

## Asthma Disease Management: Regression to the Mean or Better?

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**Objectives:** To assess the effectiveness of disease management as an adjunct to treatment for chronic illnesses, such as asthma, and to evaluate whether the statistical phenomenon of regression to the mean is responsible for many of the benefits commonly attributed to disease management.

**Study Design:** This study evaluated an asthma disease management intervention in a Colorado population covered by Medicaid. The outcomes are presented with the intervention group serving as its own control (baseline and postintervention measurements) and are compared with a matched control group during the same periods.

**Methods:** In the intervention group, 388 asthmatics entered and 258 completed the 6-month program; 446 subjects participated in the control group. Facilities charges were compared for both groups during the baseline and program periods. Both groups were well matched demographically and for costs at baseline.

**Results:** Using the intervention group as its own control revealed a 49.1% savings. The control group savings were 30.7%. Therefore, the net savings were 18.4% ( $P < .001$ ) for the intervention group vs controls. Although the demonstrated savings were less using a control group to correct for regression to the mean, they were statistically significant and clinically relevant.

**Conclusion:** When using a control group to control for the statistical effects of regression to the mean, a disease management intervention for asthma in a population covered by Medicaid is effective in reducing healthcare costs.

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During the last decade, disease management has become a widely accepted adjunct to conventional therapy.<sup>1</sup> Despite this activity, considerable debate remains as to the components of this intervention, its relative effectiveness, and, most of all, the methods of assessing its value.<sup>2</sup> Because disease management has arisen at a time when medical interventions are often measured in terms of their effects on the cost of delivering care, a significant topic of interest for disease management has been its effect on return on investment (ROI).<sup>3</sup>

Questions arise about what constitutes the best measures to be used to evaluate ROI outcomes. Equally as important as the actual measurements are the factors (intended and extraneous) that affect the observed changes when ROI is measured. A factor related to effectiveness measurements of disease management

programs is *regression to the mean*, a statistical term first coined in 1886 by Galton<sup>4</sup> when observing heights in families. The critical element in the application of the observations of Galton is that, if a series of events is tracked, the events tend on their own to return to a predictable mean. The more extreme that the initial observation is relative to the true mean, the more likely it is that regression to the mean will be observed. Most important, this regression would occur even without active intervention.<sup>5</sup>

A method of measuring the effect of an intervention is to have a control group that does not receive treatment, but still has an equal chance of being affected by other (random) events. This option is not always available when evaluating the effectiveness of certain disease management programs because of population size, ethical issues, and lack of a control population that faces the same or similar issues as the intervention group. In fact, a meticulously chosen control group should include individuals who could otherwise be substituted for those within the intervention group.

This article focuses on the results of a disease management intervention for asthma in a population covered by Medicaid. The outcomes are presented in 2 ways: (1) with the intervention group serving as its own control (ie, baseline and postintervention measurements) and (2) by comparing the intervention group with a similar matched control group during the same periods. Both of these methods are common within the literature.<sup>6</sup> By using 2 methods of assessing the same program, we are able to evaluate the principle of regression to the mean in measuring the effectiveness of disease management interventions in an asthmatic population. We also demonstrate the importance of having a matched control group rather than using only preintervention and postintervention data as a measure of the effectiveness.

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**METHODS****Study Populations**

The population studied was covered by a Colorado Medicaid health plan. Individuals were referred to the National Jewish Medical and Research Center Disease Management Program for asthma (NJDMP) based on their having had a prior diagnosis of asthma (*International Classification of Diseases, Ninth Revision [ICD-9-CM] code 493*) and a minimum level of healthcare use (hospitalization and emergency department visits) in the 12 months before their referral. The population of asthmatics was divided into 2 subgroups: (1) those who participated in the NJDMP and (2) a control group that did not receive any specific intervention. Both subgroups were followed up for 6 months. The observation was limited to the short period during which an asthmatic would be most likely to experience an exacerbation of his or her illness, primarily during the fall and winter months. To ensure complete evaluation of baseline and postintervention costs, all individuals from both subgroups had to have been enrolled with the health plan for at least 1 year.

