INTEGRATED BENEFITS INSTITUTE

The Impact of Medication Adherence on Workplace Productivity Outcomes – 2023 UPDATE

A discussion of the scientific evidence for calculating savings from a diagnosis of depression and anxiety

Joseph Aller DHA, MBA, CPA
Director of Analytics
Integrated Benefits Institute

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Abstract

Background

In 2018 IBI launched the Medication Adherence Calculator (Medication Adherence Savings Calculator (ibiweb.org) showcasing the savings achievable by increasing medication adherence in 3 highly prevalent workforce conditions; diabetes, high cholesterol, and hypertension. The Medication Adherence Calculator derives savings estimates through measurement of the impact of higher medication adherence rates on employee absences and healthcare costs. A lower number of missed workdays grounded in improved employee health, along with healthcare utilization savings as measured by reductions in annual hospitalizations, emergency department visits, and reductions in physician office visits, create improvements in productivity and measurable cost savings. The savings are partially offset by the increased cost of regularly filling and taking prescribed medications (Medication-Aherence-Productivity.pdf (hubspotusercontent10.net), but the net gains are demonstrable using the IBI Medication Adherence Calculator.

While effective medication management of these 3 conditions continues to be important drivers of worker productivity, the intention was always to expand the tool to encompass other conditions materially affecting the workplace.

In the time since the launch of the tool, the US workforce has seen unprecedented disruption resulting in a dramatic increase in workers feelings of depression and anxiety (Mental-Health-Report-FINAL.pdf (hubspotusercontent10.net). Employee mental health is of significant concern for employers and an impactful driver of organizational productivity. While depression and anxiety were considered in the original Medication Adherence Calculator research but not included in the published version of the tool, increased condition prevalence and the availability of new research on the topic since the original launch warrants re-visiting the estimated impact of depression and anxiety as a standalone condition and as a mediating co-morbid disease.

Study Objective

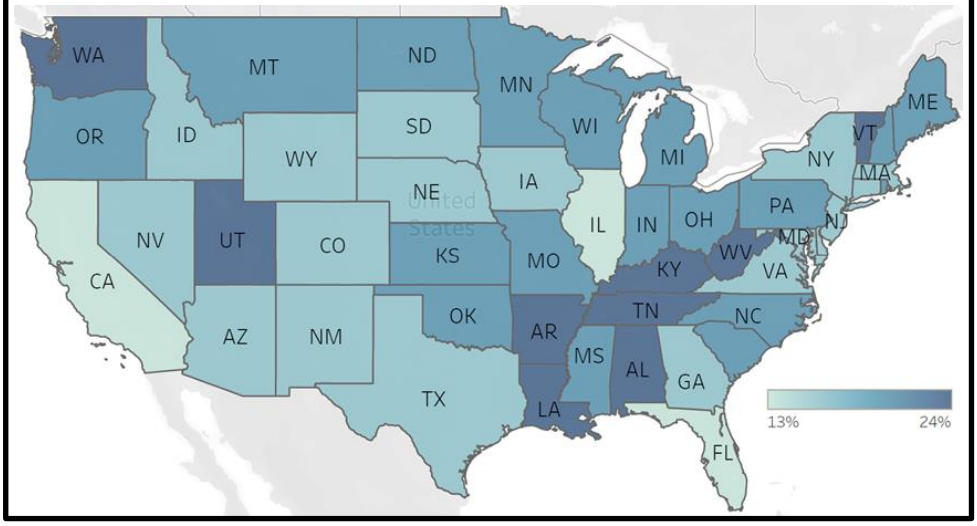
The objective of this study is to perform a systematic review of the published literature linking medication adherence to productivity outcomes for employees with depression and anxiety as a stand-alone condition as well as a mediating co-morbid condition and how productivity is affected through improved medication adherence. Based on the findings, if significant, expand the Medication Adherence Calculator to reflect the impact on productivity.

RESULTS

Research findings show there is quantifiable evidence on the statistically significant relationship between medication adherence behaviors of individuals with depression and anxiety and employee productivity both as a standalone diagnosis as well as a co-morbid mediating condition [1,3,4,5,6,7,8,9,11,12,13,14,16]. Improving the medication adherence of employees with these conditions have actual cost savings driven by fewer emergent episodes, less overall use of healthcare services, and more time spent on the job.

Introduction

Figure 1: Percent of adults with depression 2020



The IBI Medication Adherence Calculator currently reports on 3 disease conditions: Diabetes, Hypertension, and High Cholesterol. Feedback from IBI members as well as statistics found through IBI research, finds employers are extremely concerned about the prevalence of feelings of depression and anxiety in the workplace and its effect on productivity. Adding anxiety and depression as a standalone condition as well as a co-morbid mediating condition to the medication adherence calculator will provide our members with additional actionable information on the potential savings of a targeted intervention designed to improve medication adherence of employees.

