

Medical Cost Associated with Prediabetes

Yiduo Zhang, Ph.D.,¹ Timothy M. Dall, M.S.,¹ Yaozhu Chen, M.P.A.,¹
Alan Baldwin, M.S.,² Wenyang Yang, M.P.A.,¹ Sarah Mann, B.S.,¹ Victoria Moore, B.S.,²
Elisabeth Le Nestour, M.D.,³ and William W. Quick, M.D., F.A.C.P., F.A.C.E.²

Abstract

In this article, we estimate national health care resource use and medical costs in 2007 associated with prediabetes (PD), defined as either fasting plasma glucose between 100 and 125 or oral glucose tolerance test between 140 and 200.

We use Poisson regression with medical claims for an adult population continuously insured between 2004 and 2006 to analyze patterns of health care resource use by PD status. Combining rate ratios that reflect health care use patterns with national PD prevalence rates from the National Health and Nutrition Examination Survey, we calculate etiological fractions to estimate the portion of national health resource use associated with PD. The findings suggest that PD is associated with statistically higher rates of ambulatory visits for hypertension; endocrine, metabolic, and renal complications; and general medical conditions. PD is associated with a slight increase in visit rates for neurological symptoms, peripheral vascular disease, and cardiovascular disease, but the increase is not statistically significant. There is no indication that PD is associated with an increase in emergency visits and inpatient days. Extrapolating these patterns to the 57 million adults with PD in 2007 suggests that national annual medical costs of PD exceed \$25 billion, or an additional \$443 for each adult with PD.

PD is associated with excessive use of ambulatory services for comorbidities known to be related to diabetes. Our findings strengthen the business case for lifestyle interventions to prevent diabetes by adding additional economic benefits that potentially can be achieved by preventing or delaying PD. (*Population Health Management*. 2009;12:157-163)

AN ESTIMATED 57 MILLION people in the United States have prediabetes (PD), which is characterized by elevated blood glucose levels with either fasting plasma glucose between 100 and 125 or oral glucose tolerance test between 140 and 200.¹ Concerns regarding PD have focused on its role as a precursor to type 2 diabetes, a disease associated with increased risk for cardiovascular disease, renal complications, peripheral vascular disease, neurological complications, endocrine complications, and numerous other chronic health problems.²⁻⁷

There is growing evidence that even slightly elevated blood glucose levels, as is the case with PD, are associated with higher medical costs^{8,9} and increased risk for certain comorbidities of diabetes—coronary heart disease,¹⁰⁻¹⁴ retinopathy,^{15,16} hypertension,¹⁷ and even mortality.¹⁸ With nearly 1 in 4 adults (57 million out of 224 million) having PD, even a slight increase in per capita health care use and disease risk has significant implications for the health system.

While recent work highlights the significant economic burden associated with diabetes,^{19,20} few studies have investigated the economic burden of PD.^{8,9} We use recent medical claims data to estimate per capita excess health care use associated with PD, and combine this information with national estimates of health care use and medical costs to calculate national expenditures associated with PD. Such cost information is paramount to understanding the business case for interventions directed to improve prevention, screening, and treatment associated with PD.

Research Design and Methods

This study uses a Cost of Diabetes Model, originally developed to quantify the national cost of diagnosed diabetes, that contains estimates of national health care use and costs for comorbidities of diabetes. The data sources and methods used to develop this model, the national health care use and

¹The Lewin Group, Falls Church, Virginia.

²Ingenix/i3research, Basking Ridge, New Jersey.

³Ingenix/i3research, Nanterre, France.

Funding for this study was provided by the Novo Nordisk, Inc. National Changing Diabetes Program.

cost estimates in the model, and the etiological fractions used to determine the proportion of national costs attributed to diagnosed diabetes are described elsewhere.¹⁹ Following is a description of the data and methods used to adapt this model to quantify the national medical costs associated with PD.

