Value-Based Insurance Designs for Diabetes Drug Therapy:

Actuarial and Implementation Considerations

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I. Executive Summary

The health care cost crisis has spawned new techniques to control costs and to obtain more value from spending. As America's health care pushes past 16% of gross domestic product, payers and policy-makers increasingly question the value of particular health care services. Approaches to control costs and get better value from health care dollars typically fall into 4 interrelated categories:

- Benefit design: Determining services to cover and co-pay structures.
- Medical management: Using medical knowledge to determine which particular service is best for a patient and, based on that information, whether the policy should pay for it.
- Network management: Using medical knowledge and the treatment outcomes associated with particular providers to determine provider reimbursement and member cost sharing.
- Incentives: Providing positive financial incentives to members or providers for lower-cost or higher-quality choices—or imposing penalties for the opposite.

This paper focuses on value-based insurance design (VBID), a technique that has gained prominence among employers and payers as a way to encourage medically necessary utilization of evidence-based, cost-effective medical services and to discourage utilization of medical services with a weak evidence base. The approach involves creating clinically sensitive co-pay structures: low or no co-pays for cost-effective services with a strong evidence base and high co-pays or no coverage for services with a weak evidence base. Although the VBID concept applies to all medical services, much of the initial focus has been on drug therapy co-pay designs that reduce or eliminate co-pays for chronic disease drug therapy. In particular, diabetes has been a chronic condition targeted by VBIDs. We model the cost and adherence impact of several VBID programs for diabetes drug therapy for a typical employer population.

Why diabetes?

Although treatment targets for glycemic (blood glucose) control (see description of glycemic control in Appendix D) are well established by the American Diabetes Association (ADA), and efficacious and safe drug therapies are readily available, adherence to diabetes drug therapy has been disappointing. Adherence studies report relatively poor adherence with diabetic drug therapy[1-3] and other studies consistently report findings that as co-pays for diabetes drug therapy increase, adherence decreases.[4,5] The second part of the equation is also well established: poor adherence is associated with poor glycemic control. Studies report a strong correlation between medication adherence and glycemic control.[6-10] Landmark studies have established the importance of glycemic control for diabetes patients. These studies report that lower rates of complications—including heart attack, stroke, heart failure, peripheral vascular disease, amputation, retinopathy, end-stage renal disease, and cataracts—are associated with lower levels of hemoglobin A_{1c} (HbA_{1c}), a key marker of glycemic control.[11-13] However, our analysis of the 2003 to 2004 National Health and Nutrition Examination Survey (NHANES) data found only 46% of working age diagnosed diabetics have their HbA_{1c} at or below the ADA-recommended target level of 7.

Table 1 shows the prevalence and HbA_{1c} control portion for all diabetics from our analysis of NHANES 2001-2002 and 2003-2004 (NHANES 2005-2006 was not populated with drug data at the time of this analysis). We do not present control for children (aged 12 to 19 years), because target HbA_{1c} varies by age and is more sensitive to individual factors in this young age group.

Table 1. Prevalence and HbA_{1c} control for diabetics

	Adults Ages 20 to 69	
	Prevalence Among Adults	Number of People*
Diabetics	7.8%	1155
Controlled	3.1%	451
Uncontrolled	2.6%	389
Undiagnosed	2.1%	314
Prediabetics	25.3%	3730

*Among 14 721 adult health plan members aged 20 to 69 years per 10 000 employees.

Source: Milliman analysis of NHANES 2001-2002, 2003-2004.

Diabetics: Recognized diabetes or fasting blood sugar >125 mg/dL (unrecognized diabetes is defined as diabetes by drug or lab history but not recognized by patient)

Controlled: HbA_{1c} <7% (defined by ADA)

Uncontrolled: HbA_{1c} ≥7%

Prediabetics: 100 mg/dL ≤ laboratory test results for blood glucose (LBXGLU) (NHANES glucose field) ≤125 mg/dL and not diabetic

Cost and adherence impact of VBID scenarios

Table 2 displays a consistent increase in adherence for type 1 and 2 diabetics as co-pays are lowered from a standard $10/25/40 design. The incremental plan sponsor costs for type 2 diabetics, given the increased adherence and increased plan sponsor portion of drug costs, range from $19 to $42 per type 2 patient per month for our examples of model VBID plans. In keeping with benefits language, we report costs as dollars per patient per month (PPPM) and per member per month (PMPM). PPPM results are costs spread across type 1 or type 2 patients, while PMPM results are costs spread across all health plan members. Our results are from actuarial modeling rather than from treatment arm/control arm studies.

We do not model the cost offsets that might be realized with better diabetes drug therapy adherence. In section V, we make recommendations and provide a framework for how a payer/employer might reasonably model cost offsets from improved diabetes control.

Table 2. Cost and adherence impact of 3 benefit designs

		Base Standard $10/25/40	VBID 1 $0/12.5/30	VBID 2 $0/0/0	VBID 3 $10/10/10
Type 1	**Net of co-pay**				
	PPPM 2008	$127	$158	$207	$169
	PMPM 2008	$0.59	$0.74	$0.97	$0.79
	PMPM Increment to base	NA	$0.14	$0.37	$0.20
	Virtual adherence				
	Patients compliant	60%	72%	89%	75%
	Increment to base	NA	20%	48%	24%
Type 2	**Net of co-pay**				
	PPPM 2008	$60	$79	$102	$80
	PMPM 2008	$2.16	$2.82	$3.65	$2.85
	PMPM Increment to base	NA	$0.67	$1.49	$0.69
	Virtual adherence				
	Patients compliant	49%	60%	69%	57%
	Increment to base	0%	22%	41%	16%

Abbreviations: NA, not applicable; PMPM, per member per month; PPPM, per patient per month.
Source: Milliman modeling of MedStat Commercial 2006.

Even though there are many definitions of value for health care,[14] the extent of waste and inefficiency in medical care delivery[15] suggests that much progress can be made without precisely defining value. Important targets include medical services in which there is significant variation that is not explained by clinical severity or demographics.[16] Services with significant unexplained geographic variation include spinal fusions, knee arthroscopies, bariatric surgery, and high-tech imaging, as well as inpatient hospital stays and inpatient bed days. Other targets for better value include reducing obvious quality problems, such as hospital-acquired infections and other medical errors.[17]

We present the cost of several frequently covered benefits and vendor services including medical management operations that may deserve comparative valuation (Table 3). Making adjustments to co-pay designs for some benefits or reconsideration of the value and expense of particular vendor program purchases could go a long way to pay for evidence-based/value-based services such as diabetes drug VBID.

Table 3. Comparative benefits

Benefit	Typical Incremental Cost PMPM
VBID diabetes options in this report	$0.81 to $1.86
Diabetes disease management (total cost)	$0.50 to $1.00
Wellness* (total cost)	$0.40 to $14.00
Chiropractic care (total cost)	$0.30 to $2.30
Decrease inpatient admissions by 1.7 per 1000 members (typically <4% reduction)	$1.40 to $1.50
Decrease spinal surgery and bariatric surgery by 20%	$0.30 to $0.70

Abbreviations: PMPM, per member per month; VBID, value-based insurance design.
*$0.40 PMPM includes basic promotion. $14.00 PMPM includes full range of services such as health risk assessment (HRA) incentives, gym subsidy, obesity benefit, administrative costs, etc.

This report was commissioned by Takeda Pharmaceuticals North America, Inc. While the authors followed applicable Actuarial Standards of Practice,[a] this report does not form a prescribed statement of actuarial opinion. Milliman does not intend to endorse any product or to benefit any third party through this report; the report reflects the findings of the authors. As with any financial forecast, our work is based on many assumptions and cannot capture all influences. Therefore, actual experience will likely vary from that presented here. If this report is distributed, it must be distributed in its entirety, as material taken out of context can be misleading.

[a] ASOP No. 23, Data Quality (Doc No. 097; December 2004) and ASOP No. 41, Actuarial Communications (Doc No. 086; March 2002). www.actuarialstandardsboard.org/asops.asp.

II. A Primer on VBID

VBID involves creating clinically sensitive co-pay structures: low or no co-pays for cost-effective services with a strong evidence base and high co-pays or no coverage for services with a weak evidence base. Although VBID can apply to all medical services, much of the initial focus has been on drug therapy co-pays, and diabetes has been targeted by VBID programs. For years, standard actuarial practice has recognized price elasticity—that increasing/decreasing drug co-pays decreases/increases drug utilization. Recently, published studies make the same point about drug therapy adherence. In this report we add our findings on the increased pharmacy cost to employers and increased drug adherence associated with various VBIDs for diabetes drugs.

The payer community is increasingly focusing on approaches to align payment with evidence-based/value-based health care delivery including the following:

- Pay for performance (P4P) health plan initiatives
- A federal executive order for promoting quality and efficiency in programs administered or sponsored by the federal government health care programs
- Center for Medicare and Medicaid Services (CMS) policy to exclude payments for "never events"
- VBID initiatives
- Value-based purchasing initiatives
- Employer and business group and coalition initiatives, eg, eValue8 (health care vendor performance rating tool)
- Leapfrog Group (hospital rating for quality and safety practice)
- Bridges to Excellence (physician incentives for quality outcomes and care delivery processes)

A disciplined approach is required to design benefits that support this paradigm, and VBID is a useful approach if thoughtfully implemented.