Method

A search for peer-reviewed journal articles was conducted using Deep Dyve. Deep Dyve is a search engine that includes more than 100 million peer reviewed articles based on primary and advanced search criteria. Articles were extracted from Deep Dyve if their titles, abstracts, or keywords contained combinations of the following terms: medication adherence, depression or anxiety as a mediating condition, US prevalence of depression and anxiety in the workplace, and productivity and absenteeism. Criteria for inclusion in the final review were (a) English-language publications; (b) prospective, retrospective, or case studies on topic; (c) (d) comparing an adherent population to a nonadherent population, comparing periods of adherence to nonadherence, or comparing individuals with the condition to those without the condition; (e) a productivity measure in units of time (e.g., days or hours) the likelihood of having an absence from work and the associated costs of the absence.

Figure 2: Flow chart of search results

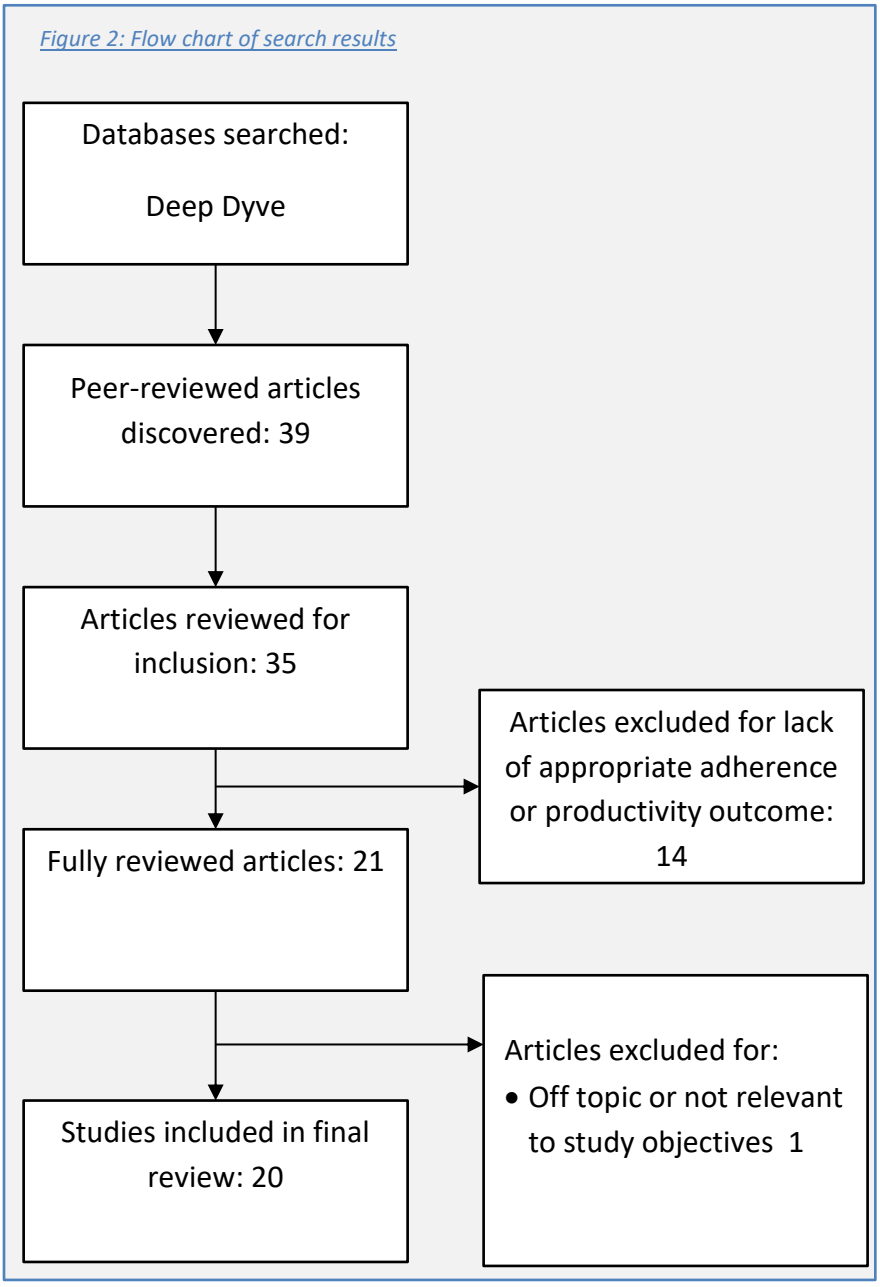


Figure 2 summarizes the search process. The search returned 39 peer-reviewed articles. Of these, 35 included outcome measures deemed to be of interest to the study and were further examined for inclusion. Of these, 20 were selected for a

full review based on their assessment of both outcome, adherence measures, and sufficient level of detail to support updating and expanding the Medication Adherence Calculator tool.