Data

The primary national data sources used are Census Bureau population estimates for 2007; the 2003–2006 National Health and Nutrition Examination Survey (NHANES) to estimate national PD prevalence; and the 2003–2005 National Ambulatory Medical Care Survey (NAMCS), the 2003–2005 National Hospital Ambulatory Medical Care Survey (NHAMCS), and the 2003–2005 Medical Expenditure Panel Survey to obtain national estimates of health resource use and associated medical costs. These data sources are publicly available and documented extensively.²¹

To calculate etiological fractions that reflect the proportion of national health care use associated with PD, we require estimates of the ratio of health care use for people with PD to health care use for people without PD, adjusting for potential confounders. To calculate these rate ratios, we analyze medical claims in the Ingenix Research DataMart (RDM) for a population of 3.5 million adults continuously insured from January 1, 2004 to December 31, 2006. The RDM population is largely commercially insured through UnitedHealth, although the database contains beneficiaries of other commercial and public insurers. Claim records for lab tests are available for all beneficiaries; however lab results are available only for tests processed by 2 national lab vendors. Among patients with no diagnosis of diabetes, a total of 796,487 patients had either a fasting plasma glucose (FPG) or an oral glucose tolerance test (OGTT) in 2004 (with test results available for 10,502 patients). In 2005, a total of 782,521 patients without a diagnosis of diabetes had either a FPG or an OGTT (with test results available for 11,406 patients). Additional detail on the RDM population is provided in the following section.

Identifying the PD and potential comparison groups

To estimate national PD prevalence, we identified people in the NHANES with a FPG between 100 and 125 mg/dL. NHANES is a stratified random sample of the US population, and a FPG test is administered to a random subset of NHANES participants. The latest wave of NHANES also contains OGTT results for a sample of participants, but for consistency with the Centers for Disease Control and Prevention estimates, we use only FPG to estimate PD prevalence for the adult population older than age 20.¹ PD prevalence rates are estimated by age, sex, and race/ethnicity (non-Hispanic white, non-Hispanic black, non-Hispanic other, and Hispanic). We use age groups 20–34, 35–44, 45–54, 55–59, 60–64, 65–69, and 70 and older. Prevalence rates are multiplied by Census Bureau population estimates for 2007 to estimate the total number of people with PD.

We used the same FPG threshold to identify individuals with PD in the RDM. To increase the accuracy of patient identification, we also use OGTT test results to capture individuals who would likely have been identified as having

PD if they had had a FPG test. According to the American Diabetes Association Clinical Guideline, the comparable threshold is OGTT between 140 and 200 mg/dL.²² People in the RDM with an FPG or OGTT test result are a nonrandom sample of the population. Among the population with a glucose test, pregnant women and people with ophthalmic complications are overrepresented, reflecting health care use and referral patterns for glucose testing. We address the nonrandom nature of the data in 2 ways. First, we use data from one year (2004 or 2005) to categorize patients by PDM status, and then use data from the following year (2005 or 2006) to analyze health care use patterns. Receiving a glucose test is endogenous to health care use in the year the test is administered. Second, we use Poisson regression analysis to statistically control for differences in health care use patterns among 5 mutually exclusive groups of patients:

- Group #1: Confirmed with PD ($n = 1642$ in 2004 and $n = 1923$ in 2005): This population meets the clinical definition of PD as confirmed by at least 1 abnormal FPG or OGTT test during the PD identification years (ie, 2004 or 2005). We exclude women with any gestational diabetes diagnosis code (648.8x).
- Group #2: Presumed no PD (comparison group 1; $n = 8860$ in 2004 and $n = 9483$ in 2005): This group consists of people with FPG below 100 mg/dL or OGTT below 140 mg/dL in the PD identification years. This group overrepresents pregnant women who receive a glucose test as part of normal prenatal care, and could possibly overrepresent those at high risk for diabetes whose physicians recommended a glucose test, as well as those who are more likely to seek medical services. To the extent that this comparison group uses more health care services than the typical non-PD person, comparing health care use patterns for this group to the confirmed PD group could bias toward 0 estimates of health care use associated with PD.
- Group #3: Had FPG, but no results available (comparison group 2; $n = 785,985$ in 2004 and $n = 771,115$ in 2005): This group consists of nondiabetic individuals who had at least 1 FPG or OGTT test, but test results are unavailable in the RDM database. This group is contaminated by those who would have been identified as PD if their test results were estimates of health care use associated with PD.
- Group #4: Patients with diagnosed diabetes (comparison group 3 used for validation; $n = 278,257$): This group consists of people with any ICD-9 diagnoses of 250.x or HbA1c test result that exceeds 7.0% during the 2004 to 2006 period.
- Group #5: No glucose test (comparison group 4; $n = 2,448,775$ in 2004 and $n = 2,462,721$ in 2005): This group consists of nondiabetic individuals who had no FPG or OGTT test in 2004 or 2005. This group is contaminated by the presence of people with PD who did not have a glucose test in 2004 or 2005; comparing PD health care use to this comparison group could bias low estimates of excess health care use associated with PD.