**Intervention Subgroup Enrollee Identification**

To maximize the statistical power to observe changes due to the NJDMP, it was the stated intention of the study to enroll a sufficient number of patients to have 250 individuals complete 6 months in the program. Given an expected dropout rate of about 35% (because of loss of eligibility, relocation, etc), approximately 385 individuals were sought for initial enrollment.

**Control Subgroup Identification**

Individuals who were eligible for inclusion in the control group were potential candidates from the base population of referrals who did not enter the program. In addition to the basic requirements, eligibility for inclusion in the control group required that the individuals had been actively enrolled in Medicaid during the baseline and program periods (so that a complete cost comparison could be made for both groups during the same periods). Because eligibility lists can be overinclusive (ie, individuals who are no longer using Medicaid insurance may still be included on Medicaid eligibility lists because they did not disenroll), active participation during the study period was defined as having at least \$1 in claims of any type (facilities, professional, or pharmacy claims, whether or not they were paid) for any reason during the 1-year period that included the 6-month program period.

Individuals in the control group did not enter the disease management program for several reasons. Eighty-

five percent of the nonparticipation was because of an inability to be reached at the initial screening telephone call. The timing of these telephone calls included day, night, and weekend times, as they were assigned to nurses in a random order. The number of available slots for participants was about a third of the number ( $n = 1249$ ) of individuals who were referred to the NJDMP as eligible for participation. Because it was the intention of the program to take participants and controls through a similar environmental exposure period, all efforts were made to quickly enroll the subjects into the program. Of 388 individuals, 98% enrolled between October 16 and November 21, 2002. This meant that most individuals who were unavailable at the time of initial contact were not telephoned again because the program had been filled. Other reasons for nonparticipation in the program included individuals with incorrect telephone numbers, individuals who were not on the initial list sent for screening but who appeared in the subsequent month's list, and individuals who declined to participate. This last group accounted for about 8% of individuals. To ensure statistical rigor, these individuals were excluded from the control group.

The assignment of individuals to the treatment or control groups was dominated by a random variable: being at home at the time of the initial screening telephone call. Therefore, these 2 groups were statistically and clinically well matched as cases and controls.

**Data Analysis**

The data analyzed in the study came from UB-92 claims (ie, hospital and facilities charges) reported by Colorado Medicaid. Individuals with asthma were identified by analyzing the following claims: (1) any claim with a primary diagnosis of asthma (code 493.xx) and (2) any claim with a secondary diagnosis of asthma, provided that the primary diagnosis was in the respiratory system (codes 460.xx to 519.xx).

The program duration was approximately 6 months (ie, the period in which the participants would receive proactive telephone calls from the nurses). The baseline period was defined for program participants as the year before enrollment. For the control group, the periods investigated spanned November 15, 2001, to May 15, 2002, for the baseline period, and November 15, 2002, to May 15, 2003, for the program period. These dates corresponded approximately to the median entry and exit dates for program participants. A claim was counted in the analysis if the start date for a given healthcare use occurred in the time frame in question.

**Data Screening and Transformation**

Similar to symptom data and many other data sets in

healthcare, use cost data do not conform to a normal distribution. Instead, these data represent a distribution that is markedly skewed in a positive direction. That is, most individuals will have claims costs in the lower range, with a small number of individuals having much higher claims costs. The effect of this type of distribution is that the mean value deviates from the median value and the standard deviation is minimally informative in terms of denoting extreme scores. In this case, many more people will fall into the range of extreme scores than would be expected if the data were normally distributed.

As a result of this nonnormality, mean differences may be misleading; therefore, data should be transformed so that the distribution approaches normality before any inferential statistical analyses are performed. In this case, the most appropriate transformation is a log transformation of the data; therefore, for the purpose of analysis, the data are redefined as the natural log of the original cost plus \$1. (The adding of \$1 ensures that any individuals with \$0 in claims for a given period are still counted in the analysis.)