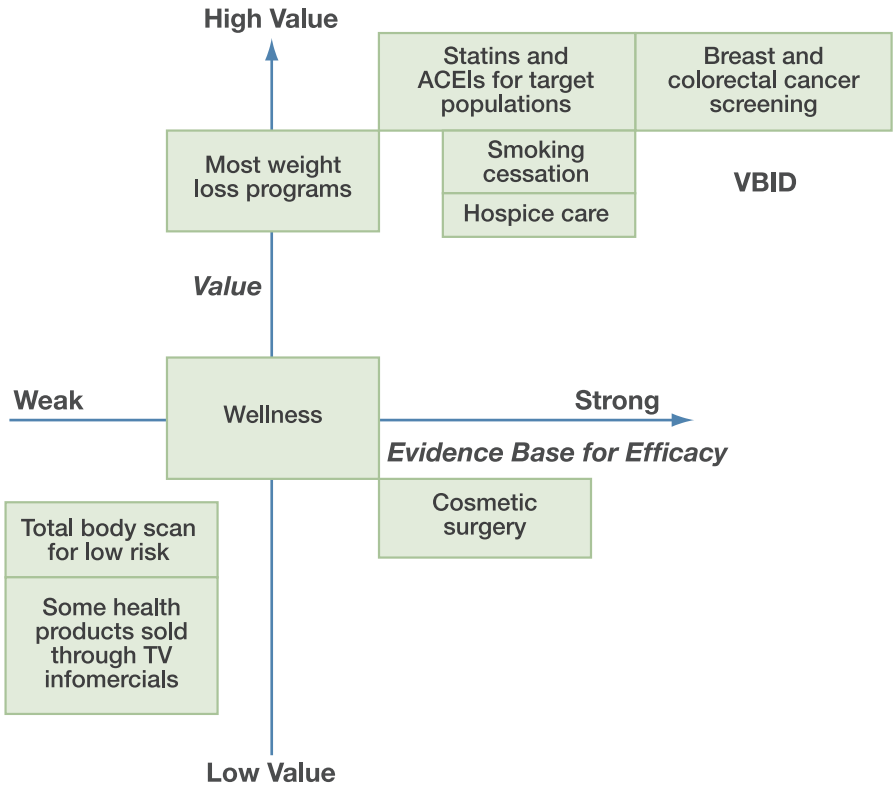
Mark Fendrick and Michael Chernew, noted advocates of the concept, coined VBID in 2004 after developing the concept of benefit-based co-pay (BBC) in 2001. They propose VBID as a response to the likely adverse clinical effects of the current trend toward higher co-pays and advocate that co-pay rates be set based on the value of clinical services (benefits and costs)—not exclusively the costs.[18] They suggest that VBID will encourage more appropriate utilization of medical services as cost sharing is adjusted to account for the value of medical services.[18] Other terms for similar concepts are value-based benefits, clinically sensitive benefit designs, and, more broadly, value-based health care.

VBID shifts the benefit design from one based on legacy or price to one based on value and price. The design tailors co-pays at the point of service to the evidence base and value of specific services for targeted groups or individual patients where value is measured by clinical and economic benefit.

VBID strategies may adjust co-pay designs for a variety of targeted health services including physician services, hospital services, ancillary services, and prescription drugs. The intent is to evaluate the value and evidence base of specific benefits in making benefit design decisions. Chart 1 provides a potential framework for evaluating benefits within that context. The benefits were identified and placed in quadrants based on the authors' view of medical evidence from the literature and value in terms of size of target population and cost of treatment. The placement of benefits in particular quadrants is illustrative rather than definitive and designed to encourage readers to create their own quadrant interpretation. For example, the authors considered that landmark statin and angiotensin-converting enzyme inhibitor (ACEI) therapy studies, for indicated populations, report significant reduction in adverse health events. We placed these in what we label the VBID quadrant. Smoking cessation therapies have an established evidence base, and a significant portion of working-age adults (24% based on Milliman analysis of NHANES 2005-2006) smoke; therefore, we placed a smoking cessation benefit in the VBID quadrant. We straddled weight loss programs across the VBID quadrant and the left upper quadrant. The evidence base for weight loss programs is mixed, although on the value access, the benefit would be high since 35% of working-age adults are considered obese, with a body mass index (BMI) $\geq$ 30 (Milliman analysis of NHANES 2005-2006 Appendix A). Disease management and

wellness programs are positioned midway on the value- and evidence-base axes, because success with these programs and financial savings outcome reports have been weak.

Chart 1. Framework for evaluating the value of benefits



Abbreviation: ACEI, angiotensin-converting enzyme inhibitor.

Key design concepts for VBID:

- Target services known to be of high value without differentiating among individuals who receive the intervention (eg, ACEIs, flu shots, tobacco cessation, hospice)
- Target patients with select clinical diagnoses
  - Lower co-pays for high-value services (eg, diabetic members' annual eye exams, diabetic prescriptions); the design may adjust co-pay by condition severity level (eg, lower statin co-pay for high risk individuals)

- Target providers meeting quality outcome criteria
  - Lower co-pay for members utilizing quality providers
- Target patient adherence behavior
  - Adjust co-pays accordingly

VBID fits well with current health care trends including consumerism, consumer-driven health plans (CDHPs), evidence-based medicine, comparative effectiveness research, P4P, disease management and wellness/prevention. And support is growing for VBID, spearheaded by the University of Michigan Center for VBID (Mark Fendrick) and the Center for Health Value Innovation (David Hom). Uptake is slowly growing, with several large corporations such as Marriott, IBM, Johnson & Johnson, and Procter & Gamble adopting VBID along with several states and municipalities.

Outcomes studies are sparse, with only 3 reported in peer-reviewed journals:

1. An outcomes study from Pitney Bowes was published in 2005, several years after the company shifted all diabetes drugs and diabetes devices (test strips, glucometers, etc) to tier 1.[19] The study reports significant increases in medication possession ratio (MPR), 6% decrease in overall claim costs, 26% decrease in emergency department visits, and 7% decrease in average overall pharmacy costs for diabetics.
2. A recent study by Active Health Management[20] reduced co-pays by approximately 50% for brand-name ACEIs, angiotensin-receptor blockers (ARBs), beta-blockers, diabetes medications (oral therapies and insulin), inhaled corticosteroids, and statins. Nonadherence was reduced by 7% to 14% for all medication classes except for inhaled corticosteroids, for which there was no statistically significant difference in adherence.
3. The Asheville project waived co-pays for diabetes drugs and supplies and provided intensive pharmacy and diabetes education programs.[21] The study reports reductions in costs and sick time and improved HbA_{1c} and lipid control.

Several considerations for payers arise when integrating VBID into benefit strategies:

- *Potential for short-term increase in utilization and cost.* VBID increases compliance with the targeted drugs, which directly increases pharmacy spending for those drugs. The expectation is that with better control there will be fewer exacerbations of chronic conditions requiring emergency department and inpatient care, but this outcome is uncertain.
- *Cost of operational implementation*. Implementation will be more costly for programs that target patients as opposed to services. To target patients, eligibility data must be transferred from the payer to the point of service, which is more administratively burdensome.
- *Information technology (IT) infrastructure (point-of-service identification)*. The systems for point-of-service claims administration need to be developed. If particular patients are targeted, algorithms will be needed to identify specific disease states, compliance levels, etc.
- *Insufficient evidence/research to target services and patient groups—ie, lack of comparative value agency such as the UK's National Institute for Clinical Excellence.* Some disease areas do not have adequate research to differentiate between high- and low-value services, yet sufficient evidence is available to support VBID in selected diseases.
- *Communications/human resources role*. Effectively communicating to all members/employees about VBID is essential to avoid confusion and to encourage any target patient groups to use and appreciate the benefit.
- *Antidiscrimination barriers.* Some individuals may raise discrimination concerns as to why particular diseases are being targeted for VBID. This must be addressed on a case by case basis, as well as by education on the VBID paradigm.
- *Privacy*. For programs that vary by patient group, identification of members/employees with specific conditions is required, and Health Insurance Portability and Accountability Act (HIPAA) privacy regulations will need to be followed.

- *Unintended incentives*. If co-pays are lowered on brand-name drugs to the same level as generics, patients may not have enough incentive to use generics when there is an option. VBID designs typically reduce co-pays for generics significantly more than for brand-name drugs.
- *Adverse selection*. There is some concern that plans offering a VBID may attract a disproportionate number of patients with chronic conditions, although VBID could positively impact member/employee retention.

III. About Diabetes

Why focus on diabetes?