Analysis of health resource care use patterns

We used Poisson regression to analyze patterns of health care resource use associated with neurological symptoms, peripheral vascular disease, cardiovascular disease, renal complications, endocrine complications, ophthalmic complications, and other complications of diabetes. The diagnosis

codes used to define these complication categories are described elsewhere.¹⁹ In addition, we analyze an “other” category that includes care provided for all reasons not included in the 8 categories previously specified but excluding care associated with injuries and pregnancy.

For each comorbidity group we estimate separate regressions for ambulatory visits, emergency visits, and inpatient days. Poisson regression allows us to isolate the relationship between PD status and health care service use, controlling for other determinants of health care use. The estimating equation is:

$$\text{Log}(\text{annual visits}_i) = \beta_0 + \beta_1 \times \text{PD}_i + \beta_2 \times \text{Gr1}_i + \beta_3 \times \text{Gr2}_i + \beta_4 \times \text{Gr3}_i + \beta_5 \times \text{control}_i$$

where PD, and Gr1 through Gr3 are dichotomous variables: PD=1 if identified with PD in identification year and 0 otherwise; Gr1 through Gr3 correspond to being in comparison groups 1 through 3 (1 in comparison group, 0 otherwise). Comparison group 4 has been omitted as the reference group. The row vector control_i represents an array of dichotomous variables indicating age group, sex, health insurance type (either commercial or public), Census region, year, and the presence of select diabetes complications and costly health conditions during the PD identification year (ie, peripheral vascular disease, cardiovascular disease, hypertension, endocrine complications, ophthalmic complications, pregnancy, neoplasm, HIV/AIDS, and organ transplantation).

In addition to regressions that included all 3.5 million adults, to test the sensitivity of our findings we estimated separate regressions for males, non-pregnant females, and pregnant females.

Estimating attributable cost

The data and methods used to calculate national estimates of health care use (eg, ambulatory visits, medications), by diagnosis category, are described elsewhere.¹⁹ The approach combines per capita estimates of physician office visits (from the NAMCS) and outpatient visits (from the NHAMCS) with Census Bureau population estimates for 2007 by age and sex. We use the primary diagnosis code to place the visit into one of the 8 aforementioned diagnosis categories.

We calculate etiological fractions to determine the portion of national visits associated with PD.²³ Health care use attributed to PD is calculated as the proportion of visits incurred (I) by people with PD minus the visits that are likely to have occurred even in the absence of PD. To derive these estimates from national totals, we must also determine the proportion of visits incurred by people with diagnosed diabetes mellitus (DDM) and undiagnosed (UDM) diabetes mellitus. The DDM population is defined as individuals with an FPG that exceeds 125. UDM is defined as unknowingly having elevated glucose levels that meet the definition of diabetes.

The Poisson regressions, described later, produce rate ratios (RR) that reflect the ratio of annual ambulatory visits (*visits*) for people with PD compared with people with assumed normal glucose levels (NGL). Estimates of prevalence and rate ratios for DDM come from work by Dall et al¹⁹; rate ratios for UDM come from other work by the authors.²⁴

Combining rate ratios and prevalence rates (P), we calculate etiological fractions (ε) for PD by age group, sex, and complication group:

$$\epsilon_{PDM} = (1 - I_{DDM} - I_{UDM}) \times \frac{(RR_{PDM} - 1) \times P_{PDM}}{1 - (P_{DDM} + P_{UDM}) + (RR_{PDM} - 1) \times P_{PDM}}$$

where

$$I_{DDM} = \frac{RR_{DDM} \times P_{DDM}}{1 + (RR_{DDM} - 1) \times P_{DDM}}$$

$$I_{UDM} = (1 - I_{DDM}) \times \frac{RR_{UDM} \times P_{UDM}}{1 - P_{DDM} + (RR_{UDM} - 1) \times P_{UDM}}$$

$$RR_{DDM} = \frac{\overline{\text{Visits}}_{DDM}}{\overline{\text{Visits}}_{UDM + PDM + NGL}}$$

$$RR_{UDM} = \frac{\overline{\text{Visits}}_{UDM}}{\overline{\text{Visits}}_{PDM + NGL}}$$

and

$$RR_{PDM} = \frac{\overline{\text{Visits}}_{PDM}}{\overline{\text{Visits}}_{NGL}}$$

Multiplying total visits and the etiological fractions produces estimates of excess visits associated with PD by demographic and complication group. Estimates of the national average cost (including pharmaceuticals) associated with each visit, by complication group, are estimated using the Medical Expenditure Panel Survey and are described elsewhere.¹⁹

Results

When multiplied by population estimates for 2007 from the Census Bureau, PD prevalence rates from the NHANES suggest there are 57 million adults living with PD. Prevalence rates vary by demographic, ranging from approximately 9% for women age 20–34 to over 42% for males age 65 and older.