Overview of included studies

Table 1 describes the relevant characteristics of the studies included in the review, as well as a summary of the findings.

Table 1: Articles included in this review

Study	Authors	Date	Study type	Disease	Sample Population	Included productivity outcome(s)	Medication	Adherence measure	Summary results
(1)	EBI-Maurer, Roland, Flamm, Maria, Hosl, Katharina, et al.	2021	Cross-sectional survey	Depression/ Anxiety	12,405 Adult German population 18+ surveyed as part of the German Health Update	Days missed from work with associated cost of lost time	Not considered in study	8 item Patient Health Questionnaire with absenteeism measured over the past 12 months	Depression and anxiety associated with increased absence and cost based on level of severity.
(2)	Davies, A.	2022	Meta-analysis	Stress/ Depression/ Anxiety	Employed Individuals	Review of condition prevalence	Not considered in study	Varied	Stress, depression, and anxiety is materially impacting workers.
(3)	del Pino-Sedeño, T., Peñate, W., Cuevas, C., et al.	2019	Clinical Trial	Depressive disorders	400 patients aged 18-65 diagnosed with depressive disorder	Assess a multicomponent strategy to improve medication adherence both clinically and financially.	An educational program plus reminders to take prescribed medication.	Medication adherence measured at 3,6-, and 12-month intervals.	Presented in follow-on publication (4)

Study	Authors	Date	Study type	Disease	Sample Population	Included productivity outcome(s)	Medication	Adherence measure	Summary results
(4)	González de León, B., del Pino-Sedeño, T., Serrano-Pérez, P., et al.	2022	Meta-analysis	Depressive disorders	Varied	Not considered	Varied	Changes in medication adherence	Improved adherence at the 3 and 6-month mark.
(5)	Franca, M., Pereira, F., Wang, Y., et al.	2022	Cross-sectional survey	Mood, anxiety, impulse control, and substance use disorders as defined by Statistical Manual of Mental Disorders (American Psychiatric Association (1994)	5,037 adults	Absence, work performance, work loss	Not considered in study	Not considered in study	Significant relationship between lost productivity and measured conditions
(6)	Goldstein, C., Gathright, E., Garcia, S.	2017	Meta-analysis	Depression and cardiovascular disease	Varied	Hospitalizations	Not considered in study	Combination of self-reported and medication event monitoring system (MEMS)	Depression complicates a patients' ability to adhere to their medication regimen and other healthcare advise.

Study	Authors	Date	Study type	Disease	Sample Population	Included productivity outcome(s)	Medication	Adherence measure	Summary results
(7)	Wallace, K., Zhao, X., Misra, R., Sambamoorthi, U.	2018	Retrospective cross sectional study	Depression, anxiety, diabetes, and hypertension	4,560 adults >=18 diagnosed with diabetes and hypertension	Total annual healthcare expenditures health related quality of life	Not considered in study	A physical component summary index and a mental component summary index	Patients displaying depression and anxiety as a comorbid condition had demonstrably measurable differences.
(8)	Goldstein, C., Gathright, E., Gunstad, J, Dolansky, M., et al.	2017	Clinical Trial	Depression, anxiety, and congestive heart failure	372 adult age participant with a history of heart failure for at least 3 months.	Depression as a mediating co-morbidity	Not included in study	Medication adherence index based on self-reporting	Statistically significant relationship between complexity of medication regimen and medication adherence.
(9)	Schousboe, J., Vo, T., Kats, A., Langsetmo, L., et al.	2019	Prospective cohort study	Depressive symptoms	2,508 females	Total health care costs with and without depressive symptoms	Not included in study	Medication adherence index based on self-reporting	Statistically significant difference in health care costs for those participants with depressive symptoms
(10)	Brook, R., Kleinman, N., Beren, I.	2021	Retrospective longitudinal study	Mental disorders and substance use disorders	4.6 million lives; 3.0 million employed	Prevalence of conditions	Not included in study	Not included in study	Prevalence of employed individuals with mental disorders and SUD is growing

Study	Authors	Date	Study type	Disease	Sample Population	Included productivity outcome(s)	Medication	Adherence measure	Summary results
(11)	Bojanic, I., Sund, E., Sletvold, H., Bjerkeset, O.	2021	Cross sectional survey	Depression and anxiety, cardiovascular, and diabetes	Adults >=20	Depression as a mediating co-morbidity	Not considered in study	Not considered in study	Statistically significant findings on the prevalence of depression and anxiety as a mediating co-morbidity
(12)	König, H., König, H., Konnopka, A.	2020	Meta-analysis	Depressive disorders	Varied	Costs of healthcare services	Varied	Not considered in study	Depressive disorders associated with higher costs across all age groups
(13)	Xing, S., Calip, G., Leow, A., Kim, S., et al.	2018	Retrospective cohort study	Diabetes, depressive disorders	18–64-year-olds with previously treated type 2 diabetes and newly treated for depressive disorders	Depression as a mediating co-morbidity	Varied	Adherence to oral diabetic medication as prescribed	Statistically significant relationship between medication adherence and existence of depressive disorders.
(14)	Kaur, H., Scholl, J., Owens-Gary, M.	2022	Retrospective longitudinal analysis	Depression and diabetes	Behavioral Risk Factor Surveillance System (BRFSS) >= 18	Depression as a mediating co-morbidity	Not considered in study	Medication adherence index based on self-reporting	Statistically significant relationship between medication adherence and existence of diabetic disorders.