Type 2 diabetes prevalence is increasing at an alarming rate and is thought to be related to the increased prevalence of obesity. From 1997 to the first half of 2006, the National Health Interview Survey (NHIS) shows a dramatic increase in diagnosed diabetes prevalence among adults (aged 18 years and older), from 5.1% to 7.8%.[22] Table 4 presents the increase in diabetes prevalence for subjects aged 20 to 69 years in a 4-year period from our analysis of NHANES data. Although there has been a slight decline in undiagnosed diabetics, the overall prevalence of diabetes and prediabetes is on the rise, and it appears related to the increased prevalence of obesity. About 11% of prediabetics become actual diabetics each year.[23] The NHANES prevalence data include type 1 and type 2 diabetics.

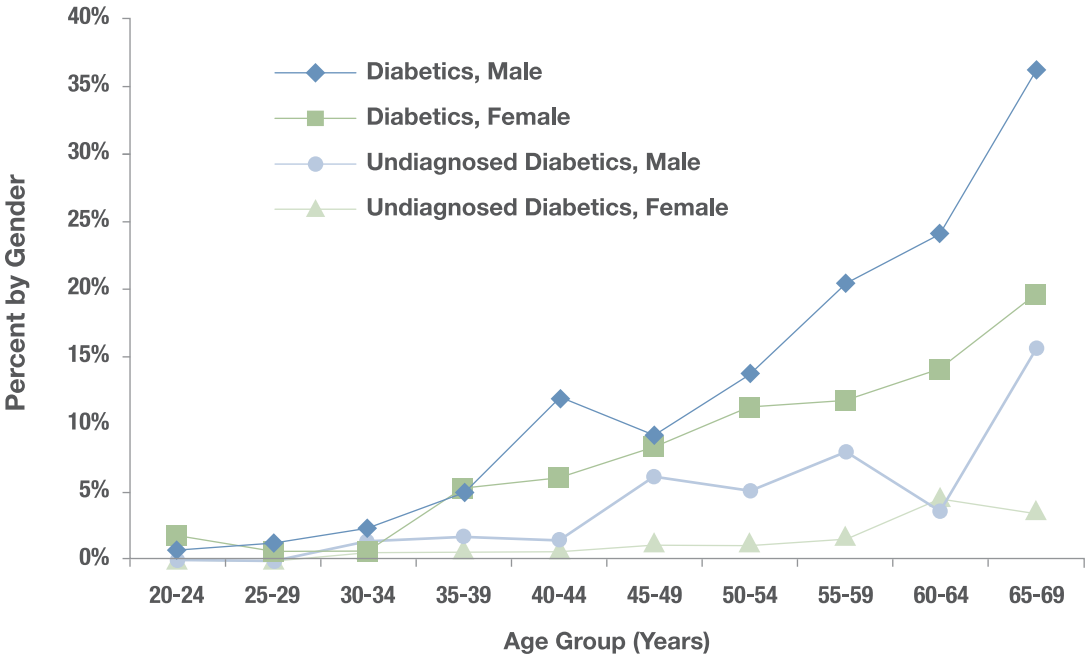
Table 4. Increasing prevalence of diabetes and prediabetes (aged 20 to 69 years)

	NHANES 1999-2000*	NHANES 2003-2004*
Prevalence of diagnosed diabetes	4.5%	5.4%
Prevalence of undiagnosed diabetes	2.5%	2.0%
Prevalence of total diabetes	6.9%	7.5%
Prevalence of prediabetes (fasting blood sugar ≥100 and <126 mg/dL)	20.9%	23.7%

Abbreviation: NHANES, National Health and Nutrition Examination Survey.
* Data in columns may not add to totals due to rounding.

The prevalence of type 2 diabetes increases with age. Chart 2 shows the prevalence of diagnosed and undiagnosed diabetes by sex and 5-year age bands. The average age of diagnosed diabetics is higher than the average age of undiagnosed diabetics. Among working-age adults (aged 20 to 69 years), the average age of those with diagnosed diabetes is 50 years based on a demographically adjusted NHANES population, versus an average age of 40 years for those without diabetes (Milliman analysis Appendix A).

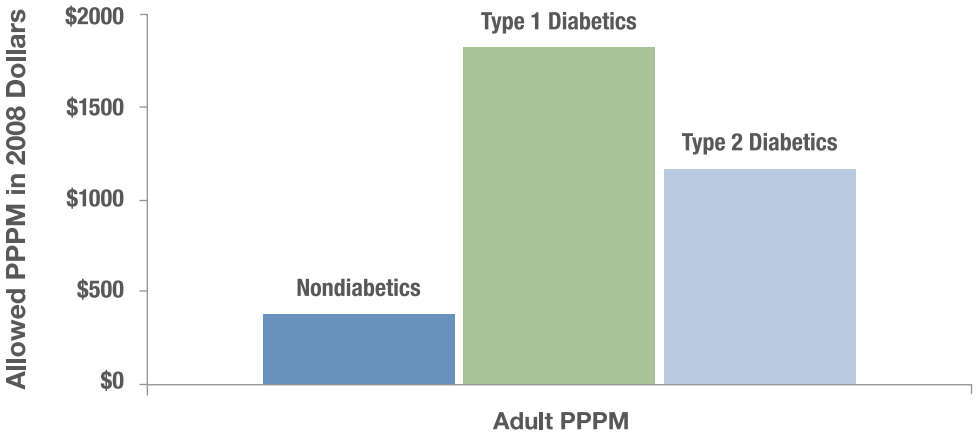
Chart 2. Prevalence of diabetes by age and gender



Source: Milliman analysis of NHANES 2001-2004.

Chart 3 provides cost data on diabetics, showing significantly higher costs for diabetics. Age alone accounts for some of the higher costs of people with diabetes. Although type 1 diabetics incur the highest cost, only 5% to 10% of Americans diagnosed with diabetes are considered type 1.[24] Therefore, it is the larger population with type 2 diabetes that drives aggregate cost of the disease.

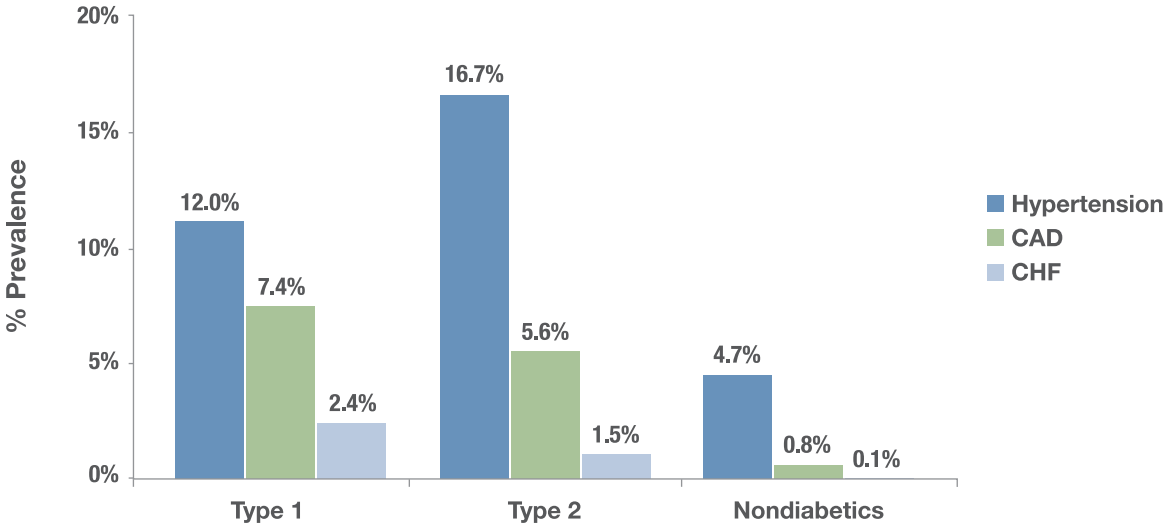
Chart 3. Diabetics have much higher costs



Abbreviation: PPPM, per patient per month.
Source: Milliman analysis of MedStat Commercial 2006, Milliman *Health Cost Guidelines* 2008.

