MILLIMAN REPORT

The impact of medication adherence on total healthcare costs for commercially insured patients

A current perspective for patients with diabetes, hypertension, and hyperlipidemia

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I. Executive Summary

We performed an analysis of medication adherence in commercially insured patients aged 18 to 64 with diabetes, hypertension, or hyperlipidemia, and observed a stronger relationship between medication adherence and lower healthcare costs for patients with high risk scores. These results suggest that employers and healthcare providers may benefit from stratifying patients by imputing health risk scores into their claims data. This process will improve insights into the relationship between adherence interventions and overall healthcare costs.

Healthcare expenditures in the United States reached $4.9 trillion in 2023 and prescription drugs account for a growing proportion of healthcare spending, reaching $449.7 billion in the same year.[1] Health plans and pharmacy benefit managers (PBMs) have developed various clinical programs designed with the goal of improving patient adherence to medications to achieve better clinical outcomes and potentially decrease total healthcare costs.[2,3]

The idea that medication adherence will result in lower healthcare costs was derived from numerous observational studies, one example being a 2005 study by Sokol et al.[4] However, we find that many of the studies are significantly dated and likely not a good reflection of the current healthcare landscape. Conversely, a study published in 2020 assessed the correlation between healthcare costs and medication adherence in privately insured (including commercial and Medicare Advantage) adults over the age of 50 and found that, for commercially insured individuals, increased adherence was associated with higher overall healthcare spending, primarily driven by higher pharmacy claims costs.[5]

Because of differing conclusions across studies and interest among health sector stakeholders, we aim to provide an updated perspective on the relationship between adherence and total healthcare costs over a one-year period for patients with three common chronic conditions: diabetes, hypertension, and hyperlipidemia.

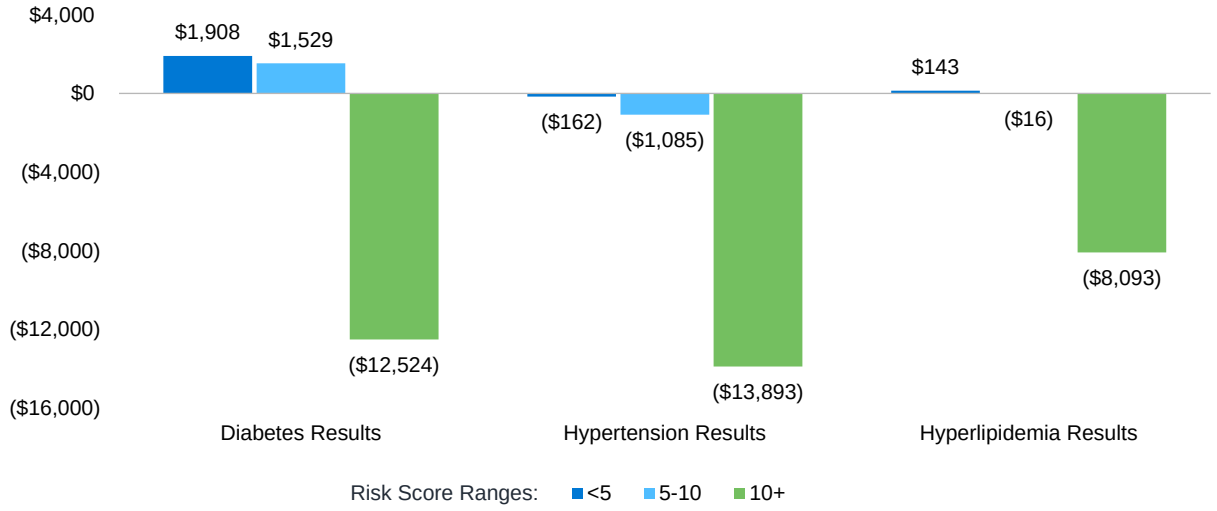
Our analysis focused on commercially insured patients aged 18 to 64 with diabetes, hypertension, or hyperlipidemia. We evaluated patient total healthcare costs in relation to adherence for patient subgroups based on age and health risk. To measure each patient's health risk, we utilized the Milliman Advanced Risk Adjusters™ (MARA™) CxXPLN prospective model. This is a linear model, using pharmacy and medical claims along with demographics to predict relative healthcare costs from one 12-month period to predict total relative healthcare resource use in the subsequent 12-month period. Each patient is assigned a numeric value reflecting their expected annual healthcare costs relative to an average-risk patient (ages 0 to 64) from MARA's development population. For instance, a patient with a risk score of two is expected to incur healthcare costs twice that of an average patient in MARA's development population. Additional details on the health risk scoring methodology are available in the paper.

Figure 1 shows the results of our healthcare cost comparisons broken out by three risk score groups for each of the disease categories included in our study. While results vary by disease category, we generally observed a much stronger relationship between adherence and lower health costs for patients within the highest risk score group. Conversely, adherent patients in the lower risk score groups often had similar or even higher total healthcare costs than non-adherent patients, which was primarily driven by higher prescription costs rather than higher medical costs.

1. Martin, A.B., Hartman, M., Washington, B., & Catlin, A. (December 18, 2024). National health expenditures in 2023: Faster growth as insurance coverage and utilization increased. Health Affairs. Retrieved February 27, 2025, from https://www.healthaffairs.org/doi/10.1377/hlthaff.2024.01375.
2. Brennan, T., Chaguturu, S., & Knecht, D. (January 29, 2020). CVS Health RxZERO solution eliminates member out-of-pocket costs for diabetes medications. CVS Health. Retrieved February 27, 2025, from https://cvshealth.com/news-and-insights/press-releases/cvs-health-rxzero-solution-eliminates-member-out-of-pocket-costs.
3. Medication adherence: Rx for success. (October 2012). OptumRx. Retrieved February 27, 2025, from https://www.optum.com/content/dam/optum3/optum/en/resources/white-papers/MedicationAdherence_WhitePaper.pdf.
4. Sokol, M.C., McGuigan, K.A., Verbrugge, R.R., & Epstein, R.S. (June 2005). Impact of medication adherence on hospitalization risk and healthcare cost. Medical Care. Retrieved February 27, 2027, from https://pubmed.ncbi.nlm.nih.gov/15908846/.
5. Gillespie, C.W., Morin, P.E., Tucker, J.M., & Purvis, L. (June 2020). Medication adherence, health care utilization, and spending among privately insured adults with chronic conditions in the United States, 2010-2016. The American Journal of Medicine. Retrieved February 27, 2025, from https://www.amjmed.com/action/showPdf?pii=S0002-9343%2820%2930031-0.

For diabetes and hyperlipidemia, we observed that adherent patients had higher healthcare costs if their risk score was under 10. However, adherent patients had significantly lower total healthcare costs when risk scores were above 10. For hypertension, we observed a positive relationship at lower risk levels, with most above a risk score of five demonstrating healthcare savings.

FIGURE 1: DIFFERENCE IN ANNUAL HEALTH COST BETWEEN ADHERENT AND NON-ADHERENT PATIENTS



II. Introduction

RISING HEALTHCARE SPEND AND THE ROLE OF ADHERENCE

National health expenditure (NHE) in the United States continues to grow each year and is expected to account for 19.7% of gross domestic product (GDP) by 2032, which represents a significant increase from the 2023 figure of 17.6%.[6] The Centers for Disease Control and Prevention (CDC) estimates that 90% of healthcare spend in the U.S. is for people with chronic and mental health conditions.[7] In 2022 alone, diabetes was estimated to cost $412.9 billion in medical costs and lost productivity.[8] Similarly, heart disease and stroke are estimated to have an average direct and indirect cost of $422.3 billion annually.[9] While some of these costs may be unavoidable or even essential, it is generally agreed upon that with proper care and optimal medication therapy, some healthcare utilization (and therefore spending) may be easily avoided. Optimal medication therapy includes two key factors: being prescribed the appropriate therapies and taking those therapies as prescribed; our focus is on the latter.