Because a significant number of individuals had \$0 claims data in both groups, even the transformed data did not conform to a normal distribution; rather, the distribution was bimodal with a small spike at \$0. Nevertheless, the resulting distribution is much closer to the normal bell-shaped distribution, and the normal parametric statistics should be robust to the small deviations from normality. However, for completeness, the nonparametric Wilcoxon rank sum test was also used to test for group differences. Because the resulting metric is not meaningful in presenting costs in their absolute terms, the data are presented in the normal metric of dollars spent, but analyses of group differences were performed on the log-transformed data.

Data screening was performed to ensure that program participants and control group subjects were statistically comparable to each other. Although the data were positively skewed for both groups, as already described, there was a small number of potential control subjects who had high use for nonasthma claims during the baseline period. Although asthma claims were similar for participants and potential controls, the inclusion of these outliers distorted the total claims by causing a large increase in nonasthma (thus, total) use. Therefore, potential control group subjects were eliminated if they had total claims that exceeded 5 standard deviations above their observed (untransformed) mean. Although this value eliminated the top 2.8% of potential individuals, it was chosen because the resultant control group was statistically appropriate in all respects. The control group was similar to the participant group in asthma,

nonasthma, and total claims. In addition, elimination of these individuals with extreme nonasthma use (>5 SDs above their untransformed mean) did not change the mean value of asthma claims for the control group; it only reduced nonasthma claims at baseline to a value comparable to that of participants.

#### **Calculation of Return on Investment**

Return on investment can be thought of as the savings a payer (such as Medicaid) realizes over and above the costs expended. Theoretically, ROI can be negative or positive. Values less than 1 indicate that the cost of the program was greater than any savings provided, values equal to 1 indicate that the cost of the program was equal to the savings provided, and values greater than 1 indicate that there were savings over and above the cost of the program. The formula used to calculate ROI is as follows: (year-1 costs minus year-2 costs) divided by disease management program costs.

#### **Interventions in the National Jewish Medical and Research Center Disease Management Program for Asthma**

The main activities that took place within the intervention group were physician education, patient education, and case management. Based on the needs and previous patterns of healthcare access of this population, we focused on 3 areas: (1) increasing the use of anti-inflammatory medications, (2) having the participants telephone our reactive care line early in an attack instead of going to an emergency department, and (3) decreasing nighttime symptoms, the most frequent time for emergency services. Physician and patient education was provided in different ways and included many topics.

Case management was implemented through a team of specialized respiratory nurses. Patients received between 5 and 7 proactive telephone calls following an initial questionnaire. Patients were encouraged to contact nurses when their asthma was symptomatic. If this occurred, they received follow-up telephone calls to ensure that appropriate care was being pursued.

In a timely manner, physicians received reports from the case managers summarizing their patients' status and providing healthcare use and productivity data. Physicians were also encouraged to follow the most recent national guidelines<sup>7</sup> in the care of their patients. Each patient's physician was asked to provide a written asthma action plan. If this was not provided, the patient provided a description of his or her medications and information on how to use them. This was recorded in an asthma action plan and sent to the patient's physician for verification. If plans were not in accord with

national guidelines, the physician's office was contacted and appropriate recommendations made. Physicians were encouraged to contact the NJDMP with any changes in their recommendations.

## RESULTS

From the population of referred individuals, 388 entered the program and 258 had continuous participation for 6 consecutive months in the intervention group. Rapid enrollment was used in an attempt to control for variations in climatic, viral infection, and pollution exposures among patients. The peak of the flu season in Colorado occurred approximately at the same time as all patients completed entry into the program.

There were 17 864 asthmatics (48% male) aged between 1 and 89 years in the total population of Colorado Medicaid. From this asthmatic population, a subgroup was identified for referral to the NJDMP consisting of individuals who (1) had a code-493 asthma claim in the year before program commencement and (2) had a minimum of 2 emergency department or hospital claims submitted to Medicaid (whether or not they were paid) for any reason during the previous year. Colorado Medicaid members have a mean of 0.6 hospital or emergency department visits per year. There were 1249 individuals referred to the NJDMP for possible enrollment, and the total claims paid for these individuals was \$2 210 813.