The RDM data contain 10,502 people with a glucose test result in 2004 in the normal or PD range. This represents only 0.3% of the analyzed population. The comparison group (ie, those with no test or no test results) therefore contains a significant number of people with PD (which could bias toward 0 the estimates of differences between the PD and comparison groups). Pregnant women are overrepresented in the population receiving a glucose test in 2004; they constitute 6% of the population who test positive for PD and 14.7% of the population who test negative for PD. Women with a glucose level indicating gestational diabetes are excluded from the analysis (Table 1).

The Poisson regression analysis suggests that PD is associated with increased ambulatory visits, but we found no consistent evidence of an association between PD and increased risk of emergency visits and inpatient days. Consequently, we assume PD is not associated with medical

TABLE 1. SAMPLE SUMMARY STATISTICS FOR THREE-YEAR CONTINUOUSLY INSURED INDIVIDUALS IN RDM AS OF 2004 BASELINE IDENTIFICATION PERIOD

	<i>Test positive for PD</i>	<i>Test negative for PD</i>	<i>Glucose tested, results unavailable¹</i>	<i>Established diabetes</i>	<i>No glucose test</i>
Number of RDM Individuals	1,642	8,860	785,985	278,492	2,448,775
Age group					
20–34	37.0%	36.0%	47.4%	7.6%	18.6%
35–64	49.8%	57.7%	50.1%	57.6%	64.7%
65+	13.2%	6.3%	2.4%	34.8%	16.7%
Gender					
Female	52.3%	15.2%	9.5%	52.0%	42.6%
Male	47.7%	84.8%	90.5%	48.0%	57.4%
Region					
Northeast	21.7%	20.3%	24.5%	12.0%	9.6%
Midwest	16.6%	17.0%	14.7%	30.9%	29.6%
South	59.1%	59.7%	58.6%	45.3%	46.9%
West	2.6%	2.9%	2.2%	11.7%	13.9%
Insurance type					
Private	99.6%	99.7%	99.9%	96.5%	97.6%
Medicaid	0.4%	0.3%	0.1%	3.5%	2.4%
Health status at baseline					
Pregnant	6.0%	14.7%	19.7%	1.2%	1.9%
Have neoplasm	12.8%	19.3%	18.2%	22.8%	22.3%
Have HIV/AIDS	0.4%	0.2%	0.3%	0.3%	0.5%
Have organ transplantation	0.0%	0.0%	0.0%	0.2%	0.1%
Have peripheral vascular disease	0.9%	1.8%	1.5%	4.7%	2.4%
Have cardiovascular disease	7.7%	5.4%	2.6%	15.0%	7.4%
Have hypertension	20.0%	12.1%	5.9%	28.9%	20.0%
Have endocrine or metabolic complications	15.7%	13.3%	8.3%	25.5%	24.4%
Have ophthalmic complications	5.5%	3.7%	2.8%	15.6%	6.7%

¹The research team obtained lab results from only 2 national lab vendors. RDM, Research DataMart; PD, prediabetes.

services that might stem from emergency visits and hospitalizations (eg, hospice care, nursing home care, home care).

Regression coefficients in the form of rate ratios are reported in Table 2. A coefficient greater than 1 implies an increased rate of health care use associated with that characteristic. The increase in per capita ambulatory visits from PD for the 7 complication categories is slight, and for some complication groups the increase is not statistically significant (Table 2). With the exception of hypertension and endocrine-related care, we observed a dose-response relationship by comparison group, where people diagnosed with diabetes have the greatest adjusted rates for ambulatory visits in the follow-up year, followed by individuals who had at least 1 glucose test, and individuals who had no test. People who had a glucose test in the year preceding analysis of medical claims, regardless of the results, have higher rates of health care use than the population who did not have a glucose test, even after controlling for baseline health status, demographics, and other factors.

We use the adjusted rate ratio between confirmed PD and the reference group (ie, individuals without either diabetes diagnosis or glucose test) to calculate the incremental ambulatory visits associated with PD. Patients with confirmed PD have approximately 34% more ambulatory visits per year compared to the reference population—ranging from 9%

more visits for cardiovascular disease and peripheral vascular disease to 92% more visits for hypertension.