6. Martin, A.B., Hartman, M., Washington, B., & Catlin, A. (December 18, 2024). National health expenditures in 2023: Faster growth as insurance coverage and utilization increased. Health Affairs. Retrieved February 27, 2025, from https://www.healthaffairs.org/doi/10.1377/hlthaff.2024.01375.
7. Centers for Disease Control and Prevention (July 12, 2024). Fast facts: Health and economic costs of chronic diseases. Retrieved February 27, 2025, from https://www.cdc.gov/chronic-disease/data-research/facts-stats/index.html.
8. Parker, E.D., Lin, J., Mahoney, T., Nwanneamaka, U., Yang, G., Gabbay, R.A., El Sayad, N.A., & Bannuru, R.R. (November 1, 2023). Economic costs of diabetes in the U.S. in 2022. Diabetes Care. 2024;47(1):26–43. Retrieved April 9, 2025, from https://diabetesjournals.org/care/article/47/1/26/153797/Economic-Costs-of-Diabetes-in-the-U-S-in-2022.
9. Martin, S.S., Aday, A.W., Almarzooq, Z.I., et al. (February 20, 2024). 2024 heart disease and stroke statistics: A report of US and global data from the American Heart Association. Circulation. 2024;149,8:e347–e913. Retrieved February 27, 2025, from https://www.ahajournals.org/doi/epub/10.1161/CIR.0000000000001209.

The extent to which patients take medications as prescribed by their doctors is referred to as medication adherence. There are two primary methods used to measure medication adherence: proportion of days covered (PDC) and medication possession ratio (MPR). We elected to calculate adherence using PDC in our study to align with adherence measures created by the Pharmacy Quality Alliance (PQA). Optimal adherence is often defined as a PDC of 80% or greater, meaning that the patient is estimated to have the medication on hand at least 80% of the days in a given time period.[10] Adherence to medications for chronic conditions is generally low.[11,12] A 2020 study by Gillespie et al. estimates that less than half of patients in the U.S. adhere to their medications for four evaluated chronic conditions (atrial fibrillation, chronic obstructive pulmonary disease, diabetes, or hyperlipidemia)[13]. When patients are non-adherent, they may be more at risk for preventable, more costly health events, such as heart attacks, strokes, cardiovascular disease, and kidney disease.

There are many perceived benefits of adherence, such as improved quality of life and prevention of complications from chronic diseases. However, these benefits are difficult to capture in claims experience. As a result, analysis of healthcare cost is a common method of measuring the benefits of adherence. Medication adherence inherently results in increased pharmacy costs in the short term, since patients are filling medications more frequently. Nonetheless, the assumption is that adherent patients will utilize fewer medical services over the long term. The question then becomes whether the increased pharmacy spend is offset by decreased medical service utilization, therefore resulting in lower overall healthcare costs. Multiple studies on this topic have found that this tends to be the case, although much of that research is outdated or limited in scope.[14,15,16] Additionally, pharmacy spend in most studies, including this one, does not consider the effect of drug manufacturer rebates, which are not typically included in the pharmacy claims data analyzed. If rebates were included, healthcare savings may be higher, as the additional pharmacy cost related to higher medication adherence would be reduced on rebated products. Lastly, the emergence of more recent studies that have demonstrated inconsistent results may cause one to question whether improved adherence truly leads to decreased total healthcare costs.

ADDRESSING THE NEED FOR CURRENT ADHERENCE RESEARCH

One of the most frequently cited studies in this area concluded that better adherence was associated with statistically significant lower all-cause healthcare costs for diabetes, hypertension, and hyperlipidemia, but not congestive heart failure (CHF).[17] In this 2005 study, Sokol et al. evaluated claims from 1997 through 1999. More recently, a 2011 study published in *Health Affairs* found that adherent patients with CHF, diabetes, hypertension, and hyperlipidemia had significantly lower healthcare spend than non-adherent patients.[18] The study used data from 2005 to 2008, and was

10. Pharmacy Quality Alliance. (April 19, 2022). PQA adherence measures. Retrieved February 27, 2025, from https://www.pqaalliance.org/adherence-measures.

11. Neiman, A.B., Ruppar, T., Ho, M., et al. (November 17, 2017). CDC Grand Rounds: Improving medication adherence for chronic disease management—innovations and opportunities. CDC Morbidity and Mortality Weekly Report. 2018 Feb;18(2):514-517. Retrieved April 9, 2025, from https://www.cdc.gov/mmwr/volumes/66/wr/mm6645a2.htm.

12. Kleinsinger, F. (September 1, 2018). The unmet challenge of medication nonadherence. The Permanente Journal. Retrieved on April 9, 2025, from https://www.thepermanentejournal.org/doi/10.7812/TPP/18-033.

13. Gillespie, C.W., Morin, P.E., Tucker, J.M., & Purvis, L. (June 2020). Medication adherence, health care utilization, and spending among privately insured adults with chronic conditions in the United States, 2010-2016. The American Journal of Medicine. Retrieved February 27, 2025, from https://www.amjmed.com/action/showPdf?pii=S0002-9343%2820%2930031-0.

14. Sokol, M.C., McGuigan, K.A., Verbrugge, R.R., & Epstein, R.S. (June 2005). Impact of medication adherence on hospitalization risk and healthcare cost. Medical Care. Retrieved February 27, 2027, from https://pubmed.ncbi.nlm.nih.gov/15908846/.

15. Roebuck, M.C., Liberman, J.N., Gemmill-Toyama, M., & Brennan, T.A. (January 2011). Medication adherence leads to lower health care use and costs despite increased drug spending. Health Affairs. Retrieved February 27, 2025, from https://www.healthaffairs.org/doi/abs/10.1377/hlthaff.2009.1087?journalCode=hlthaff.

16. Balkrishnan, R., Rajagopalan, R., Camacho, F.T., et al. (November 2003). Predictors of medication adherence and associated health care costs in an older population with type 2 diabetes mellitus: A longitudinal cohort study. Clinical Therapeutics. Retrieved February 27, 2025, from https://www.clinicaltherapeutics.com/article/S0149-2918(03)80347-8/abstract.

17. Sokol, M.C., McGuigan, K.A., Verbrugge, R.R., & Epstein, R.S. (June 2005). Impact of medication adherence on hospitalization risk and healthcare cost. Medical Care. Retrieved February 27, 2027, from https://pubmed.ncbi.nlm.nih.gov/15908846/

18. Roebuck, M.C., Liberman, J.N., Gemmill-Toyama, M., & Brennan, T.A. (January 2011). Medication adherence leads to lower health care use and costs despite increased drug spending. Health Affairs. Retrieved February 27, 2025, from https://www.healthaffairs.org/doi/abs/10.1377/hlthaff.2009.1087?journalCode=hlthaff

authored by employees of a large PBM, which may impact the perceived credibility of the results by some stakeholders in the healthcare sector. The healthcare system has seen several changes within the last 20 years. Prescription drug spending as well as patient out-of-pocket spending both increased significantly.[19] At the time of these studies, many of the medications used to treat the conditions were only available as brand products and have since had generics that became available. High-deductible health plans (HDHPs) were also not yet available at the time of the Sokol study; therefore, based on studies that have compared healthcare utilization in HDHP and non-HDHP-enrolled patients, it is possible that in the absence of HDHPs, patients may have been more likely to seek treatment in the emergency department (ED).[20] Additionally, patients now have access to medical care through practice sites such as urgent care and nurse practitioner clinics that typically bear lower costs than the ED. For these reasons, there is a need for updated information regarding the association between adherence and healthcare costs. This is particularly important because PBMs and payers often cite these studies to support a need for programs designed to promote medication adherence, with some using the findings to calculate program savings guarantees.[21,22]

In contrast to the studies previously described, the Gillespie et al. (2020) study evaluated the association of adherence with healthcare costs and utilization in commercial and Medicare Advantage enrollees over the age of 50, and did not see decreased costs for adherent patients.[23] For commercial health insurance enrollees, the study found that adherent patients had overall spending of up to $3,000 more than non-adherent patients. The study presents results that conflict with what has been previously observed; thus, it further supports the need for updated research in this area.