Chart 4 shows that adults aged 20 to 69 years with diabetes carry a greater burden of comorbidities than the nondiabetic population. The prevalence of hypertension, coronary artery disease (CAD), and congestive heart failure (CHF) are dramatically higher in diabetics compared to nondiabetics. (Blood pressure ≥130/80 is considered uncontrolled hypertension for diabetics.) In addition, 54% of diabetics are considered obese with a BMI ≥30, while the prevalence of obesity drops to 27% for nondiabetics.[25]

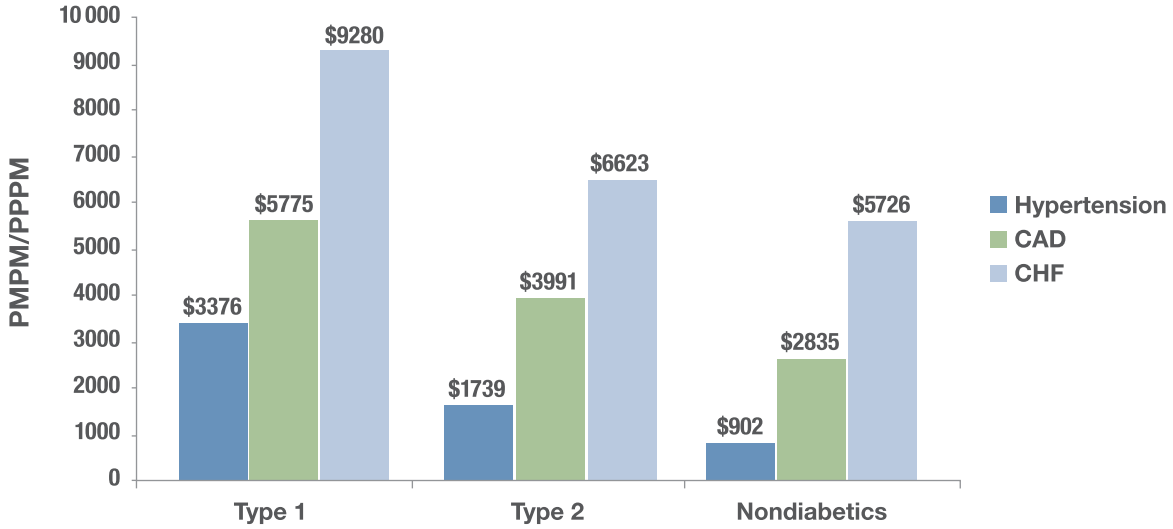
Chart 4. Distribution of prevalence of comorbidities (adults aged 20 to 69 years)



Abbreviations: CAD, coronary artery disease; CHF, congestive heart failure.
Source: Milliman analysis of NHANES 2001-2004, Milliman *Health Cost Guidelines* 2008 Standard Demographics.

Even when controlling for comorbidities, the cost of covering diabetics is significantly higher than the cost of covering nondiabetics (Chart 5).

Chart 5. Cost of covering adults with comorbidities

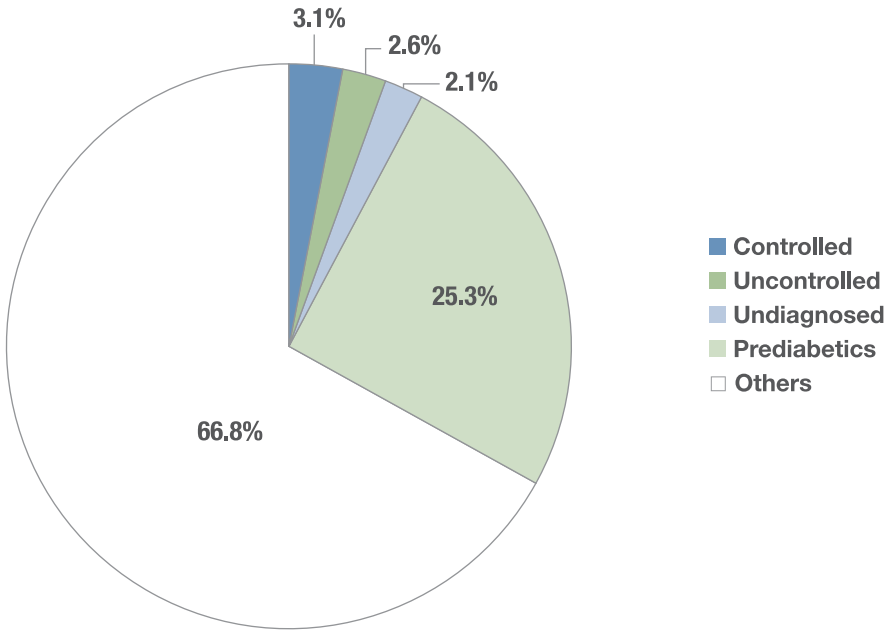


Abbreviations: CAD, coronary artery disease; CHF, congestive heart failure; PMPM, per member per month; PPPM, per patient per month.

Source: Milliman analysis of Medstat Commercial 2006, Milliman *Health Cost Guidelines* 2008.

Our analysis of 2001-2004 NHANES survey data shows that only 54% of diagnosed diabetic adults aged 20 to 69 years have their glycemic levels controlled (HbA_{1c} <7 as recommended by the ADA). Chart 6 displays those findings.

Chart 6. Prevalence of diabetes among adult health plan members



Source: NHANES 2001-2004.

Studies show relatively poor adherence with diabetic drug therapy. In a meta-analysis of 20 adherence studies with oral hypoglycemic drug therapy, adherence ranged from 36% to 93% in retrospective analyses and 67% to 85% in prospective monitoring studies.[1] Insulin adherence for patients with type 2 diabetes ranged from 62% to 64%.[1] In a subsequent study of 11 532 managed care diabetic patients, 79% of patients were identified as being adherent with their oral hypoglycemic agents or insulin where adherence was defined as taking drug therapy ≥80% of the year.[2] In another study of 900 managed care type 2 adult diabetics, 71% of patients were reported to be adherent with oral hypoglycemic drug therapy, where adherence was defined as taking drug therapy ≥80% of the year.[3]

Some of the poor adherence is related to co-pay cost burden. Studies consistently report that, as co-pays for diabetes drug therapy increase, adherence decreases. A meta-analysis of prescription drug cost sharing impact on adherence cited several studies reporting a correlation between increasing co-pays for diabetes drugs and

reduced adherence.[4] A study examining pharmacy claims data and health plan benefit designs from 30 employers and 52 health plans reported that doubling of co-pays for diabetes drugs reduced the use of antidiabetic drugs by patients with diabetes by 23%.[5]

The second part of the equation is also well established: namely, that poor adherence is associated with poor glycemic control. Studies report a strong correlation between medication adherence and glycemic control.[6-10]

IV. Findings: Cost and Adherence Impact of VBID Strategies

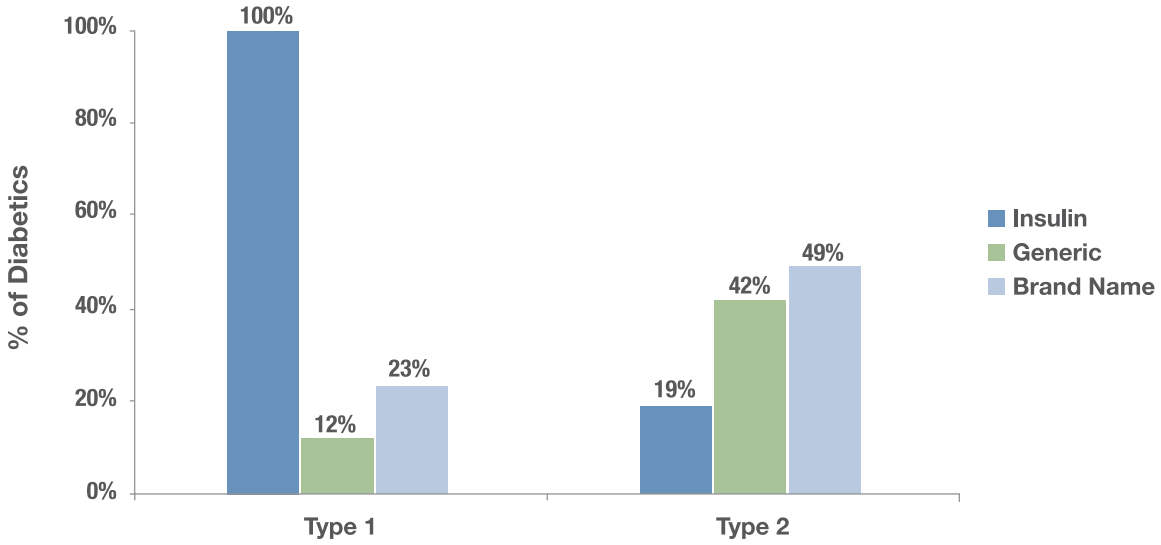
This section contains summary information about diabetics and their use of prescription drugs. We also present results from our modeling of VBID for diabetes drugs.

Utilization of diabetes drugs

Because type 1 and type 2 diabetics have significantly different characteristics, we report descriptive data separately. The data we show are taken from MedStat 2006, a large database that includes a wide range of benefit designs and employer-sponsored health plans. These data indicate current typical practice, but many factors can cause actual results for any particular group to vary from these data.

Chart 7 shows the portion of type 1 or type 2 diabetics on broad classes of drugs. All type 1 diabetics take insulin, which reflects both medical sense and the way we identified type 1 diabetics in the data. A minority of type 2 diabetics use insulin. The percentages shown reflect one or more prescriptions during the year, not utilization.