The additional visits associated with PD translate into approximately 1 additional physician office visit per year, 1/10th of an additional hospital outpatient visit per year, and 2.7 additional prescriptions per year—for a total additional cost of \$443 per case of PD (Table 3). The majority of PD-associated costs per year are for general medical conditions that are not identified comorbidities of diabetes (\$355), followed by hypertension (\$57), endocrine and metabolic complications (\$11/person year), and renal complications (\$9/person year) (Table 3).

Extrapolated to the national level by patient demographics, the national cost of PD would exceed \$25 billion, with about \$21 billion associated with general medical conditions not directly linked to diabetes. For diagnosed diabetes, approximately one third of the cost of ambulatory care associated with diabetes is attributed to excess visits for general medical conditions.¹⁹ Close to half of the total cost is in the form of medications prescribed during ambulatory visits.

Discussion

Our findings differs from those of Nichols et al who report that predicted impaired glucose tolerance is associated with

TABLE 2. POISSON REGRESSION RATE RATIOS FOR AMBULATORY VISITS

Rate Ratio from Poisson Regression	Peripheral		Cardiovascular		Hypertension		Renal		Endocrine		Ophthalmic		General		All	
	Neurological Symptoms	Vascular Disease	Disease	Disease	Complications	Complications	Complications	Complications	Complications	Complications	Medical Visits	Medical Visits	Medical Visits	Medical Visits	Comorbidity Combined	All Visits
Nondiabetic with no glucose test (reference group)	1.48**	1.42**	1.28**	1.28**	1.28**	1.28**	1.28**	1.28**	1.28**	1.28**	1.28**	1.28**	1.28**	1.28**	1.28**	1.28**
Glucose test results unavailable	1.23	1.86**	1.03	1.03	1.31**	1.31**	1.31**	1.31**	1.31**	1.31**	1.31**	1.31**	1.31**	1.31**	1.31**	1.31**
No PDM based on FPG/OGTT Test	1.41	1.09	1.09	1.09	1.92**	1.92**	1.92**	1.92**	1.92**	1.92**	1.92**	1.92**	1.92**	1.92**	1.92**	1.92**
Has PDM based on FPG/OGTT Test	2.97**	2.69**	1.87**	1.87**	1.34**	1.34**	1.34**	1.34**	1.34**	1.34**	1.34**	1.34**	1.34**	1.34**	1.34**	1.34**
Confirmed diabetes	1.25**	0.94*	0.58**	0.58**	0.96*	0.96*	0.96*	0.96*	0.96*	0.96*	0.96*	0.96*	0.96*	0.96*	0.96*	0.96*
Male	1.31**	1.41**	1.11**	1.11**	1.02	1.02	1.02	1.02	1.02	1.02	1.02	1.02	1.02	1.02	1.02	1.02
Census region (reference group = Northeast)	1.18**	1.04	0.92**	0.92**	1.11**	1.11**	1.11**	1.11**	1.11**	1.11**	1.11**	1.11**	1.11**	1.11**	1.11**	1.11**
Midwest	1.03	1.04	0.83**	0.83**	0.79**	0.79**	0.79**	0.79**	0.79**	0.79**	0.79**	0.79**	0.79**	0.79**	0.79**	0.79**
South	1.15	1.10	1.22**	1.22**	2.28**	2.28**	2.28**	2.28**	2.28**	2.28**	2.28**	2.28**	2.28**	2.28**	2.28**	2.28**
West	1.14**	1.17**	1.09**	1.09**	1.09**	1.09**	1.09**	1.09**	1.09**	1.09**	1.09**	1.09**	1.09**	1.09**	1.09**	1.09**
Payer type (reference group = private)	4.37**	3.40**	3.41**	3.41**	4.73**	4.73**	4.73**	4.73**	4.73**	4.73**	4.73**	4.73**	4.73**	4.73**	4.73**	4.73**
Medicaid	7.75**	5.03**	8.12**	8.12**	6.81**	6.81**	6.81**	6.81**	6.81**	6.81**	6.81**	6.81**	6.81**	6.81**	6.81**	6.81**
Year (reference year = 2005)	10.19**	6.21**	13.53**	13.53**	7.84**	7.84**	7.84**	7.84**	7.84**	7.84**	7.84**	7.84**	7.84**	7.84**	7.84**	7.84**
Age group (reference group = 20-34)	12.36**	6.69**	17.19**	17.19**	8.35**	8.35**	8.35**	8.35**	8.35**	8.35**	8.35**	8.35**	8.35**	8.35**	8.35**	8.35**
35-44	12.11**	6.01**	16.38**	16.38**	6.24**	6.24**	6.24**	6.24**	6.24**	6.24**	6.24**	6.24**	6.24**	6.24**	6.24**	6.24**
45-54	17.47**	6.31**	20.16**	20.16**	4.99**	4.99**	4.99**	4.99**	4.99**	4.99**	4.99**	4.99**	4.99**	4.99**	4.99**	4.99**
55-59	1.27**	1.23**	1.10**	1.10**	1.09**	1.09**	1.09**	1.09**	1.09**	1.09**	1.09**	1.09**	1.09**	1.09**	1.09**	1.09**
60-64	0.98	1.50**	1.02	1.02	0.69**	0.69**	0.69**	0.69**	0.69**	0.69**	0.69**	0.69**	0.69**	0.69**	0.69**	0.69**
65-69	1.37	1.18	3.48**	3.48**	1.06	1.06	1.06	1.06	1.06	1.06	1.06	1.06	1.06	1.06	1.06	1.06
70+	0.98	1.50**	1.02	1.02	0.69**	0.69**	0.69**	0.69**	0.69**	0.69**	0.69**	0.69**	0.69**	0.69**	0.69**	0.69**
Have cancer	2.21**	24.00**	1.45**	1.45**	1.34**	1.34**	1.34**	1.34**	1.34**	1.34**	1.34**	1.34**	1.34**	1.34**	1.34**	1.34**
Have HIV/AIDS	1.83**	1.50**	12.04**	12.04**	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97
Have transplantation	1.36**	1.12**	1.10**	1.10**	10.11**	10.11**	10.11**	10.11**	10.11**	10.11**	10.11**	10.11**	10.11**	10.11**	10.11**	10.11**
Pregnant	1.07*	0.82**	1.04*	1.04*	1.04**	1.04**	1.04**	1.04**	1.04**	1.04**	1.04**	1.04**	1.04**	1.04**	1.04**	1.04**
Baseline health condition	1.36**	1.18**	1.11**	1.11**	1.08**	1.08**	1.08**	1.08**	1.08**	1.08**	1.08**	1.08**	1.08**	1.08**	1.08**	1.08**
Peripheral vascular disease																
Cardiovascular disease																
Hypertension																
Endocrine complications																
Ophthalmic complications																
Number of unique observations																