In this observational study, we aim to provide an updated analysis and additional perspective regarding the correlation between medication adherence and healthcare costs using a large dataset of commercial enrollees. The analysis covers three highly prevalent chronic conditions—diabetes, hypertension, and hyperlipidemia—which affect approximately 5%, 12%, and 11% of the commercially insured population, respectively. Long-term use of prescription drugs is thought to play a major role in managing disease outcomes and costs for the chosen conditions according to the adherence studies reviewed.[24,25] We evaluate the difference in total annual healthcare costs between commercially insured adherent and non-adherent patients between the ages of 18 and 64, considering differences in age and health risk. As mentioned in the executive summary, we utilized the MARA CxXPLN prospective model to measure each patient's health risk. This is a linear model, using pharmacy and medical claims and demographics to predict relative healthcare costs from a 12-month period to predict total relative healthcare resource use in the subsequent 12-month period. Thus, CxXPLN offers a comprehensive assessment of risk by including both pharmacy and medical data and is predictive of future healthcare utilization. In this model, each patient is assigned a numeric

19. Wager, E., Telesford, I., Cox, C., & Amin, K. (September 15, 2023). What are the recent and forecasted trends in prescription drug spending? Health System Tracker. Retrieved February 27, 2025, from https://www.healthsystemtracker.org/chart-collection/recent-forecasted-trends-prescription-drug-spending/.

20. Chou, S.C., Hong, A.S., Weiner, S.G., & Wharam, J.F. (June 28, 2021). Impact of high-deductible health plans on emergency department patients with nonspecific chest pain and their subsequent care. Circulation. Retrieved on April 9, 2025, from https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.052501.

21. Brennan, T., Chaguturu, S., & Knecht, D. (January 29, 2020). CVS Health RxZERO solution eliminates member out-of-pocket costs for diabetes medications. CVS Health. Retrieved February 27, 2025, from https://cvshealth.com/news-and-insights/press-releases/cvs-health-rxzero-solution-eliminates-member-out-of-pocket-costs

22. Medication adherence: Rx for success. (October 2012). OptumRx. Retrieved February 27, 2025, from https://www.optum.com/content/dam/optum3/optum/en/resources/white-papers/MedicationAdherence_WhitePaper.pdf

23. Gillespie, C.W., Morin, P.E., Tucker, J.M., & Purvis, L. (June 2020). Medication adherence, health care utilization, and spending among privately insured adults with chronic conditions in the United States, 2010-2016. The American Journal of Medicine. Retrieved February 27, 2025, from https://www.amjmed.com/action/showPdf?pii=S0002-9343%2820%2930031-0

24. Brennan, T., Chaguturu, S., & Knecht, D. (January 29, 2020). CVS Health RxZERO solution eliminates member out-of-pocket costs for diabetes medications. CVS Health. Retrieved February 27, 2025, from https://cvshealth.com/news-and-insights/press-releases/cvs-health-rxzero-solution-eliminates-member-out-of-pocket-costs

25. Medication adherence: Rx for success. (October 2012). OptumRx. Retrieved February 27, 2025, from https://www.optum.com/content/dam/optum3/optum/en/resources/white-papers/MedicationAdherence_WhitePaper.pdf

risk score based on their expected annual total healthcare costs relative to the average in the MARA development population. Note that MARA's CxXPLN models use information on individual diagnoses and drugs, but do not consider individual costs in producing a prediction. We use and view risk adjustment as a proxy for population morbidity. Individuals with higher risk scores typically have a higher disease (and cost) burden, and patients with lower risk scores have lower disease (and cost) burden. Using this methodology, we hope to provide additional insights to stakeholders interested in the impact of medication adherence on healthcare costs.

III. Results

We identified more than 2.5 million commercially insured patients that met our inclusion criteria, which is described in more detail in the following Methodology section. Overall, 64.1% of patients were adherent. We identified 460,410 patients in the diabetes cohort, with 67.2% of patients classified as adherent. In the hypertension cohort, we observed 1.3 million patients, with 67.5% classified as adherent. In the hyperlipidemia cohort, 768,098 patients were identified, with 56.5% classified as adherent. Additional characteristics of the patients in each cohort may be found in **Figure 2**.

FIGURE 2: CHARACTERISTICS OF CONDITIONS COHORTS

Condition	Sample Size (n)	Mean Age (SD)	Percent Female
Diabetes (n = 460,410)			
MARA < 5			
PDC Less than 80%	125,674	52.0 (8.7)	43.4%
PDC Greater than 80%	239,768	53.9 (7.6)	40.5%
MARA 5+			
PDC Less than 80%	25,567	53.9 (8.0)	51.0%
PDC Greater than 80%	69,401	55.4 (6.9)	44.8%
Hypertension (n = 1,320,969)			
MARA < 5			
PDC Less than 80%	385,012	51.5 (9.0)	43.1%
PDC Greater than 80%	761,402	53.5 (8.0)	42.0%
MARA 5+			
PDC Less than 80%	44,888	53.6 (8.4)	51.2%
PDC Greater than 80%	129,667	55.3 (7.3)	45.7%
Hyperlipidemia (n = 768,098)			
MARA < 5			
PDC Less than 80%	294,229	53.7 (7.9)	37.8%
PDC Greater than 80%	370,335	55.1 (7.1)	36.3%
MARA 5+			
PDC Less than 80%	39,748	55.4 (7.1)	46.9%
PDC Greater than 80%	63,786	56.4 (6.4)	42.0%

For all conditions studied, adherence increased with age, and adherence rates were consistently higher for those with a MARA CxXPLN risk score of five or greater. Figures 4, 5, and 6 present a detailed analysis of patients categorized by MARA CxXPLN risk score and age group for diabetes, hypertension, and hyperlipidemia, respectively. Each figure includes the number of patients studied, the percentage of adherent patients, the average total healthcare cost per person within each MARA CxXPLN risk score and age group in 2022, the average disease-related healthcare cost

per person for each condition in 2022 (e.g., disease-related healthcare cost in Figure 4-2 presents diabetes-related healthcare costs), and disease-related cost as percentage of total healthcare cost. The average total healthcare cost and average disease-related healthcare cost are based on aggregated data for each risk score and age group for each condition. Linear regression was used to evaluate the difference in total healthcare costs and difference in total disease-related health cost between adherent and non-adherent patients for each condition within each risk score and age group, with adherence status as the sole predictor variable of costs. The results herein represent a weighted-average summary of the regression modeling completed and therefore does not include any p-values. Detailed results from the linear regression, including p-values, are provided in Appendix C.

We did not find a consistent relationship between adherence and total healthcare costs or disease-related healthcare costs in our analysis when looking at the overall population identified for each disease state. This is likely due to wide variability in healthcare costs of patients due to age, comorbidities, and disease severity. However, when looking within specified MARA CxXPLN risk score bands and age groups, we observed that adherent patients more often had lower total healthcare costs as risk score and age increased. In addition to age and MARA CxXPLN risk score, we evaluated the healthcare cost for adherent and non-adherent patients across different genders and plan types but did not see any significant differences. We also investigated patients with comorbidities that required use of higher-cost specialty medications and found that the inclusion/exclusion of those patients did not have a material impact on the results. The regression analysis resulted in low R-squared values, indicating a high level of variance within the model. Overall results across all three conditions are listed in Figure 3. Results are broken out by diseases and three different MARA CxXPLN risk score groupings (less than five, five to 10, and 10 or greater). The figure provides total patients observed, percent optimally adherent, and total and disease-related healthcare costs, along with the average differences between adherent and non-adherent patients.

FIGURE 3: ADHERENCE AND HEALTHCARE COSTS BY DISEASE AND MARA RISK SCORE GROUP

Disease	MARA Risk Score	N	Percent Optimally Adherent	Average Total Healthcare Cost	Average Disease Related Healthcare Cost	% Disease-Related Cost	Difference in Total Healthcare Costs Between Adherent and Non-Adherent Patients	Difference in Disease Related Healthcare Costs Between Adherent and Non-Adherent Patients
Diabetes	< 5	365,442	65.6%	$10,944	$6,371	58%	$1,908	$3,088
	5-10	72,294	74.1%	$36,071	$13,865	38%	$1,529	$5,218
	10+	22,674	69.9%	$102,542	$17,723	17%	-$12,524	$3,289
Hypertension	< 5	1,146,414	66.4%	$7,156	$1,066	15%	-$162	$85
	5-10	125,905	74.4%	$38,414	$4,912	13%	-$1,085	$350
	10+	48,650	74.0%	$114,482	$11,555	10%	-$13,893	$1,033
Hyperlipidemia	< 5	664,564	55.7%	$7,632	$1,242	16%	$143	$154
	5-10	77,788	62.0%	$38,371	$6,068	16%	-$16	$545
	10+	25,746	60.5%	$107,257	$13,265	12%	-$8,093	-$655

* Adherence defined as PDC ≥ 80%

DIABETES RESULTS

For the highest-risk patients with diabetes (MARA CxXPLN risk score of 10 or greater), we observed that adherent patients experienced between $10,075 and $24,833 of average annual healthcare cost savings relative to non-adherent patients, depending on age group. However, for those with a MARA CxXPLN risk score lower than 10, we found that total healthcare costs were typically higher for adherent patients than non-adherent patients. This is primarily because, based on our analysis, the medical cost savings are often not sufficient to offset the higher prescription costs associated with adherence. As shown in Figure 4-1, the savings in medical costs are insufficient to offset the higher prescription drug expenses.

