An estimation of the effect of 100% Compliance with Diabetes Treatment: Can we reduce cost of illness with higher compliance rates?

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Abstract
Introduction: The current study was designed to estimate the direct cost of noncompliance of diabetes patients to the US health system. Understanding these expenses can inform screening and education budget policy regarding expenditure levels that can be calculated to be cost-beneficial.
Materials and Method: The study was conducted in three parts. First, a computer search of National Institutes of Health websites and professional society websites for organizations with members that treat diabetes, and a PubMed search were performed to obtain the numbers required for calculations. Second, formulas were developed to estimate the risk of non-compliance and undiagnosed diabetes. Third, risk calculations were performed using the information obtained in part one and the formulas developed in part two.
Results: Direct risk reduction for diabetes-related kidney disease, stroke, heart disease, and amputation were estimated for 100% compliance with diabetes treatment. Risk, case and yearly cost reduction calculated for a 100% compliance with diabetes treatment were 13.6%, 0.9 million and US$ 9.3 billion, respectively.
Conclusion: Society, insurers, policy makers and other stakeholders could invest up to these amounts in screening, education and prevention efforts in an effort to reduce these costly and traumatic sequelae of noncompliant diabetes patients.

Introduction

Diabetes is the one of most common chronic diseases throughout the world. In the USA, it was reported that annual care visits for diabetes total 28.6 million per year.[1] Direct, indirect and total costs of diabetes to the USA`s health system per year were reported as $116 billion, $58 billion and $174 billion, respectively in 2007 dollars.[2] There are 23.6 million people suffering from diabetes.[2]

It has been estimated that the cost of diabetes per patient was $7,372 in 2007 dollars ($ 174 billion / 23.6 million patients). Treatments can control patients' symptoms and can reduce comorbities and costs of diseases. But if patients cannot be diagnosed or be compliant with their treatments, the risks of comorbities and cost of comorbities may increase. There are huge numbers of undiagnosed and diagnosed but non-compliant patients. It was reported that 17.9 million of 23.6 million diabetes patients are aware they have it (approximately 76%)[3] and nearly 72 (mean of 52-93%) percent of treated patients are compliant[4] with their treatment. Based on the Markov Model presented in Figure 1, only 55 percent of all diabetes patients are under full current treatment.

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Diabetes doesn't have known separate risk points for gender, age or blood glucose level. It has known risk points for only being diabetic or not being diabetic. Risk points, incidence and prevalence of diabetes were published by the National Diabetes Information Clearinghouse.[5,6] In addition, compliance and noncompliance of diabetics were reported in Breitscheidel's review in 2009.[4] Prevalence of the comorbidities of diabetes was published by the Centers for Disease Control and Prevention's Statistics[7,8,9] and the cost of comorbidities was published in Heart Disease and Stroke Statistics 2009[10], Atlas of Chronic Kidney Diseases 2009[11] and Kolansky's[12] review which was published in 2009.

Data were published about diabetes regarding incidence, prevalence, risks and comorbidities. However, there are some unknown areas such as the cost of non-compliance. The current study was designed to calculate the direct cost of non-compliant diabetes patients to the US health system. Understanding these expenses can inform screening and education budget policy regarding expenditure levels that can be calculated to be cost-beneficial.

Materials and Method
The study was conducted in three parts. First, a computer search of National Institutes of Health websites and professional society websites for organizations with members that treat diabetes, and a PubMed search were performed to

obtain the numbers required for calculations. Second, formulas were developed to estimate the risk of noncompliance and undiagnosed diabetes. Third, risk calculations were performed using the information obtained in part one and the formulas developed in part two.

First part
An internet search was performed at the National Institutes of Health's web sites. If there were data for the U.S. for diabetes which were published by the National Institutes of Health, they were included. If data were not published by National Institutes of Health for the U.S, the web sites of the societies related to diabetes were searched. If data for the U.S. were not published in the society's web sites, a PubMed search was performed. The published studies which include the widest and newest data in PubMed were included for calculations. After including data, estimations were made. The findings from the computer search and estimations are listed in Table 1.

Second part
Group percentages were estimated from the known numbers. Groups were defined as compliant, noncompliant and undiagnosed for diabetes. The undiagnosed group's percentage was taken as 24% (1-0.76=0.24).[3] The compliant group's percentage was taken as 55% depending on diagnosed group's percentage (76%)[3] multiplied with compliant percentage (72% - mean of 52-93%)[4] (0.76 x 0.72 = 0.55). The noncompliant group percentage was taken as 21% based upon 76%[3] (all diagnosed patients in all diabetes patients) and 55% (compliant patients in all diabetes patients) (0.76-0.55 = 0.21).