The demographic data for the intervention group can be found in **Table 1**. The 130 subjects who did not complete the program were disenrolled for various reasons. The most frequent reason was that these individuals lost eligibility for insurance through Medicaid; the second most common reason was that nurses were unable to contact the patients because they had moved or lost telephone service. Only 2 individuals dropped out of the program because they no longer wanted to participate in it.

Of those who were referred for enrollment to the NJDMP, 840 did not enter the program (potential control group). The reasons for their not entering the disease management program are listed in the "Control Subgroup Identification" subsection of the "Methods" section. The demographic data for the control group can be found in **Table 1**.

From this group of 840 potential control group subjects, 446 met the selection

criteria for inclusion. The remaining 394 were eliminated for the following reasons: 38 were missing all payment data during the baseline period, 237 had lost eligibility by Colorado Medicaid, 62 had no charges (facilities, professional, or pharmacy) in the 12 months following the baseline period and were presumed to be no longer eligible for insurance through Medicaid, 30 had baseline expenditures exceeding 5 SDs above their group mean, and 27 refused to participate in the program.

For the intervention and control groups, claims were available for analysis for the year before enrollment and for the enrollment period. Six months of claims data were used as the baseline costs for each group (**Table 2**). The final analysis of claims during the program period was conducted on a data set generated 90 days after the end of the intervention period to allow sufficient time for billing and payment of most claims (estimated by the state to be  $\geq 95\%$  of the claims).

The clinical results related to the 3 focus areas for the intervention group were positive. The level of use of anti-inflammatory medications rose from 72.6% of patients using these medications to 85.2% at 6 months (12.6% improvement). We tracked 21 individuals who telephoned early during the course of an asthma exacerbation, and an emergency department visit was averted in all of these cases. The last index we followed was the number of nighttime symptoms. At the conclusion of the study, the intervention group recorded 75% fewer nighttime symptoms than at baseline. All of these focus areas played a part in the reduction in the use of asthma-emergency department visits from 253 during the baseline period to 36 during the intervention period.

The total costs for all emergency department visits and hospitalizations for the intervention group in the baseline period were \$544 847 (\$351.97 per member per month [PMPM]). The total costs for the control group were \$991 710 (\$361.79 PMPM). The costs during the 6-month intervention period (including the cost of the program) were \$341 856 (\$220.84 PMPM) for the intervention group and \$755 173 (\$250.75 PMPM) for the control group.

**Table 1.** Demographics of Participants, Control Subjects, and the Total Asthmatic Population in the Colorado Medicaid Program

Group	Age, Mean (SD) [Range], y	% of Men/Woman
Intervention group (n = 258)	14.6 (12.2) [2-53]	48/52
Control group (n = 446)	18.4 (14.7) [2-56]	49.5/50.5
Total asthmatic population (n = 17 864)	[1-89]	48/52

Table 2 presents total PMPM costs and the percentage change from the baseline period to the program period for both groups. All differences were statistically significant in parametric and nonparametric statistical analysis, and probability values are reported for log-transformed data, as already described.

As can be seen from Table 2, costs for the 2 groups were similar at baseline. During the program period, costs for both groups declined: total costs for the control group decreased by 30.7%, while costs for the intervention group (without the costs of the program included) declined by 49.1%. A statistical comparison of the log-transformed value of these difference scores for the 2 groups yielded a *t* value of 117.1 (*P* < .001). For completeness, the difference scores were also compared using the nonparametric Wilcoxon rank sum statistic (which is treated as *t* for samples > 20), and the results were unchanged (*P* < .001).

**Calculated Return on Investment for the Intervention**

As shown in Table 2, the total cost for the intervention group during the program period was \$179.17. The cost of the NJDMP was \$41.67 PMPM. Therefore, the total costs for asthma and nonasthma care plus the cost of the program were \$220.84 PMPM. Return on investment was calculated as follows: (\$351.97 minus \$179.17) divided by \$41.67 equals \$4.15.