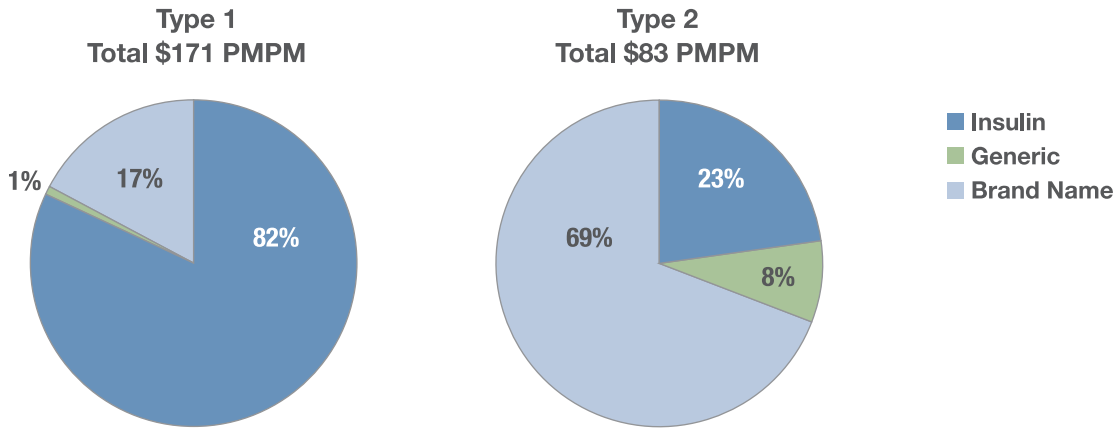
Chart 7. Percent of type 1 and type 2 diabetics with one or more scripts for diabetes drugs split by insulin, generic drugs, and brand-name drugs



Source: Milliman analysis of MedStat Commercial 2006. Insulin is not included in generic or brand-name category. Individuals may be on multiple generic or brand-name drugs.

Chart 8 shows the allowed cost for type 1 and type 2 diabetics by category of drug, along with total drug cost. Allowed cost includes both the plan-paid amounts and the member co-pays. For both types of diabetics, generic drugs are the smallest portion of cost.

Chart 8: Distribution of allowed cost per diabetic patient per month



Abbreviation: PMPM, per member per month.
Source: MedStat Commercial 2006, Standard Demographics from Milliman *Health Cost Guidelines* 2008.
Cost trended to 2008.

Contrasting utilization and adherence

Payers traditionally measure prescription use as (aggregate) utilization, typically, the number of scripts per 1000 members per year. By contrast, clinicians measure adherence of individual patients, which is the fill rate of the prescriptions the patient receives from the physician. Adherence (filling the prescription) is associated with compliance (taking the drug), which is what drives health outcomes. Utilization, however, is the measure associated with claims and cost.

There is no easy translation between the 2 measures, for the following reasons:

- A patient may change therapy during the year. For example, the patient may start with 1 prescription, and, through changing health status, end the year with 2 prescriptions. Without chart audits or clinical information, it is impossible to identify such cases through claims data.

- Physicians may change prescription drugs and/or doses during the year, which makes it difficult to determine whether the patient should be compliant with 1 or 2 prescriptions.
- Some patients may be prescribed more or less than a year's worth of drugs. For example, it is not unusual for a diabetic to receive prescriptions for both long-acting and short-acting insulins.

From a practical standpoint, because employers will not be able to measure adherence directly, a surrogate approach is needed. We believe the nature of prescription changes and the progressive nature of diabetes mean that simple approaches to tabulating adherence from utilization data will tend to understate adherence. For VBID to be measured, standards for "virtual adherence" that translate available utilization into useful information will need to be developed. We suggest the following methodology:

- Distinguish between type 1 and type 2 diabetics
- Identify utilization of multiple pharmacies within broad drug categories
- Make assumptions for changing therapies and doses

As described in the methodology section, we used this approach to develop our figures. As interest in VBID grows, the need for such standard methodology will become more urgent as organizations try to compare results.

Impact of VBID for diabetes drugs

Using the data and methodology described in Appendices A and B, respectively, we found that reducing the co-pays on a typical prescription drug plan for diabetes drugs will significantly increase adherence.

Although VBID advocates point to the health-improving consequences of better adherence, we have not attempted to model any medical cost offsets. It is difficult to model medical cost offsets, because there is little medical knowledge about the impact of incremental improvements in adherence on health status. For example, if reducing co-pays helps someone take their medicine for 9 months out of 12 instead of 8 months, does their health status improve? If so, by how much? These issues have not been

resolved in the scientific literature. For individual patients, if adherence rate increases to 80% MPR or higher, one would expect a reduction in micro- and macrovascular side effects associated with poor glycemic control.

In keeping with common prescription drug designs, we modeled 3 VBID tier structures, where co-pays are set lowest for generics, middle level for preferred brand-name drugs, and highest for nonpreferred brand names. We modeled the 3 plans shown in Table 5. The base plan was chosen to represent a common structure,[26] while the VBID plans were chosen to reflect a range of dramatically lower cost-sharing options.

Table 5. VBID co-pay structures

	Co-pay Structure		
	Generic	Preferred Brand	Nonpreferred Brand
Base (10/25/40)	$10	$25	$40
VBID 1 (0/12.5/30)	$0	$12.50	$30
VBID 2 (0/0/0)	$0	$0	$0
VBID 3 (10/10/10)	$10	$10	$10

As shown in Table 6, each of the VBID plans increases costs and virtual adherence. The most dramatic increase is for VBID 2, with no co-pays. Costs increase $0.37 for type 1 diabetics and $1.49 for type 2 diabetics—a total of $1.86 PMPM. Virtual adherence increased by about 48% for type 1 diabetics and about 41% for type 2 diabetics.

Table 6. Cost and adherence impact of 3 benefit designs

		Base Standard $10/25/40	VBID 1 $0/12.5/30	VBID 2 $0/0/0	VBID 3 $10/10/10
Type 1	**Net of co-pay**				
	PPPM 2008	$127	$158	$207	$169
	PMPM 2008	$0.59	$0.74	$0.97	$0.79
	PMPM Increment to base	NA	$0.14	$0.37	$0.20
	Virtual adherence				
	Patients compliant	60%	72%	89%	75%
	Increment to base	NA	20%	48%	24%
Type 2	**Net of co-pay**				
	PPPM 2008	$60	$79	$102	$80
	PMPM 2008	$2.16	$2.82	$3.65	$2.85
	PMPM Increment to base	NA	$0.67	$1.49	$0.69
	Virtual adherence				
	Patients compliant	49%	60%	69%	57%
	Increment to base	0%	22%	41%	16%

Abbreviations: NA, not applicable; PMPM, per member per month; PPPM, per patient per month.
Source: Milliman modeling of MedStat Commercial 2006.

Adherence is typically defined as diabetes scripts or MPR ≥80% of the days in a year, and we followed that convention in Table 6. However, because of the disconnect between utilization and adherence, the "increment to base" figures are more significant than the absolute values of virtual adherence.

Reducing co-pays increases cost for 2 reasons. Our modeling captures both these dynamics:

1. Some members who were not filling their prescriptions will now do so, which increases drug spending.
2. Members who were filling prescriptions will now have lower co-pays, which means the payer will incur these additional costs.

It is beyond the scope of this report to determine whether the clinical outcomes of better adherence can offset additional drug utilization costs associated with lower co-pays. The next section of this report, however, describes a methodology by which a plan may measure projected net value from a VBID program of reduced co-pays.

V. How to Measure Value From VBID Programs

The goal of implementing a VBID diabetes drug program is to improve adherence to diabetes drug therapy and, in so doing, improve diabetes glycemic control (see Appendix D). With this in mind, 2 outcomes metrics need to be measured and monitored:

- Diabetes drug adherence rates
- HbA_{1c} levels

Although reducing the medical cost trend is an expected outcome of VBID programs, we caution that diabetes cost trends could easily be overwhelmed by other factors, including changes in other benefit designs, provider reimbursement, demographics, and medical management policies, as well as random fluctuations. One approach to modeling costs savings is to monetize the improved health status associated with glycemic control that is reported in medical literature, such as reduced amputations, end-stage renal disease, and retinopathy. Landmark studies report a lower incidence of micro- and macrovascular adverse events associated with lower HbA_{1c} levels.[11,12]

Prior to the start of implementing a program, we suggest estimating baseline drug therapy adherence rates in the plan's pharmacy claims data. We note that utilization (scripts/1000) is a standard actuarial measurement, while adherence is difficult to measure through claims data. In particular, because many diabetics are on more than 1 diabetes drug, it is difficult to distinguish between changes in multipharmacy, intended switches in drug therapy, and nonadherence. Consequently, with claims data, improvements in estimated adherence are generally more meaningful than absolute adherence rates.

The following is a simplified description of how to create this estimate. Diabetics on diabetes drug therapy will need to be identified for a baseline period, probably 12 months long. The identified members should be stratified by days of medication possession, eg, 30 days, 60 days, 90 days, etc. This will allow for measuring the number of individuals currently adherent, as measured by medication possession ≥80% of the days in the year, and the number who increase adherence to achieve a rate of possession ≥80%. Change in aggregate utilization of diabetic drugs should also be measured. Shift of utilization from brand name to generic is another metric to note.