Diabetes doesn't have known separate risk points of comorbidities for each gender, age and blood glucose level. It has known risk points for only being diabetic or not being diabetic. Risk points for comorbidities were estimated and risk points of sub-groups were calculated. The risk points were converted based on the compliance risk point as 1.

The calculations were repeated for each group and these results were summed for calculating the main risk points of comorbidities which could be caused by diabetes. The calculations were performed for compliant, noncompliant and undiagnosed groups. Then the calculation was performed for a 100% Compliant Strategy which means that all patients who were diagnosed with diabetes in the U.S. would take nearly 100% of doses prescribed or follow nearly 100% of recommendations. The Compliance Strategy led to control of blood HbA1c values, with blood HbA1c control defined as blood HbA1c values less than 6.5%[14].

The difference in risk points of current patients and a 100% Compliant Strategy were used for calculation of cost reduction. The percentage of difference between risk points of current patients and a 100% Compliant Strategy were calculated. The percentage of risk reduction was used for calculation; the case reduction and the direct cost reduction by muliplication with current cases and direct costs.

Formulas are shown below:
1. $\sum$(Percentage of Group * Risk Points)
2. Total Risk Point: $\sum$ Risk Points
3. % Risk Point Reduction for Compliance: 100 x (Total Base Risk Point -Total Estimated Compliance Risk Point)/Base Risk Point
4. Case Reduction: Base Disease Prevalence * % Risk Point Reduction
5. Cost of Illness per Patient: Cost of Illness / Prevalence of Illness
6. Cost of Illness Reduction: Case Reduction * Cost of Illness per Patient

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Example 1:
Calculation of Kidney Diseases for Diabetes in Compliant Patients

If risk point of compliance strategy is 1, the noncompliant risk point of kidney diseases according to increased risk point of kidney diseases in patients with diabetes in all kidney diseases[5] is 50%.
= 1 / 50% = 2
Compliant Group Base Risk Point = 0.55*1 (Percentage of Compliant Groups*Stroke Risk Point) = 0.55
Incompliant Group Base Risk Point = 0.21*2 (Percentage of Incompliant Groups*Stroke Risk Point) = 0.42
Undiagnosed Group Base Risk Point = 0.24*2 (Percentage of Undiagnosed Groups*Stroke Risk Point) = 0.48
Total Base Risk Point = 0.55 + 0.42 + 0.48 = 1.45
%100 Compliant Strategy Risk Point = (0.55+0.21)*1 + 0.48 = 1.24
% Risk Point Reduction of Kidney Diseases for Compliance Strategy: (1.45-1.24)/1 * 100 = 14 %
Case Reduction: 1,628,000 x 14 % = 235,779
Cost of Illness per Patient: US$ 63 billion / 3,700,000 = US$ 17132
Cost Of Illness Reduction: 235,779 * US $17132 = US $ 4.0 billion

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Risk Point: Risk point of comorbidities of diabetes at estimated situations.
Base Risk Point: Risk point of comorbidities of diabetes at now.
Total Risk Point: Risk point of comorbidities of diabetes at estimated situations.
Total Base Risk Point: Risk point of comorbidities of diabetes now.

Third Part
The calculation was completed as shown in Example 1 for the diabetes compliance population stroke risk calculation.

Estimations
Percentage of compliance with diabetes treatment was estimated from the Breitscheidel et al. study.[4] It was reported that the range of compliance to diabetes treatment were 52-93%. The mean value of 52% and 93% were taken for our calculations; which is 72%.

The direct cost of lower extremity amputation was reported to be $24,000-40,000 in 1990 US$.[9] So these numbers were converted to 2009 US$ by adding a yearly 5% inflation rate and by calculating mean average which equaled US $ 80,000. In addition, heart failure risks were taken as heart diseases risks.

Direct cost per patient was estimated from known direct costs and number of patients. For example, the direct cost of stroke per patient was calculated by dividing the direct cost of stroke by the numbers of adults who ever had a stroke.

Risk points of undiagnosed and noncompliant patient were accepted as the same.