**Cost Differences Between the Intervention and Control Groups**

As already described, the total savings in facilities charges between the baseline and program periods realized for the intervention group were 49.1%. After the costs of the program were added, the savings were 37.3% (\$131.13 PMPM), while the reduction in total costs for the control group was 30.7% (\$111.04 PMPM). Therefore, the net savings over and above the cost of

the program were 9.1% greater for the intervention group than the control group. The differences in percentage reductions (including program costs) were analyzed and found to be statistically significantly different (*P* < .001).

One way to look at ROI would be to consider this difference of 9.1% as the actual effect of the NJDMP on the Colorado population covered by Medicaid. This would mean a savings of 9.1% on the total initial costs of \$544 847, or \$49 582, for this small population of 258 individuals. This recharacterization would yield an actual ROI of \$1.77 during the 6 months of the program. Using the equation presented herein, this would mean a savings of \$0.77 for every dollar spent over and above the savings accounted for by regression to the mean.

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**DISCUSSION**

Disease management is rapidly growing in practice and in the issues surrounding its definition and measurement. A key area of dispute is defining measurements to evaluate the outcome variables used to assess the efficacy of disease management.<sup>2</sup>

This study addresses some of the most common disputes about measurement of disease management intervention effectiveness in a single population of asthmatics. These are discussed in detail herein and include (1) the effects of seasonality when individuals enter the program during an extended period, (2) the results of measuring the effect on different populations in the baseline and intervention periods, (3) the problem of having a population serve as its own control, and (4) the effects of regression to the mean.

Many asthmatics are affected by seasonal exposures due to allergy, weather, or infections. In this study, we provided disease management for 6 consecutive months during the fall and winter months for the entire population, thus avoiding the potential confounding effects of seasonality.

A second common problem in analyzing data from asthma disease management programs is that the individuals evaluated in the baseline period may not be the same as those evaluated in the intervention period. In this study, we only enrolled those individuals who had previously been enrolled in the Colorado Medicaid program

**Table 2.** Per-Member-Per-Month Asthma, Nonasthma, and Total Costs Among the Medicaid Population

Variable	Intervention Group (n = 258)			Control Group (n = 446)		
	Asthma	Nonasthma	Total	Asthma	Nonasthma	Total
Baseline	\$57.87	\$294.10	\$351.97	\$62.15	\$299.64	\$361.79
Intervention year	\$32.59	\$146.58	\$179.17	\$44.50	\$206.26	\$250.76
% Difference*	43.7	50.2	49.1	28.4	31.2	30.7

\*All differences are statistically significant within measures between groups, between years within groups, and between groups for difference scores.

for a minimum of 1 year. This allowed us to have access to data for a full year before the study. In this way, we were able to track the members within the intervention and control groups during the same 6 months for 2 consecutive years.

The third issue in evaluating data from disease management programs, using a single population as its own control, is a common one. In this study, there were sufficient numbers of asthmatic members to have defined intervention and control groups. As already shown, these groups were similar in their demographics and prior total healthcare use.

If we had used only the preintervention and postintervention data for the intervention group in this analysis, we would have demonstrated a 49.1% reduction in costs, with an ROI of \$4.15. The use of a control group, although not perfect in evaluating the effect of programs, allows controlling for the effect of exposures and other unknown variables (including regression to the mean) on the evaluation process. In this study, the control group also experienced a significant reduction in costs during the same period of observation, but this reduction was statistically smaller than the reduction experienced by the intervention group. By having a control group, we were able to better evaluate the effect of the disease management program on this population.

The last area that is often mentioned as being of concern in evaluating data for disease management outcomes is the statistical effect of regression to the mean. We assume that the 30.7% reduction in costs for the control group from the baseline period to the program period is predominantly due to this. The intervention group, in contrast, showed a reduction of 49.1%. Therefore, subtracting the 30.7% that is presumed to be due to regression to the mean, the remaining (statistically significant) 18.4% reduction is attributable to program intervention. Furthermore, these results are practical. On a PMPM basis, the savings for the intervention group were more than \$45 per month beyond regression to the mean and beyond program costs; that totals nearly \$550 per year in savings for each member.