Study	Authors	Date	Study type	Disease	Sample Population	Included productivity outcome(s)	Medication	Adherence measure	Summary results
(15)	Jüngst, .C., Gräber, .S., Simons, .S., Wedemeyer, .H., & Lammert, .F.	2019	Cross-sectional survey	Chronic disease	Adult pharmacy customers	Medication adherence	Varied	Morisky medication adherence scale	Approximately 59% of respondents were fully adherent.
(16)	Fernandez-Piciochi, C., Martín-Saborido, C., Bimbela-Pedrola, J., & Sarria-Santamera, A.	2022	Cross-sectional survey	Chronic co-morbid	Working age adults diagnosed with depression, anxiety, and diabetes	Economic burden	Varied	Direct and indirect costs	Statistically significant relationship between standalone and co-morbid disease

Depression and Anxiety as a Stand-Alone Condition

The reviewed literature provides specific statistically significant guidance on the relationship between feelings of depression and anxiety and worker productivity in a variety of associations, measures, and directionally consistent outcomes. The utilized literature can be further broken down into two general classifications of studies. The first classification investigates the relationship between behaviors of the study participants regarding time away from work defined as absenteeism and sick days. The second classification investigates the behaviors of participants regarding their adherence to prescribed medication protocols.

One of the most comprehensive studies falling into the first classification is the EBI-Maurer study (2021). Using cross sectional survey data, the authors investigate both lost time and increased costs associated with depressive symptoms. Maurer concludes increases in the severity of depressive symptoms are associated with higher prevalence of absenteeism and employer costs. The research measures two outcome variables to evaluate productivity losses due to reported feelings of anxiety and depression.

Measured changes in absenteeism and sick days over the past 12 months between a cohort with no/minimal reported feelings of depression and anxiety and subsequent cohorts at four

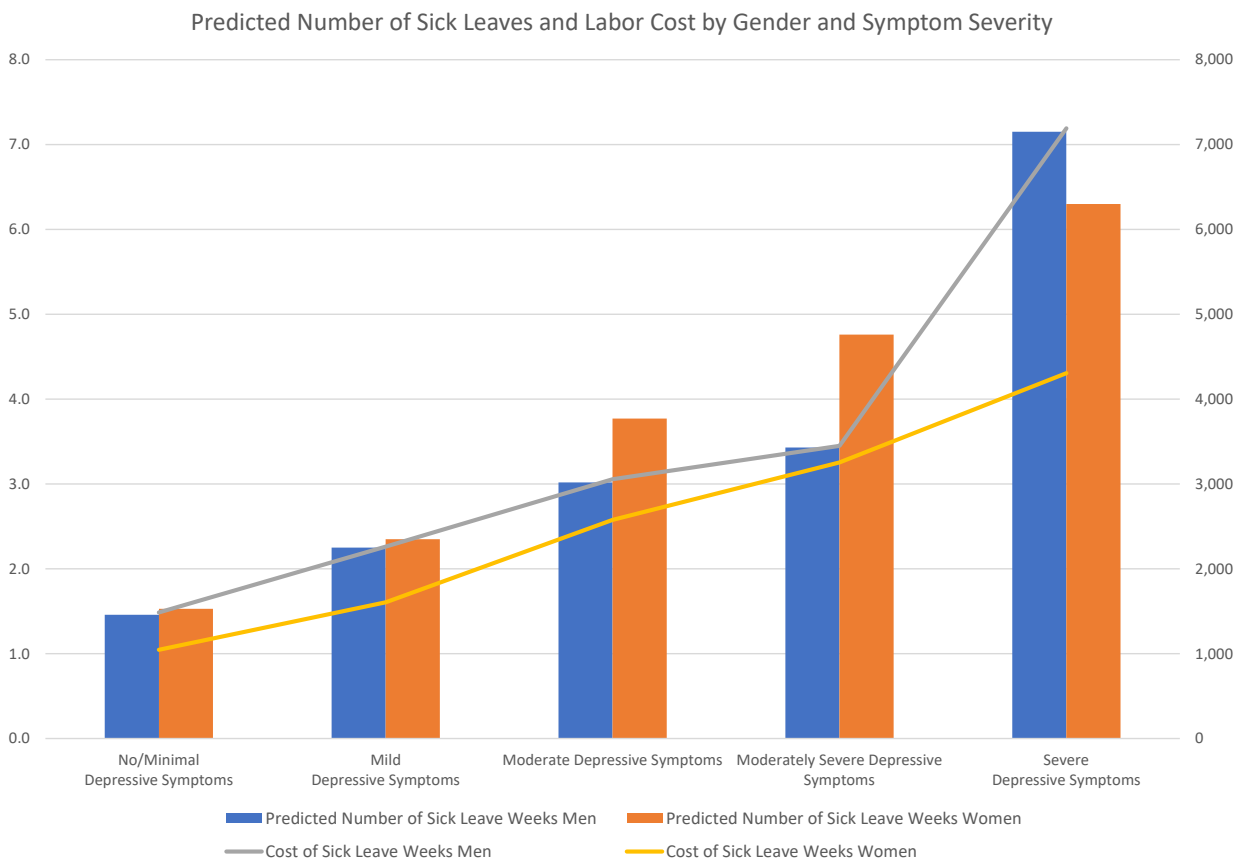
Table 2: Lost time of the study population as a total and by depressive symptom severity