Results
Risk of kidney disease, stroke, heart disease (heart failure) and amputation caused directly by diabetes were calculated from known numbers and estimations. (Tables 1 & 2) Direct risk reduction caused by diabetes for kidney disease, stroke, heart disease, amputation were calculated for a 100% Compliant Situation (Table 3).

Risk, case and cost reduction for kidney disease caused by diabetes with a 100% Compliant strategy were 14%, 0.23 million and US$ 4.0 billion, respectively. Risk, case and cost reduction for stroke caused by diabetes with a 100% Compliant strategy were 17%, 0.18 million and US$ 1.2 billion, respectively. Risk, case and cost reduction for heart diseases (heart failure) caused by diabetes with a 100% Compliant strategy were 10%, 0.48 million and US$ 3.3 billion, respectively. Risk, case and cost reduction for amputation caused by diabetes with a 100% Compliant strategy were 12%, 0.008 million and US$ 0.6 billion, respectively.

Total risk, case and yearly cost reduction calculated for a 100% Compliant Strategy were 13.6%, 0.9 million and US$ 9.3 billion, respectively.

Discussion
Noncompliance with prescribed drug regimens is a widespread phenomenon which results in needless trauma, decreased efficacy and is often associated with increased medical expenditures. Despite this, economic evaluations based on decision-analytic models rarely incorporate noncompliance to allow for the differences in compliance observed between controlled clinical trials and routine clinical practice.[15]

For example, a population based study was performed for comparing direct health care costs related to the treatment of osteoporosis and osteoporotic fractures among compliant and noncompliant users of alendronate and risedronate. Compared to compliant women, noncompliant women incurred significantly higher physician care and hospital care costs. Due to lower drug costs, total direct health care costs were lower among noncompliant women.[16]

In addition, a study was performed with kidney transplantation patients for examining relationships between compliance with allograft outcomes and costs. Immunosuppression medication possession ratios indicative of less than the highest quartile of compliance predicted increased risk of graft loss and elevated costs. These findings suggest that interventions to improve medication compliance among kidney transplant recipients should emphasize the benefits of maximal compliance, rather than discourage low compliance.[17]

Noncompliance with cardiovascular and antidiabetic medication is a significant problem. It was reported in Cramer's review about compliance and persistence in the treatment of diabetes, hypertension and dyslipidaemia that 30% of days 'on therapy' was not covered by medication and only 59% of patients were taking medication for more than 80% of their days 'on therapy' in a year. Good compliance has a positive effect on clinical outcomes, suggesting that the management of CVD may be improved by improving patient compliance.[19]

Moreover, it was reported that direct risk reduction for stroke caused by hypertension, heart attack, kidney disease and heart disease was calculated for a 100% Compliant Strategy. Risk, case and cost reduction for a 100% Compliant Strategy for Hypertension were 32%, 8.5 million and US$ 72 billion, respectively. [20]

Limitations
There were numerous assumptions and estimates such as multiplying the known numbers for calculating the percentages of compliant, noncompliant and undiagnosed groups in all diabetic populations. So it is necessary to perform this analysis depending on a separate trial which will report the percentage of compliant, noncompliant and undiagnosed groups.

Risk and costs of eye diseases were taken as risk and costs of blindness which were lead by diabetes. It is necessary to perform this analysis depending on the actual risks and costs of blindness.

Risk and costs of heart failure were taken as risk and costs of heart diseases which were led by diabetes. It is necessary to perform this analysis depending on the actual risks and costs of heart diseases.

The number of patients who had kidney diseases, stroke, heart diseases and amputations which were led by diabetes was estimated from the published data. On the other hand, there were no precise incidence numbers for the comorbidities of diabetes. The published data were estimated from known numbers as well. It is necessary to perform this analysis depending on the clean incidence numbers for the comorbidities of diabetes.