FIGURE 4-1: MEDICAL COST AND PRESCRIPTION DRUG COST - DIABETES PATIENTS
DIABETES PATIENTS BY MARA RISK SCORE GROUP

MARA Risk Score	Average Total Medical Cost (Adherent Patients)	Average Total Medical Cost (Non-Adherent Patients)	Average Total Prescription Drug Cost (Adherent Patients)	Average Total Prescription Drug Cost (Non-Adherent Patients)	Medical Cost Difference Between Adherent and Non-Adherent Patients	Prescription Drug Cost Difference Between Adherent and Non-Adherent Patients
< 5	$4,200	$5,538	$7,332	$4,086	-$1,338	$3,246
5-10	$18,030	$22,041	$18,432	$12,891	-$4,012	$5,541

The differences in healthcare costs between adherent patients and non-adherent patients were statistically significant for all MARA CxXPLN risk score/age group categories except for a few MARA CxXPLN risk score categories for the 18–34 age group. For more details on the statistical modeling results, please refer to the appendix. When looking at MARA CxXPLN risk scores less than five on a more granular level (Appendix C1), the differences in cost for the adherent population varied by MARA CxXPLN risk score and age group but, in most MARA CxXPLN risk score and age categories, there was a statistically significant relationship between adherent patients and higher healthcare costs. This finding was even more evident when looking at disease-related healthcare costs, indicating that the cost of increased adherence to diabetes medications exceeded any diabetes-related medical cost savings these patients may have experienced.

FIGURE 4-2: DIABETES ADHERENCE AND HEALTHCARE COSTS BY MARA RISK SCORE AND AGE GROUP

MARA Risk Score	Age Group	N	Percent Optimally Adherent	Average Total Healthcare Cost	Average Disease Related Medical Cost	% Disease-Related Cost	Difference in Total Healthcare Costs Between Adherent and Non-Adherent Patients	Difference in Disease Related Healthcare Costs Between Adherent and Non-Adherent Patients
< 5	18-34	10,900	46.0%	$10,728	$6,275	58%	$1,123	$2,388
	35-44	46,763	57.5%	$10,407	$6,428	62%	$1,750	$2,926
	45-54	128,442	64.8%	$10,993	$6,549	60%	$2,170	$3,192
	55-64	179,337	69.5%	$11,062	$6,235	56%	$1,809	$3,097
5-10	18-34	1,344	52.8%	$35,924	$13,377	37%	-$327	$2,750
	35-44	6,326	66.6%	$37,330	$14,015	38%	$1,019	$4,673
	45-54	22,857	72.2%	$36,503	$14,111	39%	$1,927	$5,088
	55-64	41,767	76.9%	$35,648	$13,724	38%	$1,448	$5,452
10+	18-34	296	51.7%	$108,330	$19,125	18%	-$24,833	-$1,544
	35-44	1,726	63.7%	$103,253	$17,499	17%	-$10,075	$4,938
	45-54	6,915	68.1%	$103,055	$18,017	17%	-$12,260	$3,140
	55-64	13,737	72.0%	$102,070	$17,573	17%	-$12,699	$3,260

* Adherence defined as PDC ≥ 80%

HYPERTENSION RESULTS

For patients with hypertension, we observed that adherent patients typically demonstrated total healthcare savings relative to non-adherent patients across all risk levels. However, we found that these results had varied statistical significance as shown in Appendix C2. In addition, when looking at a more granular level (Appendix C2), we also found that the lowest-risk adherent patients (MARA CxXPLN risk score less than one) still had higher total healthcare costs than non-adherent patients. Similar to diabetes, the highest-risk score group (greater than 10) demonstrated the highest healthcare savings result for adherent patients.

FIGURE 5: HYPERTENSION ADHERENCE AND HEALTHCARE COSTS BY MARA RISK SCORE AND AGE GROUP

MARA Risk Score	Age Group	N	Percent Optimally Adherent	Average Total Healthcare Cost	Average Disease Related Medical Cost	% Disease-Related Cost	Difference in Total Healthcare Costs Between Adherent and Non-Adherent Patients	Difference in Disease Related Healthcare Costs Between Adherent and Non-Adherent Patients
< 5	18-34	43,703	50.2%	$5,860	$751	13%	-$384	$57
	35-44	165,722	59.0%	$6,141	$850	14%	-$243	$78
	45-54	389,550	65.3%	$7,011	$1,002	14%	-$88	$98
	55-64	547,439	70.8%	$7,671	$1,203	16%	-$172	$80
5-10	18-34	2,632	55.5%	$39,683	$3,185	8%	-$3,074	-$32
	35-44	11,889	66.4%	$40,048	$3,539	9%	-$832	$433
	45-54	37,851	72.1%	$39,085	$4,616	12%	-$638	$134
	55-64	73,533	77.5%	$37,760	$5,348	14%	-$1,285	$461
10+	18-34	1,114	60.8%	$144,751	$11,658	8%	$7,289	$6,279
	35-44	4,474	67.2%	$119,626	$10,883	9%	-$9,438	-$89
	45-54	14,527	71.4%	$112,667	$10,683	9%	-$13,631	$1,101
	55-64	28,535	76.8%	$113,418	$12,101	11%	-$15,553	$970

* Adherence defined as PDC ≥ 80%

HYPERLIPIDEMIA RESULTS

Results for the hyperlipidemia population were the least consistent of the three conditions evaluated. For the 18–34 age group, we observed that the number of patients is limited, thus the statistical significance of the results were typically unreliable. For patients over the age of 35, the highest-risk adherent patients (MARA CxXPLN risk score greater than 10) experienced average annual healthcare savings of $1,980 to $9,105 when compared to the non-adherent patients (Figure 6). The highest savings were associated with the older age groups, while the 35–44 adherent age group had lower savings. For those with MARA CxXPLN risk scores between five and 10, we found some marginal but inconsistent savings for adherent patients relative to non-adherent patients. When looking at a more granular level within this group (Appendix C3), we found that total healthcare costs for adherent patients are higher than non-adherent patients for some categories. When reviewing lower-risk patients (MARA CxXPLN risk score less than five), we found that total healthcare costs of adherent patients were slightly higher than that of the non-adherent population. The differences in healthcare costs between adherent and non-adherent hyperlipidemia patients was not statistically significant for most risk score/age band groups studied. When looking at MARA CxXPLN risk scores less than five on a more granular level, the differences in cost were inconsistent and did not follow a meaningful pattern.

FIGURE 6: HYPERLIPIDEMIA ADHERENCE AND HEALTHCARE COSTS BY MARA RISK SCORE AND AGE GROUP

MARA Risk Score	Age Group	N	Percent Optimally Adherent	Average Total Healthcare Cost	Average Disease Related Medical Cost	% Disease-Related Cost	Difference in Total Healthcare Costs Between Adherent and Non-Adherent Patients	Difference in Disease Related Healthcare Costs Between Adherent and Non-Adherent Patients
< 5	18-34	12,663	39.9%	$6,468	$862	13%	$42	$72
	35-44	68,787	47.8%	$6,697	$951	14%	$138	$191
	45-54	214,912	53.6%	$7,493	$1,151	15%	$198	$170
	55-64	368,202	59.0%	$7,927	$1,362	17%	$115	$140
5-10	18-34	801	45.8%	$39,607	$3,570	9%	$2,968	-$424
	35-44	5,417	54.3%	$39,972	$4,778	12%	-$533	$628
	45-54	22,289	59.1%	$39,265	$5,530	14%	-$287	$315
	55-64	49,281	64.4%	$37,771	$6,494	17%	$115	$656
10+	18-34	244	47.1%	$123,068	$11,888	10%	$23,460	$8,782
	35-44	1,573	52.3%	$108,194	$11,658	11%	-$1,980	-$251
	45-54	7,021	58.5%	$106,436	$12,470	12%	-$9,105	-$1,329
	55-64	16,908	62.3%	$107,283	$13,764	13%	-$8,697	-$548

* Adherence defined as PDC ≥ 80%

IV. Discussion

For the overall population included in our study, medication adherence was not consistently associated with decreased total healthcare costs for any of the conditions studied. Differences in healthcare costs for adherent patients did not follow a meaningful pattern until the population was divided into groups based on age and risk score. Our analysis found that for patients with higher healthcare costs and greatest health risks (MARA CxXPLN risk score of 10 or greater), adherent patients' total healthcare costs were generally lower than those of the non-adherent population for most conditions and age groups studied, except for hypertension and hyperlipidemia patients aged 18 to 34. With older patient age groups, the observed differences in healthcare costs were greater. This would indicate that, for these patients, the higher pharmacy costs attributed to adherence were more than offset by reduced medical spending. From a health plan's perspective, stratifying the patient population by health risk and age may assist in decision making when reviewing the benefits of medication adherence-based programs, especially programs that have guarantees or pricing based on return on investment (ROI). These results may also be useful in the development of interventions targeted at improving medication adherence.

