2002.1245]
 - 15 **Demir T, Akinci B, Yesil S.** Diagnosis and treatment of diabetic foot ulcers. *Dokuz Eylul Medical Journal* 2007; **21**: 63-70
 - 16 **Arıkan Y, Kuzgun U, Sever C, Armagan R.** The role of orthopedic's in multidisciplinary approach to diabetic foot wounds. *The Medical Bulletin of Sisli Etfal Hospital* 2010; **44**: 106-112
 - 17 **Republic of Turkey Social Security Institution.** The Medical Enforcement Declaration. 2014
 - 18 **Altındas M, Kilic A, Cinar C, Bingol UA, Ozturk G.** The epidemiology of foot wounds in patients with diabetes: a description of 600 consecutive patients in Turkey. *J Foot Ankle Surg* 2011; **50**: 146-152 [PMID: 21353997 DOI: 10.1053/j.jfas.2010.12.017]
 - 19 **Tabur S, Eren MA, Çelik Y, Dağ OF, Sabuncu T, Sayiner ZA, Savas E.** The major predictors of amputation and length of stay in diabetic patients with acute foot ulceration. *Wien Klin Wochenschr* 2015; **127**: 45-50 [PMID: 25398288 DOI: 10.1007/s00508-014-0630-5]
 - 20 **Akgül EA, Karakaya J, Aydin S.** Role of comorbidities as limiting factors to the effect of hyperbaric oxygen in diabetic foot patients: a retrospective analysis. *Diabetes Ther* 2014; **5**: 535-544 [PMID: 25273365]
 - 21 **Keskek SO, Kirim S, Yanmaz N.** Estimated costs of the treatment of diabetic foot ulcers in a tertiary hospital in Turkey. *Pak J Med Sci* 2014; **30**: 968-971 [PMID: 25225508 DOI: 10.12669/pjms.305.5182]
 - 22 **Karakas A, Arslan E, Cakmak T, Aydin I, Akgul EO, Demirbas S.** Predictive Value of Soluble CD14, Interleukin-6 and Procalcitonin For Lower Extremity Amputation in People with Diabetes with Foot Ulcers: A Pilot Study. *Pak J Med Sci* 2014; **30**: 578-582 [PMID: 24948983 DOI: 10.12669/pjms.303.4575]
 - 23 **Mutluoglu M, Sivrioglu AK, Eroglu M, Uzun G, Turhan V, Ay H, Lipsky BA.** The implications of the presence of osteomyelitis on outcomes of infected diabetic foot wounds. *Scand J Infect Dis* 2013; **45**: 497-503 [PMID: 23384323 DOI: 10.3109/00365548.2013.765589]
 - 24 **Aydin F, Kaya A, Karapinar L, Kumbaraci M, Imerci A, Karapinar H, Karakuzu C, Incesu M.** IGF-1 Increases with Hyperbaric Oxygen Therapy and Promotes Wound Healing in Diabetic Foot Ulcers. *J Diabetes Res* 2013; **2013**: 567834 [PMID: 23671876 DOI: 10.1155/2013/567834]
 - 25 **Korkmaz M, Erdoğan Y, Balcı M, Senarslan DA, Yılmaz N.** Preoperative medical treatment in patients undergoing diabetic foot surgery with a Wagner Grade-3 or higher ulcer: a retrospective analysis of 52 patients. *Diabet Foot Ankle* 2012; **3** [PMID: 22919456 DOI: 10.3402/dfa.v3i0.18838]
 - 26 **Altay FA, Sencan İ, Şentürk GÇ, Altay M, Güvenman S, Ünverdi S, Açıkgöz ZC.** Does treatment affect the levels of serum interleukin-6, interleukin-8 and procalcitonin in diabetic foot infection? A pilot study. *J Diabetes Complications* 2012; **26**: 214-218 [PMID: 22521320 DOI: 10.1016/j.jdiacomp.2012.03.018]
 - 27 **Ertugrul BM, Oncul O, Tulek N, Willke A, Sacar S, Tunccan OG, Yilmaz E, Kaya O, Ozturk B, Turhan O, Yapar N, Ture M, Akin F.** A prospective, multi-center study: factors related to the management of diabetic foot infections. *Eur J Clin Microbiol Infect Dis* 2012; **31**: 2345-2352 [PMID: 22354524 DOI: 10.1007/s10096-012-1574-1]
 - 28 **McCartan B, Dinh T.** The use of split-thickness skin grafts on diabetic foot ulcerations: a literature review. *Plast Surg Int* 2012; **2012**: 715273 [PMID: 22666573 DOI: 10.1155/2012/715273]
 - 29 **Puttirutvong P.** Meshed skin graft versus split thickness skin graft in diabetic ulcer coverage. *J Med Assoc Thai* 2004; **87**: 66-72 [PMID: 14971537]