While this analysis will be first in the literature for diabetes, further analysis and estimations are needed to be performed for undiagnosed diabetes populations also. In total, it is possible to save nearly $8.1 billion per year by increasing the percentage of compliant patients in the ongoing treatment of diabetes. These are hypothetical and full compliance would be hard or probably impossible to achieve but it reveals the amount of improvement that is possible.
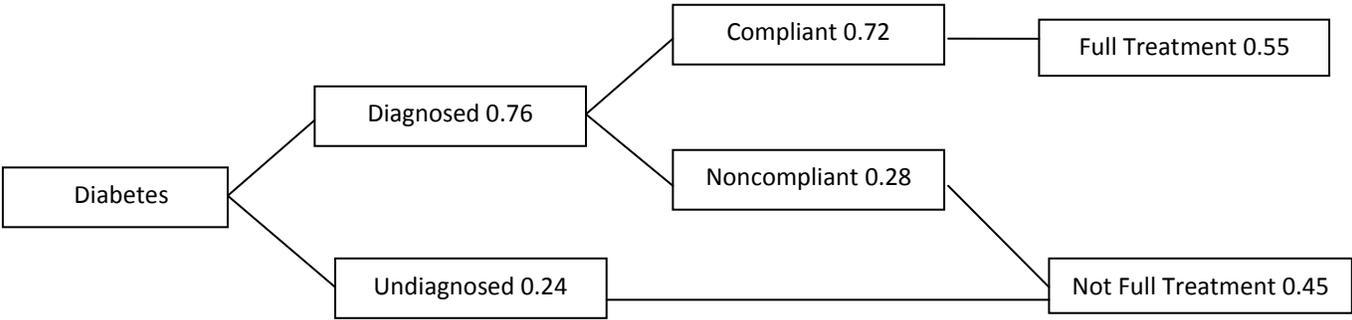
In conclusion, our analysis suggests that society, insurers, policy makers, and other stakeholders could invest up to these amounts in screening, education and prevention efforts in an effort to reduce these costly and traumatic sequelae of noncompliant diabetes patients.

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Figure 1: Percentage of noncompliant, undiagnosed and untreated patients by Markov Model

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                                        ┌──────────────────┐      ┌────────────────────┐
                                        │  Compliant 0.72  │──────│ Full Treatment 0.55│
                                        └──────────────────┘      └────────────────────┘
                    ┌──────────────────┐
                    │ Diagnosed 0.76   │
                    └──────────────────┘
                                        ┌────────────────────┐
                                        │ Noncompliant 0.28  │
  ┌──────────┐                          └────────────────────┘
  │ Diabetes │
  └──────────┘
                    ┌──────────────────┐                          ┌──────────────────────┐
                    │ Undiagnosed 0.24 │──────────────────────────│ Not Full Treatment 0.45│
                    └──────────────────┘                          └──────────────────────┘
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Table 1: Numbers and estimation for calculation

Data	Numbers
USA Population[1]	306 million
Number of adults who ever had a stroke[7]	6.5 million
Number of adults with diagnosed kidney disease[7]	3.7 million
Number of adults with diagnosed heart disease[7]	26.6 million
Numbers of adults with diabetes[5]	23.6 million
Numbers of adult with amputations by diabetes(yearly)[5,6]	71.000
Percentage of diagnosed diabetes[5]	76%
Percentage of compliance to diabetes treatment[4]	72%* (mean value of 52-93%)
Percentage of stroke by directly diabetes in all stroke[5]	16%
Percentage of kidney diseases by directly diabetes in all kidney diseases[5]	44%
Percentage of heart diseases by directly diabetes in all heart diseases[5]	17%*
Direct cost of stroke per patient[10]	US$ 7,061*
Direct cost of kidney diseases per patient[11]	US$ 17,132*
Direct cost of heart diseases per patient[10]	US$ 6,879*
Direct cost of amputation per patient[9]	US$ 80,000*

*Estimated

Table 2: Risk Points & Estimated Risk Points for Diabetes

Diabetes Groups	Kidney Diseases		Stroke		Heart Diseases (Heart Failure)		Amputation	
	Risk Rdct.	Est. Risk	Risk Rdct.	Est. Risk	Risk Rdct.	Est. Risk	Risk Rdct.	Est. Risk
Compliance	50%[5]	1	57%[5]	1	42%[5]	1	56%[5]	1
Noncompliant		2		1.78		1.66		2.32
Undiagnosed		2		1.78		1.66		2.32

Table 3: Estimation of Effect of 100% Compliant Strategy for Diabetes

Data	100% Compliant Strategy for Diabetes		
	Direct Risk Reduction	Direct Case Reduction	Direct Cost Reduction (US$)
Kidney Disease Estimation	14%	0.23 million	4.0 billion
Stroke Estimation	17%	0.18 million	1.2 billion
Heart Disease(Heart Failure) Estimation	10%	0.48 million	3.3 billion
Amputation Estimation	12%	0.008 million	0.6 billion
Total	13.67 % (mean value)	0.90 million	9.3 billion