Apart from hypertension, these same relationships were not found for patients with lower healthcare risk (MARA CxXPLN risk score less than five). In fact, total healthcare costs for diabetes and hyperlipidemia patients tended to be higher for those who were adherent and, in some cases, this difference was statistically significant. It is possible that for these patients, the increased pharmacy costs associated with adherence outweighed any potential savings on the medical benefit. The healthy user effect may play a role as well, which occurs when adherent patients are more likely to engage in other healthy behaviors, like vaccinations and screenings, therefore increasing healthcare costs.[26] Additionally, since we are only looking at one year of data, our study does not capture the potential long-term savings that may be associated with adherence. Lastly, regression modeling resulted in low R-squared values, indicating a low level of predictability within the model. This was expected due to the large variability of healthcare costs from patient to patient and does not negate the overall findings of this study.

26. Shrank, W.H., Patrick, A.R., & Brookhart, M.A. (January 4, 2011). Healthy user and related biases in observational studies of preventive interventions: A primer for physicians. Journal of General Internal Medicine. Retrieved February 27, 2025, from https://pmc.ncbi.nlm.nih.gov/articles/PMC3077477/.

Our results suggest that for patients who have more complex health issues, adherence to medications for chronic conditions may provide more of a clinical benefit, resulting in lower total healthcare costs. This becomes more apparent in the older patient cohorts. These results are expected and in line with the results of a 2016 study, which found that adherent patients with more comorbidities saw higher savings than those with fewer comorbidities.[27] In a broader sense, compared to other studies, our results landed somewhere in the middle, which is not surprising given the inconsistency seen among previous studies. To our knowledge, this is the first study to specifically evaluate the impact of adherence on healthcare costs among patients of different health risks, therefore providing a new perspective on this relationship. Payers should consider these differences in savings across different patient cohorts when determining savings guarantees for adherence programs, as our findings suggest that savings for adherent patients vary considerably depending on age, condition, and health risk.

Further study is needed to determine the long-term cost savings of a younger/less diseased population being highly adherent to medications. There are likely little to no short-term savings as supported by our study, but a longitudinal study evaluating long-term ROI could provide evidence that this group significantly reduces long-term medical costs if they are highly adherent. Further studies on this topic are needed to answer these questions. Risk adjustment models such as MARA may be useful in identifying patients to target for clinical programs, particularly those focused on medication adherence. As patients approach a higher disease burden corresponding to a higher risk score, indicating that their expected recurring healthcare costs are higher than the average patient, their adherence may have a larger impact on their health outcomes and near-term healthcare costs. Payers should consider stratifying their membership by risk score and evaluating higher-risk members for opportunities to improve medication adherence. An analysis of the long-term implications of adherence on risk score may provide an interesting point of view into the relationship between these two factors and total healthcare costs as a whole.

LIMITATIONS

The analysis presented in this white paper has many limitations. First and foremost, as this was an observational study, it is not possible to draw definitive conclusions about the causal relationship between adherence and cost. Observational studies have the potential to introduce biases that we are unable to see or account for, such as the healthy user effect as was discussed previously. Additionally, evaluating adherence through claims comes with its own challenges. Claims do not provide the full picture, leading to potential interpretive problems when labeling patients as adherent or non-adherent. There are multiple scenarios in which patients could be mislabeled, leading to variation within each of the study groups. For example, patients who are supposed to take multiple medications within a drug class but only fill one of them consistently would be labeled as adherent, even though they are not truly adherent to all of their medications. Conversely, patients who were on a drug for a short period of time would be labeled as non-adherent, even though there may have been a clinical reason for drug discontinuation. In addition, medications received outside of the pharmacy benefit (i.e., cash pay, discount cards, physician samples) are not captured in claims data. While this methodology is generally consistent with industry standards and those used in other adherence studies, these are important limitations of adherence studies based on claims data.[28,29]

27. Kymes, S.M., Pierce, R.L., Girdish, C., et al. (August 2016). Association among change in medical costs, level of comorbidity, and change in adherence behavior. American Journal of Managed Care. Retrieved February 27, 2025, from https://www.ajmc.com/view/association-among-change-in-medical-costs-level-of-comorbidity-and-change-in-adherence-behavior.

28. Sokol, M.C., McGuigan, K.A., Verbrugge, R.R., & Epstein, R.S. (June 2005). Impact of medication adherence on hospitalization risk and healthcare cost. Medical Care. Retrieved February 27, 2027, from https://pubmed.ncbi.nlm.nih.gov/15908846/

29. Neiman, A.B., Ruppar, T., Ho, M., et al. (November 17, 2017). CDC Grand Rounds: Improving medication adherence for chronic disease management—innovations and opportunities. CDC Morbidity and Mortality Weekly Report. 2018 Feb;18(2):514-517. Retrieved April 9, 2025, from https://www.cdc.gov/mmwr/volumes/66/wr/mm6645a2.htm

Manufacturer rebates are also not included in the data used for this study and therefore not reflected in our prescription drug cost measurements. Per the 2023 Nephron Research on Trends in Profitability and Compensation of PBMs & PBM Contracting Entities report, rebates as a percentage of brand sales to commercial payers were 36.97% in 2022.[30] Rebates are primarily paid by manufacturers on brand-name and specialty drugs. We observed that brand drugs as a percent of total prescription drug cost was 92% for the diabetes cohort, 85% for the hypertension cohort, and 86% for the hyperlipidemia cohort. If rebates were included for these drugs, the pharmacy cost associated with higher adherence would be lower and therefore healthcare savings would be higher.

Another limitation associated with evaluating adherence through claims is that because this was not a longitudinal study, we were unable to differentiate between incident and prevalent cases, or whether a patient was new to a medication or has been on it for many years. These are important considerations, as we are unable to determine if the correlation between adherence and healthcare costs is immediate or cumulative over time. Additionally, to maintain a large sample size and provide a current perspective, we limited our analysis to one year of data. It is likely that the impact of medication adherence/non-adherence takes time to materialize in claims data. Future analyses should conduct a longitudinal study to evaluate the long-term impact of adherence on total healthcare costs.

In our analysis, we also saw higher adherence rates than the averages typically cited in the literature. As previously mentioned, many studies note average adherence rates to chronic disease treatments to be around 50%; however our analysis saw rates of 57%– 67% depending on the condition. A likely contributor to this difference is the short time frame of study. By calculating adherence over a consecutive 12-month period, we only see a small snapshot of chronic disease treatment. With a longer period of study, we expect that adherence rates would align more closely with those found in the literature. Complexities and nuances associated with calculating adherence through claims may have also contributed to these higher adherence rates.

Lastly, in most cases where we observed healthcare cost savings associated with better adherence, a majority of the savings is being driven by lower non-disease-related medical costs. While the regression analysis suggests a strong correlation between higher adherence and these costs being lower for most of these groups, we did not conduct any additional analysis to validate whether the adherence to the medications observed influenced this result. Future analyses may be necessary to further explore this dynamic.

Despite these limitations, we feel that these results provide a valuable perspective on the relationship between adherence and healthcare costs. While overall we did not see a correlation between medication adherence and healthcare costs for all patients with diabetes, hypertension, and hyperlipidemia, we were able to identify a subpopulation in which adherence was associated with significantly lower healthcare costs for all three conditions studied. Optimally adherent high-risk patients consistently realized lower healthcare costs than the non-adherent group of high-risk patients, indicating that population stratification may pose as a useful tool in identifying target populations for adherence interventions, and that a one-size-fits-all approach to calculating adherence savings may not be appropriate.