	Total (N=12,405)	No/Minimal Depressive Symptoms (N=8,573)	Mild Depressive Symptoms (N=2,864)	Moderate Depressive Symptoms (N=704)	Moderately Severe Depressive Symptoms (N=214)	Severe Depressive Symptoms (N=50)
Full-time Employment %	71.8%	73.6%	68.3%	66.8%	66.4%	60.0%
Average Weeks sick leave past 12 Months	1.89	1.41	2.40	4.06	5.25	9.08
Percent Change from Prior Category			70.2%	69.2%	29.3%	73.0%

distinct levels of depression and anxiety severity: mild, moderate, moderately severe, and severe. Lost time is reported as an average for each stratification. Results are shown in Table 2. When combining the lost work time with the associated costs, as expected, they have a relatively linear relationship as shown in Figure 3. The Maurer study finds both the number of

sick leaves attributable to feelings of anxiety and depression as well as the associated utilization of healthcare services as measured by cost, increases with increasing levels of severity.

Table 3: Predicted Number of Sick Leaves and Labor Cost by Gender and Symptom Severity



Another directionally supportive study of the relationship between feelings of anxiety and depression and productivity includes findings from König, H., König, H., Konnopka, A. (2020). The researchers, using a meta-analysis, find feelings of anxiety and depression are associated with higher costs in all age groups. Higher costs are observed both as a standalone and co-morbid condition.

The conclusions of König, et al, are based on 48 articles covering approximately 675,000 individuals of which 55,898 are classified as depressive. Using a Ratio of Means (RoM), the

percentage change of mean costs between the groups (depressed v non-depressed study participants) , König, et al conclude statistically significant higher costs as shown in Table 4.

Table 4: Significance of Change in Mean Cost by Age Group

	Adolescents	Adults	Elderly	Co-Morbid
RoM (Range)	2.79 (1.69-4.59)	2.58 (2.01-3.31)	1.73 (1.47-2.03)	1.39 (1.24-1.55)
Level of Significance	p<.0001	p<.0001	p<.0001	p<.0001

In addition, König, et al find indirect cost, defined as inpatient, outpatient, medication, emergency, and other costs, to be statistically significantly higher in the adult age category having an RoM=2.28 and p<.0001. This is particularly important as this group generally represents working age individuals and are most applicable to the cohort of interest.

The research done by Schousboe, J., Vo, T., Kats, A., Langsetmo, L., et al. (2019) also supports the statistically significant relationship between healthcare cost and feelings of anxiety and depression. In this study, Schousboe finds depressive symptoms are significantly associated with higher healthcare costs in part driven by functional limitations, multi-morbidity, and the severity of the condition. Evaluating a cohort of 2,908 elderly women in 4 U.S. states, Schousboe finds annualized total healthcare costs to be $4,654 in those having little or no feelings of anxiety and depression, $7,871 (cost ratio=1.34 CI=95%) in those with mild symptoms, and $9,010 (cost ratio=1.29 CI=95%) in those with moderate to severe symptoms.

Measuring the effectiveness of an intervention designed to modify the behaviors of participants' medication adherence is the González de León (2022) research. González de León use a meta-analysis to conclude adherence interventions have a positive statistically significant effect for up to 6-12 months into the program.

Using Odds ratios calculated at a 95% CI; p<.01, the authors conclude the likelihood of an intervention being successful on the adherence of the participant. Depending on the specific type of adherence severity classification, the odds ratios varied, but the statistical significance was evident and consistent throughout.