If utilizing a diabetes disease management program, this analysis should be performed by the disease management vendor and reported on a quarterly basis. Alternatively, the contracted pharmacy benefits manager (PBM) can perform these specialized analyses.

Employers buying a disease management program for diabetes should obtain annual reports on changes in HbA_{1c} levels among enrolled members. Disease management vendors typically gather baseline HbA_{1c} levels on individuals as they enroll in disease management programs and additional values periodically thereafter. However, the vendor may find it hard to obtain follow-up values from many enrollees, and data on HbA_{1c} changes may be based on a small portion of diabetics. Outside a disease management program, an employer will find it challenging and cumbersome to collect HbA_{1c} data. While employers can examine the HbA_{1c}-related scores of health plans compiled in the Healthcare Effectiveness Data and Information Set (HEDIS), these figures are generally reported for the whole health plan's population and not for members in VBID or for a particular employer.

Employers may wish to consider other impact measures:

- Surveying members/employees regarding impact of lower co-pays for diabetes drugs on other health behaviors, including impact on medication adherence for other comorbid conditions
- Member/employee satisfaction and retention
- Workplace productivity/absenteeism

These measurements are also complex and difficult to associate with a particular benefits program such as VBID.

VI. Comparing Value to Current Benefits

VBID is intended to apply to all medical benefits and adjust co-pays or benefit coverage based on value and evidence. We identify several changes in benefit design or medical care efficiency that employers and health plans can consider to offset the additional costs associated with increased adherence with VBIDs. Making adjustments to co-pay designs for some benefits or reconsideration of the value and expense of particular vendor program purchases could go a long way toward paying for value-based services such as diabetes drug VBID.

Table 7 compares the VBID incremental costs developed in Table 6 to typical costs for other types of benefit options employers can choose.

Table 7. Comparative value

Benefit	Typical Incremental Cost PMPM
VBID diabetes options in this report	$0.81 to $1.86
Diabetes disease management (total cost)	$0.50 to $1.00
Wellness* (total cost)	$0.40 to $14.00
Chiropractic care (total cost)	$0.30 to $2.30
Decrease inpatient admissions by 1.7 per 1000 members (typically <4% reduction)	$1.40 to $1.50
Decrease spinal surgery and bariatric surgery by 20%	$0.30 to $0.70

Abbreviations: PMPM, per member per month; VBID, value-based insurance design.

*$0.40 PMPM includes basic promotion. $14.00 PMPM includes full range of services such as health risk assessment (HRA) incentives, gym subsidy, obesity benefit, administrative costs, etc.

Appendix C describes the methodology behind these estimates. Costs certainly vary among employers and by geographic region, as does the opportunity for some of the improved utilization figures we show. The decreased inpatient admissions and decreased surgery we show are often available to employers through more aggressive utilization management.

VII. Conclusion

Despite well-established treatment targets and the availability of numerous diabetes drugs, adherence to therapeutic regimens remains poor.[1-3] Adherence correlates with glycemic control—good adherence leads to better control, while poor adherence leads to poor control.[6-9]

To encourage adherence with cost-effective therapies, some employers and payers have experimented with VBID and related concepts. VBID sets cost sharing to support evidence-based interventions—for example, lower cost sharing for cost-effective services with a strong evidence base; higher cost sharing or denial of coverage for interventions with a weak evidence base. While VBID can apply to all medical services, our focus has been on medication therapy co-pays. For prescription drugs, the rationale for focusing on co-pays is that adherence is inversely proportional to the level of co-pay. As shown in Milliman modeling for types 1 and 2 diabetes, adherence is higher in lower co-pay benefit designs.

When co-pays are reduced under VBID, increasing levels of adherence may be accompanied by incrementally higher drug costs. Our analysis suggests that reducing co-pays elevates utilization and drug costs for diabetes drugs, because more members begin to fill prescriptions for which the payer assumes more of the cost and because members who were already adherent pay less out-of-pocket.

It is beyond the scope of this report to model cost offsets that might accrue from better adherence. However, we note that plans can assign reasonable health improvements and cost reductions associated with better adherence and assumed glycemic control—reduced amputations, end-stage renal disease, retinopathy, and other complications. These improvements can then be compared to the costs of VBID or other plan costs. Plans may also consider effects such as impact on HEDIS measures, member and physician satisfaction, and disability.

VBID dovetails with current health care trends, such as consumerism, evidence-based medicine, and concern over the management of chronic disease.

Appendix A: Description of Key Data Sources and Their Application

MedStat claims data. This dataset contains all paid claims generated by over 4 million commercially insured lives. Member identification codes are consistent from year to year and allow for multiyear longitudinal studies. Information includes diagnosis codes, procedure codes, diagnosis-related group (DRG) codes, and national drug codes (NDCs), along with site of service information and the amounts paid by commercial insurers. For this study, we used data for 2006.

NHANES 1999-2000, 2001-2002, 2003-2004 and 2005-2006 datasets. This is from the series of National Health and Nutrition Examination Surveys. A department within the Centers for Disease Control (CDC) National Center for Health Statistics (NCHS) produces NHANES. Each year, the survey contains information from roughly 5000 completed forms plus details of laboratory results and physical examinations. A representative sample of the noninstitutionalized civilian population aged 12 years and older is selected by using a stratified, multistage sampling design. The data items list contains well over 1000 items that measure an individual's clinical, demographic, and health status.

Milliman's 2008 Health Cost Guidelines. The Guidelines provide a flexible but consistent basis for the determination of health claim costs and premium rates for a wide variety of health plans. The Guidelines are developed as a result of Milliman's continuing research on health care costs. First developed in 1954, the Guidelines have been updated and expanded annually since that time. The Guidelines are continually monitored to ensure that they are useful in measuring the experience and evaluating the rates of health plans. The Guidelines are also compared to other data sources. The standard demographics in the Guidelines were developed to be representative of the age and sex distribution for a typical large insured group. The standard demographics were developed using data from large insurers combined with Department of Labor sources.

Appendix B: Study Methodology

We used NHANES 2001-2004 to identify the prevalence of diabetes, comorbidities among diabetics, and the HbA_{1c} levels of diabetics. We applied criteria from the ADA to the following NHANES fields to identify diabetics:

DIQ010 Doctor told you have diabetes

DIQ050 Now taking insulin

DIQ070 Now taking diabetic pills to lower blood sugar

LBXGLU Fasting blood glucose (we use >125 mg/dL as the criterion for diabetes and 100 to 125 mg/dL for prediabetes)

We use the following NHANES fields to identify patients on diabetes drug therapy:

Description Orals	NHCODE
chlorpromamide phenformin	85200
chlorpromamide	13700
diabetes drug unspecified	87100
glimepiride	27300
glipizide	27400
glucagon hydrochloride	27500
glyburide	27600
glyburide; metformin hydrochloride	90100
metformin hydrochloride	38500
tolazamide	57100
insulin	32800

We use the LBXGH (glycohemoglobin) field in the NHANES lab data file to capture HbA_{1c} levels and determine diabetes control according to the ADA guidelines: HbA_{1c} <7% (controlled) or ≥7% (uncontrolled).

We applied the portions of diabetes lives identified in NHANES by quinquennial age groups and sex to the Guidelines' standard employee/spouse/dependent population (10 000 employees, 4721 spouses and 7844 children) covered through a typical large employer.

The logic for identifying diabetics in MedStat follows:

Definition of Diabetes Patients

One inpatient admit or 1 emergency department claim with a diabetes ICD-9 in any position of the claim or 2 outpatient physician evaluation and management (E&M) claims with a diabetes ICD-9 in any position of the claim or 1 claim for a diabetes drug, excluding metformin and glucophage.

Description	ICD-9-CM Diabetes Diagnosis Codes
Diseases of other endocrine glands – diabetes	250.xx
Polyneuropathy in diabetes	357.2x
Diabetic retinopathy	362.0x
Diabetic cataract	366.41
Description	**CPT Codes**
Physician E&M codes	92002-92014, 99201-99205, 99211-99215, 99217-99220, 99241-99245, 99271-99275, 99301-99303, 99311-99313, 99321-99323, 99331-99333, 99341-99355, 99384-99387, 99394-99397, 99401-99404, 99411, 99412, 99420, 99429, 99499

Abbreviation: HEDIS, Healthcare Effectiveness Data and Information Set.
Code source: HEDIS 2006.