30. Percher, E. (September 18, 2023). Trends in profitability and compensation of PBMs & PBM contracting entities. Nephron Research. Retrieved February 27, 2025, from https://nephronresearch.com/trends-in-profitability-and-compensation-of-pbms-and-pbm-contracting-entities/.

V. Methodology

DATA SOURCES

For this analysis, we utilized Milliman's proprietary Consolidated Health Cost Guidelines Sources Database (CHSD) data for commercial enrollees from 2022 and 2023. CHSD contains about 60 million lives from the commercial (i.e., self-insured and fully insured group) line of business, and is a consolidation of medical and pharmacy member experience data contributed by numerous health plans throughout the nation. In addition to the demographic and claims data contributed by these health plans, Milliman applies data quality indicators and analyzes the data to ensure reasonable quality results.

STUDY POPULATION

Separate study cohorts for each of the three conditions under study—diabetes, hypertension, and hyperlipidemia—were identified for the purposes of analysis. Patients were included in a study cohort if they had medical and pharmacy coverage for the entire study period, received a prescription drug for the specified condition, and utilized medical services for that same condition. Following, we describe the full inclusion criteria for each condition. Patients were required to meet the criteria in each bullet to be included. Patients who met the inclusion criteria for more than one of the medical conditions were included in multiple condition cohorts.

- A patient was included in the study cohort for a given condition if they received one or more prescription drugs for the target condition during the study period during 2022 and the first prescription drugs occurred in first quarter of 2022. The first fill occurring in the study period was used as the index drug claim for that patient. For each medical condition under study, the list of drug classes used for identification may be found in **Appendix A**. Note that insulins were not included in this study. Insulins are often excluded from standard measures for adherence, including the CMS diabetes adherence STAR measure, due to the complexities/inaccuracies of days' supply of insulins in pharmacy claims data. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors were also excluded from the study due to the low volume of claims in our data.
- Once a patient with an eligible prescription drug claim for a given condition was identified, we evaluated whether the patient received medical services for the condition in 2022 after the index drug claim. For each medical condition under study, medical services were identified using primary and secondary International Classification of Diseases, 10th Revision (ICD-10) codes in each patient's claim records. This can be found in **Appendix B**.
- To be included in the final analysis, patients meeting the previously discussed criteria had to be commercially insured, between the ages of 18 and 64, and continuously enrolled with medical and prescription coverage throughout 2022 and 2023 in order to track health cost. This population included PPO, HMO, POS, and EPO groups. No partial-year groups were included in the study due to the eligibility criteria. Members were also excluded if their medical costs fell within the top 1% of the studied population, to control for outliers. Our analysis focused on the health cost incurred in 2022.

CALCULATING ADHERENCE

Once patients were identified for inclusion, medication adherence was calculated using PDC, which is defined as the percentage of days during the analysis period that patients had a supply of one or more maintenance medications for the specified condition. The analysis period started with the index drug claim until the end of 2022.

The calculation is based on actual fill dates and days' supply data in the prescription claims dataset. Adjustments were made to account for overlapping days' supply and for cases where the last fill spilled over the analysis period. A PDC of 80% or greater was considered adherent, and a PDC of less than 80% was considered non-adherent. This is consistent with the threshold set by the PQA and is frequently used in the industry.[31]

31. Neiman, A.B., Ruppar, T., Ho, M., et al. (November 17, 2017). CDC Grand Rounds: Improving medication adherence for chronic disease management—innovations and opportunities. CDC Morbidity and Mortality Weekly Report. 2018 Feb;18(2):514-517. Retrieved April 9, 2025, from https://www.cdc.gov/mmwr/volumes/66/wr/mm6645a2.htm

STRATIFICATION AND STATISTICS

Medication adherence was used as the primary independent variable for our analysis, and the primary dependent variable was total healthcare cost. We analyzed a variety of subsets of the population to evaluate differences in age, gender, plan type, and overall health status/risk. The age bands used were 18–34, 35–44, 45–54, and 55–64.

To adjust for variations in health status, we relied on proprietary MARA total relative risk scores. MARA is a population stratification tool that combines medical and pharmacy claims with machine learning and statistical methods to calculate a total risk score for each member in the population under consideration. These scores represent expected overall healthcare resource utilization for each member relative to the average member in MARA's development data, which includes patients between the ages 0 and 65. The prospective model is useful for projecting trends in a future period where data is not yet available and more heavily influenced by chronic conditions. MARA CxXPLN risk scores start just above zero and do not have a set maximum, although scores greater than five are generally associated with patients who are high cost and have multiple complex medical conditions. For the purposes of this analysis, to split our population into lower-risk and higher-risk subgroups, MARA CxXPLN risk scores were grouped into two primary categories: less than five (lower risk) and five or greater (higher risk). A more granular breakdown of results by MARA CxXPLN risk score may be found in Appendix C for each of the conditions under study.

We used multiple linear regression to evaluate the association between medication adherence and healthcare costs for each condition, and overall fit of the regression models was tested using adjusted R-squared. Statistical significance of the difference in healthcare costs for adherent patients compared to the overall cohort population was indicated by a p-value below 0.05. Most but not all findings met this definition of statistical significance and are detailed in Appendix C.

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Appendix A: Drug classes used for patient identification and claims analysis

Condition	Class Name
Diabetes	Antidiabetic Combinations
	Biguanide Antidiabetics
	Dipeptidyl Peptidase-4 (DPP-4) Inhibitors
	Glucagon-like Peptide-1 (GLP-1) Receptor Agonists
	Insulin Sensitizing Agents
	Sodium Glucose Co-Transporter 2 (SGLT2) Inhibitors
	Sulfonylureas Antidiabetics
	Thiazolidinediones
Hypertension	Alpha Blockers
	Angiotensin II Receptor Blockers
	Angiotensin-Converting Enzyme (ACE) Inhibitors
	Antihypertensive Combinations
	Beta Blockers
	Calcium Channel Blockers
	Centrally Acting Alpha Agonists
	Diuretics
Hyperlipidemia	Antilipemic Nicotinic Acid and Derivatives
	Bile Acid Sequestrants and Ion-exchange Resins
	Fibric Acid Derivatives
	HMG CoA Reductase Inhibitors (Statins)
	Lipid Modifying Agents/Antilipemic Combinations Omega-3 Dyslipidemic Agents

Source: Clinical Pharmacology, Elsevier, retrieved on June 26, 2024

Appendix B: ICD-10 diagnostic indicators used for patient identification and claims analysis

Condition	ICD-10 Diagnosis Code
Diabetes	E08; E10; E11; E13
Hypertension	I10; I11; I12; I13; I15; I16
Hyperlipidemia	E78; G45.8; G45.9; G46; I21; I25.9; I63; I67.9; I70; I97.81; I97.82