 - 30 **Yaman E.** As Scintigraphic Determination of the Amputation Levels on the Diabetic Foot. Isparta, Turkey: Süleyman Demirel University, 2009
 - 31 **Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG, Deery HG, Embil JM, Joseph WS, Karchmer AW, Pinzur MS, Senneville E.** 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis* 2012; **54**: e132-e173 [PMID: 22619242 DOI: 10.1093/cid/cis346]
 - 32 **Malhan S, Oksuz E, Babineaux SM, Ertekin A, Palmer JP.** Assessment of the Direct Medical Costs of Type 2 Diabetes Mellitus and its Complications in Turkey. *Turk Jem* 2014; **2**: 39-43 [DOI: 10.4274/tjem.2441]
 - 33 **Harrington C, Zagari MJ, Corea J, Klitenic J.** A cost analysis of diabetic lower-extremity ulcers. *Diabetes Care* 2000; **23**: 1333-1338 [PMID: 10977028 DOI: 10.2337/diacare.23.9.1333]
 - 34 **Stockl K, Vanderplas A, Tafesse E, Chang E.** Costs of lower-extremity ulcers among patients with diabetes. *Diabetes Care* 2004; **27**: 2129-2134 [PMID: 15333473 DOI: 10.2337/diacare.27.9.2129]
 - 35 **Sargen MR, Hoffstad O, Margolis DJ.** Geographic variation in Medicare spending and mortality for diabetic patients with foot ulcers and amputations. *J Diabetes Complications* 2013; **27**: 128-133 [PMID: 23062327 DOI: 10.1016/j.jdiacomp.2012.09.003]
 - 36 **Margolis DJ, Malay DS, Hoffstad OJ, Leonard CE, MaCurdy T, Tan Y, Molina T, de Nava KL, Siegel KL.** Economic burden of diabetic foot ulcers and amputations. Diabetic Foot Ulcers. Data Points 3 (prepared by the University of Pennsylvania DEcIDE Center, under Contract No. HHS290200500411). Rockville, MD: Agency for Healthcare Research and Quality, 2011
 - 37 **Kerr M, Rayman G, Jeffcoate WJ.** Cost of diabetic foot disease to the National Health Service in England. *Diabet Med* 2014; **31**: 1498-1504 [PMID: 24984759 DOI: 10.1111/dme.12545]
 - 38 **Girod I, Valensi P, Laforêt C, Moreau-Defarges T, Guillon P, Baron F.** An economic evaluation of the cost of diabetic foot ulcers: results of a retrospective study on 239 patients. *Diabetes Metab* 2003; **29**: 269-277 [PMID: 12909815]
 - 39 **Prompers L, Huijberts M, Schaper N, Apelqvist J, Bakker K, Edmonds M, Holstein P, Jude E, Jirkovska A, Mauricio D, Piaggese A, Reike H, Spraul M, Van Acker K, Van Baal S, Van Merode F, Uccioli L, Urbancic V, Ragnarson Tennvall G.** Resource utilisation and costs associated with the treatment of diabetic foot ulcers. Prospective data from the Eurodiale Study. *Diabetologia* 2008; **51**: 1826-1834 [PMID: 18648766 DOI: 10.1007/s00125-008-1089-6]
 - 40 **Rezende KF, Ferraz MB, Malerbi DA, Melo NH, Nunes MP, Pedrosa HC, Chacra AR.** Predicted annual costs for inpatients with diabetes and foot ulcers in a developing country—a simulation of the current situation in Brazil. *Diabet Med* 2010; **27**: 109-112 [PMID: 20121897 DOI: 10.1111/j.1464-5491.2009.02871.x]
 - 41 **Ali SM, Fareed A, Humail SM, Basit A, Ahmedani MY, Fawwad A, Miyan Z.** The personal cost of diabetic foot disease in the developing world—a study from Pakistan. *Diabet Med* 2008; **25**: 1231-1233 [PMID: 19046203 DOI: 10.1111/j.1464-5491.2008.02529.x]
 - 42 **Rice JB, Desai U, Cummings AK, Bimbaun HG, Skomicki M, Parsons N.** Medical, Drug, and Work-Loss Costs of Diabetic Foot Ulcers. *Value in Health* 2013; **16**: A12 [DOI: 10.1016/j.jval.2013.03.075]

P- Reviewer: Navedo MF, Tarantino G, Zhao J **S- Editor:** Gong XM
L- Editor: A **E- Editor:** Li D





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>