Appendix C: Description of VBID Modeling

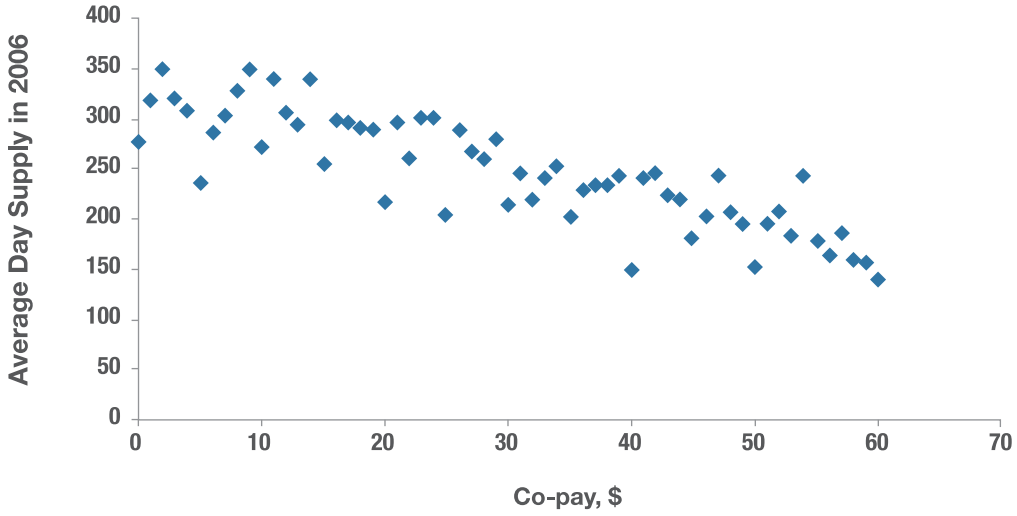
Our approach to modeling the increase in adherence due to reduced co-pays required several steps, which we describe in this section. We emphasize that we used data on the actuarial impact of co-pays on aggregate utilization. We used assumptions to convert utilization into adherence. Benefit pricing rarely, if ever, uses randomized controlled trials to determine relationships among different benefits—such data are simply not available. In our approach, we used the methods that actuaries working for health insurers could use to set rates.

We classified each diabetes drug claim from a large database of prescription claims paid under a 3-tier benefit structure into tiers (tier 1, tier 2, or tier 3) by linking each claim to plan descriptions. We also classified each diabetes drug claim into component class (pen insulin, other insulin, generic, or brand) by NDC and therapeutic class. We used ICD-9 codes on medical claims to determine whether the patient had type 1 or type 2 diabetes.

We developed elasticity curves by component class and type of diabetes. The elasticity curve shows the relationship between co-pay (x-axis) and utilization (y-axis), as illustrated in Chart 9. Higher co-pay plans have lower utilization, so the curve has negative slope.

We calculated the total day supply of diabetes prescriptions for patients with full-year membership by component class, as well as the co-pay for each component class. After averaging total day supply of patients in the same co-pay, we constructed 8 sets of data (2 types of diabetes and 4 component classes) for regression analysis. Chart 9 shows the utilization of generic drugs for type 2 diabetics by co-pay level.

Chart 9. Utilization of generic prescriptions for type 2 diabetics by co-pay



To develop mathematical relationships, we assumed a family of curves using a normative actuarial elasticity curve from the Milliman 2008 *Health Cost Guidelines* (HCGs), which were developed for all drug classes and patients. We assumed the elasticity curves for each of the 8 combinations (2 diabetes types and 4 component classes) could be represented by the HCGs curve and 2 parameters, θ and ς. We solved for the 2 parameters by the least square method for each type and component class.

$$\text{Smoothed Curve} = \theta\,(\text{HCGs Curve}+(1-\text{HCGs Curve})\varsigma)$$

Chart 10 shows the elasticity curve for generic drugs used by type 2 diabetics.

Chart 10. Elasticity curve of generic prescriptions for type 2 diabetics

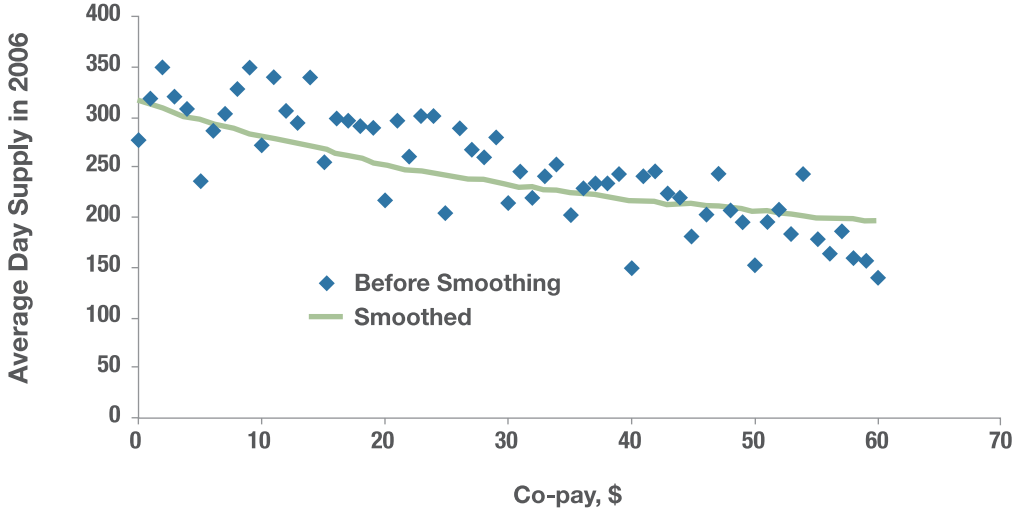
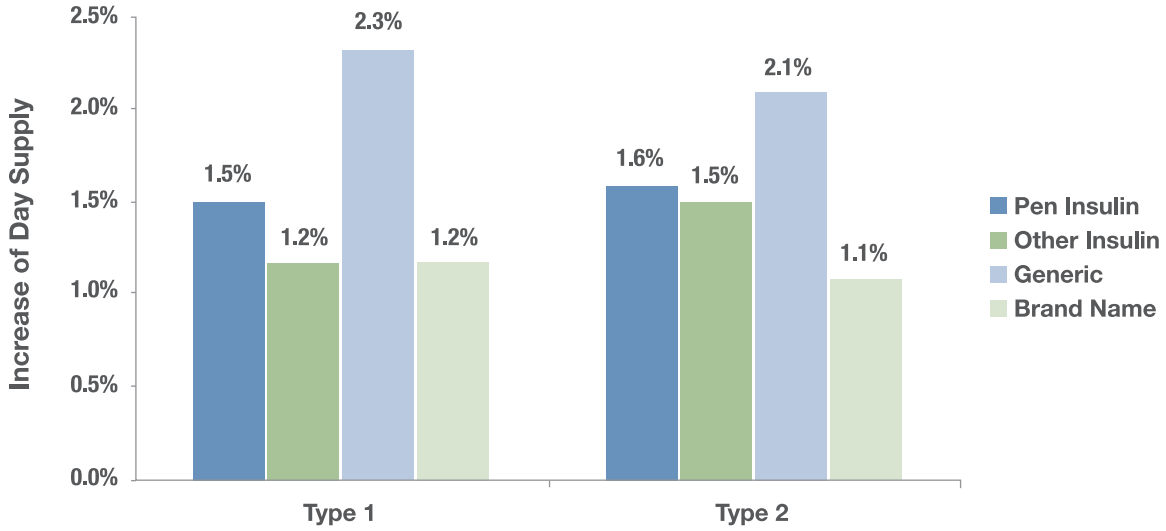


Chart 11 shows the percentage increase of average total day supply if co-pay goes down from $10 to $9 calculated by the smoothed elasticity curves.

Chart 11. Increase of utilization if co-pay goes down from $10 to $9



We used the derived least-squares elasticity curves to calculate average days' supply of diabetes drugs in 2006 per diabetes patient in different co-pay structures.

This average days' supply included the days' supply of second drugs for patients who used more than 1 prescription. We distinguished patients who take more than 1 prescription and adjusted their days' supply by dividing by 2. After making this adjustment, the aggregate percentage adherence (adjusted days' supply divided by 365) was 61% for type 1 diabetics and 43% for type 2 diabetics, across MedStat 2006 plans.

In developing adherence rates, our model recognizes 2 groups of patients—the adherent group, and the nonadherent group. We assumed the following:

- 70% of type 1 diabetes patients and 55% of type 2 diabetes patients are compliant
- For the compliant group, the adherence rate is 80%

Using the elasticity curves, we calculated the aggregate adherence rate in each of the 4 co-pay structures described in Table 5. We calculated the percent of virtual adherence in each co-pay structure with the above assumptions.

Comparative benefits

This section describes the cost development of comparative benefits shown in section VI.

Chiropractic

This benefit provides for visits to a licensed chiropractor's office including visits involving manipulations with a $15 co-pay per visit. Radiology services are not included in the cost. We used 2007 national average Medicare Resource-Based Relative Value Scale (RBRVS) allowed amounts adjusted to 2008 using trends reported in the Milliman Medical Index. We used utilization for loosely managed and well-managed health plans from the Milliman 2008 *Health Cost Guidelines*.

Reduction of inpatient days through improved medical management

To produce the range shown for reducing 1.7 inpatient admits per 1000, we applied national average Medicare DRG allowed amounts to commercial inpatient admission distributions by DRG. We used 2 different distributions of DRGs: loosely managed and well-managed health plans from the Milliman 2008 *Health Cost Guidelines*.