Appendix C: Expanded results for all MARA CXXPLN risk scores

Appendix C1 - Regression Analysis Details - Diabetes

MARA Risk Score	Age Group	N	% of Members Using Specialty Drugs	Average Total Healthcare Cost	Average Disease Related Healthcare Cost	% Disease-Related Cost	Difference in Total Healthcare Costs Between Adherent and Non-Adherent Patients (95% CI)	P-Value	Difference in Disease Related Healthcare Costs Between Adherent and Non-Adherent Patients (95% CI)	P-Value
0 to 1	18-34	2,227	0.4%	$2,037	$936	46%	$14 (-$235 to $263)	0.9122	$194 ($57 to $331)	0.0056
	35-44	8,728	0.3%	$1,924	$899	47%	$208 ($111 to $306)	<0.0001	$237 ($175 to $299)	<0.0001
	45-54	16,841	0.2%	$1,925	$803	42%	$359 ($294 to $425)	<0.0001	$242 ($202 to $282)	<0.0001
	55-64	14,765	0.1%	$1,684	$651	39%	$239 ($176 to $303)	<0.0001	$172 ($133 to $210)	<0.0001
1 to 2	18-34	3,298	0.5%	$7,120	$4,372	61%	$1,624 ($1,249 to $2,000)	<0.0001	$2,661 ($2,384 to $2,938)	<0.0001
	35-44	14,034	0.6%	$6,680	$4,412	66%	$1,808 ($1,647 to $1,970)	<0.0001	$2,478 ($2,346 to $2,610)	<0.0001
	45-54	37,433	0.5%	$6,094	$3,598	59%	$1,592 ($1,492 to $1,692)	<0.0001	$1,979 ($1,901 to $2,057)	<0.0001
	55-64	50,241	0.5%	$5,029	$2,616	52%	$1,138 ($1,054 to $1,222)	<0.0001	$1,378 ($1,319 to $1,438)	<0.0001
2 to 3	18-34	2,740	1.2%	$12,635	$7,813	62%	$1,595 ($978 to $2,211)	<0.0001	$3,446 ($3,019 to $3,873)	<0.0001
	35-44	12,273	0.9%	$12,222	$8,026	66%	$2,539 ($2,271 to $2,808)	<0.0001	$3,992 ($3,796 to $4,188)	<0.0001
	45-54	35,514	0.9%	$11,743	$7,545	64%	$2,956 ($2,791 to $3,120)	<0.0001	$3,957 ($3,837 to $4,078)	<0.0001
	55-64	51,408	1.0%	$10,796	$6,544	61%	$2,262 ($2,115 to $2,409)	<0.0001	$3,533 ($3,429 to $3,638)	<0.0001
3 to 4	18-34	1,656	1.6%	$19,037	$10,924	57%	$1,116 (-$74 to $2,306)	0.0661	$3,015 ($2,238 to $3,792)	<0.0001
	35-44	7,511	1.4%	$17,414	$10,644	61%	$2,090 ($1,602 to $2,578)	<0.0001	$4,337 ($3,999 to $4,675)	<0.0001
	45-54	23,998	1.5%	$16,995	$10,275	60%	$2,858 ($2,567 to $3,150)	<0.0001	$4,821 ($4,626 to $5,017)	<0.0001
	55-64	37,925	1.4%	$16,230	$9,381	58%	$2,322 ($2,065 to $2,579)	<0.0001	$4,584 ($4,422 to $4,745)	<0.0001
4 to 5	18-34	979	2.7%	$23,256	$12,669	54%	$646 (-$1,178 to $2,470)	0.4874	$2,442 ($1,183 to $3,701)	0.0001
	35-44	4,217	2.3%	$22,610	$12,417	55%	$1,839 ($928 to $2,749)	<0.0001	$4,368 ($3,794 to $4,943)	<0.0001
	45-54	14,656	2.0%	$22,280	$12,178	55%	$2,697 ($2,174 to $3,219)	<0.0001	$5,160 ($4,850 to $5,470)	<0.0001
	55-64	24,998	2.1%	$21,431	$11,398	53%	$2,372 ($1,949 to $2,794)	<0.0001	$5,127 ($4,879 to $5,375)	<0.0001
5 to 7	18-34	889	6.2%	$30,838	$13,280	43%	-$413 (-$3,146 to $2,321)	0.7670	$3,754 ($2,246 to $5,262)	<0.0001
	35-44	3,991	6.5%	$30,780	$13,494	44%	$722 (-$588 to $2,032)	0.2799	$4,360 ($3,655 to $5,066)	<0.0001
	45-54	14,322	4.4%	$30,168	$13,676	45%	$1,800 ($1,043 to $2,557)	<0.0001	$5,064 ($4,671 to $5,457)	<0.0001
	55-64	26,124	3.7%	$29,692	$13,201	44%	$1,345 ($733 to $1,958)	<0.0001	$5,301 ($4,997 to $5,605)	<0.0001
7 to 10	18-34	455	16.5%	$45,860	$13,569	30%	-$160 (-$5,845 to $5,524)	0.9558	$789 (-$1,506 to $3,083)	0.4997
	35-44	2,335	19.5%	$48,527	$14,906	31%	$1,526 (-$1,293 to $4,345)	0.2887	$5,207 ($4,086 to $6,328)	<0.0001
	45-54	8,535	16.3%	$47,134	$14,842	31%	$2,140 ($620 to $3,661)	0.0058	$5,128 ($4,503 to $5,752)	<0.0001
	55-64	15,643	12.4%	$45,595	$14,596	32%	$1,620 ($413 to $2,826)	0.0085	$5,704 ($5,204 to $6,205)	<0.0001
10+	18-34	296	37.2%	$108,330	$19,125	18%	-$24,833 (-$51,936 to $2,269)	0.0724	-$1,544 (-$11,532 to $8,445)	0.7613
	35-44	1,726	35.2%	$103,253	$17,499	17%	-$10,075 (-$19,172 to -$978)	0.0300	$4,938 ($2,782 to $7,095)	<0.0001
	45-54	6,915	33.8%	$103,055	$18,017	17%	-$12,260 (-$16,924 to -$7,597)	<0.0001	$3,140 ($1,816 to $4,464)	<0.0001
	55-64	13,737	29.3%	$102,070	$17,573	17%	-$12,699 (-$15,941 to -$9,457)	<0.0001	$3,260 ($2,344 to $4,176)	<0.0001

Appendix C2 - Regression Analysis Details - Hypertension

MARA Risk Score	Age Group	N	% of Members Using Specialty Drugs	Average Total Healthcare Cost	Average Disease Related Healthcare Cost	% Disease-Related Cost	Difference in Total Healthcare Costs Between Adherent and Non-Adherent Patients (95% CI)	P-Value	Difference in Disease Related Healthcare Costs Between Adherent and Non-Adherent Patients (95% CI)	P-Value
0 to 1	18-34	21,610	0.2%	$1,817	$437	24%	-$22 (-$101 to $57)	0.5872	$88 ($66 to $110)	0.5872
	35-44	71,702	0.3%	$1,666	$420	25%	$42 ($8 to $76)	0.0166	$71 ($59 to $83)	0.0166
	45-54	125,187	0.2%	$1,774	$410	23%	$121 ($97 to $146)	<0.0001	$72 ($64 to $81)	<0.0001
	55-64	118,274	0.2%	$1,607	$379	24%	$142 ($119 to $165)	<0.0001	$71 ($63 to $78)	<0.0001
1 to 2	18-34	12,236	1.0%	$6,015	$819	14%	-$677 (-$927 to -$427)	<0.0001	$4 (-$63 to $72)	<0.0001
	35-44	49,767	0.9%	$5,427	$814	15%	-$407 (-$517 to -$297)	<0.0001	$57 ($17 to $98)	<0.0001
	45-54	131,802	0.8%	$4,968	$799	16%	-$89 (-$153 to -$25)	0.0064	$71 ($44 to $98)	0.0064
	55-64	199,701	0.7%	$4,333	$763	18%	-$62 (-$113 to -$11)	0.0180	$71 ($48 to $94)	0.0180
2 to 3	18-34	5,396	2.1%	$11,436	$1,161	10%	-$791 (-$1,388 to -$194)	0.0094	$60 (-$124 to $243)	0.0094
	35-44	24,466	1.9%	$10,855	$1,249	12%	-$319 (-$577 to -$61)	0.0155	$93 (-$2 to $188)	0.0155
	45-54	70,520	1.5%	$10,387	$1,352	13%	-$225 (-$382 to -$69)	0.0048	$151 ($81 to $220)	0.0048
	55-64	117,481	1.5%	$9,777	$1,469	15%	-$309 (-$444 to -$174)	<0.0001	$71 ($05 to $136)	<0.0001
3 to 4	18-34	2,746	2.9%	$16,479	$1,507	9%	-$852 (-$1,941 to $237)	0.1253	$51 (-$291 to $393)	0.1253
	35-44	12,634	2.6%	$16,273	$1,741	11%	-$935 (-$1,451 to -$420)	0.0004	$137 (-$67 to $341)	0.0004
	45-54	39,456	2.3%	$15,939	$1,932	12%	-$229 (-$535 to $76)	0.1409	$204 ($64 to $345)	0.1409
	55-64	69,705	2.1%	$15,720	$2,284	15%	-$469 (-$730 to -$209)	0.0004	$103 (-$30 to $236)	0.0004
4 to 5	18-34	1,715	5.8%	$21,154	$1,729	8%	-$814 (-$2,505 to $878)	0.3455	$57 (-$430 to $544)	0.3455
	35-44	7,153	4.3%	$21,950	$2,458	11%	-$474 (-$1,375 to $427)	0.3021	$136 (-$240 to $512)	0.3021
	45-54	22,585	3.1%	$21,819	$2,746	13%	-$570 (-$1,117 to -$23)	0.0411	$44 (-$226 to $313)	0.0411
	55-64	42,278	2.9%	$21,272	$3,067	14%	-$696 (-$1,130 to -$263)	0.0017	$143 (-$81 to $368)	0.0017
5 to 7	18-34	1,666	14.8%	$32,254	$2,796	9%	-$2,354 (-$4,929 to $220)	0.0730	$211 (-$871 to $1,294)	0.0730
	35-44	7,288	13.7%	$32,876	$3,183	10%	-$1,692 (-$2,983 to -$401)	0.0102	-$36 (-$549 to $477)	0.0102
	45-54	23,069	9.2%	$31,762	$3,870	12%	-$1,112 (-$1,863 to -$360)	0.0037	$25 (-$332 to $381)	0.0037
	55-64	44,833	6.8%	$30,780	$4,484	15%	-$1,460 (-$2,040 to -$880)	<0.0001	$300 (-$02 to $603)	<0.0001
7 to 10	18-34	966	30.6%	$52,494	$3,856	7%	-$4,316 (-$9,477 to $845)	0.1011	-$452 (-$2,052 to $1,147)	0.1011
	35-44	4,601	29.3%	$51,410	$4,103	8%	$531 (-$1,780 to $2,841)	0.6526	$1,176 ($325 to $2,027)	0.6526
	45-54	14,782	26.3%	$50,514	$5,781	11%	$103 (-$1,257 to $1,462)	0.8824	$304 (-$367 to $975)	0.8824
	55-64	28,700	20.0%	$48,662	$6,697	14%	-$1,011 (-$2,053 to $31)	0.0572	$712 ($168 to $1,257)	0.0572
10+	18-34	1,114	37.1%	$144,751	$11,658	8%	$7,289 (-$11,138 to $25,717)	0.4378	$6,279 ($1,220 to $11,338)	0.4378
	35-44	4,474	40.5%	$119,626	$10,883	9%	-$9,438 (-$16,435 to -$2,440)	0.0082	-$89 (-$2,692 to $2,513)	0.0082
	45-54	14,527	39.8%	$112,667	$10,683	9%	-$13,631 (-$17,289 to -$9,972)	<0.0001	$1,101 (-$269 to $2,472)	<0.0001
	55-64	28,535	36.4%	$113,418	$12,101	11%	-$15,553 (-$18,373 to -$12,732)	<0.0001	$970 (-$54 to $1,993)	<0.0001