While the author's acknowledge additional work needs to be done to measure intervention efficacy beyond the 6–12-month window, for modeling purposes and potential return-on investment, the conclusions provide an important benchmark given wellness programs and

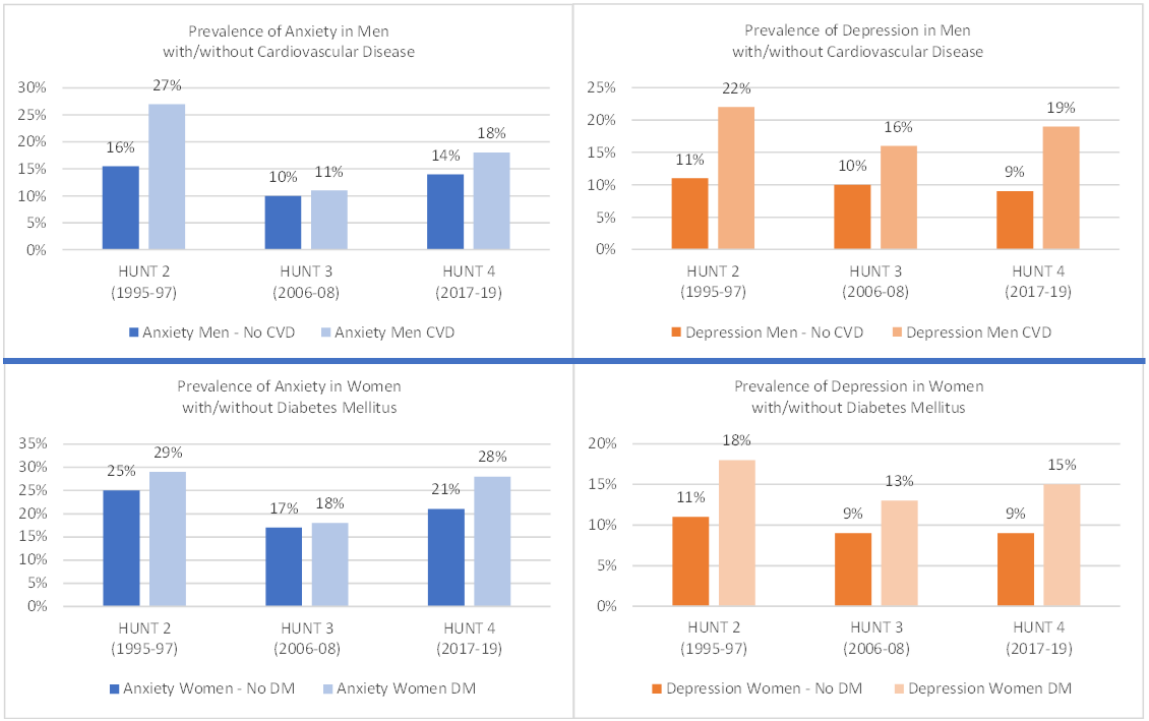
intervention results are often measured annually based on program renewals, employee turnover, and organizational budget cycles.

Depression and Anxiety as a Mediating Co-Morbidity

Research shows there is a strong relationship between the prevalence of depression and anxiety as a mediating co-morbidity (6,7,8,11,14) in individuals with cardiovascular disease and diabetes, conditions currently included in the Medication Adherence Calculator.

According to one such study (Bojanic, I., Sund, E., Sletvold, H., Bjerkeset, O. (2021), the prevalence of depression is more than 3x higher in individuals with Type I diabetes and almost twice as high in individuals with Type II diabetes. When Including anxiety as a co-morbid condition, this increases the overall prevalence to an even greater degree. The relationship between individuals experiencing symptoms of depression and anxiety and cardiovascular disease is equally significant. Bojanic (2021), concludes upwards of 1 in 3 individuals suffering from cardiovascular disease also shows symptoms of depression and anxiety.

Figure 2: Co-morbid mediating effect of anxiety and depression on men and women with Cardiovascular disease and diabetes mellitus



The Bojanic (2021) study, is based on 3 serial entry health questionnaires given to the entire Norway population 19 and older every 10 years. Respondent information available to researchers for this analysis was 65,228, 50,800, and 56,042 in HUNT 2,3, and 4 respectively. Statistical significance of the increase in prevalence is evaluated using a risk ratio (95% CI) by cohort. Multi-level logistic models were used to account for repeated measurements on the

same participants. As depicted in Figure 2, Bojanic (2021) finds a significantly increased prevalence of anxiety and depression in individuals diagnosed with cardiovascular disease or diabetes mellitus.

Another such study, Goldstein, C., Gathright, E., Garcia, S. (2017), provides additional information on the behaviors of individuals with depression and anxiety in combination with cardiovascular disease. The authors conclude approximately 50% of patients with cardiovascular disease experience feelings of depression and anxiety. These feelings exacerbate the ability to adhere to their medication regimen which results in higher use of healthcare services and ultimately productivity losses. Patients with cardiovascular disease may take many medications to manage their symptoms and the existence of depression and anxiety complicates adherence. The author's used hierarchical linear regression to determine adherence rates. While the statistical significance was most pronounced as feeling of anxiety and depression were more severe ($p<.05$), the results support the conclusions that depressive symptoms moderate the relationship between medcation complexity and medication adherence.