Utilization reduction in spinal surgeries

For the utilization reduction in spinal surgeries, we used the weighted average of the 10 DRGs below from Milliman's 2008 *Health Cost Guidelines* DRG model, using admission utilization for loosely managed and well-managed health plans.

496	COMBINED ANTERIOR/POSTERIOR SPINAL FUSION
497	SPINAL FUSION EXCEPT CERVICAL W CC
498	SPINAL FUSION EXCEPT CERVICAL W/O CC
499	BACK & NECK PROCEDURES EXCEPT SPINAL FUSION W CC
500	BACK & NECK PROCEDURES EXCEPT SPINAL FUSION W/O CC
519	CERVICAL SPINAL FUSION W CC
520	CERVICAL SPINAL FUSION W/O CC
531	SPINAL PROCEDURES W CC
532	SPINAL PROCEDURES W/O CC
546	SPINAL FUSION EXC CERV WITH CURVATURE OF THE SPINE OR MALIG

For the cost per admission, we used national average 2007 Medicare DRG allowed amounts adjusted to 2008 using trends reported in the Milliman Medical Index and an estimated surgeon fee.

Utilization reduction in bariatric surgeries

For the utilization reduction in bariatric surgeries, we used the admission rates for DRG 288, OR Procedures for Obesity, from the Milliman 2008 *Health Cost Guidelines* DRG model, using admission utilization for loosely managed and well-managed health plans.

For the cost per admission, we used national average 2007 Medicare DRG allowed amounts adjusted to 2008 using trends reported in the Milliman Medical Index and an estimated surgeon fee.

Appendix D: Glycemic Control and Diabetes Drug Therapy

What is glycemic control and why is it important?

Glycemia is the concentration of glucose in the blood. Glycemic control is the cornerstone of diabetes management and requires careful short-term and long-term monitoring. Short-term monitoring involves self-monitoring of blood glucose, which is recommended several times a day for those on insulin. Long-term monitoring of blood sugar is recommended through measurement of HbA_{1c}, which reflects the level of glucose in a patient's blood for the previous 2 to 3 months. HbA_{1c} is used as a measure of how well a patient's blood sugar has been controlled in the recent past and is the measure evaluated to determine the type of drug therapy needed.

Comprehensive recommendations for management of diabetes come from the ADA[27] and the American Association of Clinical Endocrinologists (AACE)/American College of Endocrinology (ACE).[28] The ADA sets a target for HbA_{1c} <7.0% while AACE/ACE sets an HbA_{1c} target of ≤6.5%. The ADA consensus recommendation is that an HbA_{1c} of ≥7% should be a call to action to initiate or change therapy with the goal of achieving levels as close to the nondiabetic range as possible (HbA_{1c} <6% without significant hypoglycemia). This goal may not be appropriate or practical for some patients, and factors such as life expectancy, comorbidities, and risk for hypoglycemia need to be considered for every patient before intensifying drug therapy. The ADA recommends HbA_{1c} testing every 3 months while drug therapy is being adjusted (titration) and then at least every 6 months when HbA_{1c} is controlled.[27]

Diabetics, especially poorly treated diabetics, have increased risk of developing a variety of serious medical conditions. The complications of diabetes include organ damage and failure, especially involving the heart, eyes, kidneys, nerves, and blood vessels.[27] This is because hyperglycemia narrows the small and large blood vessels. In the small vessels, sugar-based substances build up on vessel walls. As a result, less blood can be supplied, especially to the nerves and the skin. In the larger vessels, plaque builds up on the inner vessel lining, as levels of fatty substances in the blood rise in the presence of hyperglycemia. This results in atherosclerosis and decreased blood flow.[29] Data consistently associate higher HbA_{1c} levels with higher

rates of micro- and macrovascular complications, including heart attack, stroke, heart failure, amputation, retinopathy, end-stage renal disease, and cataracts.[11-13] The converse is also true: lower HbA_{1c} levels are associated with lower rates of micro- and macrovascular complications.[11-13]

Diabetes drug therapy

This section gives information on guidelines for diabetic drug therapy and describes types of drug therapies available. Excellent sources for further information can be found on the Internet. Patients should follow the advice of their clinician, as we cannot capture here the significant variations that apply to patients or innovations in this rapidly evolving field.

Type 1 diabetics typically make up 5% to 10% of the diabetic population. Type 1 diabetes is characterized by the destruction of cells in the pancreas resulting in the inability to produce insulin and is referred to as insulin-dependent diabetes. In contrast, type 2 diabetics have inadequate insulin secretion and/or diminished tissue responses to insulin. Type 1 diabetics are dependent on insulin, and most type 2 diabetics are unable to achieve adequate glycemic control with lifestyle modifications alone and require drug therapy, sometimes including insulin therapy.

Several classes of antidiabetes drugs are available, and additional classes are expected to emerge soon. The choice of therapy will depend on the baseline glycemia, duration of diabetes, previous therapy, patient characteristics, and other factors, with a goal of balancing glycemic control with safety and regimen issues (side effects, patient burden, adherence, expense). According to the ADA, "when levels of glycemia are high (e.g., A_{1C} >8.5), classes with greater and more rapid glucose lowering effectiveness, or potentially earlier initiation of combination therapy, are recommended; conversely, when glycemic levels are closer to the target levels (e.g., A_{1C} <7.5%) medications with lesser potential to lower glycemia and/or a slower onset of action may be considered."[30] The following drug therapy descriptions are taken from the ADA's 2006 consensus statement.[30, 31]

Biguanides. Biguanides are often the first-line therapy for type 2 diabetes. They decrease glucose output from the liver and lower fasting blood glucose. The HbA_{1c}-lowering commonly achieved with use of this drug is 1.5% to 2.0%. As

monotherapy, biguanides infrequently cause hypoglycemia and have been used to treat prediabetic hyperglycemia. Side effects may be transient and include metallic taste, diarrhea, nausea, and anorexia.

Sulfonylureas. Sulfonylureas enhance insulin secretion. The major side effect is hypoglycemia; severe episodes are infrequent but appear more often in the elderly. Newer sulfonylureas have lower risk for hypoglycemia. Weight gain of about 2 kg is another reported side effect.

Glinides. Glinides stimulate and enhance insulin secretion. Since their duration of action is short, frequent administration is needed. A side effect includes weight gain similar to the sulfonylureas. Hypoglycemia occurs less often with glinides when compared to sulfonylureas.

*α-Glucosidase inhibitor*s. The rate of digestion is reduced with α-glucosidase inhibitors, which lower postmeal glucose levels without causing hypoglycemia or weight gain. Side effects include increased gas production and other gastrointestinal symptoms; these effects may contribute to the 25% to 45% rate of treatment discontinuation in clinical trials of these drugs.

Thiazolidinediones. Thiazolidinediones (TZDs) increase the insulin-sensitivity of the liver, muscles, and fat through several mechanisms mediated by the nuclear receptor peroxisome proliferator-activated receptor γ (PPARγ),[30] a regulator of glucose and lipid uptake and metabolism. The net result of TZD stimulation of PPARγ is decreased blood glucose levels.[32] A meta-analysis of 22 publications demonstrated that TZDs modestly reduced A_{1c} levels from baseline (weighted mean difference -0.80%; 95% CI -1.10 to -0.50).[33] Side effects include weight gain and fluid retention.[30]

Insulin. Insulin is the most efficacious drug therapy for decreasing hyperglycemia. When used in sufficient doses, it can lower any elevation of HbA_{1c} to levels at or near the therapeutic target. Although insulin has beneficial effects on fatty-substance levels in the blood, it causes weight gain of about 2 to 4 kg. Another side effect is hypoglycemia, which needs to be carefully monitored. In 2006, an inhaled insulin was approved for type 2 diabetes.

Glucagon-like peptide 1 agonists. Glucagon-like peptide 1 agonists stimulate insulin secretion, suppress glucagon secretion, and slow gastric motility without causing hypoglycemia. Side effects include nausea, vomiting, diarrhea, and weight loss (approximately 2 to 3 kg over 6 months). A new compound in this class was approved in the US in 2005 for use with metformin or sulfonylurea. It is injected subcutaneously twice per day.

Amylin agonist. Amylin agonist slows gastric emptying, inhibits glucagon production, and decreases postmeal glucose elevations. Side effects involve the gastrointestinal tract, with approximately 30% of treated patients experiencing nausea. An additional side effect is weight loss of approximately 1 to 1.5 kg over 6 months. Amylin agonist is approved in the US only as adjunctive therapy with insulin. It is injected subcutaneously before meals.

Dipeptidyl peptidase-4 (DPP-4) inhibitor. This agent prolongs the activity of proteins that increase the release of insulin after the blood sugar rises. It enhances the body's own ability to lower elevated blood sugar. DPP-4 inhibitor should not be prescribed for type 1 diabetes or to treat diabetic ketoacidosis. It can be taken with or without food. The most common side effects are upper respiratory tract infection, sore throat, and headache.

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