In healthcare, the effect of regression to the mean can lead to errant conclusions that an outcome is due to treatment when it is actually the result of chance. On the other hand, overstating the importance of regression to the mean can lead to the statistical phenomenon known as a type II error (ie, failing to find an effect when one is in fact present). This type of error can be costly if it causes decision makers to overlook a potentially valuable tool for reducing healthcare costs.

It is important to control for regression to the mean because its presence calls into question the tenability of the claims being made. In our study, without a well-

matched control group, the reduction in total healthcare costs from the baseline period to the program period could not unambiguously be attributed to the intervention. However, data were collected on a participant group and a statistically similar control group. This design allowed for assessment of the effect of regression to the mean, so that its presence could be ruled out or its magnitude estimated in explaining the decrease seen in the treatment group.

In looking at total costs, Table 2 shows that the control group costs decreased significantly from baseline to the program period. This was not an unanticipated finding, as a criterion for referral to the program was significant healthcare use during baseline. The results support the concept of regression to the mean as significantly affecting the measurement of interventions in disease management. This finding emphasizes the need for having a well-matched control group in the study process.

Regression to the mean applies most strongly in cases in which the observation is far from the true mean; the farther the observed score is from the true mean, the more likely it is that regression to the mean will occur. In the present study, the control group and the intervention group were selected for their high baseline healthcare use costs and were similar. Therefore, although regression to the mean would be expected to be (and was) present in this sample, both groups would be equally subject to its effect. The control group showed a 30.7% decline in costs from baseline to the program period; this decline was presumably due to regression to the mean. In contrast, the intervention group declined by 49.1% in the program period compared with baseline, and this change was significantly greater than the control group change. Therefore, there was a significant additional decline (18.4%) in costs for the treatment group that was not due to regression to the mean.

There is a related, albeit distinct, statistical phenomenon that could be called into question in the present study; that is, the presence of selection bias in determining cases and controls. If the assignment of individuals to treatment vs control groups was not random but somehow systematically differentiated the 2 groups, the generalizability of any findings could be limited. However, there is no statistical evidence that this was the case in the present sample. From a group assignment point of view, selection of cases and controls was close to random. In most cases in which an individual was telephoned but did not enroll, the reason was that no contact was made at the time of the telephone call. Absence from home is not a potential source of selection bias, because generally those who were not at home

were healthy and working, while those who were at home were sicker and not working. Telephone calls were made at all times of the day and evening and would not systematically exclude any particular type of participant. The 8% of potential participants who refused to participate were not included in the analysis. Asthma severity ranged from mild to severe in both groups, so there was no disparate selection by severity. Age and sex distributions were also almost identical. Finally, from an outcomes point of view, costs for treatment at baseline were similar for cases and controls. It is possible that the group of individuals who were at home for the initial telephone call was different from those who were not at home for the call. However, all individuals included in the data analysis were enrolled in the Medicaid program. This probably makes the economic differences small. In addition, it is possible that those at home had a different level of asthma severity than those who were not. However, the entry criteria were the same for both groups, and the level of baseline costs was similar. Therefore, there is no evidence that selection bias may have affected the findings.

Another potential weakness of the study is the lack of available data for pharmacy and physician visits. It is possible that there was increased pharmacy use in the intervention group, which would further narrow the difference in total costs between the 2 groups. In the self-reported data, there was an increase in the use of asthma controller medications. Costs for these medications would add to the total costs in the interven-

tion group. With respect to physician office visits, it is not clear if there would be any differences between groups. Additional studies should attempt to capture this information.

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### CONCLUSIONS

This study has looked at methods variables in the assessment of disease management intervention in an asthmatic population. A clear need was demonstrated for a control group in analyzing the effectiveness of the intervention to rule out improvement as simply being a function of regression to the mean. Using 2 methods of analysis, it is evident that disease management for asthma in a Medicaid-enrolled population is effective in reducing healthcare costs.

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