The Medication Adherence Calculator Savings Algorithm

Baseline Assumptions

The Medication Adherence Calculator is algorithm driven based on a conservative application of the findings in each of the reviewed studies. Depression and Anxiety is a bit different from the existing conditions included in the tool because not only does depression and anxiety need to be evaluated as a stand-alone condition but also as a mediating co-morbid condition. In effect, the relationship between depression and anxiety directly impacts the baseline assumptions of the model due to the compounding challenges on medication adherence in individuals with multiple conditions. The resulting improvements in medication adherence based on a targeted intervention needs to incorporate the new baseline assumptions, the additional use of healthcare resources, and the additional economic burden of co-morbid individuals. This can be better understood through a discussion of the drivers of the Medication Adherence Calculator savings algorithm.

User inputs will remain the same. The user is asked to provide estimates of employee daily wages, the cost benefits calculated at a daily rate, the short-term disability wage replacement rate shown as a percent, the percent of employees eligible for paid sick days, and the number of employees estimated to have the condition. The condition list is now expanded to include depression and anxiety as a standalone condition and as a mediating co-morbidity to the other conditions in the tool.

The user is then asked for a baseline or estimated prevailing adherence rate. This will later be compared to an input target adherence rate to calculate the potential savings based on the enhancement. The user can then better predict the quantified total savings of an intervention designed to enhance the medication adherence rate and a projected return on investment of the program.

Productivity Savings Measures

A reduction in the number of sick days is calculated based on using the user inputs and baseline assumptions for the associated condition. The reduction is based on relevant research and is table driven. The relevant studies are weighted based on the size of the cohort and then averaged. The result is shown as fewer sick days based on achieving the targeted medication adherence rate.

Sick day savings, shown in whole dollars per day is a straight calculation based on the average reduction in sick days calculated above quantified by taking the daily wages multiplied by the percent of employees eligible for paid sick days plus the cost of daily benefits.

The savings algorithm calculates the reduction in short term disability days at the targeted adherence rate in a similar fashion as the reduction in sick days. Reductions are a function of averaging the conclusions across the relevant research and providing a weighted average result based on cohort size. The result is table driven and populated based on the combination of factors selected by the user.

The resulting savings per reduction in short term disability days is again a simple calculation using the average daily wages, the wage replacement rate, and the daily cost of employee benefits, multiplied by the reduction in short term disability days.

The summary of productivity savings is derived based on the savings calculated above and the net value of savings is shown based as the difference between current adherence rate and targeted adherence rate.

Healthcare Utilization Savings

Driven by applicable research evaluating the economic impact of stand-alone and mediating co-morbid conditions, the Medication Adherence Calculator derives estimates for reductions in healthcare utilization services based on improved medication adherence. The reductions, as concluded in the applicable research, are driven by fewer hospital admissions, and less visits to the emergency department and doctor's office. The savings are partially offset by the incremental higher prescription medication cost of enhanced medication adherence as individuals fill and take their prescription drugs as prescribed.

The reduction in annual hospitalizations and ED visits per adherent employee remains supported by the Krumme study (2018) utilized in the original research related to the Medication Adherence Calculator when it was initially rolled out. The author's evaluated the behaviors of approximately 63,000 individuals to a medication synchronization program intervention designed to improve adherence. Outcome variables included patient medication adherence rates, the occurrence of a major adverse health event, and utilization of healthcare services measured by monthly number of inpatient hospitalization stays or ED visits and the number of physician office visits over eleven thirty-day intervals. The authors found a statistically significant reduction in healthcare services from those individuals who displayed higher medication adherence. On average, monthly rates of hospitalization and ED visits and of outpatient visits were 9 percent and 3 percent lower, respectively, in the synchronized group compared to the control group. Average cost per episode and changes in prescription refill cost is also used to populate the savings algorithm.

Medication Adherence Calculator Updates

Several approaches were considered in how to best represent depression and anxiety in the savings algorithm. In particular, as a mediating co-morbidity to the existing conditions. As a co-morbidity, the economic impact of the existence of depression and anxiety effectively lowers the baseline medication adherence rate, increases the utilization of healthcare services, and magnifies the overall effect of enhanced medication adherence. While the outcomes differ a bit based on the underlying conditions, the research shows this phenomenon holds regardless of the condition. While there is a relative range of applicable directionally consistent changes in service utilization, adherence rates, costs, and other stand-alone and co-morbid inputs to the model, a conservative application of the findings is employed to update the model. Additionally, because some input variables are presented as a weighted average across multiple studies, the algorithm update is in the form of a depression and anxiety co-morbidity factor. The factor accounts for the existence of the co-morbid condition and triggers additional related variables into the algorithm. Table 3 shows the effect of integrating a co-morbidity factor into the Medication Adherence Calculator savings algorithm and applicable research used as a guide.