Logged rate ratios are reported.
 *significant at 5%; **significant at 1% based on robust standard error.
 Separate regressions for split samples for males, nonpregnant females, and pregnant females found consistent coefficient estimates with the overall model.
 PDM, prediabetes mellitus; FPG, fasting plasma glucose; OGGT, oral glucose tolerance test.

TABLE 3. PER CAPITA AMBULATORY MEDICAL COSTS FOR THE ADULT POPULATION IN 2007

<i>Cost Component</i>	<i>US Average for Adults</i>	<i>Excess Associated with PD</i>
By service type*	\$1,296	\$443
Outpatient visit	\$215	\$67
Physician office visit	\$553	\$183
Medications	\$528	\$194
By complication group*	\$1,296	\$443
Neurological symptoms	\$16	\$5
Peripheral vascular disease	\$15	\$1
Cardiovascular disease	\$49	\$5
Hypertension	\$74	\$57
Renal complications	\$21	\$9
Endocrine/metabolic complications	\$16	\$11
Ophthalmic complications	\$41	\$0
All other medical conditions (excluding pregnancy and injury related visits)	\$1,017	\$355

*Numbers may not sum to totals because of rounding. PD, prediabetes.

a significant increase in hospital inpatient days but only a modest increase in ambulatory visits.⁹ The increase in hospital days observed by Nichols et al, however, disappears after controlling for hypertensive status.

The lack of statistical significance for some complication groups, despite the consistent pattern of higher rates of visits for people with PD, is not surprising for several reasons, including: (1) PD is hypothesized to be associated with the early stages of diabetes-related complications, therefore the magnitude of PD's impact on health care use is anticipated to be modest; (2) the comparison group is contaminated in that it contains people with PD for whom there is no glucose test result in the baseline year; and (3) visit rates for some complication groups are relatively low, so modest differences in health care use patterns are undetectable due to insufficient sample size.

For one complication group—ophthalmic complications—the visit rates for people with PD are lower than the rate for those with confirmed normal glucose levels. This unexpected finding may reflect an artifact of referral patterns by ophthalmologists for patients with ophthalmic problems. PD is associated with higher visit rates for general medical conditions even controlling for the presence of major chronic conditions at baseline.