Appendix C3 - Regression Analysis Details - Hyperlipidemia

MARA Risk Score	Age Group	N	% of Members Using Specialty Drugs	Average Total Healthcare Cost	Average Disease Related Healthcare Cost	% Disease-Related Cost	Difference in Total Healthcare Costs Between Adherent and Non-Adherent Patients (95% CI)	P-Value	Difference in Disease Related Healthcare Costs Between Adherent and Non-Adherent Patients (95% CI)	P-Value
0 to 1	18-34	5,690	0.4%	$1,690	$398	24%	$70 (-$41 to $182)	0.2164	$97 ($55 to $139)	0.2164
	35-44	27,871	0.2%	$1,706	$410	24%	$73 ($24 to $123)	0.0035	$70 ($52 to $89)	0.0035
	45-54	64,097	0.2%	$1,849	$398	22%	$113 ($80 to $146)	<0.0001	$51 ($40 to $63)	<0.0001
	55-64	74,732	0.3%	$1,717	$379	22%	$92 ($63 to $121)	<0.0001	$36 ($25 to $46)	<0.0001
1 to 2	18-34	3,454	0.7%	$5,569	$838	15%	-$138 (-$520 to $243)	0.4762	$36 (-$126 to $197)	0.4762
	35-44	20,329	0.7%	$5,432	$855	16%	-$13 (-$167 to $141)	0.8693	$143 ($71 to $214)	0.8693
	45-54	72,326	0.6%	$5,044	$856	17%	$130 ($51 to $209)	0.0012	$106 ($67 to $146)	0.0012
	55-64	135,285	0.7%	$4,426	$810	18%	$29 (-$29 to $86)	0.3262	$73 ($44 to $102)	0.3262
2 to 3	18-34	1,846	1.4%	$11,417	$1,107	10%	$1,126 ($298 to $1,954)	0.0077	$267 (-$49 to $583)	0.0077
	35-44	11,033	1.5%	$11,348	$1,363	12%	$635 ($284 to $986)	0.0004	$302 ($139 to $466)	0.0004
	45-54	40,985	1.3%	$10,753	$1,493	14%	$200 ($12 to $388)	0.0368	$203 ($104 to $302)	0.0368
	55-64	80,642	1.4%	$9,993	$1,627	16%	$189 ($44 to $333)	0.0107	$236 ($157 to $315)	0.0107
3 to 4	18-34	1,068	2.1%	$17,199	$1,998	12%	-$1,417 (-$3,044 to $210)	0.0877	-$284 (-$1,074 to $506)	0.0877
	35-44	6,081	2.4%	$16,546	$2,014	12%	$273 (-$371 to $916)	0.4061	$471 ($122 to $819)	0.4061
	45-54	23,774	2.0%	$16,307	$2,289	14%	$319 (-$26 to $665)	0.0698	$341 ($150 to $532)	0.0698
	55-64	48,138	2.0%	$15,752	$2,613	17%	$337 ($67 to $608)	0.0146	$230 ($75 to $386)	0.0146
4 to 5	18-34	605	4.1%	$22,491	$2,611	12%	$78 (-$2,608 to $2,764)	0.9546	$84 (-$1,336 to $1,503)	0.9546
	35-44	3,473	3.3%	$22,129	$2,677	12%	-$267 (-$1,442 to $908)	0.6561	$608 ($39 to $1,178)	0.6561
	45-54	13,730	2.6%	$21,747	$3,223	15%	$732 ($136 to $1,327)	0.0160	$664 ($320 to $1,009)	0.0160
	55-64	29,405	2.7%	$21,344	$3,628	17%	$04 (-$444 to $452)	0.9862	$305 ($44 to $566)	0.9862
5 to 7	18-34	526	10.8%	$32,474	$3,026	9%	$3,406 (-$1,070 to $7,881)	0.1356	-$291 (-$2,547 to $1,966)	0.1356
	35-44	3,394	12.2%	$33,381	$4,182	13%	-$1,397 (-$3,131 to $338)	0.1144	$141 (-$800 to $1,083)	0.1144
	45-54	13,775	8.1%	$32,339	$4,822	15%	-$120 (-$997 to $757)	0.7885	$495 ($2 to $988)	0.7885
	55-64	30,486	6.1%	$30,571	$5,444	18%	$201 (-$396 to $798)	0.5097	$681 ($330 to $1,031)	0.5097
7 to 10	18-34	275	25.1%	$53,253	$4,610	9%	$2,130 (-$7,348 to $11,607)	0.6585	-$680 (-$4,029 to $2,668)	0.6585
	35-44	2,023	26.8%	$51,031	$5,778	11%	$916 (-$2,359 to $4,192)	0.5834	$1,445 (-$85 to $2,975)	0.5834
	45-54	8,514	23.0%	$50,471	$6,674	13%	-$558 (-$2,154 to $1,037)	0.4928	$24 (-$818 to $866)	0.4928
	55-64	18,795	19.0%	$49,449	$8,196	17%	-$24 (-$1,162 to $1,113)	0.9664	$615 (-$36 to $1,265)	0.9664
10+	18-34	244	35.2%	$123,068	$11,888	10%	$23,460 (-$8,040 to $54,960)	0.1437	$8,782 (-$239 to $17,804)	0.1437
	35-44	1,573	39.1%	$108,194	$11,658	11%	-$1,980 (-$11,104 to $7,145)	0.6705	-$251 (-$4,239 to $3,736)	0.6705
	45-54	7,021	39.7%	$106,436	$12,470	12%	-$9,105 (-$13,559 to -$4,651)	<0.0001	-$1,329 (-$3,323 to $664)	<0.0001
	55-64	16,908	35.9%	$107,283	$13,764	13%	-$8,697 (-$11,604 to -$5,790)	<0.0001	-$548 (-$1,744 to $648)	<0.0001