Table 3: Example of adherence savings for diabetes as a stand-alone and co-morbid condition

USER INPUTS [a]	Diabetes Only	Diabetes with Depression and Anxiety	
Daily wages	$200	$200	
Daily benefits	$91	$91	
Wage replacement rate (STD)	63%	63%	
% of employees eligible for paid sick days	60%	60%	
Wages and benefits paid per lost STD day	$217.00	$217.00	
Wages and benefits paid per lost sick day	$211.00	$211.00	
# of Employees with Diabetes	2,000 [b]	2,000	
ADHERENCE ESTIMATE			
Adherence rate [c]	61%	61%	
Target adherence rate [d]	67%	67%	
SUMMARY OF SAVINGS			
Increasing adherence to the target rate of 67% could produce savings of $742K annually in reduced absences, office visits, ED visits, and hospitalizations.			
PRODUCTIVITY SAVINGS ESTIMATES FROM ADHERENCE			
Reduction in sick days if adherent [c]	3.6	3.9	30% of individuals with Diabetes shown to experience symptoms of depression and anxiety (Bojanic, 2021). These individuals have a 8.2% increase in absences (Fernandez-Piciochi, 2022).
Sick day savings per adherent employee [e]	$760	$822	
Reduction in STD days if adherent [c]	3.7	3.9	5% factor based on estimates aligned with hospitalization, absenteeism, and IBI benchmarking prevalence rates.
STD savings per adherent employee [f]	$803	$843	
SUMMARY PRODUCTIVITY SAVINGS			
Adherence to medications currently saves: [g]	$1.9M	$2.0M	
If adherence increased to target rate, savings would be: [h]	$2.1M	$2.2M	
The net value of increasing to target adherence rate is:	$188K	$200K	
Results based on 6 analyses with significant findings and 4 analyses with non-significant findings for articles reviewed in Aller, 2022. Results provided for example purposes only and should be			
HEALTHCARE UTILIZATION SAVINGS			
Reduction in annual hospitalizations and ED visits per adherent employee [i]	0.59	0.94	89% higher ED utilization and 40% higher hospitalization rate. Weighted average factor of .6 (Fernandez-Piciochi, 2022).
Average cost per episode [j]	$6,247	$6,247	
Hospitalization and ED savings per adherent employee	$3,687	$5,899	
Reduction in annual physician office visits per adherent employee [i]	5.9	11.39	93% increase in PC visits and specialists. (Fernandez-Piciochi, 2022).
Average cost per episode [j]	$273	$273	
Physician office savings per adherent employee	$1,611	$3,110	
Increase in annual prescription spending per adherent employee [j,k]	$681	$1,022	Based on a 3.6% increase in proportion of days with a prescription on hand among synchronized patients reported in Krumme et al, 2018. Baseline MEPS costs are assumed to reflect the share of adherent and non adherent patients in the control group from Krumme et al 2018.
SUMMARY HEALTHCARE UTILIZATION SAVINGS			
Adherence to medications currently saves:	$5.6M	$9.7M	
If adherence increased to target rate, savings would be:	$6.2M	$10.7M	
The net value of increasing to target adherence rate is:	$554K	$958K	

Limitations

While several studies matched adherent patients to nonadherent controls, this technique cannot account for unobserved factors that may influence patterns of adherence (Atella, 2017). Future studies may consider approaches that assess changes in lost productivity over time among adherent and nonadherent patients, potentially by implementing "fixed effects" approaches such as first differencing. Future studies may also consider spelling out more clearly the disease symptoms that may be affected by appropriate medication use and how occurrences of these symptoms might precipitate intermittent absences rather than relatively longer-term disability episodes. This could help establish an appropriate analytic period that allows for improvement in disease states and functioning to manifest in more-consistent work attendance.

Finally, the findings should be interpreted as reflecting the adherence measures used in the reviewed studies. The predominant approach is to dichotomously assess MPR at or above 80%. The underlying MPR method, however, as well as other approaches that use time period as a denominator, may ignore medication discontinuation and therefore overestimate adherence (Hess, 2006). Direct approaches such as measurement of drugs in blood or urine, physical observation of patients' medication-taking or the use of electronic medication packaging devices may provide a more accurate gauge of adherence (Lam, 2015) and increase confidence in the association with productivity outcomes.

Conclusions

The Integrated Benefits Institute (IBI) Medication Adherence Calculator represents another tool to assist Supplier and Employer members to effectively design and operationalize targeted interventional programs to enhance worker productivity. The tool was originally designed to accommodate an ever-growing list of conditions. As new conditions are added, IBI will continually research and represent to the best of our ability the effects of individuals with co-morbid conditions, medication complications, and contraindications. Inclusion of depression and anxiety represents our first step in this direction and establishes the framework for future enhancements.

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Integrated Benefits Institute
1901 Harrison Street
Suite 1100
Oakland, CA 94612
(415) 222-7280
ibiweb.org