Our estimate is likely conservative for several reasons. The comparison group includes people with PD who did not have a glucose test in 2004 (and who thus, by default, are placed in the comparison group).

These cost estimates understate the true cost of PD to society, as higher use of health care services and prevalence of chronic conditions such as cardiovascular disease are associated with increases in missed work days and lower productivity.^{25–28} Additionally, health problems associated with PD may result in intangible costs such as reduced quality of life.

In addition to the data limitations above that make the PD cost estimates conservative, study limitations include the following:

- The elderly, the uninsured, and the publicly insured are underrepresented in the medical claims analysis—although the regression analysis does control for insurance type, age group, and other health and demographic factors correlated with the elderly and publicly insured populations.
- We did not control for body weight status in the multivariate regression analyses. This presents challenges to isolate the impact of glucose intolerance on health outcomes independent of the changes in health outcomes via pathways other than PD. The regression analysis does control for hypertension status at baseline (which is highly correlated with body mass index).²⁹

These limitations and gaps in the literature suggest areas for additional research.

We compare use of medical services by people with PD to people with normal glucose levels. Research using a more continuous measure, such as actual glucose test results, could better determine whether there is a dose-response relationship between level of glucose impairment and use of health care services.

Although this study found no association between PD and increased use of emergency or hospital inpatient services, additional research with a larger sample is needed to verify this finding.

Small sample size limited the calculation of visit rate ratios by PD status across beneficiary characteristics (age in particular). Future research might explore the interaction between PD and other beneficiary characteristics including demographics and the presence of other complications.

Conclusions

The findings suggest that PD is associated with statistically higher rates of ambulatory visits for hypertension, endocrine and metabolic complications, renal complications, and general medical conditions. PD is associated with a slight increase in visit rates for neurological symptoms, peripheral vascular disease, and cardiovascular disease, but the increase is not statistically significant. There is no indication that PD is associated with an increase in emergency visits and/or inpatient days. Extrapolating these patterns to the 57 million adults with PD in 2007 suggests that national medical costs of PD could exceed \$25 billion, or approximately \$443 per adult with PD.

Research suggests that PD is associated with an increased risk of developing diabetes.^{2–7} Whereas adults in the United States with normal glucose levels have a 0.7% average annual risk of developing type 2 diabetes,² this risk rises to between 10% and 15% for those with PD.^{3–5} As many as 83% of persons with impaired glucose tolerance will eventually develop diabetes, barring a lifestyle intervention such as weight loss, but this lifetime risk falls to 65% among persons who lose weight and engage in moderate physical activity.^{6,7} Our findings strengthen the business case for lifestyle interventions targeted at preventing diabetes by adding additional economic benefits that can potentially be achieved by preventing or delaying PD cases.

Disclosures

Mr. Baldwin, Ms. Moore, Dr. Le Nestour, and Dr. Quick acknowledge that i3 Research has grants from sanofi-aventis,

Transition Therapeutics Inc., and Andromeda Biotech Ltd., to conduct research in diabetes. These organizations do not have control over this paper. Dr. Zhang, Mr. Dall, Ms. Chen, Ms. Yang and Ms. Mann are employed by the Lewin Group and no conflicts of interest to disclose with regard to this paper.

Funding for this study was provided by the Novo Nordisk, Inc., National Changing Diabetes Program.

References

- US Department of Health and Human Services, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. National Diabetes Statistics, 2007. Available at: http://diabetes.niddk.nih.gov/dm/pubs/staTistics/DM_Statistics.pdf.
- National Diabetes Surveillance System. Crude and age-adjusted incidence of diagnosed diabetes per 1000 population aged 18–79 years, United States, 1980–2005. Available at: <http://www.cdc.gov/Diabetes/statistics/incidence/detailtable4.htm>.
- Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346:393–403.
- Santaguida PL, Balion C, Hunt D, et al. Diagnosis, prognosis, and treatment of impaired glucose tolerance and impaired fasting glucose. Summary, Evidence Report/Technology Assessment No. 128. AHRQ Pub.No.05-E026-1. Available at: <http://www.ahrq.gov/clinic/epcsums/impglusum.htm>.
- Tuomilehto J, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med*. 2001;344:1343–1350.
- de Vegt F, Dekker JM, Jager A, et al. Relation of impaired fasting and postload glucose with incident type 2 diabetes in a Dutch population: The Hoorn Study. *JAMA*. 2001;285:2109–2113.
- Herman WH, Hoerger TJ, Brandle M, et al. The cost-effectiveness of lifestyle modification or metformin in preventing type 2 diabetes in adults with impaired glucose tolerance. *Ann Intern Med*. 2005;142:323–332.
- Nichols GA, Brown JB. Higher medical care costs accompany impaired fasting glucose. *Diabetes Care*. 2005;28:2223–2229.
- Nichols GA, Arondekar B, Herman WH. Medical care costs one year after identification of hyperglycemia below the threshold for diabetes. *Med Care*. 2008;46:287–292.
- DECODE Study Group, the European Diabetes Epidemiology Group. Glucose tolerance and cardiovascular mortality: comparison of fasting and 2-hour diagnostic criteria. *Arch Intern Med*. 2001;161:397–405.
- Bjornholt JV, Erikssen G, Aaser E, et al. Fasting blood glucose: an underestimated risk factor for cardiovascular death. Results from a 22-year follow-up of healthy nondiabetic men. *Diabetes Care*. 1999;22:45–49.
- Coutinho M, Gerstein HC, Wang Y, Yusuf S. The relationship between glucose and incident cardiovascular events. A meta-regression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. *Diabetes Care*. 1999;22:233–240.
- Cubbon R, Kahn M, Kearney MT. Secondary prevention of cardiovascular disease in type 2 diabetes and prediabetes: a cardiologist's perspective. *Int J Clin Pract*. 2008;62:287–299.
- Levitzyk YS, Pencina MJ, D'Agostino RB, et al. Impact of impaired fasting glucose on cardiovascular disease: the Framingham Heart Study. *J Am Coll Cardiol*. 2008;51:264–270.
- Wong TY, Mohamed Q, Klein R, Couper DJ. Do retinopathy signs in non-diabetic individuals predict the subsequent risk of diabetes? *Br J Ophthalmol*. 2006;90:301–303.
- Nguyen TT, Wang JJ, Wong TY. Retinal vascular changes in pre-diabetes and prehypertension: new findings and their research and clinical implications. *Diabetes Care*. 2007;30:2708–2715.
- Bjornholt JV, Erikssen G, Kjeldsen SE, Bodegard J, Thaulow E, Erikssen J. Fasting blood glucose is independently associated with resting and exercise blood pressures and development of elevated blood pressure. *J Hypertens*. 2003;21:1383–1389.
- Saydah SH, Loria CM, Eberhardt MS, Brancati FL. Subclinical states of glucose intolerance and risk of death in the U.S. *Diabetes Care*. 2001;24:447–453.
- Dall T, Mann SE, Zhang Y, Martin J, Chen Y, Hogan P. Economic costs of diabetes in the U.S. in 2007. *Diabetes Care*. 2008;31:1–20.
- Dall TM, Mann S, Zhang Y, et al. Distinguishing the economic costs associated with type 1 and type 2 diabetes. *Pop Health Manage*. 2009;12:103–110.
- National Center for Health Statistics. Survey and data collection systems. Available at: <http://www.cdc.gov/nchs/Default.htm>. Accessed July 2008.
- American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2008;31(suppl 1):S55–S60.
- Benichou J. A review of adjusted estimators of attributable risk. *Stat Methods Med Res*. 2001;10:195–216.
- Zhang Y, Dall TM, Mann SE, et al. The economic cost of undiagnosed diabetes. *Pop Health Manage*. 2009;12:95–101.
- Boles M, Pelletier B, Lynch W. The relationship between health risks and work productivity. *J Occup Environ Med*. 2004;46:737–745.
- Burton WN, Chen CY, Conti DJ, Schultz AB, Pransky G, Edington DW. The association of health risks with on-the-job productivity. *J Occup Environ Med*. 2005;47:769–777.
- Burton WN, Chen CY, Conti DJ, Schultz AB, Edington DW. The association between health risk change and presenteeism change. *J Occup Environ Med*. 2006;48:252–263.
- Goetzel RZ, Hawkins K, Ozminkowski RJ, Wang S. The health and productivity cost burden of the “top 10” physical and mental health conditions affecting six large U.S. employers in 1999. *J Occup Environ Med*. 2003;45:5–14.
- Dall T, Zhang Y, Chen YJ, et al. Cost associated with overweight and obesity, high alcohol consumption, and tobacco use within the military health system's TRICARE Prime enrolled population. *Am J Health Promotion*. 2007;22:120–143.

Address reprint requests to:
Yiduo Zhang, Ph.D.

3130 Fairview Park Drive, Suite 800
Falls Church, VA 22042

Email: yiduo.zhang@lewin.com

